Title

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Journal

Investigative Urology, 204(1)

ISSN

0021-0005

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Publication Date

2020-07-01

DOI

10.1097/ju.0000000000000749

Peer reviewed

Outcomes and Risk Factors of Revision and Replacement Artificial Urinary Sphincter Implantation in Radiated and Nonradiated Cases

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Abbreviations and Acronyms

AUS = artificial urinary sphincter

TC = transcorporal

XRT = radiation

Accepted for publication January 2, 2020.

No direct or indirect commercial, personal, academic, political, religious or ethical incentive is associated with publishing this article.

* Financial interest and/or other relationship with Boston Scientific.

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Editor's Note: This article is the fifth of 5 published in this issue for which category 1 CME credits can be earned. Instructions for obtaining credits are given with the questions on pages 194 and 195.

Purpose: Risk factors for complications after artificial urinary sphincter surgery include a history of pelvic radiation and prior artificial urinary sphincter complication. The survival of a second artificial urinary sphincter in the setting of prior device complication and radiation is not well described. We report the survival of redo artificial urinary sphincter surgery and identify risk factors for repeat complications.

Materials and Methods: A multi-institutional database was queried for redo artificial urinary sphincter surgeries. The primary outcome was median survival of a second and third artificial urinary sphincter in radiated and nonradiated cases. A Cox proportional hazards survival analysis was performed to identify additional patient and surgery risk factors.

Results: Median time to explantation of the initial artificial urinary sphincter in radiated (150) and nonradiated (174) cases was 26.4 and 35.6 months, respectively ($p=0.043$). For a second device median time to explantation was 30.1 and 38.7 months ($p=0.034$) and for a third device it was 28.5 and 30.6 months ($p=0.020$), respectively. The 5-year revision-free survival for patients undergoing a second artificial urinary sphincter surgery with no risk factors, history of radiation, history of urethroplasty, and history of radiation and urethroplasty were 83.1%, 72.6%, 63.9% and 46%, respectively.

Conclusions: Patients without additional risk factors undergoing second and third artificial urinary sphincter surgeries experience revision-free rates similar to those of their initial artificial urinary sphincter devices. Patients who have been treated with pelvic radiation have earlier artificial urinary sphincter complications. When multiple risk factors exist, revision-free rates decrease significantly.

Key Words: urinary sphincter, artificial; urinary incontinence; radiotherapy; reoperation; prostatic neoplasms

Stress urinary incontinence is a well described complication of radical prostatectomy. The gold standard treatment for moderate to severe incontinence after prostatectomy is placement of an artificial urinary sphincter. Complications of AUS surgery include urethral erosion,

0022-5347/20/2041-0110/0
THE JOURNAL OF UROLOGY®
https://doi.org/10.1097/JU.0000000000000749
Vol. 204, 110-114, July 2020
Printed in U.S.A.

infection, urethral atrophy and device malfunction. Depending on the complication, appropriate management strategies include device revision, explantation with simultaneous reimplantation or explantation with reimplantation after a period of observation. Patient reported quality of life outcomes support the value of primary AUS placement and redo surgery.[1,2]

Many candidates for AUS placement have undergone pelvic radiation as primary treatment of prostate cancer or in the adjuvant or salvage settings. Radiation therapy for prostate cancer has been shown to increase the risk of AUS cuff erosion.[3–8] Prior cuff erosion in the absence of radiation also increases patient risk of cuff erosion if a second AUS is placed.[4,5,9–11] However, given the lack of alternative surgical options for continence after an AUS has eroded, devices are often reinserted once the urethra has healed.

Few studies report on redo artificial urinary sphincter surgery in patients with a history of pelvic radiation. Specifically, it is not known whether the independent risk factors of pelvic radiation and redo AUS surgery compound to make reimplantation especially hazardous and prohibitive to perform. Known risk factors for a first AUS such as a history of urethroplasty and surgical technique, including the transcorporal approach, have also not been evaluated rigorously in the redo setting.

In the current study we evaluate the outcomes of revision or replacement AUS surgery in radiated and nonradiated cases from a large multi-institutional, multi-surgeon database. We hypothesized that patients with a history of radiation for prostate cancer and prior AUS complication would experience a higher rate of complications and shorter revision-free survival after redo surgery. The primary outcome was time to cuff revision or device explantation of a second and third AUS.

MATERIALS AND METHODS

Study Population

The multi-institutional institutional review board approved TURNS (Trauma and Urologic Reconstructive Network of Surgeons) database was queried for redo AUS surgeries, defined as cuff revision or complete device replacement, from 2008 to 2018. The cohort was subdivided by those who had been treated with primary or post-prostatectomy radiation for prostate cancer and those who had not received radiotherapy.

