FACTORS ASSOCIATED WITH SUBJECTIVE IMPROVEMENT FOLLOWING MIDURETHRAL SLING PROCEDURES FOR STRESS URINARY INCONTINENCE

A Masters Thesis Presented

By

EMILY ELISE WEBER LEBRUN

Submitted to the Faculty of the
University of Massachusetts Graduate School of Biomedical Sciences, Worcester
in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE IN

CLINICAL INVESTIGATION

MAY 11th 2010

FACTORS ASSOCIATED WITH SUBJECTIVE IMPROVEMENT FOLLOWING MIDURETHRAL SLING PROCEDURES FOR STRESS URINARY INCONTINENCE

A Masters Thesis Presented

By

EMILY ELISE WEBER LEBRUN

The signatures of the Master's Thesis Committee signifies completion and approval as to style and content of the Thesis

Robert J. Goldberg, Chair of Committee

Carol Bigelow, Member of Committee

Tiffany Moore-Simas, Member of Committee

The signature of the Dean of the Graduate School of Biomedical Sciences signifies that the student has met all master's degree graduation requirements of the school.

Anthony Carruthers, Ph.D.,
Dean of the Graduate School of Biomedical Sciences

Program
Master of Science in Clinical Investigation

May 11th 2010

Dedication

I thank my husband,

Marc,

for his

generosity, patience, understanding,
wisdom, strength, humor,
pragmatism, respect,
selflessness
and unconditional love.

My cup overfloweth.

Acknowledgements

I am grateful to the University of Massachusetts Medical Center for providing me the opportunity to expand my education in clinical research.

I am beholden to Robert Goldberg for embracing the challenge of developing and continually enhancing the Masters of Clinical Investigation program, and for inviting me to participate in the first class. Rob epitomizes mentorship as he graciously guides young investigators in their research endeavors and career path. His talent for teaching, enhanced by his generosity, is amazing to witness and is a model for all.

I am grateful to my classmates in the Masters of Science in Clinical Investigation (Christine Clemson, Steven Hatch, Olga Hardy, Chris Rosenbaum and Wendy Marsh) and to my co-fellow (Diego Illanes) for their camaraderie, sincerity and levity as they accompanied me on this journey to become effective clinician researchers.

I am thankful for having had the opportunity to learn a tremendous breadth of urogynecology and pelvic reconstructive surgery from Michael Aronson and Abraham (Nick) Morse and to know these gifted educators. Michael Aronson is unmatched in his ability to captivate, and educate, an audience. Nick Morse demonstrated the art and skill of critical surgical decision-making.

I am privileged to have enjoyed the skilled instruction of Tiffany Moore-Simas and Carol Bigelow as they helped me navigate through my earliest clinical research endeavors. Carol Bigelow is my model for professorial patience and persistence. Tiffany Moore-Simas has shown me that balancing academic excellence and personal achievement with kindness and grace is possible.

I will always regard Oz Harmanli as my first mentor in clinical research. He taught me to keep a narrow focus, select an answerable question and devise a simple approach. In this way, we can build the great wall of clinical evidence brick by brick.

I am grateful to my dear friend and colleague, Allison Howard, for her tireless dedication to my clinical and research education. She influences me to be thoughtful, careful and precise, and she makes everything I do better.

I am forever indebted to Stephen Young, for always prioritizing my academic development and personal well-being. He allowed me to spread my wings, and was always present to share in my greatest challenges and achievements. He is a true mentor, a true friend, a true mensch.

ABSTRACT

Background

Female stress urinary incontinence (SUI) greatly affects quality of life. The midurethal sling (MUS) procedure has been widely accepted as the standard of care treatment for SUI, although there is little information regarding patients' subjective reports of symptom improvement.

Objectives

The objective of this study was to identify clinical and demographic characteristics that predict subjective symptom improvement following MUS procedures in women with SUI.

Materials and Methods

The study design was retrospective cohort. Subjects included women who underwent MUS between 2006 and 2008, returned mailed surveys and met our predefined inclusion criteria. Pre-operative data included demographics, prior surgery, co-morbid diseases, urodynamics and concomitant reconstructive surgery. Subjective improvement was measured by score improvement on the UIQ-7, UDI-6, the UDI stress subscale and Question 3 of the UDI, "Do you experience urine leakage related to physical activity, coughing, or sneezing?"

Results

The mean age of the study sample was 57 years, parity was 2.5 and BMI was 28. Subjects with lower MUCP demonstrated more improvement on the UIQ-7. ΔUDI-6 stress subscale scores were more sensitive to symptom change than either the ΔUDI-6 or ΔUIQ-7. Older, menopausal subjects with urethral hypermobility and concomitant vaginal suspension showed less improvement than subjects without these characteristics. After controlling for urethral straining angle, PVR, menopause and time out from surgery, older age and concomitant vaginal suspension were associated with persistent post-op symptoms on the UDI-6 Question 3 and age remained the only variable associated with persistent symptoms on the UDI-6 stress subscale.

Conclusion

Concurrent vaginal suspension and advancing age were risk factors for persistent symptoms following MUS procedures in patients with SUI. Symptoms may recur after 24 post-operative months. Clinicians are encouraged to provide additional preoperative counseling to those women who are at greatest risk for persistent symptoms.

Table of Contents

List of Tables & Figures

List of Abbreviations

BMI	body mass index
COPD	chronic obstructive pulmonary disease
CST	cough stress test
DM	diabetes mellitus
DO	detrusor overactivity
HIPAA	Health Information Privacy & Accountability Act
ISD	intrinsic sphincter deficiency
LPP	leak point pressure
MS	multiple sclerosis
MUCP	maximum urethral closure pressure
MUS	midurethral sling
PFDI	Pelvic Floor Distress Inventory
PFIQ	Pelvic Floor Impact Questionnaire
POP-Q	Pelvic Organ Prolapse Quantification system
PVR	post-void residual
QOL	Quality of Life
SUI	stress urinary incontinence
TO MUS	transobturator tape midurethral sling (also known as TOT)
RP MUS	retropubic midurethral sling (also known as TVT)
UDI-6	Urinary Distress Inventory (short form)
UHM	urethral hypermobility
UIQ-7	Urinary Incontinence Questionnaire (short form)
USLS	uterosacral ligament suspension
UVJ	urethrovesical junction

CHAPTER I

1 Introduction

1.1 Description of the medical condition

Female stress urinary incontinence (SUI) is the involuntary transurethral loss of urine at the moment of increased intra-abdominal pressure. Upwards of 70% of women suffer from urinary incontinence during their lifetime and many undergo surgical treatment for this condition.[1] Traditional surgical procedures include the Marshall-Marchetti Krantz colposuspension, the Burch urethropexy, various needle suspension procedures and the pubovaginal sling.[2-6] The pubovaginal sling (made with either fascia lata or synthetic mesh) involves placing the suspension material at the urethrovesical junction (UVJ). The newer midurethral sling (MUS) procedures, first introduced by Ulmsted and Petros in 1995 (retropubic) and then modified by Delorme in 2001 (transobturator), have revolutionized the treatment of SUI with improved efficacy and reduced morbidity.[7-9] While a number of studies have examined objective outcomes following MUS, relatively fewer have addressed patients' reports of subjective symptom improvement.[10-12]

1.2 Overview of research problem

While there are several pathophysiologic mechanisms that may contribute to the development of SUI, there is no consensus about the relative importance of each of these in predicting successful surgical outcome. Loss of periurethral

connective tissue can result in urethral hypermobility, which is the demonstrable (>30°) rotational descent of the urethrovesical junction (UVJ) during a Valsalva's maneuver.[13] This is measured via a cotton swab test, noting the angle of the Q-tip with respect to the horizontal, at rest and during straining.[14] Shorter functional urethral length and the presence of intrinsic sphincter deficiency (ISD), diagnosed by low maximum urethral closure pressure (MUCP) or abdominal leak point pressure (LPP), may also be associated with reduced symptom improvement.[15, 16]

Other preoperative predictors of MUS success have been increasingly explored in the urogynecology literature, with little consensus. Some studies have found advanced age, menopausal status, prior anti-incontinence surgery, and urinary urgency to be independently associated with sling failure, whereas others have failed to find predictors of clinical failure.[11, 17, 18] Interpretation of the published literature is difficult due to the lack of consistent measures of clinical variables, differences in the size and characteristics of the various study populations, and definitions of treatment success and/or failure.

1.3 Quality of Life instruments as outcome measures

Much of the existing literature evaluating the efficacy of midurethral slings in patients with SUI has used an objective measure of cure, the cough stress test (CST), performed with a subjectively full bladder or 300mL, whichever is less.

