

Risk factors for urinary tract infection following incontinence surgery

Ingrid Nygaard · Linda Brubaker · Toby C. Chai · Alayne D. Markland · Shawn A. Menefee · Larry Sirls · Gary Sutkin · Phillipe Zimmern · Amy Arisco · Liyuan Huang · Sharon Tennstedt · Anne Stoddard

Received: 17 December 2010 / Accepted: 22 March 2011 / Published online: 11 May 2011
© The International Urogynecological Association 2011

Abstract

Introduction and hypothesis The purpose of this study is to describe risk factors for post-operative urinary tract infection (UTI) the first year after stress urinary incontinence surgery.

Methods Multivariable logistic regression analyses were performed on data from 1,252 women randomized in two surgical trials, Stress Incontinence Surgical Treatment Efficacy trial (SISTER) and Trial Of Mid-Urethral Slings (TOMUS). **Results** Baseline recurrent UTI (rUTI; ≥ 3 in 12 months) increased the risk of UTI in the first 6 weeks in both study populations, as did sling procedure and self-catheterization in SISTER, and bladder perforation in TOMUS. Baseline rUTI,

UTI in the first 6 weeks, and PVR > 100 cc at 12 months were independent risk factors for UTI between 6 weeks and 12 months in the SISTER population. Few (2.3–2.4%) had post-operative rUTI, precluding multivariable analysis. In women with pre-operative rUTI, successful surgery (negative cough stress test) at 1 year did not appear to decrease the risk of persistent rUTI.

Conclusions Pre-operative rUTI is the strongest risk factor for post-operative UTI.

Keywords Urinary tract infection · Stress urinary incontinence surgery · Recurrent urinary tract infection · Risk factors

I. Nygaard
Department of OB/GYN, University Utah,
Salt Lake City, UT, USA

L. Brubaker
Departments of OB/GYN and Urology, Loyola,
Chicago, IL, USA

T. C. Chai
Division of Urology, University of Maryland Baltimore,
Baltimore, MD, USA

A. D. Markland
Department of Medicine, Division of Geriatrics, Gerontology,
and Palliative Care, University of Alabama at Birmingham,
Birmingham, AL, USA

S. A. Menefee
Department of OB/GYN, Kaiser Permanente San Diego,
San Diego, CA, USA

L. Sirls
Department of Urology, William Beaumont Hospital,
Royal Oak, MI, USA

G. Sutkin
Department of OB/GYN, Magee Women's Hospital,
Pittsburgh, PA, USA

P. Zimmern
Department of Urology, University Texas Southwestern,
Dallas, TX, USA

A. Arisco
Department of Urology, University of Texas San Antonio,
San Antonio, TX, USA

L. Huang · S. Tennstedt · A. Stoddard
New England Research Institutes,
Watertown, MA, USA

I. Nygaard (✉)
University of Utah School of Medicine,
30N 1900 E,
Salt Lake City, UT 84132, USA
e-mail: Ingrid.nygaard@hsc.utah.edu

Introduction

Urinary tract infections (UTIs) are common in women and result in considerable individual and societal burden [1]. Risk factors for UTIs have been investigated predominantly in young and postmenopausal women. Little scientific investigation has been undertaken to delineate risk factors in surgical cohorts despite the fact that approximately one third of women are diagnosed with UTI after stress urinary incontinence surgery [2, 3].

Urinary incontinence (UI) is also common [4, 5]. UI and UTI are associated in multiple, large, population-based studies: women with a history of UTI are more likely to have UI, and women with UI are at increased risk for UTI [6–10]. Women with recurrent UTI, generally defined as three or more UTIs in 1 year, have up to a fivefold risk of UI and have more severe incontinence than women without recurrent UTI [11, 12].

Surgical intervention for pelvic floor disorders may modify the risk of UTI. Some risks factors for UTIs, such as prolapse, may improve after surgery. Others, such as obstruction from an anti-incontinence procedure or exposure to bladder instrumentation, may predispose to UTI. A common, but unproven, perception is that UI causes recurrent UTI and that successful stress urinary incontinence (SUI) surgery can “cure” recurrent UTI.

Given an incomplete understanding of the role of surgery in modifying the risk of UTIs, or in positively impacting recurrent UTI, the aims of this study are to describe, in two cohorts of women undergoing surgery for SUI, (1) risk factors for UTI in the post-operative period to 6 weeks and in the first post-operative year, (2) risk factors for recurrent UTIs (≥ 3 in 1 year) in the first post-operative year, and (3) the association between successful surgical treatment of patients with SUI and the persistence of recurrent UTI in women with a pre-operative history of recurrent UTI.

Methods

These analyses used data from two large randomized trials that compared operations for treatment of female stress urinary incontinence. The primary outcomes of both trials have been previously reported [9, 13]. Briefly, the Stress Incontinence Surgical Treatment Efficacy trial (SISTER) randomized 655 women to either fascial sling or Burch colposuspension; concomitant abdominal surgery was allowed. The Trial Of Mid-Urethral Slings (TOMUS) randomized 597 women to one of two synthetic mid-urethral sling routes, retropubic (RMUS) vs. transobturator (TMUS); concomitant abdominal surgery was not allowed. Nearly all women received antibiotic prophylaxis at

surgery. Participants in both trials were well characterized at baseline with regard to demographics, comorbidities, physical examination findings, sexual function, and continence status.

Both studies recorded baseline recurrent UTI history, individual UTIs during the first 6 weeks after surgery, and recurrent UTIs (3 or more) between 6 weeks and 12 months after surgery; only one trial (SISTER) recorded each individual UTI between 6 weeks and 12 months. To document baseline recurrent UTIs in both studies, the patient was asked “Have you had more than 3 episodes of a urinary tract infection, treated with antibiotics, in the past 12 months?” For recurrent UTIs after surgery in TOMUS, physicians were asked to document if there was evidence (including patient self-report) of recurrent UTI which was defined as “presumed UTI with treatment, ≥ 3 in 1 year after 6 week visit.” In SISTER, physicians were asked to document if there was evidence (including patient self-report) of all episodes of cystitis post-surgery. Recurrent UTI was defined as three or more such episodes between 6 weeks and 12 months post-surgery.

