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The female continence mechanism measured by high resolution manometry: Urethral bulking versus midurethral sling

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Abstract

Aims—Traditional technology to characterize urethral pressure changes during dynamic conditions is limited by slow response times or artifact-inducing withdrawal maneuvers. The 8F high-resolution manometry (HRM) catheter (ManoScan™ ESO, Covidien) has advantages of fast response times and the ability to measure urethral pressures along the urethral length without withdrawal. Our objective was to determine static and dynamic maximum urethral closure pressures (MUCPs) and resting functional urethral length (FUL) in women using HRM before and after transurethral bulking and compare results to other women who underwent midurethral sling (MUS).

Methods—We recorded rest, cough, and strain MUCPs and FUL in 24 women before and after transurethral bulking with polydimethylsiloxane (Macroplastique®) using the HRM catheter and compared these changes to HRM values from 26 women who had the same measures before and after MUS.

Results—At rest, MUCPs increased minimally after both urethral bulking and MUS (3 vs 0.4 cm H_2O respectively, $P = 0.4$). Under dynamic conditions there were statistically insignificant small increases in MUCP and these increases were markedly less than after MUS (cough: 1.5 vs 63.8 cm

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AUTHORS' CONTRIBUTIONS

EJW project development, data collection, data analysis, manuscript writing/editing. ACK project development, data collection, manuscript editing. ESL subject recruitment, data interpretation, manuscript writing/editing. CWN project development, subject recruitment, data analysis, manuscript writing/editing.

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H_2O, $P < 0.001$ and strain: 11.5 vs 57.7 cm H_2O, $P < 0.001$). FUL increased by 0.5 cm after transurethral bulking ($P = 0.003$), and decreased by 0.25 cm after MUS placement ($P = 0.012$).

Conclusions—The mechanism of continence after urethral bulking differs from MUS. While MUS increases dynamic MUCP, bulking may rely on increasing the length of the continence zone.

Keywords

functional urethral length; high resolution manometry; maximum urethral closures pressures; midurethral sling; stress urinary incontinence; urethral bulking

1 | INTRODUCTION

The etiology for stress urinary incontinence has been attributed to urethral hypermobility, weakness of the urethral sphincter mechanism, or a combination of both. Women have a 13.6% risk of undergoing surgical intervention for this condition.[1] The most common procedure to treat incontinence when related to urethral hypermobility is the midurethral sling (MUS). Work by our group has already demonstrated that after MUS placement there is no significant change in maximum urethral closure pressures (MUCP) at rest, but marked increases (up to 60 cm H_2O) with cough, and strain.[2] These findings suggest that the MUS does not affect the urethra at rest, but functions by augmenting the MUCP during cough, and strain maneuvers. Urethral bulking procedures are generally reserved for the 10–15% of women with intrinsic sphincter deficiency or lacking urethral mobility.[3] The proposed mechanism of action of this procedure involves reduction of the inner diameter of the urethra resulting in urethral coaptation and an increased urethral resistance to flow.[4] Its effect on urethral pressures or functional urethral length (FUL), however, is unknown.

Water perfusion techniques have been the mainstay to assess urethral pressures; however, they may not accurately measure maximum pressures during stress events, making evaluation of the physiologic impact of stress incontinence therapies a challenge. Microtip transducers or air-charged balloon catheters measure only one small area of the urethra and/or require a withdrawal technique to measure pressures, thus may miss the true MUCP. Furthermore, withdrawal can be irritating and induce urethral contractions, which can artifactually increase urethral pressure measurements. The newest technology for pressure measurements is a high-resolution manometry (HRM) catheter (ManoScan™ ESO, Covidien) which has been validated by our group for use in the urethra.[5,6] Compared to conventional technology, this catheter is easier to use with faster response times (25 ms), can measure multiple sites simultaneously, and can remain stationary for measurement recordings. Our prior work has shown that it has a high correlation with traditional water-perfusion catheters, excellent test-retest reliability, and is better tolerated by patients.[5,6] This technology has never before been used to explore urethral changes after transurethral bulking procedures.

The primary aim of this study was to investigate the effects of transurethral bulking on urethral pressure profiles at rest and during dynamic conditions using the HRM catheter. Secondary aims were to compare these pressure changes to those occurring after MUS and to compare changes in resting FUL before and after stress incontinence treatments with

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urethral bulking versus MUS placement. We hypothesized that both resting and dynamic MUCPs would increase after transurethral bulking, and that changes in MUCPs will be less with the urethral bulking than with MUS interventions.

