Effect of Radiation on Male Stress Urinary Incontinence and the Role of Urodynamic Assessment

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OBJECTIVE To evaluate the effect of radiation on male stress urinary incontinence (SUI) and to assess the relative value of preoperative urodynamic (UDS) testing in radiated vs nonradiated men with SUI.

METHODS A retrospective chart review of all male patients with SUI who underwent UDS testing from 2010 to 2016 was performed. The impact of UDS findings on treatment decision making was assessed. UDS parameters and treatment patterns of radiated vs nonradiated patients were compared as well as the fates of storage symptoms in each group.

RESULTS Two hundred seven men were identified that underwent UDS with a clinical diagnosis of SUI. Sixty-five out of 207 (31.4%) were exposed to radiation as a treatment modality for prostate cancer. All patients that underwent UDS testing moved on to surgical correction of SUI, and the UDS findings did not alter plan to treat SUI in any patients. Men who were radiated prior to surgical correction of SUI were more likely to have detrusor overactivity (70% vs 38%, P <.0001) and had lower maximum cystometric capacity (255 vs 307.4 mL, P = .01) when compared to nonradiated on UDS. After artificial urinary sphincter or sling implantation, the proportion of patients requiring overactive bladder medications was higher in radiated vs nonradiated men (44.3% vs 25.3%; P = .01).

CONCLUSION Radiation therapy appears to increase the likelihood of bladder dysfunction in male patients with SUI. The UDS findings did not alter the plan to treat SUI in any patients in our series, and its role before SUI surgery in male patients, including those receiving radiation, may be limited. UROLOGY 125: 58–63, 2019. © 2018 Elsevier Inc.

The role of urodynamics (UDS) in preoperative planning for stress urinary incontinence (SUI) in men is controversial, or at least not clearly defined.[1-3] Some clinicians use UDS routinely, while other rarely utilize it. This lack of agreement is reflected in the recently published ICS Artificial Urinary Sphincter (AUS) Consensus document which states that "UDS should be carried out at the discretion of clinicians in cases where it will help with diagnosis or counseling and follow-up".[4] Although SUI due to intrinsic sphincter deficiency is the most common etiology of urinary incontinence after prostatectomy, a significant proportion of patients have an urgency component to their incontinence.[5] One of the main arguments for UDS in men with SUI could be to objectify detrusor overactivity (DO) which may help improve storage symptoms outcomes. However, this hypothesis has rarely been investigated.[3] Patients undergoing brachytherapy or external beam radiation therapy (EBRT) have been found to have higher rates of urgency incontinence and DO than nonradiated (NR) patients.[6] In addition, radiation can cause a decrease in bladder compliance that can affect a decision to perform stress incontinence surgery.[3,7] Since radiated patients also have higher complication rates following SUI surgeries,[7] this population may draw more benefit from preoperative UDS. However, to our knowledge, the role of UDS in radiated men with SUI has not been evaluated in the literature so far.[3]

The goals of our study were to evaluate the effect of radiation on male SUI and to assess the relative value of preoperative UDS testing in radiated vs NR men with

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SUI and its ability to predict storage symptoms outcomes after SUI surgery in these 2 populations.

METHODS

Study Population

After institutional review board approval, we performed a retrospective chart review of men with a presumed diagnosis of SUI (ICD 9 code 788.32 and ICD 10 code 39.3) who underwent UDS at a single center between 2010 and 2016. Patients with SUI as a result of a neurologic condition and those who did not undergo UDS were excluded. Stress incontinence was diagnosed by history (a complaint of loss of urine with increased abdominal pressure or gravity) and on physical examination (urine loss with cough, Valsalva, or gravity). Patients were classified into 2 groups: those who were radiated and those who were NR. Patients were included in the radiated group if they received primary therapy with brachytherapy or EBRT, or if they received salvage radiotherapy or brachytherapy after their primary intervention. Symptoms of urgency, prior documentation of urgency urinary incontinence, and use of overactive bladder (OAB) medications (ie, anticholinergic and/or Beta3-agonists) were noted.