Data on UTI in the first 6 weeks were not provided by 14 women in SISTER and 9 women in TOMUS; 93 women in SISTER and 63 women in TOMUS had no evidence of UTI before 12 months follow-up, but as they did not provide complete 1-year data on UTI, they are excluded from 1-year analyses. Therefore, the analytical samples for UTI during the first 6 weeks were 641 (SISTER) and 588 (TOMUS); for recurrent UTI during the first post-operative year, were 562 (SISTER) and 534 (TOMUS), and for any UTI during the first year, 562 (SISTER only).

We defined successful treatment of SUI as a negative cough stress test at 300-cc bladder volume 1 year after surgery, cystocele as anterior wall prolapse at or below the hymen, and UTI as patient report of symptoms treated at the providers' discretion with antibiotics.

Most analyses were carried out in parallel for the SISTER and TOMUS participants as the trials had different inclusion and exclusion criteria representing different populations. For a sub-group analysis of women with pre-operative recurrent UTIs, we combined data from the two samples. Frequency distributions with percentages were reported for categorical variables, and means with standard deviation (SD) were presented for continuous variables. For each outcome measure, bivariate analyses of the outcome with participant characteristics were performed using logistic regression analysis. Multivariable logistic regression analysis models were then computed, including all the covariates that were significantly associated with the outcome in either trial or were thought to be of clinical relevance to the outcome. Odds ratios (ORs) with corresponding 95% confidence intervals (CI) are reported. Statistical analyses were performed using SAS version 9.2.

A 5% two-sided significance level was used for all statistical testings.

Results

The mean ages for the SISTER and TOMUS samples were 51.9 (SD, 10.3) and 52.9 (SD, 11.0), respectively. Three hundred twenty-nine women were randomized to Burch, 326 to sling, 298 to RMUS, and 299 to TMUS. At baseline, 30% of women in each sample were pre-menopausal, and approximately one third were on systemic hormone therapy. Seven percent had diabetes mellitus, 14% were current smokers, and 89% were parous. In the SISTER sample, 25%, 59%, and 16% had stages 0/I, II, and III/IV pelvic organ prolapse, respectively. In the TOMUS population, 45%, 47%, and 8% had stages 0/I, II, and III/IV prolapse, respectively. At surgery, 98% received prophylactic intravenous antibiotics. In the SISTER group, 58% underwent concomitant surgery, while in the TOMUS group, 25% did so. In both samples, 3% sustained a bladder perforation. After surgery, 30 (5%) and 1 (0%) of women in the SISTER and TOMUS groups, respectively, had some form of catheterization for more than 6 weeks, and 3% and 1%, respectively, underwent lysis of suture, sling, or adhesions because of voiding dysfunction.

One year after surgery, 3% had undergone surgical retreatment for SUI, 74% were sexually active, 6% had a post-void residual urine (PVR) >100 cc, and 13% had a cystocele on examination. In the SISTER sample, 4% used vaginal estrogen, and 33% used systemic estrogen, while in the TOMUS sample, 12% used vaginal estrogen and 24% used systemic estrogen. At 1 year, 12% and 19% of women in the SISTER and TOMUS samples, respectively, met the study criteria for surgical failure.

Eighty-seven women (7%) enrolled in TOMUS ($n=42$) and SISTER ($n=45$) reported a history of pre-operative recurrent UTI, as evidenced by three or more UTIs in the year preceding their study surgery. Women with diabetes pre-operatively were more likely to report recurrent UTI at baseline ($p=0.02$ in TOMUS and 0.03 in SISTER); a lower occupational score was also associated with recurrent UTI in women in the SISTER population only. Other baseline characteristics, including age, race, smoking, hormone status, prolapse stage, and genital hiatus length were not associated with baseline recurrent UTI.

During the first 6 weeks after surgery, UTI was reported by 33 of 321 (10%), 78 of 320 (24%), 34 of 293 (12%), and 21 of 295 (7%) women undergoing Burch, fascial sling, RMUS, and TMUS, respectively. Of women with 1-year data in SISTER, 141 of 562 (25%) reported at least one UTI between 6 weeks and 12 months after surgery. Thirteen women (2% of women with 1-year data) in both SISTER and TOMUS reported three or more UTIs in the year after

surgery. Characteristics of each study population between 6 weeks and 12 months after surgery are shown in Table 2.

The bivariate associations of baseline and surgical characteristics with UTI in the first 6 weeks after surgery are summarized in Table 1. Sling surgery (in SISTER only), history of recurrent UTI at baseline, advanced prolapse and bladder perforation (both in TOMUS only), and clean intermittent self-catheterization (CISC; reported in SISTER only) were significantly associated with UTI in the post-operative period on bivariate analysis. After adjusting for any variable that was significant in either population, only a history of recurrent UTI was associated with UTI in the first 6 weeks in both study populations. In addition, in SISTER, undergoing a sling (compared to Burch) and CISC (compared to self-voiding) also increased this risk. In TOMUS, bladder perforation also increased the risk.

In the SISTER population, on bivariate analysis, factors associated with UTI between 6 weeks and 12 months included history of recurrent UTI at baseline, UTI during the first 6 weeks after surgery, PVR >100 cc at 12 months, catheterization (any type) for >6 weeks after surgery, and surgical takedown of anti-incontinence procedure (Table 2). After adjusting for these variables and treatment group, catheterization for >6 weeks was no longer statistically significant, while the other variables remained significant (Table 3).

