Artificial urinary sphincter erosion after radical prostatectomy in patients treated with and without radiation

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Abstract

Introduction: There has been increasing evidence supporting the use of adjuvant radiotherapy after radical prostatectomy (RP) for prostate cancer. Significant stress incontinence after RP is not uncommon and the artificial urinary sphincter (AUS) is the gold standard of treatment. Our objective was to assess if increased use of radiotherapy after RP has changed the rate of erosion and infection in the face of improvement in radiation technique and equipment in men who had an AUS implanted in the last 10 years.
Methods: We retrospectively examined 118 patients from December 2001 to January 2012 who underwent a RP with or without postoperative radiotherapy and subsequently had an AUS implanted. We divided the patients into two cohorts (Group 1: December 2001–December 2006 and Group 2: January 2007–January 2012). We reviewed all patient records for age, cuff size implanted, history of postoperative radiotherapy, previous incontinence surgery, revisions, and complications (erosion/infection).
Results: There were 36 and 82 patients in Groups 1 and 2, respectively. The mean age was similar between groups, 67 years both groups ($p = 0.980$). The number of patients treated with postoperative radiotherapy was similar between groups (36% vs. 32%, $p = 0.640$, respectively). There was no difference in the incidence of erosion or infection between Group 1 and 2 ($p = 0.848$ and $p = 0.178$, respectively). The overall relative risk (RR) of erosion was significantly higher in those who had radiotherapy compared to those who did not (RR 4.05, 95% confidence interval 1.1–15.3).
Conclusions: Over the last 10 years, there has not been an increase in the number of patients receiving an AUS after RP and radiotherapy at our centre. During this time, the incidence of erosion and infection has not increased. However, our study reaffirms that the relative risk of erosion remains higher in patients who have had radiotherapy despite improvement in radiation treatment techniques and equipment.

Introduction

Prostate cancer is a common disease, with an estimated 23 600 new cases anticipated in 2014 in Canada.[1] Definitive treatment can be achieved using many different modalities, including radiotherapy (external beam radiotherapy or brachytherapy), radical prostatectomy (RP), or can include active surveillance in certain carefully selected patients.

Over the last 10 years, however, there has been increasing evidence supporting the use of combination therapy for prostate cancer in the form of adjuvant radiation therapy after RP.[2-4] Radiotherapy is recommended in the adjuvant setting for patients with evidence of histopathologic disease extension beyond the prostate, positive microscopic lymph node involvement, or positive resection margins. It is also commonly employed following biochemical recurrence detected by routine post-prostatectomy prostate-specific antigen (PSA) monitoring. In both settings, the literature has demonstrated a favourable effect on local disease recurrence and possibly overall survival.[5,6]

Among patients who have been treated with RP, significant stress incontinence (SUI) is not uncommon. The incidence of SUI depends on the definition employed, the amount of time elapsed since surgery, patient age, and whether or not a nerve-sparing approach was used. Data suggest that the incidence of permanent SUI is between 5% and 66%.[7-10] However, both the incidence of SUI and the severity increase when radiotherapy is combined with surgical intervention. This is secondary to a combination of factors, including increased tissue ischemia and detrusor and interstitial fibrosis leading to reduced bladder compliance.[11,12]

The artificial urinary sphincter (AUS) is the gold standard of treatment for SUI with success rates ranging from 59% to 90%.[13] With the insertion of this device, erosion and infection are a primary concern. It has been well-documented that radiation exposure can increase the risk of AUS erosion.[11,14]

There has been an increased use of radiotherapy following RP over the last 10 years. Therefore, we analyzed whether there has been a concomitant change in the rate of erosion and infection in the face of improvement in radiation technique and equipment in men who underwent prostate cancer treatment and subsequently had an AUS device implanted during this time.

Methods

Ethics approval for this study was obtained from the hospital Research Ethics Board. We retrospectively examined patients who had an AUS (American Medical Systems, Inc.) device implanted over a 10-year period: from December 2001 to January 2012. We divided patients into two cohorts, each spanning 5 years: Group 1 included patients with AUS implantation between December 2001 and December 2006; and Group 2 between January 2007 and January 2012. Patients were included in the study if they had a pathological diagnosis of prostate cancer, underwent definitive treatment with RP (with or without postoperative radiation), and subsequently had an AUS device implanted for SUI. Patients were excluded if they underwent a surgical procedure other than RP. None of the patients deactivated their AUS during the night. No patients in this study received brachytherapy.

The primary outcome of this study was the incidence of complications following AUS implantation. Complications were defined as any evidence of erosion and/or any infection requiring removal of the device. Information collected for each patient also included age, date of RP, date of AUS implantation, cuff size implanted, history of postoperative radiation, previous incontinence surgery, as well as number and reason for revision(s).