Patient demographics, radiation history and other previously identified risk factors for AUS complications were collected. Surgical technique, including use of a transcorporal approach and cuff size, was collected for each device implanted. All surgeons commonly perform the standard and transcorporal approach. AUS complications were categorized as tissue based, which includes infection, urethral atrophy and cuff erosion, or mechanical malfunction.

Statistical Analysis

Median survival and interquartile ranges were calculated for radiated and nonradiated cases for initial, second and third AUS. Comparisons were made by Kruskal-Wallis log rank testing for median survival and followup, and by chi-square testing for categorical variables, with $p < 0.05$ considered significant.

Survival analyses were conducted using the time from device implantation to device explantation for devices that failed, and the time from device implantation to the end of the study period for devices that did not fail. We performed separate survival analyses for each successive AUS surgery, as we hypothesized that each surgery contributes an additional element of risk. To limit bias secondary to technical issues around device implantation, we excluded patients with mechanical device failure from the secondary analysis, only including those with tissue based reasons for explantation.

A univariate analysis of previously identified risk factors of AUS complications was conducted. Evaluated risk factors include prior UroLume® stent placement, prior endoscopic intervention for stricture, history of urethroplasty, history of smoking, diabetes mellitus, systemic corticosteroid use and coronary artery disease. A univariate analysis was also used to evaluate surgical factors including cuff size and transcorporal cuff placement. Cuff size was defined as a categorical variable with 3.5, 4, 4.5 and 5.0+ cm cuff sizes.

Risk factors identified on univariate analysis with $p < 0.25$ were included in multivariable analysis. A Cox proportional hazards model was fit with significant predictors. No interaction terms between the predictors were significant in the model and, thus, none was included in the final model. A 4 cm cuff and standard placement were used as the referent value in the Cox proportional hazard model for evaluation of cuff size and transcorporal placement. We graphed the estimated survival function for predictors of AUS complication based on the multivariable models created for the second and third AUS surgeries. All statistical analyses were completed with Stata® version 13.1.

RESULTS

A total of 324 patients underwent cuff revision or device replacement, 150 of whom had received primary, adjuvant or salvage radiation for prostate cancer. The number of initial surgeries from which this group was collected is not known as the participating centers are largely referral centers that perform a higher proportion of revision or redo surgeries.

Median time to explantation of initial AUS was significantly shorter in the radiation group compared to the no radiation group (26.4 vs 35.6 months, $p = 0.043$). This held true after a second AUS surgery (30.1 vs 38.7 months, $p = 0.034$) but not after a third AUS surgery (28.5 vs 30.6 months,

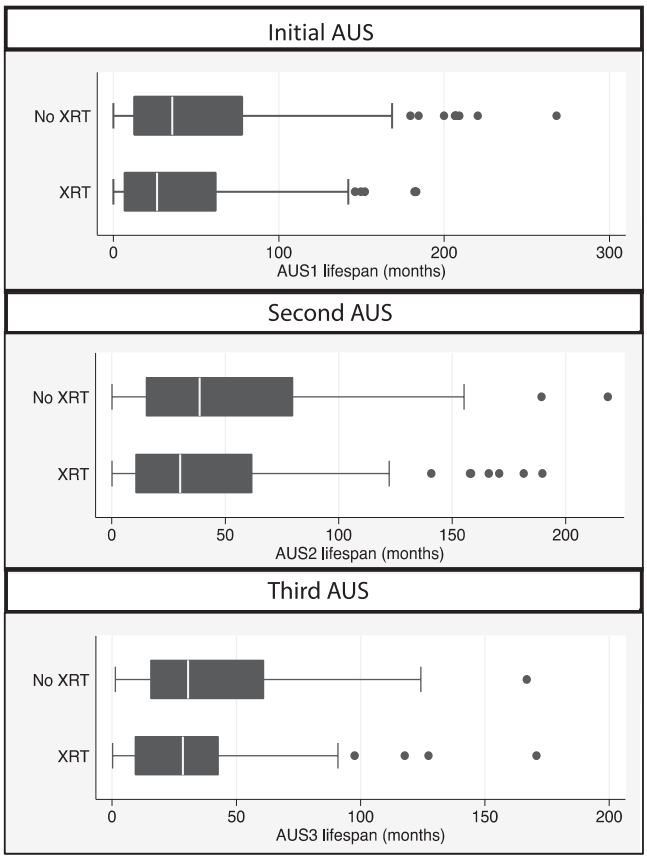

Figure 1. Box plots describing survival of initial, second and third AUS in radiated and nonradiated cases. Solid gray boxes represent IQR of AUS survival. White line is AUS median survival. Bars extending from gray IQR boxes represent 5% and 95% limits of AUS survival while dots beyond these limits are outliers.

p = 0.20). Median device survival of a second AUS was not significantly different from that of reported initial AUS survival in the radiated and nonradiated groups (fig. 1 and supplementary table, https://www.jurology.com).

