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Refined nomogram incorporating standing cough test improves prediction of male transobturator sling success

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Aims: To develop a decision aid in predicting sling success, incorporating the Male Stress Incontinence Grading Scale (MSIGS) into existing treatment algorithms.
Methods: We reviewed men undergoing first-time transobturator sling for stress urinary incontinence (SUI) from 2007 to 2016 at our institution. Patient demographics, reported pads per day (PPD), and Standing Cough Test (SCT) results graded 0-4, according to MSIGS, were assessed. Treatment failure was defined as subsequent need for >1 PPD or further procedures. Parameters associated with failure were included in multivariable logistic models, compared by area under the receiver-operating characteristic curves. A nomogram was generated from the model with greatest AUC and internally validated.
Results: Overall 203 men (median age 67 years, IQR 63-72) were evaluated with median follow-up of 45 months (IQR 11-75 months). A total of 185 men (91%) were status-post radical prostatectomy and 29 (14%) had pelvic radiation history. Median PPD and SCT grade were both two. Eighty men (39%) failed treatment (use of ≥1 PPD or subsequent anti-incontinence procedures) at a median of 9 months. History of radiation ($P = 0.03$), increasing MSIGS ($P < 0.0001$) and increasing preoperative PPD ($P < 0.0001$) were associated with failure on univariate analysis. In a multivariable model with AUC 0.81, MSIGS, and PPD remained associated ($P = 0.002$ and <0.0001 respectively, and radiation history $P = 0.06$), and was superior to models incorporating PPD and radiation alone (AUC 0.77, $P = 0.02$), PPD alone (AUC 0.76, $P = 0.02$), and a cutpoint of >2 PPD alone (AUC 0.71, $P = 0.0001$).
Conclusions: MSIGS adds prognostic value to PPD in assessing success of transobturator sling for treatment of SUI.

KEYWORDS
male stress urinary incontinence, male transobturator sling, predictive nomogram

1 | INTRODUCTION

The reported incidence of persistent post-prostatectomy stress urinary incontinence (SUI) has remained consistent,[1,2] despite the emergence of robotic-assisted laparoscopic prostatectomy (RALP).[3,4] Several factors mediating the return to post-prostatectomy continence have been studied, including baseline degree of SUI,[5] history of pelvic radiation,[6] and presence of vesicourethral anastomotic contracture.[7] For men afflicted with bothersome leakage, deciding between an artificial urinary sphincter (AUS) for

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moderate to severe SUI, or male transobturator sling for mild SUI can be challenging. The choice of AUS or male sling is dependent on multiple factors, including SUI severity and patient characteristics including age, activity, body mass index (BMI), and radiation history.[8] This decisional complexity is compounded by the long-term risks with AUS of urethral erosion, device infection, failure, and need for revision,[9,10] with most patients choosing sling when given the option.[11]

Published outcomes for male sling remain suboptimal, with up to 25-35% experiencing sling failure, defined as persistent SUI,[12] possibly due to more substantial SUI than initially estimated. The measure of SUI severity most commonly employed is the patient-reported number of pads used per day (PPD), which is inherently subjective and may not always correlate with the gold standard, 24 h pad weight testing,[13] which is often cumbersome for both patient and provider. Other adjuncts, such as urodynamic studies, are time-consuming, costly, and have not been found to more accurately characterize degree of SUI above clinical history and exam alone.[14]

To date, no decision-assisting algorithm has been developed to aid clinicians in identifying the ideal sling recipients. The objective demonstration of SUI via a standing cough test (SCT), quantified by the Male Stress Incontinence Grading Scale (MSIGS) has been shown to be a significant predictor of success following sling placement, suggesting a role in treatment selection.[15,16] We hypothesize that the addition of the SCT to predictive models of sling success would improve patient selection for male sling, with the aim of developing a clinical support tool to aid in preoperative patient evaluation and counseling.

2 | MATERIALS AND METHODS

2.1 | Patient selection

We reviewed a prospectively-maintained, Institutional Review Board approved database of all men who underwent primary (first-time) placement of AdVance transobturator sling (American Medical Systems, Minnetonka, MN) for SUI by a single surgeon at our institution between 2007 and 2016. Patients with prior anti-incontinence procedures and with follow-up less than 6 months were excluded. Clinical parameters were obtained from a standardized preoperative visit, in which baseline PPD use, history of pelvic radiation, and demonstration of SUI by SCT were routinely elicited. The SCT was administered preoperatively for all patients as previously described.[15] In brief, after ensuring that patients had not voided for at least 1 h, patients complete a series of four forceful coughs. Towels are held below the meatus to collect any leakage, and graded by the examiner according to the standardized MSIGS measure (Table 1).