Urodynamics

All UDS were performed with simultaneous fluororscopic imaging (videourodynamics) with 7F transurethral and rectal balloon catheters according to a local standardized protocol that has been previously described[8] and in line with the International Continence Society (ICS) standards.[9] Filling cystometry was then performed at a rate of 50 mL/min with radiographic contrast material, or at a decreased rate of 30 mL/min in cases of severe DO or known small functional capacity. At 150 mL (or half of bladder capacity if maximum voided volumes indicated a small bladder capacity), filling is stopped and the patient performs slow, gradually progressive straining maneuvers to increase abdominal pressures (or gradually increasing coughs if no leakage occurred with straining). A pressure-flow study was then performed and fluoroscopic images were obtained at selected times as determined by the clinical scenario (ie, filling, Valsalva, void/attempt to void, after voiding). If stress incontinence is not demonstrated with a catheter in place, a second fill is performed and the vesical catheter is removed and SUI is assessed in the same manner as described above.

The following UDS parameters were recorded: presence of DO, any leak associated with DO (DO incontinence), maximum detrusor pressure during IDC (MDP, cm H_2O), maximum cystometric capacity (MCC, mL) and demonstration of SUI. End filling pressure (EFP, cm H_2O) was used as a surrogate for bladder compliance. The presence of other clinically relevant findings such as vesicoureteral reflux or bladder outlet obstruction were noted as well.

SUI Management at the Study Site

Over the study period, 2 functional urologists, provided care for men with SUI at the study site. All patients with bothersome non-neurogenic SUI refractory to pelvic floor muscle training therapy were offered surgical treatment. All patients underwent UDS as part of the study site's routine preoperative work-up. Two surgical options were available to patients: male sling and AUS. The decision to elect one option over the other was made on an individual basis after thorough discussion with the patients (ie, no standard criteria used). The management of preoperative and postoperative OAB was not standardized and left to surgeons' discretion.

Outcomes of Interest

Patient charts were then reviewed for whether SUI surgery was performed and if so, clinical outcomes following AUS or sling placement. Treatment of urgency after surgical intervention was also documented. This included treatment with OAB medications (ie, anticholinergics and/or beta-3 agonists), as well as third-line therapy, including intradetrusor botulinum toxin injections, percutaneous tibial nerve stimulation, or sacral neuromodulation. Finally, the occurrence of upper urinary tract damage after SUI surgery, defined as upper urinary tract stones and/or hydronephrosis, was sought in patients with high EFP.

Statistical Analysis

Means and standard deviations were reported for continuous variables, and proportions for nominal variables. Comparisons between groups were performed using the χ^2 test or Fisher's exact test as appropriate for discrete variables, and Mann-Whitney *U* test for continuous variables. Change of continuous variables over time was assessed using the McNemar test. Univariate logistic regression analyzes were performed to assess statistical association between preoperative UDS parameters and the use of OAB medications after AUS implantation in radiated and NR male patients. For continuous variables, odds ratios (OR) were expressed per change in regressor for each unit increase. Statistical analyses were performed using JMP v.14.0 software (SAS Institute Inc., Cary, NC). All tests were two-sided with a level of $P < .05$ considered statistically significant.

RESULTS

Patients' Characteristics

Between 2010 and 2016, we identified 207 men who underwent UDS prior to surgical intervention for presumed non-neurogenic SUI. Of these patients, 172 (83%) of men developed SUI after undergoing radical prostatectomy (open, robotic, or laparoscopic), 6 (2.9%) as a result a transurethral resection, 21 (10.1%) as a result of EBRT, and 8 (3.9%) as a result of brachytherapy. Forty-one (19.8%) men underwent adjuvant radiotherapy for their prostate cancer. Ultimately, 65 patients (31.4%) were exposed to radiation as a treatment modality as a result of primary therapy, secondary therapy, or both. All patients that underwent UDS testing moved on to surgical correction of SUI, with 146 (70.5%) men receiving an AUS (mean follow-up 33.4 months) and 61 (29.5%) men receiving a male sling (mean follow-up 25.4 months) as a first-line SUI surgery. Fourteen men underwent AUS implantation as a second treatment due to failed sling: thus 160 of the 207 male patients of this cohort ultimately received an AUS (77.3%). The UDS findings did not alter the treatment plan for SUI in any patients.