While this test may provide a consistent tool for research, it is not always a reliable assessment of patients' daily symptoms. Patients who present postoperatively complaining of persistent incontinence deserve a thorough evaluation and treatment plan, even if they have a negative CST. In contrast, patients who are subjectively cured, but leak during a research-driven CST, generally do not need further evaluation. This common clinical paradox has prompted the selection of patient-reported subjective outcomes. Two validated quality of life (QOL) questionnaires were selected for use in the present study because of their prevalent use in clinical outcomes research and because of their ability to isolate different types of incontinence symptoms: the Pelvic Floor Distress Inventory (PFDI-20) and the Pelvic Floor Impact Questionnaire (PFIQ-7).[19] The urinary subscales of these instruments (UDI-6 and UIQ-7) were used to assess post-operative subjective satisfaction.[20, 21]

CHAPTER II

2 Related work

2.1 Measuring urethral hypermobility

In the early 1970's bead-chain cystometrograms were performed to evaluate urethral and bladder neck mobility using fluoroscopy.[22] The urethra was prepared by applying lidocaine jelly with a cotton swab. During one of these routine procedures, Crystle et al observed the dynamic deviation of the cotton swab concurrent with the patient's Valsalva's maneuver, and the "Q-tip test" was born.[14] The inexpensive and less invasive Q-tip test soon replaced more cumbersome measures of urethral mobility and a somewhat arbitrary cut-off of 30˚ categorized patients as having a "hypermobile" urethra.[23]

An assessment of urethral hypermobility (UHM) has been universally integrated into the evaluation of female urinary incontinence.[24] Efforts to standardize the Q-tip test suggest that precise placement of the cotton swab at the urethrovesical junction (UVJ) is the most critical factor.[25] Bladder volume, presence of detrusor overactivity and presence of a cystocele do not affect the measured straining angle. Replacement of the cotton swab with a straight urethral catheter yields reduces angles of excursion, and thus, these techniques are not interchangeable.[26]

Despite significant efforts to standardize this simple test, adherence to these endorsed standards is inconsistent.[27-29] In addition, the specific method of measuring the angle has not been standardized (straining angle vs. straining minus resting angle) and various methods are utilized in the published literature.

2.2 Effect of urethral hypermobility on urinary incontinence

Urethral hypermobility was implicated in the pathophysiology of stress urinary incontinence long before the development of the MUS procedure. The efficacy of the retropubic suspension procedures provided some evidence that relocation of the urethra in an abdominal and retropubic position was the key to continence.[2-5] However, the traditional pubovaginal sling incorporated tensioned suburethral support, thus providing sufficient coaptation of the urethral lumen to overcome increased intravesical pressure during straining and prevent stress incontinence.[6] The Integral Theory of incontinence supports this principle, suggesting that kinking of the urethra is the most effective means of achieving continence.[30]

2.3 Effect of urethral hypermobility on surgical outcomes

Urethral hypermobility may simultaneously contribute to the development of SUI and play a key role in achieving post-operative continence.[18, 29, 31-34] Yet, the categorical declaration of urethral mobility, as hypermobile or normal, remains a topic of interest. A recent prospective study of 134 women undergoing TO MUS

demonstrated that subjects with a Q-tip angle less than 45˚ had significantly greater postoperative incontinence.[34] A longitudinal cohort of 306 women followed over 20 years after pubovaginal sling found that incontinence cure rates were 96% for those with preoperative UHM, compared to 74% for those without UHM.[35] This evidence suggests that while a greater urethral straining angle may contribute to SUI, it is difficult to ascertain how the extent of that mobility affects post-operative continence.

CHAPTER III

3 Details of research

Using a cross-sectional survey design, an eligible cohort was identified and a retrospective chart review performed.

3.1 Subject selection

The UMass Memorial Medical Center hospital surgical log was used to identify women who underwent an MUS procedure for SUI between May, 2006 and December, 2008 by four fellowship-trained surgeons. The start date corresponded with the implementation of standardized preoperative UDI-6 and UIQ-7 questionnaires in this full-time academic urogynecology practice setting. Retropubic MUS procedures (RP) were all performed using the “bottom-up” approach (Tension-free Vaginal Tape, Gynecare, Ethicon Inc, Somerville, NJ or AdvantageFit, Boson Scientific, Natick, MA). The transobturator procedures (TO) included the “outside-in” approach (Monarc, American Medical System, Minnetonka MN or Obtryx, Boson Scientific, Natick, MA), following the manufacturer’s instructions.

In July, 2009, with Institutional Review Board approval, all potentially eligible women were mailed a survey packet which included the PFDI-20, the PFIQ-7, and a return-addressed stamped envelope.[19] (Data from the non-urologic survey subscales were used for a different study.) Once the surveys were returned, the

charts of study participants were reviewed using a standardized case report form. At the time of the chart review, subjects were selected for inclusion if they were English-speaking, had an operative note confirming that a MUS was performed, were diagnosed as having Stages I-III prolapse and completed the QOL surveys pre-operatively. Stage IV prolapse patients were excluded due to difficulty measuring UHM, greater likelihood of urinary retention, and occult SUI. Patients who underwent a concomitant vaginal obliterative procedure were also excluded, as most were undergoing MUS for occult SUI, and thus were asymptomatic preoperatively. Patients who underwent an additional anti-incontinence procedure following the index MUS were also excluded, since their current survey results would not reflect their post-MUS symptoms. A HIPAA waiver (Appendix C) granted by the UMass IRB allowed for a chart review of a random sample of non-responders.

3.2 Objective data collection

For purposes of assessing the representativeness of our responding patient sample, data collected from medical records included patient demographics, past medical and surgical history (at the time of the surgical consult) including prior SUI and prolapse repairs and preoperative urodynamic test results. Patients were categorized as having diabetes (receiving hypoglycemic medication), neurologic disease (multiple sclerosis, spinal stenosis, stroke with deficit), or pulmonary disease (asthma, chronic cough, COPD), based on the review of

information contained in hospital charts. Medications listed were reviewed and recorded if they included adrenergic (α or β receptor activity), anticholinergic (receptor) or diuretic pharmacologic activity, as these can impact urine production and/or bladder function. Urodynamic data included cough stress test results (CST), evidence of detrusor overactivity (DO), post-void residual (PVR), MUCP and LPP. Subjects without objective incontinence during the LPP test were not included in the ISD analysis. Urinary retention was defined as PVR > 100cc. ISD was defined and evaluated separately as MUCP ≤ 20cmH20 or LLP ≤ 60cmH20.[13] Prolapse severity was documented by either the Baden/Walker system or the pelvic organ prolapse quantification system (POP-Q), as noted in the chart.[36, 37] The decision to perform a RP MUS or TO MUS was based on attending physician preference. Concomitant surgeries listed in the operative report were also recorded.

Urethral angle measurements were performed with the standard Q-tip test, in which the cotton tip is placed at the urethrovesical angle (by retracting the Q-tip until resistance was encountered) in an empty bladder while the patient is resting in the dorsal lithotomy position.[25] The angle of the Q-tip with respect to the horizontal was measured at rest and during maximal Valsalva effort without reduction of prolapse. The straining and the resting angles were reported, and the straining minus resting (S-R) angle was calculated as a continuous variable.

Due to inconsistencies in the published literature, urethral hypermobility (UHM) was defined in two ways, as either straining angle ≥ 30˚ or S-R angle ≥ 30˚.

3.3 Subjective symptom measurement

Patient-reported subjective outcomes were assessed using published guidelines for calculating the UDI-6 and UIQ-7 scores (0-100, where 0 is asymptomatic and 100 is maximally symptomatic).[19] The UDI-6 can be divided into three subscales: Irritative Symptoms, Obstructive/Discomfort, and Stress Symptoms. We performed an additional analysis of the UDI-6 stress subscale (Questions 3 and 4) as well as Question 3 alone, to assess the independent contribution of these questions to symptom assessment. All outcomes used the same scale, range 0-100. Question 3 reads, “Do you experience urine leakage related to physical activity, coughing, or sneezing?” Question 4 reads, “Do you usually experience small amounts of urine leakage (that is, drops)?” The difference between the post-op scores and the pre-op scores on both of these instrument subscales were calculated and was represented by “ΔUDI-6”, “ΔUIQ-7”, “ΔUDI-6 stress subscale” and “ΔQ3”. Thus, a very negative “Δ” score indicates significant improvement in patient’s symptoms.