Compared to nonradiated cases, the initial AUS explantation or cuff revision in radiated cases was more likely to be due to a biological reason including infection, erosion or atrophy rather than mechanical malfunction (p = 0.012). When the biological reasons for AUS complication were evaluated separately, only erosion was more common in the radiated group (p = 0.049). There was no statistical difference in etiology of device explantation for a second or third AUS (supplementary table, https://www.jurology.com).

On univariate analysis history of radiation, history of urethroplasty, cuff size and transcorporal cuff placement (at third AUS surgery) were associated with shorter device survival and were included in a multivariable analysis. After correcting for covariates, multivariable analysis via Cox proportional hazards estimation demonstrated increased risk of device failure for radiation history (second AUS), urethroplasty (first and second AUS), smaller cuff size (first, second and third AUS) and transcorporal cuff placement (third AUS) (see table).

When adjusted for covariates the estimated 5 and 10-year revision-free survival rate for a second AUS in a patient with no risk factors and a 4 cm cuff size was 83.1% and 71.9%, respectively (fig. 2, *A*). Patients with a history of pelvic radiation for prostate cancer had a reduced 5 and 10-year revision-free survival rate of 72.6% and 56.4%, respectively. Those patients who had undergone urethroplasty had an even further reduced 5 and 10-year survival rate of 63.9% and 44.9%, respectively. Finally, those patients with risk factors of pelvic radiation and prior urethroplasty had 5 and 10-year survival rates of 46.0% and 24.9%, respectively.

The estimates of revision-free survival based on the multivariable model for a third AUS and no risk factors and a 4 cm cuff were 97.9% and 87.3% at 5 and 10 years, respectively (fig. 2, *B*). Those patients with an added risk factor of XRT had 5 and 10-year revision-free survival rates of 94.8% and 71.3%, respectively. Patients with TC cuff placement

Risk adjusted Cox proportional hazard multivariable analysis of AUS surgical risk factors for device explantation

	HR (95% CI)	p Value
	Initial AUS (117)	
History of XRT:		
Yes	1.38 (0.95–2.03)	0.095
No	Referent	
History of urethroplasty:		
Yes	2.12 (1.09–4.13)	0.027
No	Referent	
Cuff size (cm):		0.0081
3.5	2.71 (1.44–5.13)	
4.0	Referent	
4.5	0.89 (0.58–1.38)	
5.0+	0.96 (0.54–1.73)	
	Second AUS (223)	
History of XRT:		
Yes	1.74 (1.06–2.84)	0.029
No	Referent	
History of urethroplasty:		
Yes	2.43 (1.14–5.17)	0.022
No	Referent	
Cuff size (cm):		0.001
3.5	3.37 (1.60–7.13)	
4.0	Referent	
4.5	0.75 (0.38–1.50)	
5.0+	1.92 (1.03–3.58)	
	Third AUS (82)	
History of XRT:		
Yes	2.49 (0.92–5.24)	0.039
No	Referent	
Cuff size (cm):		0.005
3.5	24.0 (3.21–180)	
4.0	Referent	
4.5	1.50 (0.319–7.06)	
5.0+	5.12 (1.34–19.6)	
TC cuff placement:		
Yes	2.93 (0.99–8.70)	0.053
No	Referent	

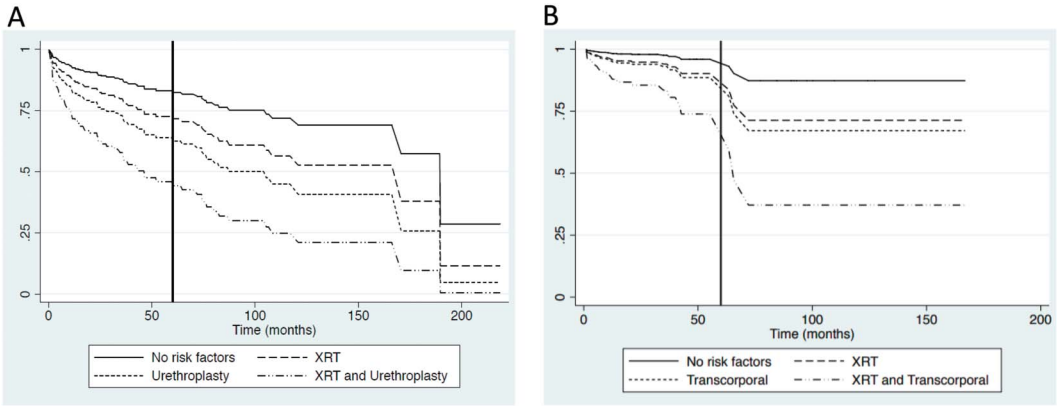

Figure 2. Adjusted survival of second (*A*) and third (*B*) AUS based on Cox regressions of risk factors identified on univariate analysis and included in multivariable model. Curves are for standard 4 cm cuff. Solid vertical line is at 60 months for reference.

experienced 93.9% and 67.2% revision-free survival at 5 and 10 years, while patients with XRT history and TC cuff placement had revision-free survival of 85.5% and 37.1% at 5 and 10 years, respectively. The high revision-free survival rates for third AUS is a reflection of limited followup of this subset, intrinsic to a study following the natural history of successive revision surgeries, and should be interpreted with caution.