2 | MATERIALS AND METHODS

Women with primary or recurrent stress urinary incontinence scheduled to undergo polydimethylsiloxane (Macroplastique®, Cogentix, Minnetonka, MN) urethral bulking injection were recruited to undergo bladder and urethral pressure measurements with the HRM catheter before and 6 weeks after urethral bulking injection. Exclusion criteria included age <18 years, an active urinary tract infection, pregnancy, and non-English-speakers. All patients had bothersome stress urinary incontinence and a positive preoperative cough stress test. We recorded age, BMI, parity, medical history, prior incontinence and prolapse surgical history, and urethral bulking volume. Each study subject completed three validated incontinence symptom questionnaires before and 6 weeks after urethral bulking injection: the Incontinence Severity Index (ISI, scale 0–12),[7] the Incontinence Impact Questionnaire Short Form (IIQ-7, scale 0–100),[8] and the Urogenital Distress Inventory short form (UDI-6, scale 0–100).[9] This urethral bulking cohort was compared to a cohort of 26 patients who underwent the same HRM measurements before and after MUS placement.[2] The study was approved by the University of California San Diego Institutional Review Board and written informed consent was obtained from each participant.

The HRM catheter is 2.75 mm in diameter (approximately 8F) and has circumferential pressure sensors along 26.5 cm of its length.[2] The miniature solid-state sensors are 4 mm long with 2 mm of active sensing area separated by 3 mm of flexible molding giving a 7.5 mm on center spacing between each of the 36 sensors.[2] Each individual sensor has 16 pressure-sensitive segments circumferentially distributed around it[2] (Figure 1).

Measurements were taken in the supine position after completely draining the bladder of urine and then filling the bladder with 250 cc of sterile water. The HRM catheter was placed such that the tip was 5 cm inside the bladder.[2] Bladder and urethral pressure measurements were taken three times at rest, during three coughs, and during three strain maneuvers.[2] For strain maneuvers, subjects were instructed to bear down or push as though trying to push out a baby or have a bowel movement.[2] Computer processing from the signal comes from the pressure-sensing elements and calculates average circumferential pressures which present as a color display.[2] MUCPs were calculated by subtracting the maximum bladder pressure, obtained 2 cm proximal to the urethrovesical junction (UVJ), from the maximum urethral pressure during each maneuver. FULs were calculated by measuring the maximum bladder pressure 2 cm proximal to the UVJ and then measuring along the distance of the urethra to determine when the urethra exceeded this pressure and then dropped below this bladder pressure. The average of the three values from each calculation were used for the final MUCP and FUL measurements. To evaluate urethral bulking efficacy, a 250 mL standard volume cough stress test was performed postoperatively.

Subject demographics between groups were compared with the Mann-Whitney U test. Continuous variables were compared with either a paired Wilcoxon rank sum test or Mann-

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Whitney test as appropriate. When comparing bulking volume subgroups the Kruskall-Wallis test was used. Our previous work comparing continent and incontinent subjects demonstrated that during dynamic maneuvers MUCPs decreased approximately 17 cm H_2O in incontinent subjects but did not change in continent subjects.[6] Therefore, we would consider clinical meaningful changes in MUCP to be approximately 17 cm H_2O. With 24 subjects there is 84% power to detect an increase of 17 cm H_2O after bulking during cough and strain maneuvers with a standard deviation of 20 cm H_2O. Analyses were performed with SPSS version 24 (IBM).

3 | RESULTS

A total of 24 women underwent Macroplastique® transurethral bulking injection. The women who underwent urethral bulking were older than those who underwent MUS, but had similar median vaginal parity, and BMI (Table 1). More women in the urethral bulking group had at least one prior anti-incontinence procedure. The mean transurethral bulking injection volume was 3.6 mL (range 1.25–5 mL).

Small statistically insignificant increases in MUCP were observed in resting and dynamic conditions after urethral bulking (Table 2). The volume of bulking injection material (<5 mL vs 5 mL) did not affect pressure changes ($P = 0.58$, $P = 0.58$, $P = 0.75$ at rest, cough, and strain, respectively) (Table 3). After bulking, 68% (15/22) had improvement on UDI-6, 68% (15/22) had improvement on ISI, 48% (11/23) had improvement on IIQ-7, and 64% (14/22) had improvement in question three of the UDI-6, which specifically targets stress urinary incontinence symptoms. 54% (13/24) had a negative cough stress test after bulking surgery. There were no statistically significant differences in FUL changes between those that improved or did not improve either subjectively or objectively ($P = 0.6$ and $P = 0.2$, respectively; data not shown).

When comparing the mean change in MUCP before and after urethral bulking to MUS, we found that at rest MUCPs increased minimally after both procedures (3 cm H_2O with urethral bulking and 0.4 cm H_2O after MUS; $P = 0.4$) (Table 4). Dynamic maneuvers, however, demonstrated minimal increases after urethral bulking but statistically significant and clinically meaningful increases after MUS (cough: 1.5 cm H_2O vs 63.8 cm H_2O, $P < 0.001$; strain: 11.5 cm H_2O vs 57.7 cm H_2O, $P < 0.001$). Table 5 shows the FUL changes pre- and post-either urethral bulking or MUS placement. FUL increased by 0.5 cm after urethral bulking ($P = 0.003$), but decreased by 0.25 cm after MUS placement ($P = 0.01$). The increase in FUL after urethral bulking was observed in subjects regardless of whether they were subjectively or objectively improved.