Significant bivariate risk factors ($p<0.05$) for post-operative recurrent UTI varied by study: in SISTER, risks were pre-operative POP stages III/IV compared to stage II (OR 4.54; 95% CI 1.35, 15.2), PVR >100 cc at 12 months (OR 7.19; 95% CI 1.76, 29.40), surgical relief of bladder neck obstruction by 12 months (OR 7.50; 1.51, 37.30), and age (per 10 years, OR 1.78; 1.04, 3.07), and in TOMUS, risks were pre-operative history of recurrent UTI (OR 12.6; 4.02, 39.8), lack of antibiotic prophylaxis at surgery (OR 11.11; 1.12, 100.0), surgical relief of bladder neck obstruction (OR 10.80; 1.12, 10.40), and higher PVR at 12 months (OR for every 10 unit 1.09; 95% CI 1.01, 1.18). The small number of women (13 in each study sample) that reported recurrent UTI post-operatively precluded multivariable analysis.

Of the 87 women with a history of pre-operative recurrent UTI in both trials, 15 did not complete the 12-month visit, and 1 received surgical retreatment prior to the 12-month visit, leaving 71 women for analysis of our aim regarding impact of successful treatment on pre-existing recurrent UTI. No woman in this sub-sample underwent surgical relief of bladder neck obstruction, and 4% (3 of 71) required some type of catheterization (urethral, suprapubic, or intermittent self-catheterization) for more than 6 weeks.

In this sub-sample of women with pre-operative recurrent UTI, 17% (12 of 71) were considered surgical treatment failures at 12 months. Eleven percent (8 of 71) reported recurrent UTI during the first post-operative year. Twenty-five percent (3 of 12) of women classified as a

Table 1 Bivariate associations of baseline and surgical characteristics with UTI in the first 6 weeks: SISTER and TOMUS

	SISTER				TOMUS					
	Total (n=641)	Yes (n=111)	No (n=530)	p value	OR	Total (n=588)	Yes (n=55)	No (n=533)	p value	OR
Treatment				<0.0001						
Burch/RMUS	321	33 (30%)	288 (54%)			293	34 (62%)	259 (49%)	0.06	
Sling/TMUS	320	78 (70%)	242 (46%)		2.81 (1.81–4.37)	295	21 (38%)	274 (51%)		0.58 (0.33–1.03)
Age, mean (SD)	641	53.1 (10.0)	51.7 (10.3)	0.18	1.01 (0.99–1.03)	588	55.2 (13.6)	52.9 (10.7)	0.13	1.02 (0.99–1.05)
Systemic hormone therapy use				0.63					0.22	
No	228	37 (33%)	191 (36%)			242	18 (33%)	224 (42%)		
Yes	217	42 (38%)	175 (33%)		1.24 (0.76–2.02)	169	21 (39%)	148 (28%)		1.77 (0.91–3.43)
Pre-menopausal	195	32 (29%)	163 (31%)		1.01 (0.60–1.70)	175	15 (28%)	160 (30%)		1.17 (0.57–2.38)
Diabetes				0.8					0.84	
No	597	104 (94%)	493 (93%)			549	51 (93%)	498 (93%)		
Yes	44	7 (6%)	37 (7%)		0.90 (0.39–2.07)	39	4 (7%)	35 (7%)		1.12 (0.38–3.27)
Smoking status				0.54					0.51	
Never smoked	347	61 (55%)	286 (54%)			314	33 (60%)	281 (53%)		
Formerly smoking	204	38 (34%)	166 (31%)		1.07 (0.69–1.68)	197	17 (31%)	180 (34%)		0.80 (0.44–1.49)
Currently smoking	90	12 (11%)	78 (15%)		0.72 (0.37–1.41)	77	5 (9%)	72 (14%)		0.59 (0.22–1.57)
Prolapse stage				0.17					0.02	
Stage 0/I	157	20 (18%)	137 (26%)			262	20 (36%)	242 (45%)		
Stage II	380	69 (62%)	311 (59%)		1.52 (0.89–2.60)	278	25 (45%)	253 (47%)		1.20 (0.65–2.21)
Stage III/IV	104	22 (20%)	82 (15%)		1.84 (0.95–3.57)	48	10 (18%)	38 (7%)		3.19 (1.39–7.32)
Pre-op GH, mean (SD)	640	3.5 (1.4)	3.6 (1.2)	0.31	0.91 (0.77–1.09)	588	3.6 (1.1)	3.4 (1.0)	0.21	1.18 (0.91–1.52)
Vaginal deliveries				0.7					0.13	
No	58	9 (8%)	49 (9%)			70	3 (5%)	67 (13%)		
Yes	583	102 (92%)	481 (91%)		1.15 (0.55–2.43)	518	52 (95%)	466 (87%)		2.49 (0.76–8.20)
Occupational scores, mean (SD)	627	58.7 (23.5)	56.7 (24.8)	0.43	1.00 (0.99–1.01)	579	58.7 (22.9)	59.7 (22.9)	0.62	1.00 (0.98–1.01)
Recurrent UTIs at baseline				0.002					0.0002	
No	599	96 (86%)	503 (95%)			545	43 (80%)	502 (94%)		
Yes	42	15 (14%)	27 (5%)		2.91 (1.49–5.68)	41	11 (20%)	30 (6%)		4.28 (2.01–9.13)
Concomitant surgery				0.59					0.08	
No	269	44 (40%)	225 (42%)			442	36 (65%)	406 (76%)		
Yes	372	67 (60%)	305 (58%)		1.12 (0.74–1.71)	146	19 (35%)	127 (24%)		1.69 (0.93–3.05)
Bladder perforation				0.49					0.004	
No	624	107 (96%)	517 (98%)			573	50 (91%)	523 (98%)		
Yes	17	4 (4%)	13 (2%)		1.49 (0.48–4.65)	15	5 (9%)	10 (2%)		5.23 (1.72–15.9)
Antibiotic prophylaxis at surgery				0.08					NA	