Continuous data were reported as mean and categorical data reported as the number of patients with percentages. Categorical data were compared using the Chi-square test. Quantitative variables were compared using the Student's t-test or analysis of variance test. Results were considered significant at the 5% critical level (two-tailed, $p < 0.05$).

Results

A total of 126 patients with prostate cancer underwent AUS implantation between December 2001 and January 2012. We excluded 8 patients who underwent surgical interventions other than RP, leaving a total sample size of 118. There were 36 patients in Group 1 and 82 patients in Group 2 (Fig. 1). The mean age in both groups was the same: 67 years (Group 1 range: 52–82 and Group 2 range: 50–82, $p = 0.980$). The number of patients treated with postoperative radiation was similar between groups (36% vs. 32%, $p = 0.640$, respectively) (Table 1).

Of the 118 patients in our study group, 39 patients had adjuvant radiation therapy. In Group 1, 13 patients had adjuvant radiotherapy. Eight patients had 3D conformal radiation therapy (3D-CRT) (66 cGy, 33 fractions). We do not know the exact radiation dose given and type for the remaining 5 patients as radiation treatment was performed outside our institution and records to confirm radiation doses and type were not available. In these 13 patients, 2 patients had erosion and were both treated using 3D-CRT with 66 cGy, 33 fractions.

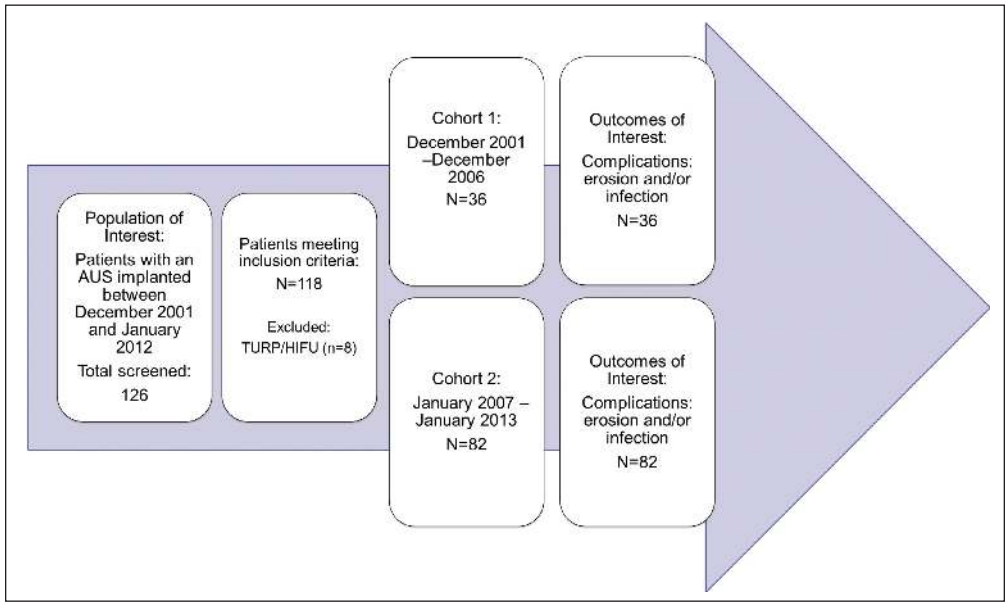

Fig. 1. Study population.

Table 1. Patient demographics

	Group 1	Group 2	*p* value
N	36	82	---
Mean age (years) (range)	67 (52-82)	67 (50-82)	0.980
Cuff size (%)			
3.5 cm	0	1	0.001
4.0 cm	5	39	
4.5 cm	26	40	
5.0 cm	5	2	
Prostatectomy alone (%)	23 (64)	56 (68)	0.640
Prostatectomy + RT (%)	13 (36)	26 (32)	
Previous incontinence surgery (%)			
None	33 (92)	76 (93)	0.749
Sling	1 (3)	3 (4)	
AUS	2 (6)	2 (2)	
ProACT	0 (0)	1 (1)	

RT: radiation therapy; AUS: artificial urinary sphincter.

Table 2. Revisions and complications

	Group 1	Group 2	*p* value
Total no. revisions	12	23	–
No. patients requiring revision(s) (%)	7 (19)	9 (11)	0.216
Reason for revision (%)			
Complication	3 (25)	10 (43)	0.013
Other	9 (75)	13 (57)	
Primary outcomes			
Erosion			
-Patients who received RT	2 (15)	4 (15)	1.000
-Patients who did not receive RT	1 (4)	2 (4)	0.870
-Overall	3 (8)	6 (7)	0.848
Infection			
-Patients who received RT	0 (0)	2 (8)	0.305
-Patients who did not receive RT	0 (0)	2 (4)	0.359
-Overall	0 (0)	4 (5)	0.178
Erosion or infection			
-Patients who received RT	2 (15)	4 (15)	1.000
-Patients who did not receive RT	1 (4)	3 (5)	0.853
-Overall	3 (8)	7 (9)	0.971

RT: radiation therapy.

