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What is the fate of artificial urinary sphincters among men undergoing repetitive bladder cancer treatment?

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Purpose: Functional characteristics and durability of the artificial urinary sphincter (AUS) among patients who develop bladder cancer has been poorly characterized. We sought to evaluate AUS outcomes among patients subsequently diagnosed with bladder cancer, in order to describe device survivability when subject to diagnostic and therapeutic procedures such as cystoscopy, transurethral resection, and cystectomy.

Materials and Methods: We retrospectively reviewed 1,803 male patients treated with AUS surgery at a single institution between 1983–2014. We describe AUS device outcomes among patients undergoing surveillance and treatment for bladder cancer.

Results: Following AUS placement, 14 (0.8%) patients were subsequently diagnosed with and treated for bladder cancer and 4 patients with bladder cancer undergoing treatment and screening, subsequently received AUS placement. The median follow-up from device placement was 7.2 years (interquartile range [IQR], 2.8–11.5), and the median time from AUS placement to bladder cancer diagnosis was 6 (IQR, 0–9). There were a total of 8 primary and 1 secondary devices failures. Despite a median of 2 diagnostic cystoscopies (IQR, 1–6) and 0 bladder tumor resections (IQR, 0–0) per patient following device implantation, only 1 (5.6%) patient experienced an iatrogenic erosion related to urethral manipulation. Among those undergoing cystectomy (n=4), 1 device was left in situ without complication.

Conclusions: Bladder cancer surveillance and treatment with an AUS device in place appears to confer minimal additional risk to AUS survival. Careful attention should be given to device deactivation and use of the smallest caliber instruments available to minimize the risk of iatrogenic urethral erosion.

Keywords: Cystoscopy; Urinary bladder neoplasms; Urinary incontinence; Urinary sphincter, artificial

INTRODUCTION

Since its introduction in 1974, the artificial urinary sphincter (AUS) has been the gold standard management option for severe male stress urinary incontinence [1]. Long-term device outcomes have been acceptable with 5 and 10-year survival rates of 75% and 65% respectively [2-5]. Notably, patients undergoing AUS placement commonly have comorbidities such as prior radiation, smoking, that increase their risk of bladder cancer [6,7]. Strategies to

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diagnose and treat this clinical entity following AUS placement may increase the risk of iatrogenic device compromise as a consequence of repetitive trans-urethral instrumentation and prolonged urinary catheterization [7-9].

In our practice, we have observed that careful cystoscopic evaluations in the population are generally well tolerated; however, more aggressive measures such as transurethral resection and prolonged catheterization may be associated with AUS complications. There is a need to identify risk factors associated with iatrogenic AUS-related complications among patients undergoing frequent transurethral manipulations for the surveillance and treatment of urothelial carcinoma. Therefore, we hypothesized that this population would be at an increased risk of AUS device compromise beyond what is generally observed in men without bladder cancer. Herein, we report our institutional experience of AUS management among patients subsequently diagnosed with urothelial malignancy.

MATERIALS AND METHODS

After obtaining Institutional Review Board approval we retrospectively identified 1,803 patients who underwent AUS implantation procedures at Mayo Clinic from 1983–2014 (approval number: 15-007373). Within this database we were able to identify 14 patients who were subsequently diagnosed with urothelial carcinoma of the bladder after device placement between 1991 and 2013, and 4 patients who were initially diagnosed with urothelial carcinoma of the bladder and subsequently underwent device placement from the year 2011–2014. Patients were excluded if they underwent AUS placement for neurogenic urinary incontinence, were younger than the age 18, or declined research consent. All implanted AUS devices were AMS 800 (Boston Scientific, Marlborough, MA, USA).

A perineal approach with proximal bulbar urethral cuff placement and preservation of the bulbospongiosus muscle is used for all AUS device implantations at our institution. Cuff size is determined after initial circumferential dissection of the bulbar urethra by the operating surgeon (Daniel S. Elliott). The 61–70 cm H_2O pressure regulating balloon is placed in a submuscular position through an abdominal counter-incision and is filled with 22 mL of iso-osmotic contrast [10].

