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The "Fragile" Urethra as a Predictor of Early Artificial Urinary Sphincter Erosion

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OBJECTIVES To identify predictors of early artificial sphincter (AUS) erosion among a cohort of men with erosion, who underwent AUS placement by either university or community-based surgeons.

METHODS The records of all patients with AUS erosions, including men who underwent AUS placement at outside facilities, were retrospectively reviewed. A Cox proportional-hazards model for time to erosion was performed with the predictors being the components of a fragile urethra (history of radiation, prior AUS, prior urethroplasty), androgen deprivation therapy (ADT), trans-corporal (TC), and 3.5 cm cuff, controlling for other risk factors. Kaplan-Meier survival curves and log-rank test compared "fragile" urethras with "not fragile" urethras. All statistical analysis was done using R version 3.5.2.

RESULTS Of the 156 men included, 36% had undergone AUS placement in the community. Median time to erosion was 16.0 months (1.0-240.0 months), and 122 (78%) met at least one fragility criteria. Radiation (HR 2.36, 95% CI 1.52-3.64) and prior urethroplasty (HR 2.12, 95% CI 1.18-3.80) were independently associated with earlier time to erosion. The Kaplan-Meier estimates demonstrate 1- and 5-year survival rates of 76.5% and 50.0%, respectively, for "non-fragile" and 44.1% and 14.8% for "fragile" urethras ($P < .0001$).

CONCLUSION In a diverse cohort of men with AUS erosion, men with "fragile" urethras eroded sooner. Radiation and prior urethroplasty were independent risk factors for earlier time to erosion, but prior AUS, ADT, TC and 3.5 cm cuff were not. UROLOGY 169: 233−236, 2022.

The artificial urinary sphincter (AUS) is the gold standard for treatment of moderate to severe male stress urinary incontinence (SUI), particularly in men who have undergone radical prostatectomy for prostate cancer. As prostate cancer survival continues to improve and new treatments are made available, more emphasis has been placed on improving the quality of life outcomes.

Patient satisfaction with this device is high, despite a 25%-45% rate of device revision.[1,2] There are several known complications associated with the AUS including erosion, urethral atrophy, infection, and mechanical failure. Urethral cuff erosion occurs in approximately 2%-15% of patients and necessitates device removal.[2,3] Various mechanisms contributing to erosion have been proposed, including iatrogenic urethral injury at the time of AUS placement, poor urethral tissue quality, urethral necrosis from tissue ischemia, or traumatic catheterization.

Some have described patients with "fragile" urethras, defined as a history of pelvic radiation, previously failed AUS, or prior urethroplasty, to be more likely to experience cuff erosion.[4] Other previously described risk factors include androgen deprivation therapy (ADT), and 3.5 cm cuff size.[5,6] Additionally, transcorporal cuff placement has been shown to have higher rates of erosion;[7] however, a recent paper suggests that transcorporal placement may actually be protective in patients with fragile urethras.[8]

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In most studies aiming to characterize risk factors for erosion, data is acquired from large tertiary care, university centers, and referral bias may skew findings. There are many community-based urologists who perform AUS placement and outcomes from patients seeking care from these surgeons have not previously been reported.[9,10] Our primary aim is to identify predictors of early device erosion amongst a more representative sample of men with AUS erosion who underwent AUS placement from either a university or community-based urologist. Additionally, we examine location of cuff erosion to determine if this is influenced by time-to-erosion; we hypothesize that dorsal erosions may occur earlier due to iatrogenic urethral injury during dissection.

METHODS

This was a multi-institutional retrospective review of patients who underwent AUS explant at 6 university institutions across the United States for cuff erosion. While all explants were performed by the university surgeons, the original devices were placed by the university or community surgeons. Patient characteristics, including age, comorbidities, history of radiation or ADT, cuff placement technique (standard vs trans-corporal, single vs tandem cuffs), cuff size, prior urethroplasty, device infection, history of catheter trauma, and center where the device was originally placed (university vs community) were obtained from the medical record through chart review. Additionally, the location of the urethral erosion (dorsal, ventral, lateral, circumferential, etc.) was recorded.

