Cystectomy and Urinary Diversion for the Management of a Devastated Lower Urinary Tract Following Prostatic Cryotherapy and/or Radiotherapy

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ABSTRACT

Introduction: We investigated the outcomes and quality of life measures in men who underwent cystectomy and urinary diversion for devastating lower urinary tract toxicity after prostatic radiotherapy and/or cryotherapy for the treatment of prostate cancer.

Methods: Records of patients who underwent cystectomy and urinary diversion for the management of a devastated lower urinary tract following prostatic radiotherapy or cryotherapy were reviewed retrospectively. A postoperative, retrospective quality of life (QOL) survey was designed specific to this patient subset and obtained by telephone interview.

Results: Extirpative surgery with urinary diversion for management of a devastated lower urinary tract was performed on 15 patients with a mean age of 72 years (range 63-82). Toxicities leading to bladder removal included bladder neck contractures, prostatic necrosis, incontinence, osteomyelitis, bladder calculi, fistulae, urethral strictures, abscesses, necrotizing fasciitis, and radiation/hemorrhagic cystitis. The mean number of failed conservative, minimally invasive interventions per patients prior to cystectomy was 3.7 (range 1-12). The average time period from major complication following radiotherapy/cryotherapy to cystectomy was 29.1 months (range 5-65). The QOL survey showed all of the patients who completed the survey (n = 13) would undergo the procedure again and 11 (85%) would have undergone the procedure an average of 13.2 months sooner (range 5-36).

Conclusion: Toxicities secondary to prostatic radiotherapy or cryotherapy may be debilitating. Our results demonstrate that cystectomy with urinary diversion can improve QOL in patients with a devastated lower urinary tract.

INTRODUCTION

Cryotherapy and radiotherapy are common primary, salvage, and/or adjuvant treatment options offered for the management of localized prostate cancer. While these interventions have documented evidence demonstrating biochemical disease-free survival benefit,[1-4] they carry the risk of toxicities to the local and surrounding tissue. Prostatic external beam radiotherapy has been reported to produce moderate to severe genitourinary complications in 3% to 23% of patients.[5-10] Severe and debilitating late complications may occur in approximately 3% of this population.[11] Late grade 2 or greater genitourinary toxicity has been seen in 14% of patients undergoing low-dose brachytherapy as a primary treatment modality.[12] Bladder outlet obstruction and tissue sloughing after cryotherapy has been documented in 3% to 21% and 4% to 15% of patients, respectively.[13-15] Reported complications after salvage cryotherapy include bladder outlet obstruction (12%), tissue sloughing (8.2%), and rectourethral fistula (RUF) in 1.6% of patients.[16]

Moderate and severe toxicities from radiotherapy and/or cryotherapy often are managed with multiple interventions of increasing invasiveness. The purpose of this study is to review the treatment outcomes of men with devastated bladder outlets following radiotherapy or cryotherapy for the management of prostate cancer ultimately treated with cystectomy and urinary diversion.

METHODS

Following institutional review board approval, we retrospectively examined the medical records of all patients that underwent cystectomy with urinary diversion for toxicities related to prostatic radiotherapy and/or cryotherapy from January 2004 to September 2014.

Recorded preoperative characteristics included patient age, prostate cancer treatment modalities, number/type/grade of toxicities related to therapy, and the number/type of interventions used to manage these complications. Cryotherapy and other surgical interven-

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tion related toxicities were graded based on the Clavien-Dindo Classification of Surgical Complications.[17] Radiotherapy-related toxicities were graded based on the Radiation Therapy Oncology Group (RTOG)/European Organization for Research and Treatment of Cancer (EORTC) late radiation morbidity scoring schema (Table 1).[18] Postoperative characteristics including duration of hospital stay, early (≤30 days) and late (>30 days) complications and patient quality of life (QOL) scores were recorded. A postoperative QOL survey (Box) was designed by the authors since no specific survey for this patient population exists. Results were obtained via telephone interview by an independent third party.