3.4 Statistical analysis

Descriptive statistics compared potential differences between survey responders and non-responders in several demographic and preoperative clinical

characteristics. Table 4.1 lists all the variables investigated as potential predictors of the four outcome variables. A total of thirty-six were considered. Continuous variables were compared with Student's t-tests and categorical variables were compared using Pearson's X^2 test. To analyze the crude association of each of the preoperative predictors with the four primary study outcomes ΔUDI-6, ΔUIQ-7, ΔUDI-6 stress subscale and ΔQ3, univariate linear regression was used. Pairwise correlations were estimated for the four outcomes, as well as for the significant predictors identified by the univariate analysis. For those variables that showed significant correlation, interaction variables were used to determine the relative association of individual potential predictors on each of the outcomes. Multivariable normal theory regression modeling was developed to explore the associations with pre and post-operative changes in self-reported symptoms. Variables identified during univariate analysis having $P \leq 0.10$ were included in the regression models. Several variables (PVR, MUCP, LPP, and UHM) were evaluated as both continuous and dichotomous variables, as described previously. Statistical analysis was performed using Stata 10.0 statistical software (StataCorp, College Station, TX).

CHAPTER IV

4 Results

4.1 Study sample

A total of five hundred and fifty-one patients were identified by surgical codes as having undergone a MUS procedure during the study period and were sent the survey packet in July, 2009. Of the 225 responses (40% response rate), 37 were excluded (14 for vaginal obliteration, 8 for inappropriate identification as having an MUS, 7 for repeat anti-incontinence procedure since the index MUS, 4 for procidentia [Stage 4 prolapse], and 4 for lack of pre-op survey), leaving 188 charts available for analysis (Figure 4.1). A random sample of non-responders (n=38) was selected and their charts reviewed for comparison. The non-responders were more likely to have diabetes and prior urethral bulking whereas more responders underwent concomitant vaginal suspension (Table 4.1).

The surveys were returned an average of 26 (range 4-84) months following initial urodynamic evaluation at consultation and 21 months (range 7-39) following the MUS procedure. The subjects in the study sample were, on average, 56 years old, with a BMI of 28 and parity of 2.5. Nearly two-thirds of the women were menopausal and almost half underwent an anterior repair or vaginal suspension at the time of the MUS. There was no difference in any concomitant urogynecologic surgery between subjects who had a RP MUS versus a TO MUS

(data not shown). Preoperative average UDI-6, UIQ-7, UDI-6 stress subscale and Q3 scores were not different between those who underwent RP MUS vs. TO MUS. The average scores of the respondents are shown in Figure 4.2 and Table 4.2. The length of office-visit follow-up also did not differ between the responders and non-responders (average 6 months).

4.2 Univariate analysis

4.2a UDI-6 and UIQ-7 scores

The average post-operative survey scores yielded an average improvement of 22 points on the UDI-6 and UIQ-7, 40 points on the UDI-6 stress subscale, and 45 points on Q3. The results of the univariate analyses for each outcome are shown in Tables 4.3 – 4.4. None of the selected pre-operative subject characteristics were crudely associated with a significant difference in UDI-6 scores. Subjects with lower MUCP (and with objective ISD) demonstrated more improvement on the UIQ-7, scoring, on average, 20 points lower than those without ISD.

4.2b UDI-6 stress subscale scores

The distribution of ΔUDI-6 stress subscale scores included more episodes of symptom improvement than either the ΔUDI-6 or ΔUIQ-7, as post-operative scores were almost 20 points lower on this scale. Older, menopausal subjects with urethral hypermobility (as measured by S-R) and concomitant vaginal

suspension showed less improvement on the ΔUDI-6 stress subscale than subjects without these characteristics. Age and menopausal status were highly correlated (0.71); hence, a single variable was defined using four levels: 1 (referent) = age < 55 and premenopausal (n=65), 2 = age < 55 and menopausal (n=23), 3 = age 55-64 (n=52), 4 = age ≥ 65 (n=46). Only three subjects in the third age group were reported as menopausal. As a result, Group 3 was comprised of all women within that age range, regardless of menopausal status. All women 65 years and older were considered to be menopausal. This summary variable was evaluated for its association with ΔUDI-6 stress subscale, showing no difference between Group 2 and the referent group, inasmuch, menopausal status was not included in the regression model. Comparison of Groups 3 and 4 to the referent group confirmed that older age was significantly associated with persistent symptoms.

Table 4.5 shows that concomitant vaginal suspension conferred a statistically significant risk of persistent symptoms on ΔUDI-6 stress subscale (+20 point difference). Greater urethral angle measurement on the Q-tip test (S-R) was significantly associated with greater subjective improvement. Similarly, the diagnosis of UHM by S-R ≥ 30˚ predicted a 20 point improvement in the UDI-6 stress subscale score. There was a negative correlation between age and UHM. Ninety-two percent of women aged < 55 years had UHM, whereas only 60% of women in the two older age categories had UHM. Therefore, these three groups

(< 55 yrs with UHM [n=7]), ≥ 55 yrs with UHM [n=27], ≥ 55 yrs without UHM [n=27]) were compared to measure the relative impact of age and UHM on the ΔUDI-6 stress subscale. Older subjects reported more symptoms (+22 points, 95%CI [5, 38] and P=0.01) than their younger counterparts, whereas similarly aged subjects who differed on UHM reported similar scores on the UDI-6 stress subscale (P=0.9).

4.2c UDI-6 Question 3 scores

Each of the factors older age, menopausal status, absence of UHM and concomitant vaginal suspension were statistically significantly associated with less subjective improvement on Q3 alone (Table 4.6). In addition, subjects with elevated PVR reported less improvement on Q3, but not when PVR was coded as the dichotomous variable “retention” (PVR > 100cc). For all outcomes, the effects of menopausal status and preoperative UHM on subjective improvement were modest compared to that of advancing age.

4.3 Consideration for duration of follow-up

The post-operative surveys were distributed at a single point in time, yielding a large range of duration of follow-up (average 21 months, range 7-39 months). Due to this significant variation, additional analyses were performed to determine if there was an association between symptom score and follow-up interval (Tables 4.7-4.9). All correlation coefficients between months of subjective follow-

up and the four outcome measures were less than 0.25. Tertiles were formed dividing the duration of follow-up into three clinically relevant groups: short term ≤ 12 months (referent group, n=35), medium term = 13-24 months (n=85) and long term ≥ 25 months (n=68). Completion of the survey greater than 24 months from the index MUS was associated with less improvement on the UDI-6, UDI-6 stress subscale and UDI-6 Question 3. Medium term (12-24 months) follow-up was also associated with persistent symptoms on the UDI-6 stress subscale. There was no association between follow-up interval and symptom score, as measured by ΔUIQ-7.

4.4 Multivariable analysis

Variables considered in multiple prediction models included those variables found to be significant on univariate analysis with a P value < 0.10 with regard to a score difference on each of the four outcomes. Three different models were created; one for ΔUIQ-7, ΔUDI-6 stress subscale and ΔQ3. Preoperative ISD (determined by MUCP < 20cmH_20) remained significantly associated with symptom improvement, as measured by the UIQ-7 (Table 4.7). Pulmonary disease retained its significant association with persistent symptoms on the UIQ-7. After controlling for menopause, PVR, and UHM, advanced age and concomitant vaginal suspension were associated with persistent symptoms on the UDI-6 Question 3. However, after controlling for these same factors for the UDI-6 stress subscale, only advanced age remained significant (Tables 4.8 and

4.9). Multivariable analysis for all UDI-6 subsets (ΔUDI-6, ΔUDI-6 stress subscale and ΔUDI-6 Question 3) showed that a longer interval between the MUS procedure (>24 months) and completion of the QOL instrument was associated with less symptom improvement.

CHAPTER V

5 Discussion

5.1 Summary of findings

In this cohort of women undergoing MUS, advanced age and concomitant vaginal suspension were statistically significant risk factors for persistent patient-reported symptoms of SUI following MUS. As the interval increased between the MUS procedure and completion of the survey, scores on the UDI-6 demonstrated significantly greater SUI symptoms. A greater urethral angle during straining and UHM (angle ≥ 30˚) were associated with statistically significantly greater symptom improvement on univariate analysis, but these variables no longer retained their significance after controlling for age.

5.2 Comparison to published data

There is a growing body of literature investigating factors associated with treatment success following MUS procedures.[10, 27, 38-41] Early studies lacked sufficient sample size to provide definitive findings about the role of demographic factors and urodynamic parameters. More recent studies have been larger, but there remains a large variety of outcome measures examined in these investigations and inconsistencies in defining surgical cure or failure.[12, 15, 34, 42] A discussion of the current literature accompanies each topic below.