In Group 2, 26 patients had adjuvant radiotherapy. Of these 26 patients, we could not determine the radiation dose and type in 10 patients as again these patients had their radiation treatment outside our institution and records were not available. Of the remaining 16, 9 had 3D-CRT (66 cGy, 33 fractions), 5 had intensity-modulated radiation therapy (IMRT) (66 cGy, 33 fractions and 46 cGy, 23 fractions), 1 had 3D-CRT at 79cGy, 42 fractions and 1 patient had 3D-CRT at 50 cGy, 25 fractions. In the 26 patients in Group 2 with radiation treatment, 4 patients had an erosion (3 had 3D-CRT at 66 cGy, 33 fractions and 1 patient's type and dose of radiation were not available).

A total of 16 patients required 35 revisions: 7 (19%) in Group 1 and 9 (11%) in Group 2 ($p = 0.216$). Revisions were categorized as "complications" (erosion, infection, or erosion + infection) and "other reasons for revision." More revisions were required in Group 2 for complications than in Group 1 (43% vs. 25%, $p = 0.013$) (Table 2). Other reasons for revisions included replacement of the cuff due to recurring incontinence (n = 7), removal of the device (n = 2), replacement of the device (n = 3), revision of the device (n = 2), addition of another cuff due to persistent incontinence (n = 5), and device malfunctioning (n = 3) (Table 3).

Among those patients who had previous incontinence surgery (AUS n = 4, sling n = 4, and ProACT n = 1), complications occurred in 2 patients who had a previous AUS implanted (1 with erosion and 1 with infection) and in 1 patient who had a previous sling (with both erosion and infection).

There was no difference in the incidence of erosion between Groups 1 and 2 (8% vs. 7%, $p = 0.848$) and among those treated with and without radiation (15% vs. 15%, $p = 1.000$ and 4% vs. 4%, $p = 0.870$, respectively). The incidence of infection was similar between Groups 1 and 2 (0% vs. 5%, $p = 0.178$), and among those treated with and without radiation (0% vs. 8%, $p = 0.305$ and 0% vs. 4%, $p = 0.359$, respectively) (Table 2). However, the overall relative risk (RR) of erosion was significantly higher in those who had previous treatment with radiation compared to those who did not (RR 4.05, 95% confidence interval [CI] 1.1–15.3).

Discussion

This retrospective cohort study aimed to capture the implication of increased use of radiotherapy and to assess if changes in technique and equipment for radiation treatment in the management of prostate cancer would affect the incidence of erosion after subsequent AUS implantation. There was not an increase in the use of radiation over the 10-year study period in those who had an AUS implanted. There was, however, an increased risk of erosion overall in patients treated with radiotherapy (15% in patients treated with radiotherapy vs. 4% in patients who did not receive radiotherapy; RR 4.05, 95% CI 1.1–15.3).

Differing rates of erosion among those previously irradiated compared to those without any prior radiation exposure have been reported. While some studies have reported no overall difference,[1,15,16] others have reported as high as a 10-fold increase in risk of erosion after radiotherapy exposure.[11,14,17] The theory behind this increased risk has been described with respect to the associated vascular changes.[14,15] Radiation may obliterate small vessels, resulting in endarteritis, local tissue hypovascularity, tissue ischemia, fibrosis, necrosis, poor wound healing, and impaired immunity against infection.

Table 3. Other reasons for revision (N = 22)	
Replacement of cuff (n = 7)	1. Recurring incontinence 2. Previous erosion 3. Recurring incontinence 4. After removal for erosion 5. After removal for erosion and infection 6. After removal for erosion 7. After removal for erosion
Removal of device (n = 2)	1. Small bowel perforation 2. Discomfort
Replacement of device (n = 3)	1. Fluid loss 2. After removal for infection 3. After removal for erosion and infection
Revision of device (n = 2)	1. High riding pump 2. Pump adherent to testicle
Addition of another cuff (n = 5)	1. Recurring incontinence 2. Recurring incontinence 3. Recurring incontinence 4. Recurring incontinence 5. Recurring incontinence
Device malfunctioning (n = 3)	1. Reservoir burst 2. Systems checked for recurring incontinence 3. Systems checked for recurring incontinence

However, these reports represent radiation treatment prior to and during the early 2000s. A recent more contemporary review by Simhan and colleagues analyzed the potential influence of cuff size on the subsequent development of AUS erosion. They found that AUS erosion occurred in 11% of those with a 3.5-cm cuff and 2.6% of those with a 4-cm or larger cuff who were radiated.[18] In this study, the type and dose of radiation were not stated. In our study, a single patient had a 3.5-cm cuff and he did not receive radiation or have a cuff erosion. We do not believe that cuff size was a factor in our study.