Urodynamic Parameters and Treatment Patterns of Radiated vs Nonradiated Patients

Comparisons between radiated and NR men are listed in Table 1. Men who were radiated prior to surgical correction of SUI were more likely to have DO (70% vs 38%, $P < .0001$) and had lower MCC (255 vs 307.4 mL, $P = .01$) when compared to NR on UDS. Moreover, radiated men were more likely to require anticholinergic therapy prior to SUI surgery (44.6% vs 29.6%, $P = .03$) and to receive an AUS as their first-line SUI surgery

Table 1. Baseline urodynamic and clinical features of radiated vs nonradiated male patients

	Radiated *N* = 65	Nonradiated *N* = 142	*P* Value
Detrusor overactivity	46 (70%)	54 (38%)	<.0001
EFP >20 cm H_2O	8 (12%)	9 (6%)	.2
	20-29 = 3	20-29 = 5	
	30-39 = 5	30-39 = 3	
	>40 = 0	>40 = 1	
MCC (mL)	253 (±126.7)	307.4 (±135.5)	.01
OAB medications use before SUI surgery	29 (44.6%)	42 (29.6%)	.03
Radical prostatectomy	28 (43.1%)	124 (87.6%)	<.0001
Type of first-line SUI surgery			
Male sling	9 (13.9%)	52 (36.9%)	.0008
AUS	56 (86.1%)	90 (73.1%)	

AUS, artificial urinary sphincter; DO, detrusor overactivity; EFP, end fill pressure; MCC, maximum cystometric capacity; OAB, overactive bladder; SUI, stress urinary incontinence.

(86.1% vs 73.1%; *P* = .0008) or at any point of their SUI management (ie, first-line or after sling's failure: 93.9% vs 69.7%; *P* <.0001). The incidence of EFP >20 cm H_2O was higher in the radiated group but this difference was not statistically significant (12% vs 6%; *P* = .2). None of these patients with EFP >20 cm H_2O, whether radiated or NR, developed upper urinary tract damage after SUI surgery.

The Fate of Storage Symptoms After Sling and AUS in Radiated vs Nonradiated Male

The fate of storage symptoms after sling and AUS in radiated vs NR men is presented in Table 2. The proportion of patients requiring OAB medications after sling placement was similar in radiated and NR men (22.2% vs 17.3%; *P* = .66), as well as the proportion of patients who discontinued OAB medications postoperatively (80% vs 73.3%; *P* = .99) and the proportion of patients who initiated OAB medications do novo after sling insertion (25% vs 13.5; *P* = .48). Conversely, after AUS implantation, the proportion of patients requiring OAB medications was higher in radiated vs NR men (44.3% vs 25.3%; *P* = .01), as well as the proportions of patients who initiated OAB medications do novo (41.2% vs 22.1; *P* = .04). Overall, eight patients (3.9%) required third-line OAB therapy (which was always intradetrusor botulinum toxin injections), after SUI surgery for storage symptoms refractory to medical treatment. Radiated men were more likely to require third-line OAB therapy after SUI surgery than NR men (9.2% vs 1.4%; *P* = .01).

Predictive Value of Urodynamics in Radiated vs Nonradiated Patients for Storage Symptoms Outcomes

Several UDS parameters were significantly associated with the use of OAB medications after AUS implantation in radiated patients (Table 3), namely DO (OR = 4.03; *P* = .03), DO incontinence (OR = 3.23; *P* = .03) and MDP during IDC (OR = 1.03; *P* = .04). In contrast, no UDS parameters were predictive of the use of OAB medications after AUS implantation in NR patients (Table 3). Radiated male patients with DO had a higher likelihood of using OAB medications after AUS implantation than those without DO at baseline (53.5% vs 22.2%; *P* = .02). Conversely, in NR male patients, DO was not associated with an

Table 2. Fate of storage symptoms after sling and artificial urinary sphincter in radiated vs nonradiated male patients

	Radiated	Nonradiated	*P* Value
After sling			
Number of patients	9	52	NA
Using OAB medications before SUI surgery			
Yes	5 (55.6%)	15 (28.9%)	.14
No	4 (44.4%)	37 (71.1%)	
Patients using OAB medications postoperatively	2/9 (17.3%)	9/52 (22.2%)	.66
Patients having discontinued OAB medications postoperatively	4/5 (80%)	11/15 (73.3%)	.99
OAB medications initiated de novo postoperatively	1/4 (25%)	5/37 (13.5%)	.48
After AUS			
Number of patients	61	99	NA
Using OAB medications before SUI surgery			
Yes	27 (44.3%)	31 (31.3%)	.10
No	34 (55.7%)	68 (68.7%)	
Patients using OAB medications postoperatively	27/61 (44.3%)	25/99 (25.3%)	.01
Patients having discontinued OAB medications postoperatively	14/27 (51.9%)	21/31 (67.7%)	.22
OAB medications initiated de novo postoperatively	14/34 (41.2%)	15/68 (22.1%)	.04

AUS, artificial urinary sphincter; NA, not applicable;
OAB, overactive bladder; SUI, stress urinary incontinence.