All patients underwent device activation 6 weeks post-operatively. Thereafter, patients were evaluated as needed for device related concerns, and as a part of our ongoing AUS registry, patients are contacted by mail regarding device function. Specifics regarding device survival and function were obtained from follow-up office visits, operative reports, and written or telephone communication.

Diagnostic cystoscopy or cystoscopy for bladder cancer surveillance was performed with a 17F flexible cystoscope, following AUS deactivation, in all cases. In the event that a biopsy or tumor resection was necessary, this was performed with the smallest rigid cystoscope feasible. The AUS device was immediately activated after cystoscopy. For cold cup biopsies a 21F rigid cystoscope was used, while transurethral resection procedures were performed with a 24F sheath, introduced under direct vision. Based on the degree of hematuria after resection, the smallest possible urethral catheter was placed following all biopsy procedures. A 12-Fr urethral catheter was used for all bladder instillations. In our practice the AUS cuff is not removed for bladder resection procedures and is activated shortly after catheter removal.

Clinical characteristics were assessed including co-morbid conditions, bladder cancer related surgical interventions, and AUS characteristics including cuff size, laterality of reservoir balloon, and number of prior AUS interventions. In particular, we reviewed all procedures related to bladder cancer surveillance and treatment including cystoscopy, instillation of intravesical therapy, endoscopic biopsy or resection, AUS device management in the event that patient required cystectomy, and the functional status of the AUS device through their treatment course. The rates of all-cause re-intervention, erosion, infection, device malfunction, and urethral atrophy are described. Continuous variables were evaluated using the nonparametric Wilcoxon rank-sum tests; categorical variables were assessed with a Fischer's exact test. A p-value of <0.05 was considered statistically significant.

RESULTS

In total, 14 of 1,803 (0.8%) men undergoing AUS placement were subsequently diagnosed with bladder cancer between the years 1997–2014 and 4 (0.2%) underwent AUS placement after bladder cancer diagnosis between the years 2004–2011. Clinical and demographic features of these patients are shown in Table 1. Radical prostatectomy was the most common etiology for AUS placement (n=17, 94.4%) and 8 (44.4%) patients underwent radiation therapy following radical prostatectomy. The most common AUS cuff size implanted was 4.5 cm (n=16, 88.9%). At last follow-up, 12 (66.7%) patients in our cohort were still alive.

Characteristics associated with evaluation and treatment of bladder cancer are provided in Table 2. The median age

Table 1. Clinical characteristics of men with artificial urinary sphincter undergoing bladder cancer therapy

Characteristic	AUS and bladder cancer (n=18)
Etiology of incontinence	
Radical prostatectomy	17 (94.4)
Pelvic radiation therapy	8 (44.4)
Pelvic radiation and radical prostatectomy	8 (44.4)
Sacrectomy	1 (5.6)
Clinical characteristics	
Age at primary device implantation (y)	73 (67–78)
Body mass index (kg/m^2)	28 (25–30)
Diabetes mellitus	4 (22.2)
Anticoagulation	8 (44.4)
Tobacco use (current or prior)	13 (72.2)
Coronary artery disease	1 (5.6)
Chronic obstructive pulmonary disease	2 (11.1)
Hypertension	10 (55.6)
Prior transurethral resection of prostate	1 (5.6)
Vesicourethral anastomotic stricture	6 (33.3)
Androgen deprivation therapy	2 (11.1)
Prior urethral collagen injection	2 (11.1)
Prior urethral sling	2 (11.1)
Primary AUS urethral cuff size (cm)	
3.5	1 (5.6)
4	1 (5.6)
4.5	16 (88.9)
Secondary AUS urethral cuff size (cm)	
3.5	1 (5.6)
4.5	4 (22.2)

Values are presented as number (%) or median (interquartile range).
AUS, artificial urinary sphincter.