Over the past 10 years, there has been a change in the way radiotherapy for prostate cancer is delivered. In their review of cancer therapy and radiation, Basker and colleagues stated that "the rapid progress in radiation oncology continues to be boosted by advances in imaging techniques, computerized treatment planning systems, radiation treatment machines (with improved X-ray production and treatment delivery), as well as improved understanding of the radiobiology of radiation therapy."[19] There has been increasing use of IMRT techniques compared to traditional methods. Available comparisons support the general conclusion that prostate radiotherapy delivered with IMRT is associated with lower acute and late urinary side effects.[20-22] This is accomplished based on the ability of this technology to manipulate beams of radiation to conform to the shape of a tumour, delivering biologically effective doses to the field of interest while avoiding nearby healthy tissue without compromising disease-specific outcomes.[20] This reduction in risk of early and late side effects could be extrapolated to include reduction in risk of erosion following AUS implantation, although this has not been previously analyzed in the literature.

Contrastingly, other studies have suggested that although IMRT reduces acute toxicity and gastrointestinal side effects, it may not reduce urinary side effects because of difficulty excluding certain areas from the treatment field.[23] Although the total number of patients who had radiation and cuff erosion in our series was small, 3D-CRT was performed mostly in those who experienced an erosion. In our series, fewer patients had IMRT than 3D-CRT (although we were not able to find documentation of radiation dose and type in all patients). We believe during our study period more patients likely underwent 3D-CRT than IMRT based on recently published data on long-term genitourinary complications after RP and radiation at our centre from 2000 to 2007. In that series, only 96 of the 652 (15%) patients received IMRT.[24]

It is possible that over the next 10 years more patients will be treated with IMRT rather than 3D-CRT, which may reduce the incidence of cuff erosion. Nevertheless, from December 2001 to January 2012, our cohort of patients treated with radiation after RP who subsequently required an AUS had a significantly increased risk of cuff erosion compared to those who did not receive radiotherapy. This has occurred despite advances in radiation treatment and technology.[19,25]

Recent literature suggests that there may be a benefit to adjuvant radiotherapy following prostatectomy for patients with specific high-risk features in reducing biochemical recurrence[2-4] and possibly metastasis-free and overall survival.[6] Despite the fact that this body of research was emerging within our 10-year study period, it appears that we did not see an increase in the number of patients having an AUS who had adjuvant radiation after RP, although we acknowledge that our cohort represents a select population. This is echoed in recent treatment patterns analyses, which have demonstrated that only 11% to 20% of patients with adverse pathologic features are being treated with adjuvant radiotherapy.[26,27] Rather, patients are being closely observed with serial PSA tests and offered salvage radiotherapy when there is an indication of biochemical recurrence.[26] Nevertheless, in our sample one-third of patients with prostate cancer were treated with radiotherapy at some point. Although their exact tumour biology was not captured, this proportion remains high and the implication of radiation exposure on future complication rates following surgical management of SUI is important to elucidate.

Our study is limited by its retrospective nature and small sample size. We were limited by the incomplete information on radiation type and dose in a number of patients. The data were also single centre and single surgeon, which may limit generalizability. Tumour pathology and radiotherapy technique employed were not reviewed among our selec-

tive study population. Despite the fact that the study was retrospective, hard end points, such as erosion and infection, were easy to directly assess and this improved the accuracy of our results.

This study confirms that radiation exposure increases the risk of erosion following AUS implantation. Furthermore, over the last 10 years, despite improvement in radiation technique and equipment, erosion rates after AUS implantation are still significantly higher in those treated with radiation compared to those who were not.

Conclusion

Over the last 10 years, there has not been an increase in the number of patients receiving an AUS after RP and radiation at our centre. During this time, the incidence of erosion and infection has not changed in those who have had radiotherapy, despite improvement in radiation technique and equipment. As documented in past reports, the relative risk of erosion remains higher in patients who have had radiation. The relationship between the occurrence of erosion and radiation dose, radiation fields and type of radiation needs to be further explored. Exploration of the patterns of practice with respect to use of adjuvant radiotherapy in high-risk prostate cancer at Canadian centres is warranted.

Competing interests: Dr. Hird declares no competing financial or personal interests. Dr. Radomski is a member of the advisory boards for Pfizer, Lilly, Astellas, Allergan, and Actavis.

This paper has been peer-reviewed.

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