4 | DISCUSSION

We did not confirm our hypothesis that resting and dynamic MUCPs would increase significantly after urethral bulking. Instead, we found modest, clinically and statistically insignificant increases in MUCPs both at rest and with dynamic maneuvers. However, we did confirm our hypothesis that MUCP changes after urethral bulking with dynamic (stress-provoking) conditions were less than after MUS.

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An important question is what is a clinically meaningful difference in MUCP. Our previous work comparing continent and incontinent subjects demonstrated that during dynamic maneuvers MUCPs decreased approximately 17 cm H_2O in incontinent subjects but did not change in continent subjects.[6] In this study there were no changes in MUCP meeting the 17 cm H_2O increase after urethral bulking. In contrast, dynamic MUCPs markedly increased after MUS. Therefore, we conclude that urethral bulking does not produce clinically meaningful changes in urethral pressures.

Closure pressure of the urethra is determined by the combined action of striated and smooth muscle with submucosal coaptation, with each element contributing one-third.[9] It has been proposed that bulking achieves continence by increasing urethral resistance during intraabdominal pressure variation through coaptation.[10] Bulking may serve as a “central filler” and the amount of filler determines the amount of change necessary in the sphincter circular smooth muscle between the “open” and “closed” states.[11] The more “filler” volume the less length change that is required by the circular smooth muscle to produce a “closed” state, that is: from the impossible 100% contraction to achieve zero length with no filler volume to 10–30% length change when the diameter of the filler volume in the closed sphincter is double or equal in size to the open lumen.[11] In our study, the amount of bulking material injected into the urethra does not appear to be associated with improved MUCP measurements. Our sub-analysis looking at volume injected and pressure changes suggest some directionality of an association with increased volume producing higher pressure changes but the small number in each subgroup precluded definitive conclusions.

At rest, neither urethral bulking nor MUS produce significant changes in MUCP, however dynamic MUCPs (both cough and strain) increased dramatically after MUS. This result is consistent with the proposed mechanism of action for MUS, which when placed tension—free does not prevent any resting pressure increases, but engages during dynamic conditions to provide a rigid backboard to counteract intraabdominal pressures, augmenting MUCPs during dynamic conditions.

Stress incontinence occurs when there is not a corresponding increase in urethral pressure that matches the increase in intraabdominal pressure (pressure-transmission ratio).

Perhaps the modest nonsignificant increases in MUCP found both at rest and with dynamic maneuvers reflect the suboptimal function of the urethral sphincter musculature in counteracting these increases in intraabdominal pressure. It has previously been found that the striated urethral sphincter in women with stress incontinence is 12.5% smaller than that in continent women matched for age, parity, and hysterectomy.[12] It is possible that this decreased striated urethral sphincter volume at baseline in combination with previous surgical intervention in this population, or the aging process itself, impairs the elasticity, and intrinsic muscular sphincter function to promote continence which reflects our patient population undergoing urethral bulking. A bulking agent could theoretically reduce incontinence during dynamic conditions if it improves the sphincter mechanism’s ability to respond to intraabdominal pressure increases, but we would expect this effect to be modest which is reflected in our data.

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The urethra becomes shorter in length and larger in diameter with aging.[12] Rather than focusing on changes in urethral pressure, perhaps attention should be turned instead to an increase in FUL with improved coaptation as the mechanism of action to achieve continence after urethral bulking. It has been suggested that urethral bulking results in the cephalad elongation of the urethra with a concomitant increase in pressure transmission in the first quarter of urethral length.[13] This elongation can also expand the periurethral tissue to further augment the pressure transmission to the proximal urethral.[14] These changes reflect adequate injection at the bladder neck or proximal urethra preventing bladder neck opening during stress.[13] Findings similar to our own and reflecting this concept have been previously reported in the literature.[13,15–17] The slight reduction in urethral length after MUS placement emphasizes the different mechanism of action of the MUS procedure, which in contrast, functions by increasing MUCPs with dynamic maneuvers. Subjective and objective continence outcomes in our study improved after transurethral bulking similar to what has been previously reported.[18]

Strengths of this study include use of a high-resolution system that measures dynamic pressures with a fast response time and without the artifact created from withdrawal common to other techniques. Limitations include a small sample size and the inherent catheter artifact encountered in all measurement systems. Although the bulking patients were older and had more previous surgery than those who had MUS, this should not significantly influence our findings because we are predominantly comparing MUCP and FUL in the same patient before and after a treatment.