	14	5 (5%)	9 (2%)	583	0 (0%)	5 (1%)
No	606	102 (95%)	504 (98%)	583	55 (100%)	528 (99%)
Yes	321	34 (31%)	287 (54%)	5	0 (0%)	5 (1%)
Voiding management at discharge to 6 weeks ^a	138	48 (44%)	90 (17%)	0.36 (0.12–1.11)	55 (100%)	528 (99%)
Self-voiding only	181	28 (25%)	153 (29%)	4.50 (2.73–7.42)	55 (100%)	528 (99%)
CISC ^a				1.54 (0.90–2.64)		
Continuous catheter drainage						N/A

GH genital hiatus length (centimeters), CISC clean intermittent self-catheterization

^a Refers to voiding management at any point between hospital discharge and 6 weeks; does not imply that catheter use was continuous for 6 weeks. The precise duration of catheter use is not known. Voiding management data were not collected for TOMUS

surgical failure at 1 year had recurrent UTI post-operatively compared to 8% (5 of 59) of women with successful surgical results; after adjusting for age and treatment assignment, this was not statistically significant (OR 2.69, 95% CI 0.38, 19.1). In women with persistent recurrent UTI post-operatively, mean age (SD) was 64.4 (11.4) years, compared to 52.4 (10.6) in women without recurrent UTI ($p=0.01$; OR 1.14, 95% CI 1.03, 1.26, controlling for treatment assignment and stress test failure). Other than age, no baseline or post-operative characteristic tested (including post-operative cystocele, sexual activity, systemic or vaginal estrogen therapy, post-void residual volume, or surgical success) was associated with recurrent UTI during this time period (all p values >0.05).

Discussion

Our study demonstrated that post-operative UTIs within the first 6 weeks after surgery were common (7–24%) and comparable to other reports of post-operative UTI following incontinence and prolapse surgery (9–45%) [10, 12, 14]. Unique to this study, we analyzed numerous potentially modifiable risk factors associated with an increased risk of post-operative UTI, with the hope of developing a clinically relevant prediction tool. However, on multivariable analysis, pre-operative recurrent UTI was the only risk factor that was consistently associated with an increased risk of UTI both in the 6-week post-operative period and the period between 6 weeks and 12 months.

While women classified as surgical successes were nearly three times more likely to resolve their recurrent UTIs than were women classified as surgical failures, this trend did not reach statistical significance. Of note, most (90%) women with pre-op recurrent UTI did not have post-op recurrent UTI, a clinically relevant finding that surgeons may use in counseling patients. The small number of women with post-operative recurrent UTI ($n=13$) limits our ability to identify significant risk factors that could be modified clinically to reduce this prevalence.

The clinical actions recommended to minimize the risk of post-operative UTI remain unclear. One randomized controlled trial using prophylactic antibiotics in women who had suprapubic catheters following POP or stress UI surgery found that prophylactic nitrofurantoin prevented post-operative UTIs [6]. We are unaware of published randomized clinical trials of prophylactic antibiotics to prevent UTI after surgery in specific high-risk groups or in women using CISC or continuous prolonged urethral drainage for voiding dysfunction after POP/UI surgery. A single decision analysis favored prophylactic antibiotics during CISC to manage post-operative voiding dysfunction after UI/POP surgery [15]. As we did not systematically

Table 2 Bivariate associations of participant characteristics with any UTI between 6 weeks and 12 months post-surgery: SISTER

	Any UTI in 6 weeks to 12 months			<i>p</i> value	OR
	Total (<i>n</i> =562)	Yes (<i>n</i> =151)	No (<i>n</i> =411)		
Treatment				0.12	
Burch	269	64 (42%)	205 (50%)		
Sling	293	87 (58%)	206 (50%)		1.35 (0.93,1.97)
Baseline characteristics					
Age, years, mean (SD)	562	52.5 (10.6)	52.4 (9.8)	0.88	1.01 (0.84–1.22) ^a
Systemic hormone therapy use				0.07	
No	203	66 (44%)	137 (33%)		
Yes	196	47 (31%)	149 (36%)		0.65 (0.42,1.02)
Pre-menopausal	162	37 (25%)	125 (30%)		0.61 (0.38,0.98)
Diabetes				0.50	
No	524	139 (92%)	385(94%)		
Yes	38	12 (8%)	26 (6%)		1.28 (0.63,2.60)
Smoking status				0.55	
Never smoked	311	79 (52%)	232 (56%)		
Formerly smoking	181	54 (36%)	127 (31%)		1.25 (0.83,1.88)
Currently smoking	70	18 (12%)	52 (13%)		1.02 (0.56,1.84)
Prolapse stage				0.68	
Stage 0/I	130	37 (25%)	93 (23%)		
Stage II	338	92 (61%)	246 (60%)		0.94 (0.60,1.47)
Stage III/IV	94	22 (15%)	72 (18%)		0.77 (0.42,1.41)
Pre-op GH, mean (SD)	561	3.7 (1.1)	3.6 (1.3)	0.6	1.04 (0.90,1.21)
Vaginal deliveries				0.74	
No	52	15 (10%)	37 (9%)		
Yes	510	136 (90%)	374 (91%)		0.90 (0.48,1.69)
Occupational scores, mean (SD)	549	54.9 (25.3)	57.9 (24.4)	0.20	1.00 (0.99,1.00)
Recurrent UTIs at baseline				0.006	
No	523	133 (88%)	390 (95%)		
Yes	39	18 (12%)	21 (5%)		2.51 (1.30,4.86)
Surgical characteristics					
Concomitant surgery				0.52	
No	232	59 (39%)	173 (42%)		
Yes	330	92 (61%)	238 (58%)		1.13 (0.77,1.66)
Bladder perforation				0.18	
No	545	144 (95%)	401 (98%)		
Yes	17	7 (5%)	10 (2%)		1.95 (0.73,5.22)
Antibiotic prophylaxis at surgery				0.20	
No	14	6 (4%)	8 (2%)		
Yes	527	142 (96%)	385 (98%)		0.49 (0.17,1.44)
Follow-up characteristics					
Voiding management at discharge to 6 weeks				0.09	
Self-voiding only	264	64 (42%)	200 (49%)		
CISC	130	45 (30%)	85 (21%)		1.65 (1.05,2.62)
Indwelling catheter only	163	42 (28%)	121 (30%)		1.08 (0.69,1.70)
UTI in the first 6 weeks				0.001	
No	447	107 (71%)	340 (84%)		
Yes	111	44 (29%)	67 (16%)		2.09 (1.35,3.23)
Sexual activity				0.52	