2.2 | Surgical technique and follow-up

Transobturator slings were placed using standardized technique by a single surgeon via a midline perineal incision, through which the sling was anchored in each quadrant to the mid-bulbar urethra to achieve urethral advancement with adequate tension. Following sling tensioning, intraoperative cystoscopy was performed to ensure satisfactory urethral coaptation. All patients were discharged the same day with a catheter overnight and underwent voiding trial the next day, followed up at 3 months for office examination, and thereafter as warranted by their reported urinary symptoms.

Treatment failure was defined as need for >1 PPD and/or subsequent anti-incontinence procedures including periurethral bulking agent injection, repeat sling, or AUS. To further evaluate the performance of the nomogram, we performed a secondary analysis of sling success using an alternative definition of ≥50% improvement in PPD because of its reported correlation with pad weight improvement.[19]

2.3 | Statistical analysis

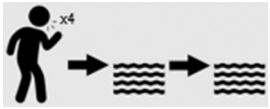
Continuous variables and categorical variables were compared with the Mann-Whitney U and Fisher's exact tests respectively. Preoperative characteristics were compared in univariate logistic regression models of sling failure using stepwise variable selection in which parameters meeting a threshold $P < 0.15$ were included in multivariable models where significance was defined as $P < 0.05$. Models were evaluated via likelihood ratio tests and comparison of areas under receiver operating characteristic (ROC) curves. A nomogram was generated from the model with greatest AUC, subjected to 200 bootstrap resamples for bias correction. Calibration was assessed by plotting predicted versus actual probability of sling failure, and the Brier score (mean squared prediction error) was determined. The *rms* package in the R statistical environment was used for all analyzes.[17]

3 | RESULTS

3.1 | Demographics

In total, 219 patients underwent transobturator sling placement during the study period, of whom 203 met selection criteria with median follow-up of 64 months (interquartile range 39-94). Median age at surgery was 67 years (IQR 63-72), with median SCT grade by MSIGS of two (IQR 1-2) and median baseline PPD use of two (IQR 1.5-3). The etiology of SUI included 164 men (81%) with history of radical prostatectomy (RP), 22 (11%) with RP and pelvic radiation, 7 (3%) with radiation alone, and 10 (5%) following transurethral resection of prostate (TURP).

TABLE 1 Standing cough test (SCT) scoring by the Male Stress Incontinence Grading Scale (MSIGS)

	Grade	Defination	Proposed management
0		Leakage by history but not an exam	Sling
1		Delayed drops only	Sling
2		Early drops, no stream	Sling
3		Drops initially, delayed stream	Aus
4		Early and persistent stream	Aus

AUS, artificial urinary sphincter.

3.2 | Treatment outcomes and preoperative predictors of sling failure

At a median of 9 months following sling placement (IQR 2-39), 80 men failed treatment as defined by the need for >1 PPD and/or subsequent procedures for incontinence. Specifically, 39/80 (49%) sling patients pursued further interventions for SUI including 30 who underwent AUS, six who had repeat sling, and three who elected for periurethral bulking agent injection. Demographic and preoperative characteristics for the population are reported in Table 2. Notably, age, body-mass index, and presence of anastomotic contracture did not differ significantly between men who had sling success versus failure.

History of radiation, SCT grade by MSIGS and baseline number of PPD met the threshold for inclusion in a multivariable logistic analysis of sling failure in which MSIGS and PPD remained significantly associated (Table 3). Several additional models were evaluated: PPD with radiation, PPD alone, and specifically use of >2 PPD on the basis of the recommendation of this cutoff for sling placement in the literature.[8] These models differed significantly from each other by chi-square based likelihood ratio tests ($P < 0.05$ for all). ROC curves for this dataset are presented in Figure 1, in which the model with MSIGS, PPD and radiation ("full model") demonstrated the greatest AUC (0.81).

3.3 | Nomogram generation and calibration

Using the full model, a nomogram was generated to predict the overall probability of sling failure (Figure 2), which had a bootstrap-corrected AUC of 0.82 and Brier score of 0.17 indicating good predictive performance.[18] Nomogram-generated probabilities of ≤30% demonstrated excellent concordance between predicted and actual sling failure (calibration plot shown in Supplementary Figure S1). The probability of ≤30% was evaluated as a natural decision-making inflection point, corresponding to a hypothetical "ideal" patient with SCT grade two by MSIGS, use of two PPD, and no prior radiation, yielding a nomogram-predicted probability of failure of 34% (95%CI: 24-45%).

3.4 | Additional value of MSIGS

The traditional parameter for gauging likelihood of sling failure, >2 PPD, was evaluated against the cutpoint of ≤30% nomogram-predicted probability of failure. In the study population, 67/80 (84%) of the men who failed sling had predicted probability of failure of ≥30%. In contrast, 54/80 (68%) patients with baseline >2 PPD failed. The full model therefore reclassified an additional 13 patients as failing sling at a decision threshold of 30%, who would have been inappropriately predicted to succeed by the >2 PPD cutoff.

