Safety and Efficacy of Sling for Persistent Stress Urinary Incontinence After Bulking Injection

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OBJECTIVES To evaluate the impact of injectable agents on subsequent incontinence surgery outcomes to assess safety and efficacy of this treatment combination. Periurethral bulking agents are a minimally invasive treatment option for stress urinary incontinence (SUI), but often lack durability necessitating further surgical intervention.

METHODS Retrospective review of 43 patients with SUI following bulking agent who underwent subsequent sling placement from November 2000 to September 2009 were evaluated for demographics, symptoms, urodynamics (UDS), bulking agent characteristics, concomitant procedures, pad requirements per day (PPD), subjective outcomes, and complications.

RESULTS Mean patient age was 67 years, with mean follow-up of 37.3 months. All demonstrated SUI, and mixed urinary incontinence (MUI) was noted in 81.4%. Almost half (48.8%) had undergone a prior antiincontinence procedure. Mean number of injections was 3. After a bulking injection, 25 autologous fascia pubovaginal slings, 13 midurethral slings, and 5 biological pubovaginal slings were placed. Concomitant pelvic surgery was performed in 37.2%. Postoperatively, mean PPD decreased from 5.3 to 0.65, with a 60.5% subjective cure rate (no pads or leakage under any circumstances). No association was seen between number or type of injection, or type of sling with regards to patient outcomes. Results were significantly related to concomitant surgery ($P = .007$). SUI recurred in 8 patients (18.6%), which was not statistically associated with other parameters. Complications included urinary retention (8 patients) de novo urgency (1 patient), UTI (4 patients), abdominal wound infection (3 patients), and cystotomy (1 patient).

CONCLUSIONS Prior treatment with bulking agents does not appear to negatively affect outcomes for future antiincontinence surgery in our patient population. UROLOGY 77: 1076–1080, 2011. © 2011 Elsevier Inc.

Periurethral bulking agents are frequently used for treatment of stress urinary incontinence (SUI) in women. Although the concept of urethral injection for SUI has been discussed for more than 70 years,[1-3] initial safety concerns delayed widespread acceptance. The introduction of glutaraldehyde crosslinked collagen (Contigen, CR Bard, Covington, GA) in 1993 shifted practice patterns by providing a potentially efficacious agent with an acceptable safety profile. Since the introduction of Contigen, multiple agents have entered the market with similar efficacy and limited complications.[4,5] In addition to safety, injectables are minimally invasive and preclude the need for a general anesthetic which dramatically enhances their use in select populations. In randomized trials, patient satisfaction and improvement in quality of life after injection therapy compares favorably with traditional surgical treatment, despite better objective outcomes with surgery.[6] In addition, complications were significantly less frequent and severe in the injection group in 1 study.[6] Several studies with at least 1-year follow-up of collagen injections report cure and improvement rates ranging from 40% to 60%.[4] Carbon-coated zirconium oxide (Durasphere, Boston Scientific, Natick, MA) and calcium hydroxylapatite (Coaptite, Boston Scientific, Natick, MA)[7] have shown efficacy rates similar to collagen in randomized control trials.[8]

Reports of durability vary by type of injectable, and comparisons are difficult because of vastly differing study methodologies. In one randomized trial comparing the efficacy and durability of Contigen to Durasphere, treatment was initially effective in 63% of both groups, but by 36 months, efficacy had decreased to 21% in the Durasphere group and to 9% in the Contigen group.[9] In addition to issues with overall durability, multiple injections may be required to achieve and maintain effect.[8] As

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such, a certain proportion of patients will ultimately decide to undergo surgery after initial injection therapy in an effort to obtain a more sustained outcome, particularly in a complex patient population. Isom-Batz et al reported a series of 31 patients with intrinsic sphincter deficiency and SUI after antiincontinence surgery who underwent collagen injection, and of these, 6 (19%) eventually underwent autologous sling procedures after failure of collagen.[10] Other than that report, currently there is little literature specifically addressing outcomes in patients undergoing surgery after urethral bulking. This study aims to assess whether injectable therapy affects the subsequent antiincontinence surgery safety profile and outcomes, and whether there is any association between objective and subjective outcomes with type of injection or number of injections.

MATERIAL AND METHODS

An institutional review board–approved retrospective review of medical records of patients with SUI after bulking agent therapy who underwent subsequent antiincontinence surgery between November 2000 and August 2009 was performed. Inclusion criteria included women aged 18 years or more with SUI demonstrated during clinical or urodynamic (UDS) evaluation after urethral bulking agent.