Table 2 (continued)

	Any UTI in 6weeks to 12months			<i>p</i> value	OR
	Total (<i>n</i> =562)	Yes (<i>n</i> =151)	No (<i>n</i> =411)		
No	137	38 (28%)	99 (25%)	0.84	0.87 (0.56,1.34)
Yes	389	97 (72%)	292 (75%)		
Stress test failure				0.84	
Missing	38	19	19		
No	466	118 (89%)	348 (89%)	0.14	0.94 (0.50,1.77)
Yes	58	14 (11%)	44 (11%)		
Surgical retreatment for SUI				0.14	
No	538	136 (96%)	402 (99%)	0.69	2.46 (0.74,8.20)
Yes	11	5 (4%)	6 (1%)		
Cystocele				0.69	
No	461	114 (88%)	347 (89%)	1.13 (0.61,2.09)	
Yes	59	16 (12%)	43 (11%)		
PVR>100 at 12 months				0.02	
No	460	108 (88%)	352 (96%)	3.26 (1.54,6.88)	
Yes	30	15 (12%)	15 (4%)		
PVR at 12 months, mean (SD)	509	40.2 (48.6)	30.97 (41.3)	0.007	1.06 (1.02–1.11) ^a
Catheterization use >6 weeks				0.02	
No	534	138 (91%)	396 (96%)	2.49 (1.15,5.36)	
Yes	28	13 (9%)	15 (4%)		
Surgical takedown				0.002	
No	547	141 (93%)	406 (99%)	5.76 (1.94,17.1)	
Yes	15	10 (7%)	5 (1%)		
Systemic estrogen use				0.18	
No	362	104 (69%)	258 (63%)	0.76 (0.51,1.13)	
Yes	200	47 (31%)	153 (37%)		
Vaginal estrogen use				0.05	
No	540	141 (93%)	399 (97%)	2.36 (1.00,5.58)	
Yes	22	10 (7%)	12 (3%)		

^a OR was based on 10 per unit change

collect detailed information about prophylactic antibiotic use in women catheterizing after surgery, our study cannot contribute to this dearth of information. Despite similarly low rates of bladder perforation in the two trials (3%), bladder perforation was a risk factor for having a UTI in the first 6 weeks post-operatively in TOMUS, but not in SISTER. This may be related to post-perforation treatment patterns, including catheter duration or antibiotic use. The low numbers of women with a bladder perforation and a UTI in SISTER and TOMUS (4 and 5 women, respectively) limit our ability to explore this further. Intraoperative bladder perforation did not increase the risk of a UTI in the 6-weeks to 12-month time period in either trial.

PVR greater than 100 ml at 12 months increased the risk of UTI from 6 weeks to 12 months, a finding also noted in some, but not other, studies [16, 17]. There is no evidence-based guidance for instituting CISC to treat an elevated

PVR. Similarly, the role of an elevated PVR in the etiology of UTI is not well understood. More research is needed in these areas [18].

We found that age was a risk factor for persistence of recurrent UTI after surgery, but not for isolated post-operative UTIs. Most of the research to date about UTI has focused on young healthy women or older infirm women; our research suggests that in the population of largely middle-aged and older women undergoing surgery, age may impact recurrent versus isolated post-operative UTIs differently.

Strengths of this study include the large number of surgical patients with a wide range of concomitant surgical procedures, thus increasing the generalizability of our results. Women were followed closely, in a standardized fashion. Most potentially relevant risk factors were measured, and all post-operative factors were collected prospectively.

Table 3 Results of multivariable logistic regression models of factors associated with UTI; OR (95% CI)

Covariates	1st 6 weeks (SISTER)	1st 6 weeks (TOMUS)	6 weeks to 12 months (SISTER)
Treatment			
Sling vs Burch	2.54 (1.58, 4.09)	N/A	1.03 (0.66, 1.60)
RMUS vs TMUS	N/A	0.60 (0.33, 1.11)	N/A
Recurrent UTIs at baseline	3.58 (1.74, 7.35)	4.87 (2.22, 10.7)	2.51 (1.16, 5.42)
UTI during 1st 6 weeks	N/A	N/A	1.90 (1.11, 3.27)
Catheter using >6 weeks	N/A	N/A	1.48 (0.54, 4.02)
Prolapse stage			
Pre-op POP stage II vs 0/I	1.37 (0.77, 2.43)	1.24 (0.66, 2.33)	–
Pre-op POP stage III/IV vs 0/I	1.58 (0.78, 3.23)	2.76 (1.13, 6.74)	–
Voiding management at discharge to 6 weeks			
Continuous catheter vs self-voiding	1.36 (0.78, 2.37)	N/A	0.86 (0.52, 1.42)
CISC vs self-voiding	3.70 (2.20, 6.22)		1.00 (0.57, 1.76)
Bladder perforation	1.77 (0.52, 6.06)	4.10 (1.26, 13.3)	–
PVR >100 cc at 12 months	N/A	N/A	2.52 (1.14, 5.60)