A Cox proportional-hazards model predicting time to erosion was performed in which the predictors of interest were the components of a fragile urethra (history of pelvic radiation, prior AUS placement, history of urethroplasty) as well as ADT, transcorporal and 3.5 cm cuff, while controlling for demographics and other previously described risk factors. Kaplan-Meier survival curves and log-rank test compared fragile and non-fragile urethras. All statistical analyses were performed using R version 3.5.2. Statistical significance was set at $P < .05$. Chi-square analysis was used to examine the relationship between erosion location and time to erosion (early vs late); early erosion was defined as <3 months after cuff placement.

RESULTS

We identified 156 men with AUS erosion who underwent device explant at 6 university hospitals across the United States. The mean patient age was 74.1 years (standard deviation (SD) 10.0), and the mean body mass index was 28.2 kg/m^2 (SD 5.1). Diabetes was present in 43 (28%) and 14 (9%) were current tobacco users. Most (122, 78%) of our patients met at least 1 criterion for having a fragile urethra: 101 (65%) had a history of pelvic radiation, 18 (12%) had a prior urethroplasty, and 51 (33%) had a prior failed AUS; 46 (29%) patients met more than one criteria. Fifty-nine (38%) patients received ADT. Most patients (66%) had a 4.0 or 4.5 cm cuff size and only 10% had a 3.5 cm cuff. Among our patients with tandem cuffs, distal and proximal cuffs were the same size in every case for which measurements were available; for clarity we chose to report only the proximal measurement.

The majority of AUS placements were performed by the university-based surgeons (63%), while 36% were placed by the surgeons at outside institutions. Forty-nine (31%) patients had device infection, and 31 (20%) patients had a documented history of catheter trauma prior to erosion (Table 1).

By nature of the way we designed the study, 100% of patients had cuff erosion; the median time from cuff placement to erosion was 16.0 months (range: 1.0-240.0 months). Patients who met one or more criteria for having a fragile urethra eroded sooner than patients without any fragility factors (12.5 months vs 59.5 months). The Kaplan-Meier estimates for AUS survival time by

Table 1. Demographic information for AUS explants performed at six university hospitals

Characteristics	N = 156
Age (Mean ± SD)	74.1 ± 10.0
BMI (Mean ± SD)	28.2 ± 5.1
Diabetes (N, %)	43 (28%)
Active Smoking (N, %)	14 (9%)
History of pelvic radiation (N, %)	101 (65%)
History of ADT (N, %)	59 (38%)
History of urethroplasty (N, %)	18 (12%)
First time AUS (N, %)	105 (67%)
Single cuff AUS (N, %)	146 (94%)
Missing	1 (1%)
Cuff Size (cm) for *single* or *proximal* tandem cuff * (N, %)- 166 cuffs	
3.5	16 (10%)
4.0	63 (41%)
4.5	39 (25%)
5.0	12 (8%)
5.5	1 (1%)
6.0	1 (1%)
Missing	23 (17%)
Transcorporal (N, %)	40 (25%)
Missing	11 (7%)
University surgeon placement (N, %)	99 (63%)
Missing	1 (1%)
Location of erosion for *single cuff* (N, %)- 146 cuffs	
Dorsal	40 (27%)
Ventral	45 (31%)
Lateral	36 (25%)
Circumferential	28 (19%)
Multiple sites	12 (8%)
Unspecified	11 (8%)
Location of erosion for *proximal* tandem cuff (N, %)- 9 cuffs	
Dorsal	0 (0%)
Ventral	2 (22%)
Lateral	1 (11%)
Circumferential	1 (11%)
Multiple sites	0 (0%)
Unspecified	5 (56%)
Location of erosion for *distal* tandem cuff (N, %)- 6 cuffs	
Dorsal	1 (17%)
Ventral	0 (0%)
Lateral	0 (0%)
Circumferential	1 (17%)
Multiple sites	0 (0%)
Unspecified	4 (67%)
Device infection (N, %) missing	49 (31%) 3 (2%)
History of catheter trauma (N, %) missing	31 (20%) 3 (2%)

* Cuff size of single cuff OR more proximal cuff if tandem placement. All tandem cuffs in this study had the same proximal and distal cuff size.