Table 3. Association between urodynamic parameters and OAB medications use after AUS implantation in radiated and nonradiated male patients

Variables	OAB Medications Use After AUS Implantation							
	Radiated Male Patients *N* = 61				Nonradiated Male Patients *N* = 99			
	Odds Ratio	Confidence Interval 95 %		*P* Value	Odds Ratio	Confidence Interval 95 %		*P* Value
		Lower	Upper			Lower	Upper	
Detrusor overactivity	4.03	1.14	14.23	.03	1.74	0.70	4.35	.24
Detrusor overactivity incontinence	3.23	1.12	9.30	.03	1.44	0.53	3.89	.47
Maximal detrusor pressure during IDC	1.03	1.01	1.07	.04	1.03	0.98	1.08	.07
End filling detrusor pressure	1.02	0.99	1.06	.18	1.01	0.98	1.05	.43
Maximum cystometric capacity	0.08	0.01	1.43	.07	0.03	0.01	1.26	.07

AUS, artificial urinary sphincter; IDC, involuntary detrusor contraction; OAB, overactive bladder.

increased use of OAB medications after AUS implantation (31.7% vs 21.1%; *P* = .23).

DISCUSSION

Although radiation therapy is largely recognized as a causative factor of SUI and bladder dysfunction, few studies have investigated the clinical and UDS features of SUI in radiated vs NR male patients.[1] There is still controversy regarding the use of UDS in the assessment of male SUI[3] and recommendations on specific patient types or characteristics are not given.[3,10-11] Since radiation is known to affect the bladder, and even caused impaired compliance, it would seem at least theoretically, that this patient group might see more of a benefit from UDS prior to surgical treatment of SUI.

Noncontrolled studies have assessed the value of UDS vs no UDS in men with SUI. UDS may be helpful to diagnose bladder dysfunction, such as DO or decreased compliance and bladder capacity as well as to assess sphincteric function with the determination of abdominal leak point pressure. However, none of these parameters have been shown to affect outcomes following AUS placement.[12-15] Furthermore, abdominal leak point pressure does not correlate well with the degree of UI, as determined by the 24-hour pad test.[14] Radiated patients could be a subgroup where this testing could be more relevant for several reasons: increased risk of complications after SUI surgery,[7] higher prevalence of DO,[16] risk of poor bladder compliance,[17] etc. However, to our knowledge, no study has examined the role of preoperative UDS specifically in this population.[3] In the present study, we found that radiated patients were more likely to have bladder dysfunction (DO, small bladder capacity, and need for OAB treatment). While the UDS findings did not alter treatment plans for either radiated or NR patients, UDS parameters were significantly associated with storage symptoms outcomes, but only in the radiated population. The fact that more patients with AUS then sling initiated OAB medications may be related to the greater severity of radiation effects that predisposed to AUS selection.

Detecting DO is often argued as one of the main goal of UDS in men with SUI.[18] However, studies have shown that the presence of preoperative DO does not affect outcomes of AUS and sling.[12,19] Not surprisingly, while DO was found in 70% and 38% of radiated and NR men respectively in the present study, it did not affect treatment decision making in any of them as all moved on to SUI surgery. No published studies have aimed to determine whether the stress or urgency component should take precedence in the management of male patients with mixed urinary incontinence. Several authors advocate that the urgency component should be treated first arguing that it could reduce the overall urinary incontinence and may make the component of SUI more apparent.[20-21] On the contrary, surgeons involved in the present series always elected to start with surgical correction of the stress component in this population, although the stress component was always predominate and often quite severe. Despite differing from other reported experts' opinion,[20-21] several arguments would support this decision. First, while some studies have been conducted in women,[22-23] there is no data to support the use of OAB treatment in male patients with mixed urinary incontinence. Moreover, while the chance to cure both the stress and urgency component of incontinence with OAB therapy is low, the female midurethral sling literature demonstrates that over a half of patients with mixed urinary incontinence could experience a resolution of urgency incontinence after SUI surgery.[24] A few series have suggested that anti-incontinence surgery, similarly, may improve OAB symptoms in a significant proportion of men with SUI.[25-26] With over 50% of patients discontinuing OAB medications after either sling or AUS implantation, our series confirm these previous findings. This improvement of OAB symptoms might be explained by an urethrogenic origin of urgency in some patients, with low outlet resistance favoring entry of urine in the proximal urethra with stimulation of urethral afferents facilitating the micturition reflex.[27-28] By increasing outlet resistance, SUI surgery would prevent this urethral mechanism. As seen in patients with end-stage renal disease with low urine output, patients with severe postprostatectomy SUI might develop artifactual DO, impaired compliance or bladder hypersensitivity.[29] Similar to what is observed after kidney transplantation, those bladder dysfunctions resolve in many cases after surgical correction of SUI restoring the physiological cycles of bladder storage and voiding.[29] The fact that in our patients DO symptoms associated with radiation were more likely to persist DO symptoms in NR patients may represent a more permanent effect on bladder overactivity caused by radiation.