5.3 Selection of appropriate subjective outcome measures

Implementation of dichotomous outcomes (“success” or “failure”) does not capture the important finding of subjective improvement since it is confined to a strict definition of cure. The UDI-6 is a well-recognized and frequently utilized instrument, which assesses urinary incontinence symptom distress. The UIQ-7 evaluates the life impact of these symptoms on women. Both instruments address a unique perspective of female urinary incontinence, and thus are not interchangeable. Score improvement on the UDI-6 and UIQ-7 showed moderate correlation; indicating that, in this cohort, symptom bother and life impact were essentially the same.

There is growing support for the use of the UDI-6 stress subscale and Q3 alone for purposes of assessing symptom change, due to their high sensitivity for SUI symptoms.[15, 17] Many patients experience temporary urinary urgency and urge-associated incontinence following the MUS procedure, and both are captured by the UDI-6. Our data suggest that administration of the UDI-6 stress subscale may facilitate a more accurate interpretation of post-operative SUI symptom improvement since this instrument specifically address SUI symptoms. Stav et al incorporated elements of several validated QOL instruments into a shorter questionnaire designed to address several outcomes of interest, effectively reducing patient survey burden.[15] While this shorter hybrid questionnaire did use Question 3 from the UDI-6, it was not independently validated. Administration of

the complete UDI-6 facilitates a more thorough subjective evaluation of patients' urinary symptoms, but research efforts may benefit from a more focused analysis on the relevant symptom subscales.

5.4 Advancing age

Women undergoing surgical treatment for SUI span a wide age-range.[9] There have been varying reports in the literature regarding the adequacy of treatment in elderly women. In an ancillary analysis of data obtained from a randomized controlled trial comparing RP and TO MUS, advancing age was found to be an independent predictor of SUI treatment failure at one year.[17] While some studies have found equal treatment effect in the elderly, those studies that include a broad range of ages more consistently show decreased efficacy with advancing age.[40, 43-46] There are several possible physiologic factors explaining these findings. Estrogen receptors in the vaginal wall and bladder base allow circulating estrogen to increase blood supply and increase thickness of surrounding connective tissue.[47] This may provide some stability to the UVJ and the continence mechanism. Additionally, age-related decline in striated muscle and connective tissue can contribute to the development of incontinence.[11, 48]

5.5 Concomitant prolapse procedures

Similar to a 2008 study evaluating the association between MUS and post-operative QOL and sexual function, we attempted to enhance the interpretability

of treatment outcome by using a QOL score improvement measure.[49] However, we elected to include all MUS procedures at our institution, regardless of concomitant prolapse surgery. This design provided insight into the impact of prolapse surgery on MUS outcomes, since these procedures are commonly performed together.

In contrast to some reports, our data suggests that concomitant vaginal suspension is a risk factor for reduced efficacy of MUS procedures.[15, 50] All of the vaginal suspension procedures in our patient population underwent the high uterosacral suspension.[51] While others have hypothesized that prolapse repairs may restore the continence mechanism, our findings suggest that manipulation of the urethrovesical angle, with suspension of the vaginal apex, may actually over-correct urethral hypermobility.

5.6 Urethral hypermobility

Subjects with elevated Q-tip angles and with de-facto UHM reported significantly better improvement following their MUS procedure than those with a more stable urethra. Among subjects who underwent a vaginal suspension, preoperative UHM was associated with a greater (21 point) score improvement. In contrast, among subjects with UHM, there was no difference in symptom improvement following MUS without suspension. This finding is consistent with the published data reporting a greater incontinence cure rate following pubovaginal sling

among subjects with UHM and complicated SUI.[35] As evidenced by these data, urethral hypermobility continues to have a place in clinical evaluation and the surgical consent process.

5.7 Body mass index

While some studies have shown that BMI is a significant risk factor for sling failure, especially for the very obese (BMI >35), our results do not support these findings. Additional analysis with standard BMI categories (normal weight 18.5-24.9, overweight 25-29.9, obese 30-34.9, morbidly obese > 35) still did not identify this as an independent risk factor for subjective failure on any of the outcome measures. While this study was not powered specifically to show a difference in BMI, other larger studies share our findings.[15, 52]

5.8 Intrinsic sphincter deficiency

We did not find any association between symptom improvement and type of MUS performed or prior urogynecologic surgery. There was an association of urethral sphincter function to the ΔUIQ-7, as measured by MUCP, expressed as both a continuous or dichotomized variable, and this relationship retained its magnitude and significance in multivariable analysis. In our practice, MUCP is more commonly used to assess urethral function and differed significantly for subjects who had a RP MUS versus a TO MUS. Interestingly, ISD in this cohort

was associated with improved UIQ-7 scores; this is in contrast to previously published literature.[53] Direct comparisons of preoperative UIQ-7 and ΔUIQ-7 scores were not different between RP MUS and TO MUS subjects, leaving uncertainty about the explanation of improved scores in subjects with ISD.

5.9 Midurethral sling durability

The durability of surgical treatment for SUI has been widely studied.[10, 53-55] A randomized controlled trial of RP MUS versus TO MUS showed that the average time to develop recurrent symptoms was approximately 19 months for both procedures.[54] We found that our RP MUS group had increasing UDI-6 stress subscales scores over time, as compared to the TO MUS group. This was not due to measurably worse disease, as these two groups did not differ on pre-op UDI-6 scores.

Across the entire cohort, the UDI-6 survey scores reflected significantly greater symptoms as the post-operative interval increased. Without surveys at several post-operative intervals, it is difficult to determine if these higher scores reflected persistent or recurrent symptoms. Interestingly, the UIQ-7 scores did not follow this same trend. In fact, as the post-operative duration increased, subjects reported less interference of their bladder symptoms on their quality of life. The UDI-6 scores increased by greater than 1 point per month, resulting in a 31 point increase in symptom severity after 2 years. Based on the 25 point score

difference between bother categories on the UDI-6 stress subscale, a 31 point score increase translates to a significant change in patient's bother category. These findings suggest that patients should be counseled about recurrence of symptoms following MUS.

5.10 Study strengths and limitations

This study has several important strengths, including the use and comparison of validated QOL outcome measures. Since SUI is largely a QOL concern, subjective measures of how much patients are bothered by their symptoms and impact on life's activities are perhaps the most appropriate. Because our study population included several different MUS types, performed in a typical academic urogynecologic practice with limited exclusion criteria, our results are likely to be generalizable to similar practices. The primary limitations of the present study are the low response rate, differences between survey responders and a random sample of non-responders, and the retrospective nature of data collection. In addition, cross-sectional administration at various post-operative intervals introduced a strong confounder. As clinician-researchers struggle to compare the effects of different treatment strategies, there has been increased attention given to the relationships between subjective and objective outcome measures. Standardized subjective assessment at regular postoperative intervals would provide more information about treatment durability.

5.11 Study conclusions and future research directions

In conclusion, concurrent vaginal suspension and advancing age were risk factors for persistent symptoms following MUS procedures in patients with SUI. Intrinsic sphincter deficiency predicted greater symptom improvement on one subjective instrument. Urethral hypermobility was also an important prognostic factor, especially in patients undergoing vaginal suspension and midurethral sling simultaneously. Following a MUS procedure, SUI symptoms may recur within two years of the surgery. Although MUS procedures are typically safe and effective, clinicians are encouraged to provide additional preoperative counseling to those women who are at greatest risk for persistent or recurrent symptoms.

Future research efforts to further elucidate the normal continence mechanism and the pathophysiology of stress urinary incontinence are needed. Population-based longitudinal observational studies would provide additional information about the natural history of SUI symptomatology. Although there is some data to suggest that symptom recurrence occurs within two years of an MUS procedure, longer follow-up with multiple measures is needed to determine if this represents a post-operative plateau, or a sustained decline in treatment effect.

The UDI-6 has proven to be an accurate instrument to measure subjective outcomes and has been widely adopted among clinician-researchers.[19, 49, 56] However, it is important to recognize that the 3 symptom domains (irritative,

obstructive and stress) all contribute equally to the UDI-6 score. Studies whose primary aim is to determine SUI symptom improvement would be well-served to perform independent analyses using the UDI-6 stress subscale. The administration of the entire UDI-6 is also important, though, as the incidence of *de novo* urgency following MUS is still in question and use of the irritative voiding subscale may provide new insight into this phenomenon. Future studies should incorporate standardized clinical and outcome measures to further enhance the surgeon's ability to provide appropriate therapeutic estimates for their patients undergoing midurethral sling procedures.