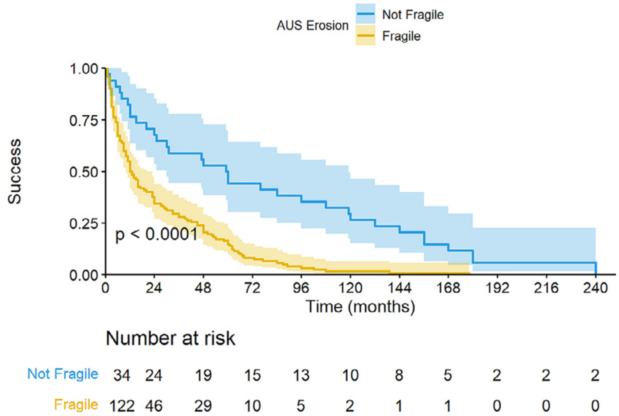

Figure 1. Kaplan-Meier Curves for fragile and non-fragile urethras. Failure is defined as device erosion. (Color version available online.)

Table 2. Predictors of early erosion based on Cox proportional hazards. Radiation and history of urethroplasty were significant predictors of earlier time to erosion

	Hazard Ratio	95% Confidence Interval	*P*-Value
Radiation	2.36	1.52-3.64	<.01*
Urethroplasty	2.12	1.18-3.80	.01*
ADT	1.01	0.65-1.55	.98
Re-do AUS	1.25	0.84-1.87	.27
Transcorporal	1.09	0.68-1.74	.72
Cuff size 3.5 cm	1.11	0.63-1.96	.71

cohort reveal survival rates of 50.0% and 76.5% at 1-year, and 14.8% and 44.1% at 5-year for fragile and non-fragile urethras respectively (P <.0001) (Fig. 1). Based on the Cox proportional hazards model, radiation (HR 2.36, 95% CI 1.52-3.64) and prior urethroplasty (HR 2.12, 95% CI 1.18-3.80) were independent predictors for earlier time to erosion (Table 2). Other factors, including prior AUS, ADT, transcorporal and 3.5 cm cuff were not predictors of time to erosion. The location of erosion (dorsal, ventral, lateral, etc.) was not associated with early erosion (Table 3).

DISCUSSION

The AUS is a highly effective treatment for moderate-to-severe male stress urinary incontinence but urethral cuff erosion remains a significant source of morbidity. Amongst a cohort of patients who had their AUS placed by either university-based or community-based surgeons and experienced device erosion, time-to-erosion was earlier amongst patients with fragile urethras. Specifically, patients with a history of pelvic radiation or prior urethroplasty eroded sooner. Other commonly cited erosion risk factors were not significant.

Table 3. Chi-square analysis comparing the relationship of early erosion to location of erosion. No significant association was found. Early explant was defined as <3 months after implant. For patients with tandem cuffs, if both cuffs eroded in the same location, this was counted as one erosion location

Location of Erosion	Early Explant	*P*-value
Dorsal (n = 41)	3 (12%)	.1458
Ventral (n = 47)	9 (36%)	.6452
Lateral (n = 37)	6 (24%)	1.0000
Circumferential (n = 29)	4 (16%)	.9341
Unspecified (n = 16)	3 (12%)	1.0000

Several studies have evaluated the longevity of the AUS and at risk factors for the *incidence* of erosion. We took a different approach here. In our study the incidence of erosion was 100% and we focused on how risk factors impacted the risk of *time to erosion*. A 10-year retrospective review of patients at a large tertiary center demonstrated a 64% ten-year device survival rate for primary AUS placement, with the majority of revision or replacement surgery occurring within the first 2 years.[11] In one cohort of 554 men undergoing primary AUS placement at a single institution, 21.4% of patients underwent device revision or replacement. That study demonstrated comparable 5-year survival between primary and secondary implants (80% and 88%, respectively); however, at 6.5 years, secondary implant survival decreased significantly. Of note, this cohort of patients had a very low rate of device erosion at 3.8%.[12]