5 | CONCLUSION

Urethral bulking injections fail to significantly alter resting or dynamic MUCP as measured with the HRM catheter, however the mechanism of action may be more reliant on an increase in FUL. The different findings in MUCP and FUL changes between MUS and transurethral bulking support a different mechanism of action for the two surgical interventions. Neither procedure significantly affects MUCPs at rest. With dynamic maneuvers, urethral bulking injections may produce continence by lengthening the continence zone and enhancing urethral coaptation with less contribution from MUCP, whereas MUS provides a backboard to counteract increases in intraabdominal pressure and produces a marked increase in MUCP during dynamic conditions.

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CONFLICTS OF INTEREST

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BRIEF SUMMARY

Urethral bulking produces modest nonsignificant increases in resting and dynamic maximum urethral closure pressures but increases functional urethral length.

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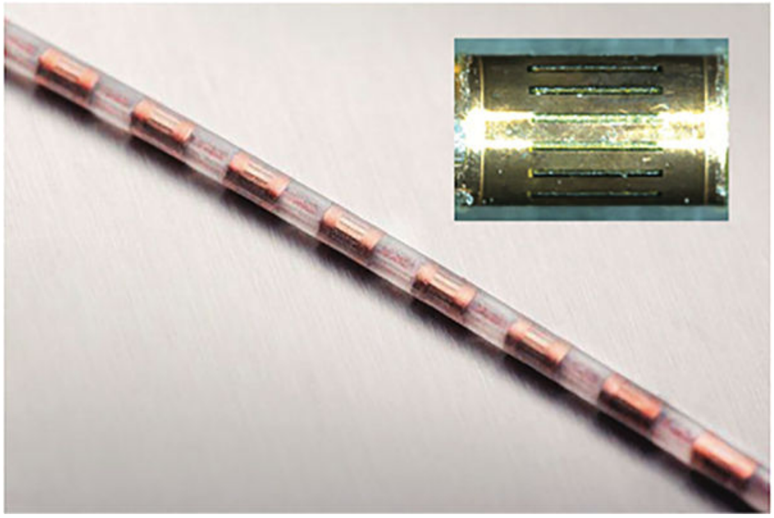

FIGURE 1.

High resolution manometry catheter. Diameter 2.75 mm with 4-mm copper pressure sensorsspaced 3 mm apart. Each sensor has 16 circumferential pressure-sensing foci (inset)

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TABLE 1

Subject demographics

	Urethral bulking (*n* = 24)	**MUS (*n* = 26)**	***P* value[a]**
Age in years	64.0 (44–84)	53.5 (38–77)	0.007
Vaginal parity	2 (0–4)	2 (0–5)	0.64
BMI (kg/m^2)	27.3 (18.9–45.7)	27.9 (20.8–37.2)	0.91
Prior anti-incontinence procedure	14 (58.3%)	7 (26.9%)	0.03

Results displayed as median (range) or *n* (%).

[a] Mann-Whitney.

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TABLE 2

MUCP before and after urethral bulking injection (*n* = 24)

	Preoperative	**Postoperative**	**Delta**	***P* value**[a]
Rest	38.4 (3.2)	41.4 (2.9)	+3	0.10
Cough	46.1 (6.5)	47.6 (4.8)	+1.5	0.89
Strain	47.0 (5.2)	58.5 (8.2)	+11.5	0.10

Results displayed as mean values in cm H_2O (SE).

[a] Wilcoxon signed ranks test.

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TABLE 3

Effect of urethral bulking volume on MUCP change

	Injection <5 mL (*n* = 13)	**Injection = 5 mL (*n* = 11)**	***P*-value[a]**
Rest	2 (4)	3 (5)	10 (8)
Cough	5 (2)	7 (9)	22 (14)
Strain	0.58	0.58	0.75

Results reported as mean MUCP in cm H_2O (SE).

[a] Kruskall-Wallis.

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TABLE 4

Mean change in MUCP before and after urethral bulking or MUS

	Urethral bulking (*n* = 23)	**MUS (*n* = 26)**	***P* value[a]**
Rest	+3	+0.4	0.40
Cough	+1.5	+63.8	<0.001
Strain	+11.5	+57.7	<0.001

Results reported as delta MUCP (MUCP postoperative minus MUCP preoperative) in cm H_2O for each maneuver.

[a] Mann-Whitney U.

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TABLE 5

Rest FUL before and after urethral bulking and MUS

	Preoperative	**Postoperative**	**Difference (95%CI)**	***P* value**[a]
Urethral bulking ($n = 24$)	3.2 (0.8)	3.7 (0.7)	0.5 (0.2, 0.7)	0.003
MUS ($n = 26$)	3.6 (0.5)	3.4 (0.5)	−0.25 (−0.42, −0.08)	0.012

Results displayed as mean (SD) in cm.

[a] Wilcoxon signed rank test.