Table 1. Radiation Toxicity and Surgical Complication Classification Systems

Clavien-Dindo Classification of Surgical Complications [17]	
Grade 1	Any deviation from the normal postoperative course without need for any type of treatment except pharmacological treatments of antiemetics, antipyretics, analgesics, diuretics, and electrolytes
Grade 2	Requiring pharmacological treatment with drugs other than allowed for Grade I complications
Grade 3	Requiring surgical, endoscopic, or radiological intervention
Grade 4	Life-threatening complication requiring intensive care unit management
Grade 5	Death of patient
RTOG/EORTC Radiation Toxicity Grading System – Genitourinary/Bladder [18]	
Grade 0	None
Grade 1	Mild urinary frequency and dysuria not requiring pharmacological treatment Microhematuria
Grade 2	Moderate urinary frequency, dysuria, bladder spasms Intermittent gross hematuria
Grade 3	Severe urinary frequency, dysuria, pelvic pain, or bladder spasms Reduction in bladder capacity Frequent gross hematuria without clot passage
Grade 4	Severe urinary frequency, dysuria, pelvic pain, or bladder spasms Necrosis/contracted bladder (capacity < 100 cc) Severe gross hematuria/hemorrhagic cystitis necessitating blood transfusion Acute bladder obstruction not secondary to clot passage, ulceration, or necrosis
Grade 5	Death

RESULTS

Fifteen men with a mean age of 72 years (range 63-82) underwent extirpation for a devastated bladder outlet secondary to prostatic radiotherapy and/or cryotherapy. Prostate cancer treatment modalities leading to extirpation are listed in Table 2. Clavien Grade 2-3, RTOG/EORTC Late Radiation Morbidity grade 2-4 toxicities and failed conservative therapies following complications after prostate cancer treatment are shown in Table 3. The mean number of failed interventions per patient prior to urinary diversion was 3.7 (range 1-12). The average time from significant prostate cancer treatment toxicity to urinary diversion was 29.1 (range 5-65) months. Incontinence was present in all but 1 patient and required a mean of 7.3 pads/day (range 1-20). Three of 4 patients (75%) with rectourethral fistulae (RUF) reported florid fecal incontinence and were omitted from the calculation of daily pad usage. One patient (25%) experienced a Clavien Grade 4 (life threatening complications requiring intensive care unit [ICU] admission) secondary to urosepsis and necrotizing fasciitis of his perineum and right lower extremity.

Ten men underwent cystectomy (66%) and 5 underwent cystoprostatectomy (33%). Thirteen patients received ileal conduit urinary diversions (87%), 1 patient chose a continent catheterizable pouch, and 1 patient with RUF underwent a colon conduit urinary diversion. Two of 4 men (50%) with RUF had fecal diversion with colostomy prior to urinary diversion. At the time of urinary diversion, they underwent completion of the pelvic exenteration. The 2 other RUF patients had a partial proctectomy and end colostomy at the time of urinary diversion. Mean hospital stay following cystectomy and diversion was 12.2 days (range 3-43). Early and late postoperative complications are included in Table 4. Two of four early complications (50%) were Clavien Grade 3 and required immediate operative intervention. The other 2 early complications were Clavien Grade 2 and managed conservatively. Of 7 late complications, 4 (57%) were Clavien Grade 3 and also required operative intervention. The other late complications were Clavien Grade 2 and managed conservatively. Average length of follow-up was 28.3 (5-88) months.