McGeady et al was the first to describe (1) history of radiation, (2) prior AUS, and (3) history of urethroplasty as predictors of AUS failure, and more specifically, device erosion or infection.[13] Hoy and colleagues later used these predictors to create the definition of a fragile urethra.[4] Risk factors for erosion amongst patients with prior AUS placement has been debated. A cohort study by Lai and Boone demonstrated a 4-fold increased the risk of urethral cuff erosion in secondary implants, while other device complications (infection, mechanical failure, and leaks) were not significantly increased.[14] However, in a larger, more recent prospective study, history of prior AUS infection or erosion was not a statistically significant predictor of requiring future device explantation (13.33% vs 7.43%; P = .06).[6] This agrees with the findings of our study where only a history of radiation and prior urethroplasty were predictive of early device erosion. Radiation is theorized to cause small vessel fibrosis and urethral atrophy which may be implicated in increasing the risk of cuff erosion amongst patients with a history of pelvic radiation.[15] In a cohort of post-prostatectomy patients with AUS, adjuvant radiation therapy significantly increased the risk of erosion or infection (HR = 4.48, P = .03).[16] In a prospective, multi-institutional study, patients with the radiation therapy were more likely to require device removal (15.94% vs 3.63%; P <.001).[6] Additionally, those with a history of radiation and urethral compromise (prior stricture, sling, or bladder neck contracture) had poor 5-year revision-free survival compared to patients with urethral compromise and no radiation history (22.4% vs 60.8%).[14] In all of the above studies, survival curves include patients who never required explant. In our cohort, where all participants eventually experienced cuff erosion, short-term survival rates appear much lower than prior studies, where the median time to erosion for all patients was 16.0 month and the 5-year survival was 44.1% and 14.8% for non-fragile and fragile urethras, respectively.

Location of cuff erosion was not associated with the early erosion. Our cohort had a relatively even distribution of dorsal, ventral, and lateral erosions. In a recent retrospective case series from Ortiz et al, dorsal erosions occurred at a much lower rate than ventral erosions, among both trans-corporal and standard AUS placements.[17] This case series was based on a single surgeon experience and may indicate that specific surgeon technique influences the location of device erosion.

The majority of studies evaluating the various risk factors for AUS erosion are from small, single-center retrospective cohort studies, including patients from university or large tertiary care centers. Although these data are valuable, there is a significant risk of referral bias; often patients from the community who are seen as "high risk" or medically complex may seek care or are referred for care at university centers. Previous data has found that only 13% of urologists perform AUS placements and only 4% perform more than 20 cases per year. Moreover, 92% of surgeons performing AUS placements report a case volume of $\leq$5 per year.[18] Outcomes are often better at higher volume surgical centers.[19] Our cohort is unique in that 36% of patients underwent original AUS placement at an outside facility and therefore our cohort may be more representative of all AUS patients.

Our study has several limitations. Most notable is the retrospective nature. Additionally, our study included only 156 patients, however 100% of patients experienced urethral erosion and were included in our analysis, making this study the largest analysis of patients with device erosion to-date. The original definition of the fragile urethra included cystoscopic evidence of urethral atrophy as an additional criterion. This finding could not be reliably quantified in our study due to the multi-institutional nature and variability of cystoscopy documentation and use amongst providers and, therefore, was not included in our analysis. Additionally, our database did not capture the specific indication for initial AUS removal in re-do cases. It is possible that prior AUS cuff erosion may predict for future cuff erosion, but devices removed for other reasons (mechanical failure, pump erosion, etc.) may not. This could also explain why prior AUS was not significantly predictive of earlier erosion. Lastly, given our multi-institutional study design as well as our inclusion of 36% of patients who received their index surgery at an outside institution, there may be variation in surgeon technique amongst sites which could not be accounted for.

CONCLUSION

Our multi-institutional retrospective cohort study includes patients undergoing AUS placement at either university- or community-based hospitals. We demonstrate that amongst patients who experienced AUS erosion, history of pelvic radiation and history of prior urethroplasty were predictive of early erosion. Patients who met criteria for having a "fragile" urethra experienced significantly shorter 1- and 5-year device survival rates.

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