Patient charts were queried for preoperative and postoperative urinary symptoms, physical examination characteristics, prior antiincontinence interventions, pad number (based on patient report), UDS data, and complications. All injections were performed transurethrally by 1 of 2 academic urologists specializing in female urology. We recorded bulking agent type and number of injections, and time from injection to surgery. Those patients who were not satisfied with their response to bulking injections or the need for repeated injections chose to pursue surgery. Sling procedures used included: rectus, fascia lata, or allograft (InteXen) pubovaginal slings, Suprapubic Arc Sling (SPARC, American Medical Systems), and Transvaginal Tape Secure (TVT-S, Ethicon). Surgery choices were based on surgeon and patient preferences in the context of the patients' prior procedural backgrounds. Subjective postoperative outcomes were delineated as cured, improved, same, and worse based on assessment by the same practitioner who performed the bulking injections and antiincontinence surgery via verbal interview. Subjective cure was defined as no leakage and no pad usage reported by patient. Patients were assessed at 1, 3, and 6 months postoperatively and then annually, unless there was reason for earlier visit. The objective measures we recorded included: pre- and post operative number of pads per day (PPD) and results of postoperative supine cough stress test performed with a physiologically full bladder. Other outcomes assessed included intraoperative and postoperative surgical complications, de novo urgency or urge incontinence, resolution of urgency, and recurrence of SUI symptoms. Statistical analysis was performed with the assistance of R version 2.7.1 (2008-06-23) and SAS/STAT software version 9.1.3 for Unix (SAS Institute, Cary, NC). Continuous variables were compared using the Wilcoxon rank sum and Kruskal–Wallis tests, while categorical variables were compared using the Fisher's exact test. All univariate statistical tests were two-tailed, with a P value of 0.05 or less considered significant.

Table 1. Presenting characteristics (n = 43)

Characteristic	Mean	Range
Age (y)	67	46-91
Follow-up (mo)	37.3	12-90
VLPP (cm H_2O)	72.1	30-110
PPD (preoperative)	5.3	0-20
	No.	%
Prior antiincontinence surgery	21	48.8
Prior hysterectomy	30	69.8
Urethral hypermobility	22	51.2
Pelvic organ prolapse	22	51.2
MUI	35	81.4

MUI = mixed urinary incontinence; PPD = pads per day.

RESULTS

A total of 43 consecutive patients were identified that met inclusion criteria (Table 1) with a mean patient age of 67.0 years (range 46-91 years). Average follow up was 37.3 months after last injection (range 12-80 months, median 31 months). Almost half of the patients (48.8%) had undergone prior surgical antiincontinence procedures before presentation to our clinic. More than half (51.2%) demonstrated concomitant pelvic organ prolapse (14 cystocele, 7 cystocele and rectocele, and 1 enterocele). The majority of prolapses were of low grade: 55.1% grade 1, 20.6% grade 2, and 13.8% grade 3. Prior hysterectomy had been performed in 30 patients (69.8%). Thirty-five (81.4%) presented with symptoms of mixed urinary incontinence, and 23.3% demonstrated detrusor overactivity (DO) on UDS. A total of 22 women (51.2%) displayed urethral hypermobility on preoperative examination, defined as 30-degree rotation of the proximal urethra and bladder neck associated with valsalva effort as detected visually without Q-Tip insertion. Mean abdominal leak point pressure (ALPP) was 72.1 cm H_2O (range 30-110 cm H_2O).

Patients underwent an average of 3 injections (range 1-4), with 41.9% undergoing Durasphere, 32.6% collagen, 20.9% Coaptite, and 4.7% more than 1 type (Table 2). There were no complications associated with initial injection therapy. After injection therapy, the average time to surgery after last injection was 9.2 months (range 1-48). All patients in this analysis underwent a sling procedure: 25 patients underwent autologous pubovaginal bladder neck sling (PVS), 13 midurethral mesh (8 TVT-S, 5 SPARC), and 5 InteXen PVS. Sixteen patients underwent concomitant surgical procedures: 7 urethrolysis, 4 cystocele repairs, 1 fistula repair, 1 rectocele repair, 1 rectocele and enterocele repair, 1 abdominal wall hernia, and 1 removal of suture from prior procedure. Urethrolysis was performed when required due to extensive fibrosis from prior surgeries.