Our findings call into question the need to diagnose DO in males with SUI, who are considering surgical treatment. Indeed, OAB medications were discontinued in the vast majority of patients, including those with DO. Several factors may contribute to the limited clinical significance of DO. First, as any other UDS parameters, DO shows a high variability and poor reproducibility.[30] Failing to elicit uninhibited contractions on a single UDS study does not exclude it as a causative factor of OAB symptoms.[10] Conversely, the finding of DO in the postprostatectomy setting has been postulated to be artifactual in many of patients with severe SUI, resulting from supraphysiological filling of chronically under filled bladder during UDS.[29] Finally, the multifactorial pathophysiology of OAB has been increasingly recognized over the past decades and it is now well established that urgency are not always DO-driven, DO lacking in over 50% of patients.[29] This relatively poor correlation with symptoms may contribute to limit its role in predicting storage symptoms outcomes after SUI surgery. Furthermore, it may be argued that simply treating OAB symptoms post operatively in those who require treatment is safe and more cost effective then preoperative UDS.

Pelvic radiation therapy is known to carry a risk of impaired bladder compliance.[17] Radiated patients with poor bladder compliance may be at risk of developing upper urinary tract damage when increasing outlet resistance by implanting an AUS (or to a lesser extent a sling). Detecting poor bladder compliance may have been an additional argument to offer UDS in radiated male with SUI. However, in our series, none of the patients with EFP >20 cm H_2O, whether radiated or NR, developed upper urinary tract damage after SUI surgery. This reinforces the idea that impaired compliance, as DO, might be artifactual in men with severe SUI resulting from supraphysiological filling of chronically under filled bladder during UDS.[13,15,29] Although this risk has been well-documented in pediatric patients with myelomeningocele, it is not known if poor bladder compliance and uncorrected storage pressure are absolute contraindications to AUS implantation in patients with non-neurogenic SUI. Hence, the ICS consensus conference on AUS recommended that such patients should be carefully followed to avoid a potentially devastating outcome of irreversible renal insufficiency with periodic upper urinary tract imaging and/or UDS.[4]

The present study has several limitations. It has all the biases inherent to its retrospective, single-center design. The surgeons involved in these series were high volume providers and then our results may not be reproducible in lower volume institutions where physicians may rely more upon UDS than on clinical judgment for treatment decision making. Also, not all patients who underwent surgical treatment of SUI had UDS. Over the time frame of this study, we relied less and less on preoperative UDS for uncomplicated patients, though until recently continued to perform UDS on radiated patients. We did not assess the predictive value of UDS parameters for SUI outcomes and voiding dysfunction outcomes which could be regarded as another significant shortcoming. However, other studies have shown that UDS findings of DO and impaired compliance do not affect outcomes of AUS or sling surgery.[12,15,19]

CONCLUSION

Radiation therapy increases the likelihood of bladder dysfunction in men with SUI with higher prevalence of DO, lower MCC at presentation and increased use of OAB medications both at baseline and after SUI surgery. There is also an increased risk of requiring third-line OAB therapy after SUI surgery in radiated vs NR men. Despite UDS being predictive of some outcomes in the subgroup of radiated patients, the UDS findings did not alter the SUI treatment plan in any patients in our series, and its role before SUI surgery in men, including those receiving radiation, may then be limited.

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