Note that only recurrent UTI was collected at 12 months for TOMUS, and therefore, 6-week to 12-month results are limited to the SISTER population

– indicates that the variable was not significant on univariate analysis and is not included in this model, N/A not applicable to this model

Some may consider the absence of urine cultures a limitation of our study. While we used a clinically rational definition of UTI in a similar way before and after surgery (as symptoms of bladder infection treated with antibiotics, regardless of whether a urinalysis or urine culture was done), patients' recall may over- or underestimate the true prevalence. Further clouding the issue is the fact that UI symptoms (e.g., urgency and frequency or voiding dysfunction) may mimic UTI, especially in this population, such that a woman with continued incontinence after surgery may or may not perceive these symptoms to be due to a UTI. We have no knowledge of the natural history of UTI in un-operated women with or without UI. This may be a condition that waxes and wanes over time. However, the important clinical question is really whether women with recurrent UTIs perceive their UTIs to be less common after successful surgery, since most clinical treatments are initiated without confirmation by urine cultures. Furthermore, the research definition for UTI is contentious and difficult. Traditional definitions, using urine cultures as a gold standard, are problematic, requiring a priori criteria for which organisms are true uropathogens, and the appropriate cut-point for colony growth. The urine culture itself is coming under scrutiny with the advent of newer bacterial detection techniques, such as polymerase chain reaction testing for bacterial products. Clinicians, however, still rely on patient symptoms, with or without bacterial cultures, to care for patients. This primarily symptom-based definition of UTI is consistent with pharmaceutical literature in which UTI

is considered present if any term sorting under the Medical Dictionary for Regulatory Activities high-level term “UTI” is recorded as an adverse event [19].

Even this large population was underpowered to answer our aim concerning the association between surgical success and resolution of pre-operative recurrent UTI. A post hoc power analysis revealed that, in this sample of 71 women with recurrent UTIs at baseline (and completed 1 year data), in order to achieve 80% power, 213 women with pre-operative recurrent UTIs would be required. If we assume that the rate of recurrent UTI in women planning surgical management of SUI is similar to that seen in TOMUS and SISTER, a population of over 3,000 women planning surgery would be needed to adequately evaluate the association between successful surgery and resolution of recurrent UTIs. Future meta-analysis of pooled and high-quality data could provide sufficient power to address this question.

The choice of outcome measure in defining surgical success is difficult. Because we were most interested in whether the actual leakage was associated with recurrent UTIs, rather than bother or quality of life related to leakage, we chose the standardized cough stress test, a measure collected the same way in both studies. Our results may have differed had we used other measures of success.

Clinicians may use our findings to counsel women considering SUI surgery that the presence of pre-operative recurrent UTI increases the risk for post-operative UTI. However, the risk of persistent or de novo recurrent UTI is low and clinically reassuring, and appears similar to the rate in the general population. Our results suggest that women questioning whether surgery can “cure” their recurrent

UTIs can be reassured that, for most women with this condition, recurrent UTIs abate in the short term (1 year) after surgery. This may be more likely in women whose surgeries are successful, but a very large population is needed to explore this more definitively.

Randomized trials are needed to determine whether prevention strategies such as post-operative antibiotic prophylaxis or catheterization type can reduce the high incidence of post-operative UTI.

Acknowledgments This study was supported by NIH grants U01 DK58231, U01 DK60379, U01 DK60380, U01 DK60401, U01 DK60397, U01 DK 58225, U01 DK60395, U01 DK58234, U01 DK60393, U01 DK58229.

Conflicts of interest The authors report no financial disclosures with the following exceptions: Linda Brubaker received grant support and honorarium from Pfizer; Toby Chai received grant support from Allergan and honorarium from Pfizer; Anne Stoddard has stocks in Bristol-Meyers Squibb, Johnson and Johnson, Elan Corp., Proctor and Gamble, and Stryker.

Appendix

For SISTEr

Steering committee

William Steers, M.D., Chair (University of Virginia Charlottesville, VA); Ananias Diokno, M.D., Veronica Mallett, M.D. (William Beaumont Hospital, Royal Oak, MI, and Oakwood Hospital, Dearborn, MI; U01 DK58231); Linda Brubaker, M.D., and MaryPat FitzGerald, M.D. (Loyola University Medical Center, Maywood, IL; U01 DK60379); Holly E. Richter, Ph.D., M.D., L. Keith Lloyd, M.D. (University of Alabama, Birmingham, AL; U01 DK60380); Michael Albo, M.D., Charles Nager, M.D. (University of California, San Diego, CA; U01 DK60401); Toby C. Chai, M.D.; Harry W. Johnson, M.D. (University of Maryland, Baltimore, M.D.; U01 DK60397); Halina M. Zyczynski, M.D.; Wendy Leng, M.D. (University of Pittsburgh, Pittsburgh, PA; U01 DK 58225); Philippe Zimmern, M.D.; Gary Lemack, M.D. (University of Texas Southwestern, Dallas, TX; U01 DK60395); Stephen Kraus, M.D.; Thomas Rozanski, M.D. (University of Texas Health Sciences Center, San Antonio, TX; U01 DK58234); Peggy Norton, M.D.; David Lesser, M.D. (University of Utah, Salt Lake City, UT; U01 DK60393); Sharon Tennstedt, Ph.D.; Anne Stoddard, ScD (New England Research Institutes, Watertown, MA; U01 DK58229); Debuene Chang, M.D.; John W. Kusek, Ph.D.; Leroy M. Nyberg, M.D., Ph.D. (National Institute of Diabetes & Digestive & Kidney Diseases); Anne M. Weber, M.D. (National Institute of Child Health and Human Development).