Tables & Figures

Figure 4.1 Flowchart of study subjects

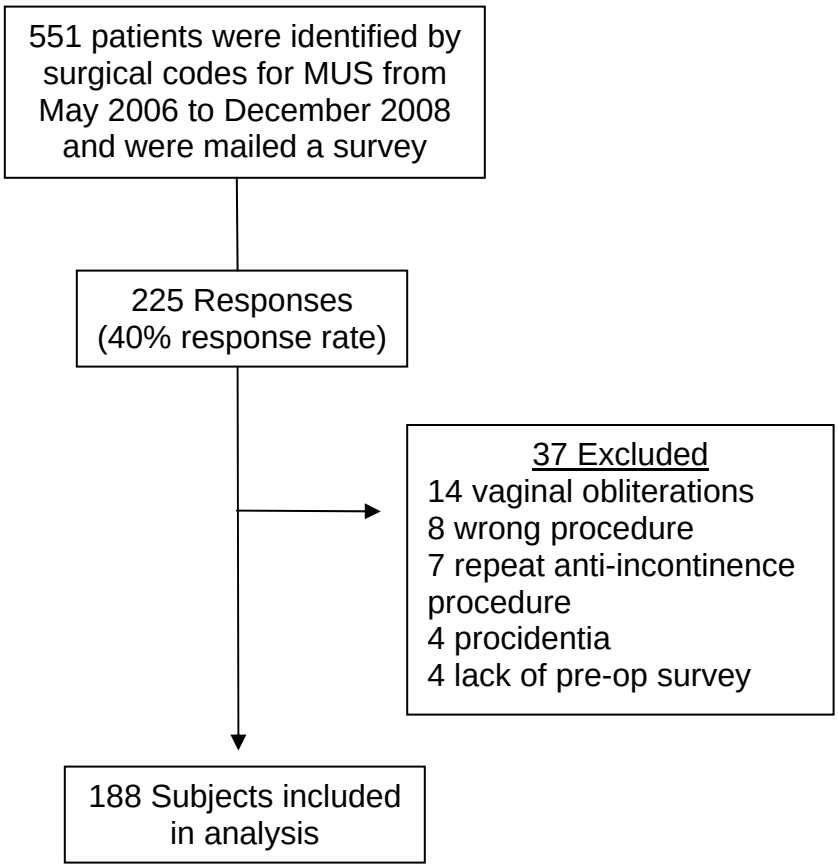

Table 4.1 Comparison of postoperative survey responders and non-responders

Table 4.1a Demographic and past medical characteristics

	Non-responders N=38	Responders N=188			
	mean / percent	mean / percent	SD	Range	P value
RP MUS	42%	48%			0.4
TO MUS	58%	51%			0.4
Characteristic					
Age, years	56	56.6	11.9	35-91	0.8
BMI, kg/m^2	28.1	28.2	5.8	18-59	0.9
parity	2.1	2.5	1.3	0-8	0.07
menopausal	64%	63%			0.9
diabetes	17%	6%			**0.03**
neurologic disease	8%	4%			0.1
pulmonary disease	8%	16%			0.2
anticholinergic medication	11%	5%			0.2
adrenergic medication	18%	12%			0.3
diuretic medication	21%	11%			0.08
smoking (within 1 year)	14%	9%			0.4

Table 4.1b Prior surgical procedures

	Non-responders N=38	Responders N=188	P value
Prior surgical procedures			
RP MUS	0%	0%	1.0
TO MUS	0%	0%	1.0
pubovaginal sling	3%	1%	0.4
Burch	3%	3%	1.0
urethral bulking	3%	0%	**0.03**
anterior repair	0%	5%	0.2
suspension	0%	1%	0.5
hysterectomy	27%	23%	0.6

Table 4.1c Pre-operative urodynamic parameters

	Non-responders N=38	Responders N=188			
	mean / percent	mean / percent	SD	Range	P value
Urodynamic data					
Q-tip resting angle	-0.3	0.9	16.9	-40 to 60	0.7
straining angle	37.9	39.5	21.5	-25 to 85	0.7
straining-resting angle	38.2	38.6	15.7	-6 to 80	0.9
UHM (straining angle)	74%	75%			0.8
UHM (S-R)	79%	77%			0.7
MUCP	42.2	43.5	23.0	4-165	0.8
ISD (MUCP≤20cmH20)	10%	13%			0.6
LPP	43.9	87.8	28.0	27-187	0.8
ISD (LPP≤60cmH20)	16%	11%			0.4
PVR	18.8	30.7	39.2	0-225	0.07
retention (PVR>100cc)	0%	7%			0.1
urethral length	2.9	2.6	0.7	1-4.8	0.9
Positive CST	100%	95%			0.2
Destrusor Instability	9%	9%			0.9

Table 4.1d Concomitant surgical procedures (anterior and apical)

	Non-responders N=38	Responders N=188	P value
Concomitant procedures			
anterior repair	32%	47%	0.07
hysterectomy	24%	29%	0.5
vaginal suspension (USLS)	8%	41%	**0.04**

Figure 4.2 Pre and post-operative QOL scores

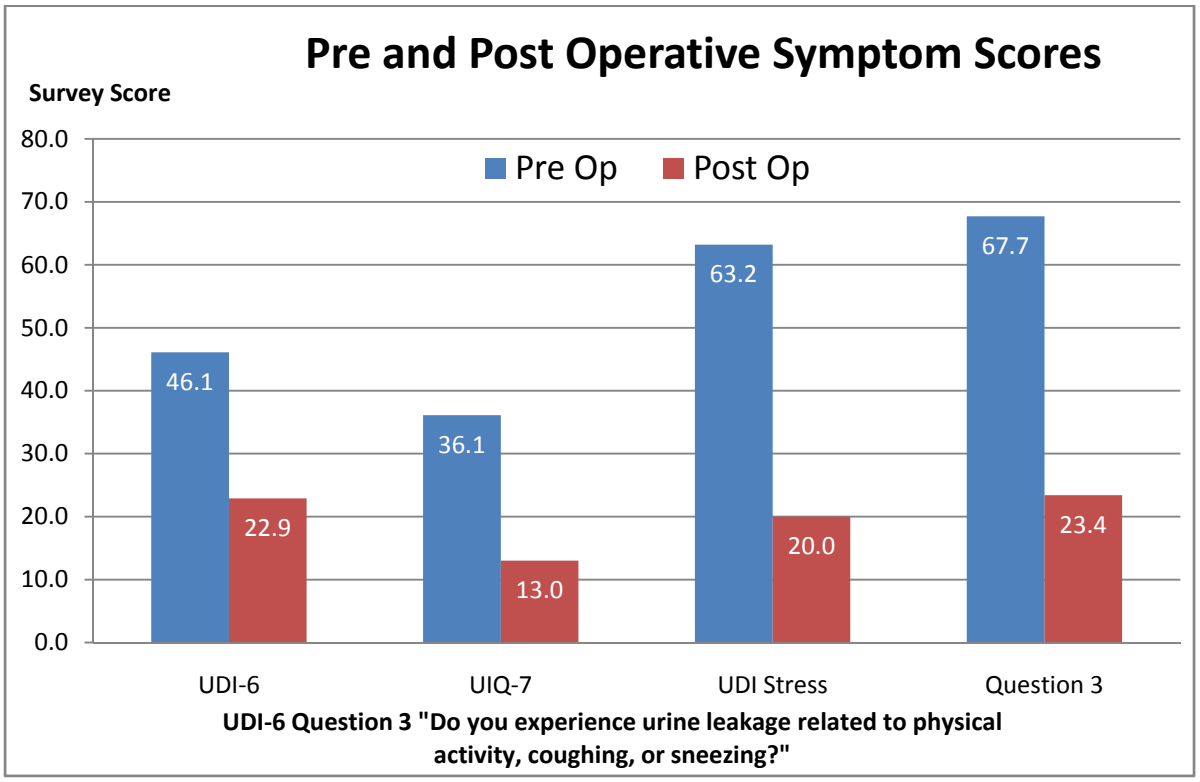

Table 4.2 Pre and post-operative QOL scores

	Pre-Op	**Post-Op**	**Delta**		
	mean	mean	mean	SD	range
UDI-6	46.1	22.9	-22.7	28	-100 to 50
UIQ-7	36.1	13.0	-22.9	30	-100 to 67
UDI-6 stress subscale	63.2	20.0	-40.0	41	-100 to 75
UDI-6 Question 3	67.7	23.4	-45.8	46	-100 to 100