3.5 | Alternate definitions of failure

Secondary analysis of an alternative definition of success (<50% improvement in pad use or need for subsequent anti-incontinence procedures) revealed an identical failure rate (39.4%, 80/203). On univariate analysis, baseline PPD use, SCT grade by MSIGS, and history of radiation were again predictive of failure (Supplementary Table). On multivariable analysis, only MSIGS remained significantly associated with this outcome.

TABLE 2 Demographic and preoperative characteristics of patients undergoing transobturator sling placement, stratified by treatment failure

	Failure		
Parameter	**No ($n = 123$)**	**Yes ($n = 80$)**	***P***
Age, years	67 (62-71)	68 (63-73)	0.5
Body-mass index, kg/m^2	28 (25-30)	27 (25-31)	0.3
History of (no., %)			
Androgen deprivation therapy	4 (3%)	4 (5%)	0.7
Hypertension	62 (50%)	42 (53%)	0.8
Erectile dysfunction	90 (73%)	57 (71%)	0.9
Smoking	62 (50%)	42 (53%)	0.8
Type 2 diabetes	19 (15%)	14 (18%)	0.7
Prior (no., %)			
Anastomotic contracture	11 (9%)	10 (13%)	0.5
Inflatable penile prosthesis	5 (4%)	4 (5%)	0.7
Pelvic radiation	12 (10%)	17 (21%)	**0.03**
Urethroplasty	0	1 (1%)	0.4
Type of prostate procedure (RP vs TURP)	114 (93%)	70 (88%)	0.2
Pads per day, no.	1.5 (1-2.5)	3 (2-4)	**<0.0001**
SCT grade by MSIGS	2 (1-2)	2 (2-3)	**<0.0001**

Continuous variables are presented as medians with interquartile ranges in parentheses.
MSIGS, Male Stress Incontinence Grading Scale; RP, radical prostatectomy; SCT, standing cough test; TURP, transurethral resection of prostate.
P values demonstrating statistical significance are highlighted with bold text.

4 | DISCUSSION

Determining the severity of male SUI is critical to patients and providers in deciding between transobturator sling and AUS, but a significant portion of otherwise well-selected men fail sling despite use of PPD-based cutoffs.[20] Other potential risk factors for sling failure have been studied attempting to predict a degree of residual urinary sphincteric function.[21,22] We present a novel non-invasive clinical tool incorporating the physical demonstration of SUI, represented as SCT grade, in conjunction with baseline PPD use, and history of pelvic radiation which was superior to PPD alone in identifying ideal sling candidates.

The nomogram developed from this multivariable model performs optimally at a risk threshold of ≤30% of sling failure, implying that patients who score above this value should be counseled on AUS rather than sling. This threshold corresponds to a patient with SCT grade two, without history of radiation, who uses two PPD. In our population, 81% of men with SCT grade 0-2 by MSIGS, ≤2 PPD, and no history of radiation had a successful outcome following transobturator sling placement.

Compared to the guidelines for the evaluation of SUI in women, the role of the physical examination in determining the degree of male SUI is underemphasized, and the definitions of mild and moderate SUI remain nebulous.[23,24] The SCT, formalized from patterns of urinary leakage observed in our practice, represents an adjunctive measure with negligible expense, or time added to the preoperative visit. In order to estimate the likelihood of success before surgery, more invasive testing, such as cystoscopy or urodynamics, may be pursued, but may not correlate with SUI severity and postoperative success.[14] Patients may therefore be subjected

TABLE 3 Univariate and multivariable logistic regression of factors predicting sling failure

	Univariate		Multivariable	
Parameter	**OR**	***P***	**OR**	***P***
MSIGS, per increment	2.3 (1.7-3.2)	<0.0001	1.7 (1.2-2.4)	**0.005**
Pads per day, per pad	2.1 (1.6-2.8)	<0.0001	1.8 (1.4-2.4)	**<0.0001**
History of radiation, yes/no	2.5 (1.1-5.7)	0.03	2.2 (0.9-5.6)	0.099

Odds ratios (OR) are presented with 95% confidence intervals in parentheses.
MSIGS, Male Stress Incontinence Grading Scale.
P values demonstrating statistical significance are highlighted with bold text.