Box. Quality-of-Life Survey

1. How would you categorize your overall satisfaction with the procedure?
1. Completely unsatisfied
2. Mostly unsatisfied
3. Halfway satisfied
4. Mostly satisfied
5. Completely/considerably satisfied

2. Did the treatment meet your expectations?
1. Did not meet expectations at all
2. Did not meet expectations moderately
3. Met expectations halfway
4. Met expectations moderately
5. Completely/considerably met expectations

3. Overall how big a problem has urinary function been during the last 4 weeks?
1. No problem
2. Very small problem
3. Small problem
4. Moderate problem
5. Big problem

4. Would you elect to have a cystectomy again if you were given the choice?
YES / NO
If you answered NO: Please explain why
_____
_____
_____
_____

5. Would you have chosen to have the cystectomy earlier?
YES / NO
If you answered YES: How soon after your complications began would you have agreed to have the procedure? _____months

Table 2. Prostate Cancer Treatments

Treatment Modalities (n = 15)	Number
RP with adjuvant XRT	6
XRT with salvage cryotherapy	5
Brachytherapy	1
XRT	1
XRT and brachytherapy	1
TURP followed by XRT	1

Abbreviations: RP, radical prostatectomy (robotic or retropubic); XRT, external beam radiotherapy; TURP, transurethral resection of prostate.

Table 3. Treatment Toxicities and Failed Conservative Therapies

Toxicities	Number
Bladder neck contracture	17
Incontinence	13
Prostate tissue necrosis/sloughing	12
Pubic osteomyelitis	7
Pelvic abscess	6
Recurrent bladder calculi	4
Recto-urethral fistula	4
Radiation/hemorrhagic cystitis	3
Prostatic stricture/stone	3
Necrotizing fasciitis	2
Urethral stricture	1
Radiation induced osteonecrosis	1
Failed Conservative Interventions	**Number**
Transurethral bladder neck incision	20
Suprapubic tube placement	9
Drainage of pelvic abscess	5
Hyperbaric oxygen therapy	4
Intravesical instillations	3
Nephrostomy tube insertion	3
Urethral dilation	2
Fecal diversion with colostomy	2
Artificial urinary sphincter insertion	2
Clean intermittent catheterization	2
Transobturator sling implantation	1
Urethral stenting	1
Osteoplasty of pubic ramus	1

At the time of extirpation, residual prostate cancer was found in 4 patients (27%). Three of the patients had primary radiotherapy followed by salvage cryotherapy and one had primary brachytherapy followed by salvage cryotherapy.

The postoperative QOL telephone survey was completed by 13 of 15 patients (87%). One patient refused to complete the questionnaire, and 1 was unreachable. The survey results showed that patients were satisfied with the surgical outcome and would undergo the extirpative surgery an average of 13.2 months (range 5-36) sooner (Table 5).

DISCUSSION

Most toxicity related to prostatic radiotherapy and/or cryotherapy is successfully managed conservatively. Unfortunately, some patients experience debilitating Clavien Grade 2-3 and RTOG/EORTC Grade 3-4 complications that are refractory to medical management or minimally invasive interventions. This patient subset often undergoes futile procedures over a protracted time period before the patient and urologist decide to pursue cystectomy with urinary diversion. This study retrospectively investigates our experience with such a patient population and assesses postoperative QOL.

Our retrospective analysis demonstrates that men may present with a myriad of toxicities after radiotherapy and/or cryotherapy. Depending on the degree of bother, the toxicities can be managed with a wide range of interventions. While these treatment modalities are successful for many, others require more invasive therapies. Unfortunately, the method of determining which patient is a candidate for conservative interventions versus cystectomy with urinary diversion is not algorithmic. We discuss extirpation early in the treatment course, so patients are aware that if conservative interventions fail, a more radical approach is available. Recommendations for urinary diversion are often made because of the near impossibility of successful conservative management of toxicities resulting from pelvic radiotherapy and/or cryotherapy. It is difficult to assess the number of patients who needed or were given the recommendation for cystectomy with urinary diversion because of the referral nature of our institution. Additionally, patient medical comorbidity was rarely a surgical contraindication; it was the patient who would choose to avoid or defer surgery.

While no metric exists to predict which patient will benefit from urinary diversion, findings from the postoperative QOL survey provide qualitative evidence that men with significant pelvic comorbidities from radio/cryotherapy are satisfied with the outcome and would undergo the procedure again. In addition, patients reported that, if possible, they would have undergone surgical extirpation with diversion an average of 13.2 months sooner.