Table 4.3 Factors associated with persistent or improved symptoms following MUS, as measured by the change in UDI-6 score (univariate)

	Δ UDI-6 (univariate)			
Factor	**mean**	**Beta**	**95% CI**	**P value**
follow-up ≤ 12 months	referent			
follow-up 13-24 months		6.8	(-4.3, 17.8)	0.3
follow-up ≥ 25 months		16.8	(5.3, 28.4)	0.005

Table 4.4 Factors associated with persistent or improved symptoms following MUS, as measured by the change in UIQ-7 score (univariate)

	ΔUIQ - 7 (univariate)			
Factor	**mean**	**Beta**	**95% CI**	**P value**
BMI		0.7	(-.05, 1.5)	0.07
pulmonary disease		10.6	(-1.3, 22.5)	0.08
present	-14			
absent	-24			
ISD (MUCP≤20cmH20)		-19.0	(-33.4, -4.6)	0.01
present	-37			
absent	-18			
follow-up ≤ 12 months	referent			
follow-up 13-24 months		-9.3	(-21, 2.7)	0.13
follow-up ≥ 25 months		-10.8	(-23.4, 1.7)	0.09

Table 4.5 Factors associated with persistent or improved symptoms following MUS, as measured by the change in UDI-6 stress subscale score (univariate)

	ΔUDI - 6 stress subscale (univariate)			
Factor	**mean**	**Beta**	**95% CI**	**P value**
age < 55		referent		
age 55-64		21.1	(7.0, 35.2)	0.004
age ≥ 65		19.3	(4.4, 34.3)	0.01
menopause*		17.9	(5.5, 30.3)	0.005
present	-33			
absent	-51			
neurologic disease		26.8	(-4.3, 57.8)	0.09
present	-14			
absent	-41			
straining angle*		-0.3	(-0.6, 0.01)	0.06
S-R*		-0.6	(-1.0, -0.2)	0.007
UHM (S-R)*		-16.0	(-31.6, -0.4)	0.04
present	-44			
absent	-28			
PVR		0.13	(-0.2, 0.3)	0.10
hysterectomy		12.3	(-0.9, 25.5)	0.07
present	-31			
absent	-43			
suspension		19.5	(7.5, 31.6)	0.002
present	-29			
absent	-49			
follow-up ≤ 12 months		referent		
follow-up 13-24 months		17.1	(1.0, 33.3)	0.04
follow-up ≥ 25 months		29.3	(12.5, 46.1)	0.001

Table 4.6 Factors associated with persistent or improved symptoms following MUS, as measured by the change in UDI-6 Question 3 score (univariate)

	ΔUDI-6 Question 3 (univariate)			
Factor	**mean**	**Beta**	**95% CI**	**P value**
age < 55		referent		
age 55-64		26.4	(10.7, 42.1)	0.001
age ≥ 65		29.5	(12.9, 46.1)	0.001
menopause*		24.4	(10.6, 38.3)	0.001
present	-37			
absent	-61			
straining angle*		-0.4	(-0.7, -0.04)	0.03
S-R*		-0.8	(-1.2, -0.3)	0.00
UHM (S-R)*		-20.2	(-37.9, -2.5)	0.03
present	-50			
absent	-30			
PVR		0.2	(0.003, 0.4)	0.05
hysterectomy		13.4	(-1.4, 28.2)	0.08
present	-36			
absent	-50			
suspension		23.4	(9.9, 37.0)	<0.001
present	-33			
absent	-56			
follow-up ≤ 12 months		referent		
follow-up 13-24 months		14.2	(-4.1, 32.5)	0.10
follow-up ≥ 25 months		30.7	(11.7, 49.7)	0.002

Table 4.7 Factors associated with persistent or improved symptoms following MUS, as measured by the change in UIQ-7 score (multivariable)

	ΔUIQ - 7 (multivariable)		
Factor	**Beta**	**95% CI**	**P value**
BMI	0.6	(-0.3, 1.4)	0.20
pulmonary disease	13.0	(0.3, 25.7)	**0.05**
ISD (MUCP≤20cmH20)	-16.3	(-30.7, -2.0)	**0.03**
follow-up ≤ 12 months	referent		
follow-up 13-24 months	-9.8	(-22.7, 3.2)	0.14
follow-up ≥ 25 months	-12.9	(-25.9, 0.2)	**0.05**

Table 4.8 Factors associated with persistent or improved symptoms following MUS, as measured by the change in UDI-6 stress subscale score (multivariable)

	ΔUDI - 6 stress subscale (multivariable)		
Factor	**Beta**	**95% CI**	**P value**
age < 55	referent		
age 55-64	15.3	(0.8, 29.8)	**0.04**
age ≥ 65	18.6	(3.1, 34.2)	**0.02**
neurologic disease	22.1	(-7.7, 51.9)	0.15
PVR	0.09	(-0.06, 0.2)	0.2
hysterectomy	-2.2	(-21.4, 16.9)	0.8
suspension	16.6	(-1.7, 34.9)	0.08
follow-up ≤ 12 months	referent		
follow-up 13-24 months	8.3	(-8.6, 25.2)	0.3
follow-up ≥ 25 months	22.7	(5.1, 40.3)	**0.01**

Table 4.9 Factors associated with persistent or improved symptoms following MUS, as measured by the change in UDI-6 Question 3 score (multivariable)

	ΔUDI-6 Question 3 (multivariable)		
Factor	**Beta**	**95% CI**	**P value**
age < 55	referent		
age 55-64	21.0	(5.0, 37.1)	**0.01**
age ≥ 65	26.0	(8.9, 43.1)	**0.003**
PVR	0.1	(-0.03, .3)	0.1
hysterectomy	-5.3	(-26.1, 15.6)	0.6
suspension	22.7	(2.5, 42.8)	**0.03**
follow-up ≤ 12 months	referent		
follow-up 13-24 months	4.1	(-14.5, 22.8)	0.6
follow-up ≥ 25 months	23.8	(4.5, 43.1)	**0.02**

APPENDIX A

Pelvic Floor Distress Inventory – Short Form 20

Instructions:
Please answer these questions by putting a **X** in the appropriate box. If you are unsure about how to answer a question, give the best answer you can. While answering these questions, please consider your symptoms over the **last 3 months.** Thank you for your help.

Name:_____Date: _____/_____/

1. Do you usually experience *pressure* in the lower abdomen? ☐ No; ☐ Yes
0

   If yes, how much does this bother you?
   ☐ **1** ☐ **2** ☐ **3** ☐ **4**
   Not at All - Somewhat - Moderately - Quite a bit

2. Do you usually experience *heaviness or dullness* in the pelvic area? ☐ No; ☐ Yes
0

   If yes, how much does this bother you?
   ☐ **1** ☐ **2** ☐ **3** ☐ **4**
   Not at All - Somewhat - Moderately - Quite a bit

3. Do you usually have a bulge or something falling out that you can see or feel in the vaginal area? ☐ No; ☐ Yes
0

   If yes, how much does this bother you?
   ☐ **1** ☐ **2** ☐ **3** ☐ **4**
   Not at All - Somewhat - Moderately - Quite a bit

4. Do you usually have to push on the vagina or around the rectum to have or complete a bowel movement? ☐ No; ☐ Yes
0

   If yes, how much does this bother you?
   ☐ **1** ☐ **2** ☐ **3** ☐ **4**
   Not at All - Somewhat - Moderately - Quite a bit

5. Do you usually experience a feeling of incomplete bladder emptying? ☐ No; ☐ Yes
0

   If yes, how much does this bother you?
   ☐ **1** ☐ **2** ☐ **3** ☐ **4**
   Not at All - Somewhat - Moderately - Quite a bit

6. Do you ever have to push up on a bulge in the vaginal area with your fingers to start or complete urination? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**

Not at All - Somewhat - Moderately - Quite a bit

7. Do you feel you need to strain too hard to have a bowel movement? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**

Not at All - Somewhat - Moderately - Quite a bit

8. Do you feel you have not completely emptied your bowels at the end of a bowel movement?

☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**

Not at All - Somewhat - Moderately - Quite a bit

9. Do you usually lose stool beyond your control if your stool is well formed? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**

Not at All - Somewhat - Moderately - Quite a bit

10. Do you usually lose stool beyond your control if your stool is loose or liquid? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**