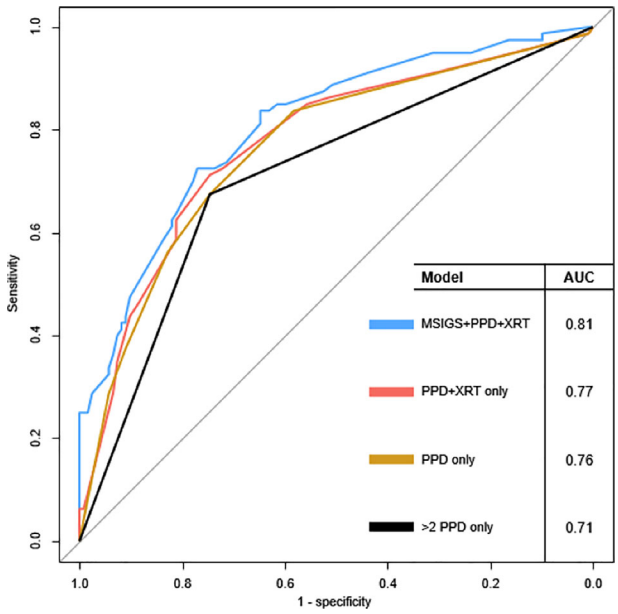


FIGURE 1 Comparison of receiver-operating characteristic curves of models incorporating parameters predictive of sling failure. AUC = area under curve. MSIGS = male stress incontinence grading scale. PPD = pads per day. XRT = radiation therapy

to laborious and costly diagnostic maneuvers with questionable additional value.[15] This report builds on our previous examinations of patient selection prior to sling, in which increasing success as well as patient satisfaction was noted with deployment of MSIGS at our institution,[16] to describe the additive benefit of the SCT to PPD.

We propose that mild grades of SUI observed via the SCT correspond to greater residual urinary sphincter function and healthier periurethral tissue. This is supported by the association between history of pelvic radiation and sling failure on multivariate analysis. Lack of clarity in the

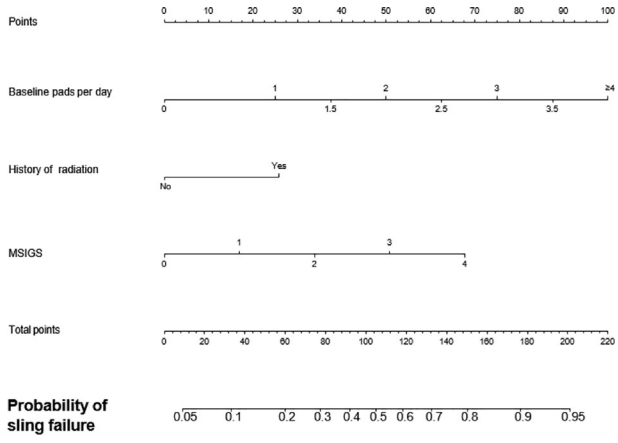


FIGURE 2 Nomogram predicting the probability of sling failure, which can be calculated by obtaining the value for each parameter by drawing a straight line to the points axis, adding the points together, and finding the sum on the total points axis

definition and measurement of SUI severity complicates standardized patient selection and outcomes. While more invasive assessment of incontinence and sphincter function such as urodynamic studies and cystoscopic evaluation have been described, variable definitions of SUI severity and sphincteric function result in inconsistent prediction of surgical success.[25,26] Reproducible objective testing is therefore needed to describe more accurately the severity of incontinence. The SCT graded by MSIGS may fill this niche, and the nomogram described in this study may be useful not only as a predictive tool, but also in raising awareness of male SUI and setting appropriate patient expectations in preoperative counseling, as has been shown for similar nomograms in other urologic conditions.[27]

As the multivariable analysis and model development was based on data from a single surgeon, practice patterns unique to our institution may limit its generalizability. Although the rate of anastomotic contracture was low, previous reports indicate the adverse effects of peri-sphincter fibrosis. We believe the rate of contracture may be lower in general post-RALP as compared to open RP.[28] Nevertheless, more severe baseline SUI exhibited either via PPD or SCT grade remained significant predictors of sling failure. The definition of failure in this study was relatively stringent (>1 PPD and/or need for subsequent anti-incontinence procedures) and does not account for patient-reported outcomes, but for the purposes of generating a predictive tool this cutoff was selected as patients with ≤1 PPD use are generally satisfied with this degree of SUI.[29] Furthermore, SCT grade by MSIGS remained predictive of sling success on secondary multivariable analysis using ≥50% improvement in PPD use. Lastly, variable selection for our nomogram was limited to factors derived from the available data, which was reviewed retrospectively; nonetheless, bootstrap resampling and internal validation offered some degree of bias correction. External validation and study of the reliability of the SCT are warranted and may bear out its utility and simplicity.

5 | CONCLUSIONS

Outcomes following transobturator sling placement can be predicted with a nomogram incorporating readily available clinical factors. An ideal candidate for sling has SCT grade 0-2, baseline ≤2 PPD, and no history of radiation. This clinical tool outperforms PPD alone in selecting patients for sling placement.

CONFLICTS OF INTEREST

Dr Allen Morey receives honoraria for being a guest lecturer/meeting participant for Boston Scientific and Coloplast Corp. No other authors have disclosures to report.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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