Overall, pad use decreased from a mean of 5.3 PPD preoperatively to a mean 0.65 PPD postoperatively (P = .2095) based on patient report. After sling surgery, no patients demonstrated leakage on postoperative cough-stress test. Subjectively, 60.5% of patients reported themselves cured (no pads or leakage), 34.9% improved, and 1

Table 2. Treatment

			Correlation With:			
	Mean	Range	Subjective Outcome	Change in PPD	Recurrent SUI	De Novo UUI
No. of injections	3.0	1-4	$P = .832$	0.793	0.090	0.933
Time to surgery (months)	9.2	1-48				
	No.	%				
Type of injection			$P = .881$	0.811	0.433	0.015
Durasphere	18	41.9				
Contigen	14	32.6				
Coaptite	9	20.9				
> 1 Type	2	4.7				
Type of sling			$P = .500$	0.604	0.484	0.424
Autologous	25	58.1				
Mesh	13	30.2				
Biological	5	11.6				
Concomitant surgery			$P = .007$	0.161	1.00	0.847
Urethrolysis	7	16.3				
Cystocele repair	4	9.3				
Rectocele repair	1	2.3				
Recto and enterocele	1	2.3				
Other	3	7.0				

PPD = pads per day; SUI = stress urinary incontinence; UUI = urge urinary incontinence.

Table 3. Outcomes

	No.	%
Leakage on postop cough stress	0	0.0
Decrease in mean ppd	4.67	—
Subjective outcome		
Cured/no leak	26	60.5
Improved	15	34.9
Same	1	2.3
Insufficient data	1	2.3
Resolution of UUI (of 35 patients with preop MUI)	22	62.9
Completely	10	45.5
Significantly	7	31.8
Partially	5	22.7
Recurrence of SUI	8	18.6

MUI = mixed urinary incontinence; SUI = stress urinary incontinence; UUI = urge urinary incontinence; preop = preoperative.

patient reported no change (Table 3) Patients with longer follow-up intervals did not significantly differ from those with shorter intervals in terms of outcome (Table 4). Interestingly, patients undergoing simultaneous procedures showed only a 33.3% subjective cure rate ($P = .007$) compared with the overall rate of 60.5% in the collective group. However, the majority (66.7%) of patients undergoing concomitant procedures reported "improved" status and none worsened. Of 35 patients with preoperative urge urinary incontinence (UUI), 62.9% improved with surgery and appropriate anticholinergic therapy (45.5% completely, 31.8% significantly, and 22.7% partially) (Table 3). SUI recurred in 8 patients (18.6%), at an average of 13 months after surgery (range 3-34). Three of these patients experienced recurrence within 4 months, and as such may be characterized as a treatment failure as opposed to late recurrence. There was no statistically significant relationship between number or type of injection, UDS parameter (including DO, voiding or storage pressures, ALPP), or type of sling on subjective outcomes, postoperative pads per day, or recurrence of SUI (Table 2).

With regard to postoperative adverse effects and operative complications, the most prominent finding was transient urinary retention in 8 patients (18.6%), with all cases resolving in the immediate postoperative period. One patient (12.5% of 8 patients with preoperative pure SUI) reported de novo urgency after surgery. Continuation of urgency and occurrence of de novo urgency showed a statistically significant correlation with injection type (Table 2). Three patients had superficial abdominal wall wound infections, 2 cases of which resolved with oral antibiotics and 1 of which required incision and drainage. Two patients had documented UTIs within 6 months of their operation, and 2 patients developed recurrent UTIs presenting more than 1 year after surgery. Both cases eventually resolved with vaginal estrogen therapy for vaginal mucosal atrophy. One patient had an intraoperative cystotomy in an area of scarring where an eroded sling had previously been removed. There was no incidence of sling erosion or extrusion and no episodes of particle migration.

COMMENT

Urethral bulking agents have emerged as a reasonable, minimally invasive alternative to surgical repair, both as a primary treatment and as a secondary procedure for recurrent SUI. As a primary procedure, injections fall short of surgery in terms of durability and objective cure, but are less invasive and show diminished complication rates. In a complex patient who has already undergone prior procedures, injection is a valid method of attempting to restore or optimize cure.[10] In patients undergoing injectable therapy either primarily or secondarily, a sub-

Table 4. Outcomes with follow-up

Length of follow-up, y (No. of Patients)	1-2 y (17 patients) n (%)	2-3 y (7 patients) n (%)	3-4 y (5 patients) n (%)	4-5 y (7 patients) n (%)	> 5 y (7 patients) n (%)
Subjective outcome					
Cured/no leak	10 (58.8%)	3 (42.9%)	4 (80.0%)	5 (71.4%)	4 (57.1%)
Improved	6 (35.2%)	4 (57.1%)	1 (20.0%)	2 (28.6%)	2 (28.6%)
Same	1 (5.9%)	0	0	0	0
Insufficient data	0	0	0	0	1 (14.3%)

set will choose to pursue a more definitive surgical procedure, either because of recurrence or because of the need for multiple injections. We sought to characterize our experience with this complex patient group, and to assess the safety and efficacy of sling after urethral bulking agents.