Co-investigators

Rowell S. Ashford II, M.D.; Jan Baker, APRN; Diane Borello-France, PT, Ph.D.; Kathryn L. Burgio, Ph.D.; Seine Chiang, M.D.; Ash Dabbous, M.D.; Patricia S. Goode, M.D.; Lee N. Hammontree, M.D.; Kimberly Kenton, M.D.; Salil Khandwala, M.D.; Karl Luber, M.D.; Emily Lukacz, M.D.; Shawn Menefee, M.D.; Pamela Moalli, M.D.; Kenneth Peters, M.D.; Elizabeth Sagan, M.D.; Joseph Schaffer, M.D.; Amanda Simsiman, M.D.; Larry Sirls, M.D.; Robert Starr, M.D.; R. Edward Varner, M.D..

Study coordinators

Rosemary Bradt, RNC; Karen Debes, RN; Rosanna Dinh, RN, CCRC; Judy Gruss, RN; Lynn Hall, RN, MSN, CURN; Alice Howell, RN, BSN, CCRC; Kathy Jesse, RN; D. Lynn Kalinoski, Ph.D.; Kathryn Koches, RN; Barbara Leemon, RN; Karen Mislanovich, RN; Shelly O'Meara, RN; Janese Parent, RN; Norma Pope, RN; Caren Prather, RN; Terry Rogers, RN; Sylvia Sluder, CCRP; Mary Tulke, RN.

Biostatistical coordinating center

Kimberly J. Dandreo, MSc; Corinne J. Leifer, BA; Susan M. McDermott, MPH, GNP; Anne Stoddard, ScD (Co-PI); Sharon Tennstedt, Ph.D. (PI); Liane Tinsley, MPH; Lisa Wruck, ScD; Yan Xu, MS.

Data safety and monitoring board

Elizabeth A. Gormley, M.D. (Chair), Dartmouth-Hitchcock Medical Center, Lebanon NH; Paul Abrams, M.D., Bristol Urological Institute, Bristol, UK; Diedre Bland, M.D., Blue Ridge Medical Associates, Winston Salem NC; J. Quentin Clemens, M.D., Northwestern University Medical School, Chicago, IL; John Connett, Ph.D., University of Minnesota, Minneapolis, MN; William Henderson, Ph.D., University of Colorado, Aurora, CO; Dee Fenner, M.D., University of Michigan, Ann Arbor, MI; Sheryl Kelsey, Ph.D., University of Pittsburgh, Pittsburgh, PA; Deborah Myers, M.D., Brown University School of Medicine, Providence, RI; Jacek Mostwin, M.D., Johns Hopkins Hospital, Baltimore, MD; Bassem Wadie, MBBCh, MSc, M.D., Mansoura Urology and Nephrology Center, Mansoura, Egypt.

For TOMUS

Steering committee

Elizabeth A. Gormley, Chair (Dartmouth-Hitchcock Medical Center, Lebanon, NH); Larry Sirls, M.D.; Salil Khandwala,

M.D. (William Beaumont Hospital, Royal Oak, MI, and Oakwood Hospital, Dearborn, MI; U01 DK58231); Linda Brubaker, M.D.; Kimberly Kenton, M.D. (Loyola University Chicago, Stritch School of Medicine, Maywood, IL; U01 DK60379); Holly E. Richter, Ph.D., M.D.; L. Keith Lloyd, M. D. (University of Alabama, Birmingham, AL; U01 DK60380); Michael Albo, M.D.; Charles Nager, M.D. (University of California, San Diego, CA; U01 DK60401); Toby C. Chai, M.D.; Harry W. Johnson, M.D. (University of Maryland, Baltimore, MD; U01 DK60397); Halina M. Zyczynski, M.D.; Wendy Leng, M.D. (University of Pittsburgh, Pittsburgh, PA; U01 DK 58225); Philippe Zimmern, M. D.; Gary Lemack, M.D. (University of Texas Southwestern, Dallas, TX; U01 DK60395); Stephen Kraus, M.D.; Thomas Rozanski, M.D. (University of Texas Health Sciences Center, San Antonio, TX; U01 DK58234); Peggy Norton, M.D.; Ingrid Nygaard, M.D. (University of Utah, Salt Lake City, UT; U01 DK60393); Sharon Tennstedt, Ph.D.; Anne Stoddard, ScD (New England Research Institutes, Watertown, MA; U01 DK58229); Debuene Chang, M.D. (until 10/2009), John Kusek, Ph.D. (starting 10/2009), Rebekah Rasooly, Ph.D. (National Institute of Diabetes & Digestive & Kidney Diseases).

Co-investigators

Amy Arisco, M.D.; Jan Baker, APRN; Diane Borello-France, PT, Ph.D.; Kathryn L. Burgio, Ph.D.; Ananias Diokno, M.D.; MaryPat Fitzgerald, M.D.; Chiara Ghetti, M.D.; Patricia S. Goode, M.D.; Robert L. Holley, M.D.; Yvonne Hsu, M.D.; Margie Kahn, M.D.; Jerry Lowder, M. D.; Karl Luber, M.D.; Emily Lukacz, M.D.; Alayne Markland, DO, MSc; Shawn Menefee, M.D.; Pamela Moalli, M.D.; Elizabeth Mueller, M.D.; Leslie Rickey, M. D., MPH; Elizabeth Sagan, M.D.; Joseph Schaffer, M.D.; Robert Starr, M.D.; Gary Sutkin, M.D.; R. Edward Varner, M.D.; Emily Whitcomb, M.D..

Study coordinators

Laura Burr, RN; JoAnn Columbo, BS, CCRC; Tamara Dickinson, RN, CURN, CCCN, BCIA-PMDB; Rosanna Dinh, RN, CCRC; Judy Gruss, RN; Alice Howell, RN, BSN, CCRC; Chaandini Jayachandran, MSc; Kathy Jesse, RN; D. Lynn Kalinoski, Ph.D.; Barbara Leemon, RN; Karen Mislanovich, RN; Elva Kelly Moore, RN; Caren Prather, RN; Jennifer Tabaldo; Tia Thrasher; Mary Tulke, RN; Robin Willingham, RN, BSN; Kimberly Woodson, RN, MPH; Gisselle Zazueta-Damian.