Table 2. Bladder cancer surveillance and treatment characteristics among men with *in situ* artificial urinary sphincter

Variable	Value
Age at bladder cancer diagnosis (y)	76 (72–86)
AUS implantation prior to UC Dx	14 (77.8)
Years from AUS implantation to UC Dx	6 (0–9)
AUS implantation after UC Dx	4 (22.2)
Years from UC Dx to AUS implantation	6 (3–8)
Treatment modalities in patients with intact AUS	
Flexible cystoscopies per patient	2 (1–6)
Mean±SD	4±5
TURBT per patient	0 (0–0)
Mean±SD	0±0
CBF per patient	1 (0–1)
Mean±SD	1±2
BCG instillations per patient	0 (0–2)
Mean±SD	3±6
Cystectomies in patient with intact AUS	4 (22.2)
AUS explantation with cystectomy	3 (16.7)

Values are presented as median (interquartile range), number (%), or mean±standard deviation
AUS, artificial urinary sphincter; UC, urothelial carcinoma; Dx, diagnosis; SD, standard deviation; TURBT, transurethral resection of bladder tumor; CBF, cystoscopy with biopsy and fulguration; BCG, bacillus Calmette-Guérin.

at AUS implantation among patients in this cohort was 73 years (interquartile range [IQR], 67–78 years). Among the 14 patients (77.8%) who underwent AUS implantation prior to bladder cancer diagnosis, the median time from AUS implantation to urothelial carcinoma diagnosis was 6 years (IQR, 0–9 years) and the median age at cancer diagnosis was 76 years (IQR, 72–86). Among the 4 patients (22.2%) who underwent AUS implantation after the diagnosis of bladder cancer and continued to receive cancer treatment and screening following AUS device placement, the median time from diagnosis to device implantation was 6 years (IQR, 3–8). The median number of flexible cystoscopies per patient with an intact AUS device was 2 (IQR, 1–6), transurethral resection of bladder tumor (TURBT) 0 (IQR, 0–0), cystoscopy with biopsy and fulguration (CBF) 1 (IQR, 0–1), and bacillus Calmette-Guérin instillations 0 (IQR, 0–2).

The median follow-up after AUS placement was 7.2 years (IQR, 2.8–11.5 years) during which time a total of 8 primary AUS device related adverse events occurred and 8 AUS revision procedures were performed. Two revision procedures for mechanical failure of the AUS device took place prior to the diagnosis of urothelial carcinoma. Of primary devices requiring revision after urothelial cancer diagnosis, 2 (11.1%) underwent revision for mechanical failure (median, 6.4 years), 1 (5.6%) for urethral atrophy (2 years), 2 (11.1%) for erosion/infection (median, 3.5 years), and 1 (5.6%) for hematoma formation (3 months). Only one patient (7.1%) required a tertiary device due to mechanical failure without subsequent AUS complication.

In this case series, there was no relationship between AUS adverse events and the number or type of urethral instrumentations among patients with and without an adverse AUS event (Table 3). Only 1 (5.6%) patient experienced an AUS complication directly related to the treatment of urothelial carcinoma. This was due to a traumatic urethral catheterization across an activated AUS device resulting in urethral erosion. One other patient (5.6%) in our cohort experienced urethral erosion after primary device placement, which occurred 1 month after initial placement of the device. This patient received external beam radiation for carcinoma of the prostate one year prior to placement of the device, and underwent no urethral manipulations for bladder cancer in the time between

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Table 3. Clinical characteristics stratified by any-cause adverse AUS event

Characteristic	AUS re-intervention (n=8)	No AUS re-intervention (n=10)	p-value
Transurethral instrumentations	3 (0.75–21)	4 (1.75–18.75)	0.37
Mean±SD	10±10	8.6±8.9	0.75
Flexible cystoscopies	2 (1.5–3.5)	2 (1–4)	0.40
Mean±SD	4.7±6.6	3.9±3.4	0.74
TURBT	0 (0–0)	0 (0–0)	0.96
Mean±SD	0.3±0.7	0.2±0.6	0.74
CBF	0 (0–1)	1 (0–1.25)	0.18
Mean±SD	1.1±2.4	1.6±1.9	0.62
BCG	0 (0–0)	0 (0–1.5)	0.66
Mean±SD	3.7±7.1	2.9±5.6	0.80
Cystectomy	4 (50.0)	1 (10.0)	0.06
Traumatic catheterization	1 (12.5)	0 (0.0)	0.27

Values are presented as median (interquartile range), mean±standard deviation, or number (%).
AUS, artificial urinary sphincter; SD, standard deviation; TURBT, transurethral resection of bladder tumor; CBF, cystoscopy with biopsy and fulguration; BCG, bacillus Calmette-Guérin.

placement of the device and removal. Of the 4 cystectomies performed on patients with an intact AUS device, 3 of those patients had their AUS devices explanted for reasons unrelated to device failure or device associated complications. The one patient with an AUS device left in-situ following cystectomy experienced no subsequent component related complications (Supplemental Table 1).