Representing a tertiary care population, the described patient group was particularly complicated, with half having previously undergone one or more prior antiincontinence procedures. In this group, ALPP did not significantly correlate with subjective or objective outcome measures. Of the patients, 51% demonstrated pelvic organ prolapse, and 16 patients underwent concomitant surgery, which was significantly associated with subjective outcome ($P = .007$). Patients undergoing simultaneous procedures showed only a 33.3% subjective cure rate, whereas the majority improved.

Despite complicating factors in the study population, patients undergoing sling following bulking agents in general demonstrated favorable outcomes with an acceptable morbidity profile. Because of the diversity of preinjection surgical procedures, heterogeneity of the patient population, and the lack of standardization of outcome reporting in other comparative study groups, it is difficult to compare our results with published success rates for various sling types. Yet, our rates of subjective improvement and cure appear fairly comparable. For PVS, a series of 14 women who underwent rectus fascia PVS for recurrent SUI after prior suburethral sling procedure reported 86% cure or improvement by the Blaivas-Groutz antiincontinence surgery response score.[11] In another series of 38 women with primary SUI and 29 women with recurrent SUI who underwent autologous PVS, 74% were cured (by a strict outcome score); 18% improved in the primary SUI group and 59% were cured and 24% improved in the recurrent SUI group.[12] Transvaginal tape success rates of 81-91% have been recorded in various studies,[13] and objective success rates have been found to be comparable between TVT, SPARC™[14] and TVT-S (80-88% objective cure and 76-77% subjective cure in 1 trial).[15] By subjective report, 60.5% of our patients reported cure (no pads or leakage), and 34.9% reported improvement. Objectively, our patients showed a significant reduction in pad usage and leakage on physical examination.

One potential concern in patients undergoing sling after urethral injectable might be whether the injected implant would alter urethral anatomy or physiology in such a way that the attendant risks of sling or injection might be enhanced, ie, increased rates of sling erosion, urinary retention, new or worsening DO, or particle migration. In our experience, prior injections did not change the complication profile of sling placement. There were no incidences of sling erosion, persistent urinary retention, or particle migration. In all, 81% of our patients complained of stress-predominant MUI preoperatively, with 23.3% having documented DO. After sling surgery, most patients with MUI improved, and only 1 case of de novo urgency after sling (12.5% of pure SUI patients) was reported, which is fairly comparable to reported rates for de novo urgency rates after TVT.[16] The type of injection showed a statistically significant correlation with overall occurrence of de novo urgency and continuation of preoperative urgency ($P = .015$), but de novo urgency occurred in a single case (a patient who underwent autologous sling after collagen injection), and this is not likely to be representative of a clinical trend.

Limitations of this study include its retrospective nature and a patient population varied in their presentations and management. As discussed, half of our patients had undergone prior antiincontinence procedures. These procedures were varied, ranging from colposuspension, to removal of eroded slings, to the ubiquitous patient-reported "bladder suspension/tack." The variety of the group is a weakness in 1 sense, as we do not have a pure group. However, it is a group of patients who would be more prone to morbidity and failure, and in a study assessing safety, it adds emphasis to the low rate of complications. In addition, injection therapy is a feasible option for SUI-recurrent patients who would like to avoid or prolong the interval until repeat surgery, and in that sense, our mixed patient group is appropriate. Our outcome measures are not as stringent as those of prospective trials, making it difficult to compare our rates of success to other series. The fact that our subjective improvement data are based on verbal patient report to the operative physician introduces an element of bias. Therefore, our study is better suited to remark on safety and complications, which we were able to record with consistent objectivity. However, despite this, it should be noted that this is the largest series of its type addressing this difficult clinical scenario.

CONCLUSIONS

Treatment of patients with recurrent SUI after urethral or periurethral procedures represents a therapeutic challenge. In our experience, sling placement after urethral injection is safe and efficacious. Patient selection and determination of the proper procedure for each clinical situation contributes to success in the management of these complex presentations. This analysis demonstrated no significant relationship between sling type, injection type or number, or UDS parameter on objective or subjective outcomes or on development of post or intraoperative complications. In this group, performance of concomitant procedures was significantly related to decreased subjective cure, although most showed improvement. In our approach, injectables are a safe first line agent for SUI (with or without low grade prolapse or stress predominant MUI) that may be used in patients who decline or would prefer to defer surgery with the understanding that they may lack durability. In our patients with recurrent SUI after injectable, sling surgery has been demonstrated to be safe and efficacious.

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