DISCUSSION

AUS complications occur more frequently in patients with tissue that has been compromised by surgery or who have a systemic disease that affects wound healing or vascularity. Previously identified factors include prior UroLume stent placement, prior urethroplasty, smoking, diabetes mellitus and coronary artery disease.[4,5,9,12,13]

There is a strong mechanistic basis for increased risk of AUS complications in patients with a history of pelvic radiation. Radiation causes progressive local fibrosis and endarteritis, which leads to avascularity and decreased capacity for tissue healing and fighting infection. A preponderance of studies has confirmed that a history of radiation is an independent risk factor for AUS erosion.[3,5,6,14–16] However, there are no prospective randomized trials to inform definitively on the issue. Prior AUS cuff erosion or device infection similarly creates local fibrotic tissue that is lacking in robust vascularity, portending a likelihood of repeat erosion.

It had been previously unknown whether a combination of prior AUS complication and history of radiation makes repeat AUS surgery prohibitively hazardous. The present data do not support that notion. Patients who required device removal without a history of radiation had a median survival of 35.6 months for the initial AUS and 38.7 months for a second AUS. Those with a history of radiation who required device removal had a median survival of 26.4 and 30.1 months for an initial and second AUS, respectively. Although complications occur earlier and are more likely from biological reasons vs mechanical malfunction in the radiated case, the survival of a second device is similar to that of an initial device in both settings. Our data suggest that a patient treated with radiation who previously experienced an AUS complication can be offered a second device with the expectation of a similar replacement-free survival as their initial device.

History of urethroplasty and small cuff size are additional factors that contribute to device complication and should be considered in a risk assessment conducted before repeat AUS surgery. A history of urethroplasty and radiation also appears to compound as seen in the estimated survival curves adjusted for significant covariates (fig. 2). Counseling for those patients considering a second AUS can now include a risk stratified approach based on these data. The 5-year revision-free survival for patients given a 4 cm cuff with no risk factors, history of radiation, history of urethroplasty, and a history of radiation and urethroplasty is 83.1%, 72.6%, 63.9% and 46%, respectively.

Survival in the case of the third AUS is likely inflated by the limited followup for these devices as they were often placed late in the study period and complications requiring removal had not yet occurred. However, the trend is similar as seen for a second AUS. Radiation places the patient at increased risk for erosion and additional risk factors compound. In the case of the third AUS an identified risk factor was use of a transcorporal technique.

The most common technique used to mitigate the risk of AUS erosion in the setting of prior pelvic radiation or previous AUS complication is transcorporal placement, in which the tunica albuginea is

interposed between the urethra and AUS cuff on the vulnerable dorsal aspect of the urethra. Despite the logic of a transcorporal approach, there has not been convincing efficacy in the literature. Randomized prospective data do not exist in this arena and retrospective data do not show superiority of the transcorporal approach.[17–21]

Transcorporal placement was not associated with increased survival at the time of second AUS surgery in the studied cohort and it was identified as a risk factor for complication at the time of a third AUS, which most likely reflects a higher risk cohort (see table). This study does not answer the question on the utility of the transcorporal technique. Without a prospective randomized trial it is not possible to determine whether the technique is protective. Surgeon bias heavily dictates the surgical approach based on patient clinical parameters. Given the small number of patients receiving a third AUS the validity of the finding may be skewed, while there are other risk factors that may not be accounted for within our multivariable model.

The limitations of the study include the lack of randomization. In a nonrandomized fashion it is difficult to assert a given surgical technique or cuff size used selectively based on clinical concern is protective or not against complication. Cuff size cannot be randomized as it is based on intraoperative measurement but a randomized trial of transcorporal placement would be useful in the future.

CONCLUSIONS

When no additional risk factors are present patients undergoing second and third AUS surgeries experience revision-free rates similar to those of initial AUS devices. Patients who have been treated with pelvic radiation have earlier AUS complications. However, overall revision-free rates remain high for second and third AUS placement. When multiple risk factors exist, revision-free rates decrease significantly. These data are helpful when counseling patients about the expected outcome of redo AUS surgery.

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