The majority of publications describing cystectomy and diversion after prostate irradiation are for concomitant urothelial carcinoma of the bladder[19-22] or for bladder invasion by prostate cancer.[23] The authors subjectively note that extirpation is an effective and durable treatment, despite increased perioperative morbidity compared to patients who underwent cystectomy without prior prostate irradiation. The findings in our patient population mirror these results.

The largest previous series describing radical extirpation for prostate cancer treatment toxicity focused on 11 patients with RUF secondary to brachytherapy. The authors also concluded that anterior pelvic exenteration with urinary diversion for RUF can be associated with good results.[24] In another study, Izawa et al focused on toxicities related to salvage prostatic cryotherapy in 6 patients. Similarly, they reported that radical intervention with extirpation and urinary diversion is justifiable and safe.[25]

In our cohort, 10 (66%) men underwent cystectomy and 5 (33%) cystoprostatectomy. The decision to remove the prostate was made at the time of surgery and was determined by perceived ease

of prostatectomy and overall health of the surrounding pelvic tissue. No postoperative complications could be attributed directly to either prostatectomy or the retained prostate.

The weaknesses of this study include the variation in treatment methods leading to cystectomy with urinary diversion. Although this is true, all patients in this cohort began their course with prostate cancer, ultimately requiring cystectomy with urinary diversion. In addition, the sample size is small and limits interpretation. Also, the survey specifically designed for this study has not been validated for effectiveness, but does provide a qualitative understanding of the patient's postoperative quality of life. Last, each patient completed the survey at different post-operative time periods, which may lead to recall bias.

The severity of toxicities secondary to prostatic cryotherapy and/or radiotherapy can be debilitating. Our series, the largest to date, demonstrates that cystectomy with urinary diversion is safe and improves the quality of life in patients with a devastated lower urinary tract following prostatic radiotherapy and/or cryotherapy.

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Table 4. Post Cystectomy Complications

Complications	Type	Number
Early (< 30 days)	Abdominal dehiscence	2
	Bowel leak	1
	Clostridium difficile colitis	1
Late (> 30 days)	Incisional hernia	2
	Pelvic abscess	2
	Enterocutaneous fistula	1
	Parastomal hernia	1
	Ureteroenteric stricture	1

Table 5. Postoperative Quality-of Life Survey Results

Quality of Life Survey Results (n=13)		
Question	**Average score**	**Range**
Satisfaction	4.3	3-5
Expectation	4.2	3-5
Problematic urinary function	2.5	1-5
Question	**Yes**	**No**
Undergo again	13	0
Sooner	11	2
How much sooner	*Mean 13.2 months*	

REFERENCES

1. Bahn DK, Lee F, Badalament R, Kumar A, Greski J, Chernick M. Targeted cryoablation of the prostate: 7-year outcomes in the primary treatment of prostate cancer. *Urology.* 2002;60(2 Suppl 1):3-11.

2. Bolla M, van Poppel H, Collette L, et al. Postoperative radiotherapy after radical prostatectomy: a randomised controlled trial (EORTC trial 22911). *Lancet.* 2005;366(9485):572-578.

3. Fonteyne V, Soete G, Arcangeli S, et al. Hypofractionated high-dose radiation therapy for prostate cancer: long-term results of a multi-institutional phase II trial. *Int J Radiat Oncol Biol Phys.* 2012;84(4):e483-490.

4. Zelefsky MJ, Kuban DA, Levy LB, et al. Multi-institutional analysis of long-term outcome for stages T1–T2 prostate cancer treated with permanent seed implantation. *Int J Radiat Oncol Biol Phys.* 2007;67(2):327-333.

5. Lawton CA, Won M, Pilepich MV, et al. Long-term treatment sequelae following external beam irradiation for adenocarcinoma of the prostate: analysis of RTOG studies 7506 and 7706. *Int J Radiat Oncol Biol Phys.* 1991;21(4):935-939.