Data coordinating center

Kathleen Cannon, BS; Kimberly J. Dandreo, MSc; Liyuan Huang, MS; Rose Kowalski, MA; Heather Litman, Ph.D.;

Marina Mihova, MHA; Anne Stoddard, ScD (Co-PI); Kerry Tanwar, BA; Sharon Tennstedt, Ph.D. (PI); Yan Xu, MS.

Data safety and monitoring board

J. Quentin Clemens, M.D. (Chair) Northwestern University Medical School, Chicago IL; Paul Abrams, M.D., Bristol Urological Institute, Bristol, UK; Deidre Bland, M.D., Blue Ridge Medical Associates, Winston Salem, NC; Timothy B. Boone, M.D., The Methodist Hospital, Baylor College of Medicine, Houston, TX; John Connett, Ph.D., University of Minnesota, Minneapolis, MN; Dee Fenner M.D., University of Michigan, Ann Arbor, MI; William Henderson, Ph.D., University of Colorado, Aurora, CO; Sheryl Kelsey, Ph.D., University of Pittsburgh, Pittsburgh, PA; Deborah J. Lightner, M.D., Mayo Clinic, Rochester, MN; Deborah Myers, M.D., Brown University School of Medicine, Providence, RI; Bassem Wadie, MBBCh, MSc, M.D., Mansoura Urology and Nephrology Center, Mansoura, Egypt; J. Christian Winters, M.D., Louisiana State University Health Sciences Center, New Orleans, LA

References

1. Foxman B (2002) Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med* 113(Suppl 1A):5S–13S
2. Albo ME, Richter HE, Brubaker L, Norton P, Kraus S, Zimmern PE et al (2007) Burch coloposuspension versus fascial sling to reduce urinary stress incontinence. *N Engl J Med* 356:2143–2155
3. Anger JT, Litwin MS, Wang Q, Pashos CL, Rodriguez LV (2007) Complication of sling surgery among female Medicare beneficiaries. *Obstet Gynecol* 109:707–714
4. Kunin CM (1994) Urinary tract infections in females. *Clin Infect Dis* 18:1–10
5. Melville JL, Katon W, Delaney K, Newton K (2005) Urinary incontinence in US women: a population-based study. *Arch Intern Med* 165:537–542
6. Hooton TM, Scholes D, Hughes JP, Winter C, Roberts PL, Stapleton AE, Stergachis A, Stamm WE (1996) A prospective study of risk factors for symptomatic urinary tract infection in young women. *NEJM* 335:468–474
7. Brown JS, Grady D, Ouslander JG, Herzog AR, Varner RE, Posner SF (1999) Prevalence of urinary incontinence and associated risk factors in postmenopausal women. *Heart & Estrogen/Progestin Replacement Study (HERS) Research Group. Obstet Gynecol* 94:66–70
8. Brown JS, Vittinghoff E, Kanaya AM, Agarwal SK, Hulley S, Foxman B et al (2001) Urinary tract infections in postmenopausal women: effect of hormone therapy and risk factors. *Obstet Gynecol* 98:1045–1052
9. Foxman B, Somsel P, Tallman P, Gillespie B, Raz R, Colodner R et al (2001) Urinary tract infection among women aged 40 to 65: behavioral and sexual risk factors. *J Clin Epidemiol* 54:710–718
10. Hu KK, Boyko EJ, Scholes D, Normand E, Chen CL, Grafton J et al (2004) Risk factors for urinary tract infections in postmenopausal women. *Arch Intern Med* 164:989–993

11. Raz R, Gennesin Y, Wasser J, Stoler Z, Rosenfeld S, Rottensterich E, Stamm WE (2000 Jan) Recurrent urinary tract infections in postmenopausal women. *Clin Infect Dis* 30(1):152–156
12. Moore EE, Jackson SL, Boyko EJ, Scholes D, Fihn SD (2008 Feb) Urinary incontinence and urinary tract infection: temporal relationships in postmenopausal women. *Obstet Gynecol* 111(2 Pt 1):317–323
13. Richter HE, Albo ME, Zyczynski HM et al (2010 Jun 3) Retropubic versus transobturator midurethral slings for stress incontinence. *N Engl J Med* 362(22):2066–2076
14. FitzGerald MP, Richter HE, Bradley CS, Ye W, Visco AC, Cundiff GW, Zyczynski HM, Fine P, Weber AM (2008) Pelvic support, pelvic symptoms, and patient satisfaction after colposcleisis. *Int Urogynecol J* 19:1603–1609
15. Sutkin G, Lowder JL, Smith KJ (2009) Prophylactic antibiotics to prevent urinary tract infection during clean intermittent self-catheterization (CISC) for management of voiding dysfunction after prolapse and incontinence surgery: a decision analysis. *Int Urogynecol J* 20:933–938
16. Stern JA, Hsieh Y, Schaeffer AJ (2004) Residual urine in an elderly female population: novel implications for oral estrogen replacement and impact on recurrent urinary tract infection. *J Urol* 171:768–770
17. Hampson SJ, Noble JG, Rickards D, Milroy EJ (1992) Does residual urine predispose to urinary tract infection? *Br J Urol* 70:506
18. Phipps S, Lim YN, McClinton S, Barry C, Rane A, N'Dow J (2006) Short term urinary catheter policies following urogenital surgery in adults. *Cochrane Database Syst Rev* 19(2): CD004374
19. Hammar N, Farahmand B, Gran M, Joelson S, Andersson SW (2010) Incidence of urinary tract infection in patients with type 2 diabetes. Experience from adverse event reporting in clinical trials *Pharmacoepidemiol Drug Saf* 19:1287–1292