DISCUSSION

In a retrospective database review of a large series of men undergoing AUS procedures, we noted a ≈1% incidence of bladder cancer. In this small case series of 18 men, we found no evidence suggesting that careful urethral instrumentation for the diagnosis and treatment of bladder cancer contributes to AUS device related adverse events. Specifically, there was no difference in the number of urethral manipulations among men with and without an adverse AUS event. Additionally, the rate of AUS re-intervention in this cohort (33%) was similar to other reported series in those without bladder cancer (37%) [3].

Importantly, we emphasize the need for judicious and careful urethral instrumentation in the setting of concurrent AUS device implantation, as this poses the theoretical risk for complications such as iatrogenic urethral erosion, mechanical failure of the device, and infection resulting in device failure and urethral complications [11]. This is best illustrated by the one patient in our cohort who experienced traumatic urethral erosion as a direct consequence of catheterization across an activated device for gross hematuria as a consequence of bladder cancer treatment. The risk of this devastating complication can be mitigated with patient and provider education regarding the delicate nature of the AUS device, proper AUS deactivation prior to urethral instrumentation, use of the smallest catheter possible (12 Fr), and minimization of catheterization time to <48 hours [8].

While some have proposed a staged approach for any AUS placement and concomitant aggressive transurethral manipulation for the treatment of recalcitrant bladder neck contracture or bladder tumor resection [12,13], we have found that the removal of the AUS urethral cuff prior to manipulation is often unnecessary. In our experience, when possible, iatrogenic urethral injury can be mitigated with the use of small caliber resectoscopes. However, in the event that there is a large tumor burden which may require repetitive aggressive interventions, we would caution against AUS placement until there is evidence of disease control. In the event that an AUS has previously been placed, clinicians should educate patients regarding the risk of such transurethral interventions.

Do we need to remove all AUS device components at the time of cystectomy; evidence would suggest that this is not the case. Although infrequent, in the setting of an existing AUS, some patients may require urinary diversion for end-stage bladder as a consequence of pelvic radiation related complications or for bladder cancer. To our knowledge, this is the first study to address this complex question.

In our series, of 4 patients undergoing cystectomy with an intact AUS device, 3 had complete removal at the time of cystectomy and 1 patient had the AUS cuff left in situ without complication. A "drain and retain" approach appears to be safe in the setting of an uncompromised device without evidence of urethral erosion or infection. In a large

series of 120 re-operative urinary prosthetic cases, Cefalu et al. [14] demonstrated no difference in complication rates among those with retained defunctionalized components. Accordingly, in the majority of men, we would propose that leaving a deactivated AUS cuff in situ at the time of cystectomy should be considered as it minimizes the morbidity associated with prolonged cystectomy operative times, the high lithotomy position, and a separate perineal incision.

This is a retrospective review of a large AUS database from a single tertiary referral institution. The frequency and applicability of these findings may not be generalizable to other practices with a low volume of AUS procedures. As this is a limited case series, it is difficult to draw definitive conclusions regarding the safety of repetitive endoscopic urethral manipulation with an indwelling AUS. Pending further investigation, we believe that these findings highlight the need for awareness and education regarding the careful and judicious manipulation of a fragile AUS system, and its potential complications, in the setting of concomitant bladder cancer.

CONCLUSIONS

Bladder cancer surveillance and treatment following AUS device placement appears to confer minimal additional risk to AUS survival. Deactivation of the device prior to instrumentation and use of small caliber instruments appears to mitigate the risk of traumatic urethral erosion.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

SUPPLEMENTARY MATERIAL

Scan this QR code to see the supplementary material, or visit https://www.icurology.org/src/sm/icurology-59-44-s001.pdf.

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