6. Zelefsky MJ, Cowen D, Fuks Z, et al. Long-term tolerance of high dose three-dimensional conformal radiotherapy in patients with localized prostate cancer. *Cancer.* 1999;85(11):2460-2468.

7. Schultheiss T, Hanks G, Hunt M, et al. Incidence of and factors related to late complications in conformal and conventional radiation treatment of cancer of the prostate. *Int J Radiat Oncol Biol Phys.* 1995;32(3):643-649.

8. Beard C, Lamb C, Buswell L, et al. Radiation-associated morbidity in patients undergoing small-field external beam irradiation for prostate cancer. *Int J Radiat Oncol* Biol Phys. 1998;41(2):257-262.

9. Koper P, Stroom J, Putten W, et al. Acute morbidity reduction using 3DCRT for prostate carcinoma: a randomized study. *Int J Radiat Oncol Biol Phys.* 1999;43(4):727-734.

10. Dearnaley D, Khoo V, Norman A, et al. Comparison of radiation side effects of conformal and conventional radiotherapy in prostate cancer: a randomized trial. *Lancet.* 1999;353(9149):267-272.

11. Zelefsky MJ, Levin EJ, Hunt M, et al. Incidence of late rectal and urinary toxicities after three-dimensional conformal radiotherapy and intensity-modulated radio-therapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys.* 2008;70(4):1124-1129.

12. Kollmeier MA, Fidaleo A, Pei X, et al. Favourable long-term outcomes with brachytherapy based regimens in men ≤ 60 years with clinically localized prostate cancer. *BJU Int.* 2013;111(8):1231-1236.

13. Long JP, Fallick ML, LaRock DR, et al. Preliminary outcomes following cryosurgical ablation of the prostate in patients with clinically localized prostate carcinoma. *J Urol.* 1998;159(2):477-484.

14. Shinohara K, Rhee B, Presti JC, et al. Cryosurgical ablation of prostate cancer: patterns of cancer recurrence. *J Urol.* 1997;158(6):2206-2209.

15. Wilt TJ, MacDonald R, Rutks I, et al. Systematic review: comparative effectiveness and harms of treatments for clinically localized prostate cancer. *Ann Intern Med.* 2008;148(6):435-448.

16. Parekh A, Graham PL, Nguyen PL. Cancer control and complications of salvage local therapy after failure of radiotherapy for prostate cancer: a systematic review. *Semin Radiat Oncol.* 2013;23(3):222-234.

17. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg.* 2009;250(2):187-196.

18. Cox, JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). *Int J Radiat Oncol Biol Phys.* 1995;31(5):1341-1346.

19. Tolhurst SR, Rapp DE, O'Connor RC, et al. Complications after cystectomy and urinary diversion in patients previously treated for localized prostate cancer. *J Urol.* 2005;66(4):824-829.

20. Bostrom PJ, Soloway MS, Manoharan M, Ayyathurai R, Samavedi S. Bladder cancer after radiotherapy for prostate cancer: detailed analysis of pathological features and outcome after radical cystectomy. *J Urol.* 2008;179(1):91-95.

21. Schuster TG, Marcovich R, Sheffield J, Montie JE, Lee CT. Radical cystectomy for bladder cancer after definitive prostate cancer treatment. *Urology.* 2003;61(2):342-347.

22. Jayram G, Katz MH, Steinberg GD. Radical cystectomy in patients previously treated for localized prostate cancer. *Urology.* 2010;76(6):1430-1433.

23. Leibovici D, Kamat AM, Pettaway CA, et al. Cystoprostatectomy for effective palliation of symptomatic bladder invasion by prostate cancer. *J Urol.* 2005;174(6):2186-2190.

24. Moreira SG, Seigne JD, Ordorica RC, et al. Devastating complications after brachytherapy in the treatment of prostate adenocarcinoma. *BJU Int.* 2004;93(1):31-35.

25. Izawa JI, Ajam K, McGuire E, et al. Major surgery to manage definitively severe complications of salvage cryotherapy for prostate cancer. *J Urol.* 2000;164(6):1978-1981.

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