Not at All - Somewhat - Moderately - Quite a bit

11. Do you usually lose gas from the rectum beyond your control? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**

Not at All - Somewhat - Moderately - Quite a bit

12. Do you usually have pain when you pass your stool? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**

Not at All - Somewhat - Moderately - Quite a bit

13. Do you experience a strong sense of urgency and have to rush to the bathroom to have a bowel movement? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**
Not at All - Somewhat - Moderately - Quite a bit

14. Does a part of your bowel ever pass through the rectum and bulge outside during or after a bowel movement? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**
Not at All - Somewhat - Moderately - Quite a bit

15. Do you usually experience frequent urination? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**
Not at All - Somewhat - Moderately - Quite a bit

16. Do you usually experience urine leakage associated with a feeling of urgency, that is a strong sensation of needing to go to the bathroom? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**
Not at All - Somewhat - Moderately - Quite a bit

17. Do you usually experience urine leakage related to coughing, sneezing, or laughing? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**
Not at All - Somewhat - Moderately - Quite a bit

18. Do you usually experience small amounts of urine leakage (that is, drops)? ☐ No; ☐ Yes **0**
If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**
Not at All - Somewhat - Moderately - Quite a bit

19. Do you usually experience difficulty emptying your bladder? ☐ No; ☐ Yes **0**

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**
Not at All - Somewhat - Moderately - Quite a bit

20. Do you usually experience *pain* or *discomfort* in the lower abdomen or genital region? ☐ No; ☐ Yes
0

If yes, how much does this bother you?

☐ **1** ☐ **2** ☐ **3** ☐ **4**

Not at All - Somewhat - Moderately - Quite a bit

APPENDIX B

PELVIC FLOOR IMPACT QUESTIONNAIRE – SHORT FORM 7

Pelvic Floor Impact Questionnaire – short form 7

Instructions: Some women find that bladder, bowel or vaginal symptoms affect their activities, relationships, and feelings. For each question, place an X in the response that best describes how much your activities, relationships or feelings have been affected by your bladder, bowel or vaginal symptoms or conditions <u>over the last 3 months</u>. Please be sure to mark an answer in **all 3 columns** for each question. Thank you for your cooperation.

How do symptoms or conditions related to the following →→→→ usually affect your ↓	***Bladder or urine***	***Bowel or rectum***	***Vagina or Pelvis***
1. ability to do household chores (cooking, housecleaning, laundry)?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
2. ability to do physical activities such as walking, swimming, or other exercise?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
3. entertainment activities such as going to a movie or concert?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
4. ability to travel by car or bus for a distance greater than 30 minutes away from home?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
5. participating in social activities outside your home?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
6. emotional health (nervousness, depression, etc.)?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit
7. feeling frustrated?	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit	☐ Not at all ☐ Somewhat ☐ Moderately ☐ Quite a bit

Pelvic Floor Impact Questionnaire – short form 7 © Cleveland Clinic Foundation Gynecology

APPENDIX C

HEALTH INFORMATION PRIVACY & ACCOUNTABILITY ACT - FORM

University of Massachusetts Medical School
UMASS

Office of the Vice Provost for Research
Human Subjects/IRB
University of Massachusetts Medical School
55 Lake Avenue North
Worcester, MA 01655-0002 USA
508.856.4261 (office) 508.856.5004 (fax)

IRB Approval of Request for Waiver of Authorization

June 3, 2009

Emily Weber LeBrun, M.D.
Department of Obstetrics & Gynecology
Memorial Campus
Docket 13301

Title: Clinical predictors of surgical success following midurethral sling procedure for stress urinary incontinence

The University of Massachusetts Medical School Institutional Review Board (IRB) has reviewed and approved the attached Request for Partial or Full Waiver of Authorization for the study referenced above. In granting the requested waiver, the IRB has made the following determinations:

1) The disclosure of protected health information (PHI) involves no more than a minimal risk to the privacy of individuals, because

- An adequate plan exists to protect the identifiers from improper use and disclosure:
- An adequate plan exists to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law; and
- The researcher has provided adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, or for authorized oversight of the research study.

2) The research could not practicably be conducted without the waiver; and

3) The research could not practicably be conducted without access to and use of the PHI.

This waiver of authorization is contingent upon the researcher providing the covered entity with the information needed to fulfill its obligations to account for these disclosures in accordance with 45 CFR 164.528.

The attached Accounting of Disclosures form (Attachment A) that can also be found at www.umassmed.edu/Subjects/human/hipaa should be used for those projects that will review under 200 medical records. This form will be completed for each disclosure and filed in the subjects medical record. **For those projects using 200+ records, please contact Laurie Richard in the Privacy Office at 508-856-6589 for additional instruction.**

In making the determination, the Committee for the Protection of Human Subjects in Research, followed the requirements of the Common Rule and approved this waiver of authorization by Expedited review.

REFERENCES

1. Olsen ALM, Smith VJM, Bergstrom JOM, Colling JCRNP, Clark ALM. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstetrics & Gynecology. 1997;89(4):501-6.

2. Burch JC. Urethrovaginal fixation to cooper's ligament for correction of stress incontinence, cystolcele and prolapse. Am J Obstet Gynecol. 1961;81:281.

3. Marshall VD, Marchetti AA, Krantz KE. The correction of stress incontinence by simple vesicourethral suspension. Surg Gynecol Obstet. 1949;88:509.

4. Peyeyra AJ. Simplified surgical procedures for the correction of stress incontinence in women. West J Surg. 1959;67:223.

5. Stamey TA. Endoscopic suspension of the vesical neck for urinary incontinence. Surg Gynecol Obstet. 1975;136:547.

6. Aldridge AH. Transplantation of fascial relief of urinary stress incontinence. Am J Obstet Gynecol. 1942;44:398,398-411.

7. Ulmsten U, Petros P. Intravaginal slingplasty (IVS): An ambulatory surgical procedure for treatment of female urinary incontinence. Scand J Urol Nephrol. 1995 Mar;29(1):75-82.

8. Delorme E. Transobturator urethral suspension: Mini-invasive procedure in the treatment of stress urinary incontinence in women. Prog Urol. 2001 Dec;11(6):1306-13.

9. Oliphant SS, Wang L, Bunker CH, Lowder JL. Trends in stress urinary incontinence inpatient procedures in the united states, 1979-2004. Am J Obstet Gynecol. 2009 May;200(5):521.e1,521.e6.

10. Lee KS, Choo MS, Doo CK, Han DH, Lee YS, Kim JY, et al. The long term (5-years) objective TVT success rate does not depend on predictive factors at multivariate analysis: A multicentre retrospective study. Eur Urol. 2008;53(1):176-82.

11. Chen HY, Yeh LS, Chang WC, Ho M. Analysis of risk factors associated with surgical failure of inside-out transobturator vaginal tape for treating urodynamic stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2007;18(4):443-7.

12. Lukacz ES, Luber KM, Nager CW. The effects of the tension-free vaginal tape on proximal urethral position: A prospective, longitudinal evaluation. Int Urogynecol J Pelvic Floor Dysfunct. 2003;14(3):179,84; discussion 184.

13. Abrams, P. Cardoza, L. Fall,M. The standardisation of terminology of lower urinary tract function: Report from the standardisation subcommittee of the INternational COntinence soceity. Neurourol Urodyn. 2002;21:167-78.

14. FAU CC, FAU CL, WE C. Q-tip test in stress urinary incontinence. (0029-7844; 0029-7844).

15. Stav K, Dwyer PL, Rosamilia A, Schierlitz L, Lim YN, Lee J. Risk factors of treatment failure of midurethral sling procedures for women with urinary stress incontinence. Int Urogynecol J Pelvic Floor Dysfunct. 2010 Feb;21(2):149-55.

16. Houwert RM, Venema PL, Aquarius AE, Bruinse HW, Roovers JP, Vervest HA. Risk factors for failure of retropubic and transobturator midurethral slings. Am J Obstet Gynecol. 2009 Aug;201(2):202.e1,202.e8.

17. Barber MD, Kleeman S, Karram MM, Paraiso MF, Ellerkmann M, Vasavada S, et al. Risk factors associated with failure 1 year after retropubic or transobturator midurethral slings. Obstet Gynecol. 2008;199(6):666 e1-7.

18. Bakas P, Liapis A, Creatsas G. Q-tip test and tension-free vaginal tape in the management of female patients with genuine stress incontinence. Gynecol Obstet Invest. 2002;53(3):170-3.

19. Barber MDMHS, Walters MDa, Bump RCb. Short forms of two condition-specific quality-of-life questionnaires for women with pelvic floor disorders (PFDI-20 and PFIQ-7). American Journal of Obstetrics & Gynecology. 2005 July;193(1):103-13.

20. Lemack GE, Zimmern PE, Foster B. RELATIONSHIP BETWEEN UROGENITAL DISTRESS INVENTORY-6 QUESTIONNAIRE AND URODYNAMIC FINDINGS. J Urol. 1999 April;161(4S) (Supplement):77.

21. Shumaker SA, Wyman JF, Uebersax JS, McClish D, Fantl JA. Health-related quality of life measures for women with urinary incontinence: The incontinence impact questionnaire and the urogenital distress inventory. J Urol. 1998 June;159(6):2255.

22. Robertson JR. Ambulatory gynecologic urology. Clinical Obstetrics & Gynecology. 1974 September;17(3):255-76.

23. Caputo RM, Benson JT. The Q-tip test and urethrovesical junction mobility. Obstet Gynecol. 1993;82:892,892-6.

24. Nager CW, Albo M. Testing in women with lower urinary tract dysfunction. Clinical Obstetrics & Gynecology. 2004;47(1):53,53-69.

25. Karram MM, Bhatia NN. The Q-tip test: Standardization of the technique and its interpretation in women with urinary incontinence. Obstet Gynecol. 1988;71(6):807-11.

26. Weber LeBrun EE, Harmanli OH, Lidicker J, Dandolu V. Can we use a catheter to do the Q-tip test? Obstet Gynecol. 2007;110(6):1297,1297-1300.

27. Paick JS, Cho MC, Oh SJ, Kim SW, Ku JH. Is proximal urethral mobility important for transobturator tape procedure in management of female patients with stress urinary incontinence? Urology. 2007;70(2):246,50; discussion 250-1.

28. Walsh LP, Zimmern PE, Pope N, Shariat SF, Urinary Incontinence Treatment N. Comparison of the Q-tip test and voiding cystourethrogram to assess urethral hypermobility among women enrolled in a randomized clinical trial of surgery for stress urinary incontinence. J Urol. 2006;176(2):646,9; discussion 650.

29. Klutke JJ, Carlin BI, Klutke CG. The tension-free vaginal tape procedure: Correction of stress incontinence with minimal alteration in proximal urethral mobility. Urology. 2000;55(4):512-4.

30. Petros PE, Ulmsten U. An integral theory and its method for the diagnosis and management of female urinary incontinence. Scand J Urol Nephrol. 1993;153:1,1-93.

31. Liapis A, Bakas P, Christopoulos P. Tension free vaginal tape for elderly women with stress urinary incontinence. Int J Gynaecol Obstet. 2006;92:48,48-51.

32. Frietel X, Zabak K, Pigne A. Predictive value of urethral mobility before suburethral tape procedures for urinary stress incontinence in women. J Urol. 2002;168:2472,2472-2475.

33. Mutone N, Mastropietro M, Brizendine E. Effect of tension free vaginal tape procedure on urodynamic continence indices. Obstet Gynecol. 2001;98:638,638-645.

34. Minaglia S, Urwitz-Lane R, Wong M, Ozel B. Effectiveness of transobturator tape in women with decreased urethral mobility. J Reprod Med. 2009;54(1):15-9.

35. Young SB, Howard AE, Illanes DS, Weber LeBrun EE, Hardy JR, Kambiss SMDO, et al. Long-term efficacy of the pubovaginal mersilene mesh sling. American Journal of Obstetrics & Gynecology. 2009 November;201(5):516e1-7.

36. Baden W, Wallace T. Surgical repair of vaginal defects. In: Philadelphia: Lippincott; 1992.

37. Bump RC, Mattiasson A, Bo K, Brubaker LP, DeLancey JO, Klarskov P, et al. The standardization of terminology of female pelvic organ prolapse and pelvic floor dysfunction. Am J Obstet Gynecol. 1996 Jul;175(1):10-7.

38. Meschia M, Pifarotti P, Gattei U, Bertozzi R. Tension-free vaginal tape: Analysis of risk factors for failures. Int Urogynecol J Pelvic Floor Dysfunct. 2007;18(4):419-22.

39. Koops SE, Bisseling TM, van Brummen HJ, Heintz AP, Vervest HA. What determines a successful tension-free vaginal tape? A prospective multicenter cohort study: Results from the netherlands TVT database. Obstet Gynecol. 2006;194(1):65-74.

40. Nager CW, FitzGerald M, Kraus SR, Chai TC, Zyczynski H, Sirls L, et al. Urodynamic measures do not predict stress continence outcomes after surgery for stress urinary incontinence in selected women. J Urol. 2008 Apr;179(4):1470-4.

41. Guerette NL, Bena JF, Davila GW. Transobturator slings for stress incontinence: Using urodynamic parameters to predict outcomes. Int Urogynecol J Pelvic Floor Dysfunct. 2008;19(1):97-102.

42. Viereck V, Nebel M, Baden W, Harms L, Lange R, Hilgers R, et al. Role of bladder neck mobility and urethral closure pressure in predicting outcome of tension-free vaginal tape (TVT) procedure. Ultrasound Obstet Gynecol. 2006;28(2):214-20.

43. Moore RD, Miklos JR. Colpocleisis and tension free vaginal tape sling for severe uterine and vaginal prolapse and stress urinary incontinence under local anesthesia. J Am Assoc Gynecol Laparosc. 2003;179:1470,1470-1474.

44. Sevestre S, Ciofu C, Deval B, Traxer O, Amarenco G, Haab F. Results of the tension-free vaginal tape technique in the elderly. Eur Urol. 2003;44:128,128-131.

45. Walsh K, Generao SE, White MJ, Katz D, Stone AR. The influence of age on quality of life outcome in women following a tension-free vaginal tape procedures. J Urol. 2004;171:1185,1185-8.

46. Nilsson CG, Kuuva N. The tension-free vaginal tape procedure is successful in the majority of women with indications for surgical treatment of stress urinary incontinence. BJOG. 2001;108:414,414-9.

47. Hall G, Phillips TJ. Estrogen and skin: The effects of estrogen, menopause and hormone replacement therapy on the skin. J Am Acad Derm. 2005;53:555,555-68.

48. Perucchini D, DeLancey JO, Ashton-Miller JA, Galecki A, Schaer GN. Age effects on urethral striated muscle. II. anatomic location of muscle loss. 2002. Am J Obstet Gynecol;186:356,356-360.

49. Murphy M, van Raalte H, Mercurio E, Haff R, Wiseman B, Lucente VR. Incontinence-related quality of life and sexual function following the tension-free vaginal tape versus the "inside-out" tension-free vaginal tape obturator. (0937-3462; 0937-3462).

50. Anger JT, Litwin MS, Wang Q, Pashos CL, Rodriguez LV. The effect of concomitant prolapse repair on sling outcomes. (1527-3792; 0022-5347).

51. Aronson MP, Aronson PK, Howard AE, Morse AN, Baker SP, Young SB, et al. Low risk of ureteral obstruction with "deep" (dorsal/posterior) uterosacral ligament suture placement for transvaginal apical suspension. American Journal of Obstetrics & Gynecology. 2005;192(5):1530-6.

52. Rechberger T, Futyma K, Jankiewicz K, Adamiak A, Bogusiewicz M, Skorupski P. Body mass index does not influence the outcome of anti-incontinence surgery among women whereas menopausal status and ageing do: A randomised trial. Int Urogynecol J Pelvic Floor Dysfunct 2010(1433-3023; 0937-3462).

53. Houwert RM, Renes-Zijl C, Vos MC, Vervest HA. TVT-O versus monarc after a 2-4-year follow-up: A prospective comparative study. Int Urogynecol J Pelvic Floor Dysfunct. 2009 Nov;20(11):1327-33.

54. Barber MDMDMHS, Kleeman SMD, Karram MMMD, Paraiso MFRMD, Walters MDMD, Vasavada SMD, et al. Transobturator tape compared with tension-free vaginal tape for the treatment of stress urinary incontinence: A randomized controlled trial. Obstetrics & Gynecology. 2008;111(3):611-21.

55. Bjelic-Radisic VMD, Dorfer MP, Greimel EP, Frudinger AMD, Tamussino KMD, Winter RMD. Quality of life and continence 1 year after the tension-free vaginal tape operation. American Journal of Obstetrics & Gynecology. 2006;195(6):1784-8.

56. Rizvi RM. Clinical and quality-of-life (QoL) outcomes in women treated by tension free vaginal tape (TVT). J Pak Med Assoc. 2009 May;59(5):274-7.