



Research Article

Role of Urinary Diversion in Management of Failed Bladder Due to Radiation Damage

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Introduction

Radiation damage to the lower urinary tract, as a late complication of radiotherapy for pelvic malignancies, can manifest with a wide range of symptoms and presentations. Pelvic malignancies treated with radiation therapy create a group of patients with various outcomes including, for some, complications associate with that radiotherapy. [1] Despite improved techniques for targeting pelvic tumors during radiotherapy, there remains potential for radiation damage to adjacent structures including bladder, urethra and distal ureters. [2] Increased cancer survivorship has led to emergence of a number of long-term sequelae of radiation therapy. [3] Because symptoms may take years to present, data regarding the exact incidence of the long-term complications and their treatment is scarce, and the incidence of adverse outcomes may be higher than reported. [4] Complications associated with radiation damage can greatly affect a patient's quality of life, necessitating multiple hospital admissions and interventions [4]. The optimum care of these group of patients remains unclear. Definitive surgical intervention in this group of patients, including urinary diversion, is often considered only as a last resort. We present our experience with surgical management of the severely damaged lower urinary tract as a consequence of pelvic radiation. Continent and incontinent urinary diversion have been used to treat patients over an 8-year period at a tertiary center. We also provide a review of current literature on role of urinary diversion in this specific subgroup of patients.

Methods

After receiving institutional ethical committee approval, we identified 13 patients who underwent urinary diversion on the background of treatment refractory radiation damage due to

previous non-urothelial malignancies between 2010 to 2018 in our institution. All were adult patients who had previously received radiation treatment for various pelvic malignancies, excluding malignancies of urinary tract. They had all received multiple previous medical treatments and surgical intervention in multiple attempts to alleviate their symptoms. A retrospective review of patients' charts was performed. Clinical and demographic variables were recorded including age at time of urinary diversion, primary malignancy, preoperative symptoms, including recurrent infections, hematuria, incontinence, pelvic or suprapubic pain, previous treatments or interventions, time between radiotherapy and diversion surgery, type of diversion (ileal conduit formation vs, formation of continent diversion (neobladder with Mitrofanoff channel), primary or subsequent simple cystectomy, revision surgeries, complications and final outcome regarding patient satisfaction. Due to lack of validated questionnaire applicable to our diverse group of patients, a retrospective post-operative quality of life questionnaire was designed to evaluate the patient's symptoms at time of follow up and compare their quality of life to before diversion surgery.

Results

13 patients who suffered from various end-stage complications relating to previous radiotherapy for pelvic malignancies between 2010 and 2018 were identified. Table 1 summarizes patient's demographic data. Seven (53%) were female and six (46%) were male. Median age was 68 years (36-77). Primary malignancy in men was prostate cancer. Most common malignancy in female patients was cervical cancer (n=4), followed by anal cancer (n=1), rectal cancer (n=1) and rhabdomyosarcoma (n=1). Range of time between radiotherapy and urinary diversion was 0.5 years to 37

years. Manifestations of radiation related complications varied amongst these patients. The most common bothersome symptom was incontinence in 12 (92.30%) patients. Six (46.10%) reported chronic pelvic or suprapubic pain. Six patients (46%) had recurrent intermittent hematuria needing intervention, and recurrent Urinary Tract Infection (UTI) were recorded in 5 patients. There were two male patients with urethrocutaneous fistulas and one female patient, with a vesicovaginal fistula. All patients had signs of severe radiation cystitis on cystoscopy.

Prior Surgical Interventions	Suprapubic catheter n=3 (23%)
	Urethrotomy n=2 (15%)
	Artificial Urinary Sphincter n=3 (23%)
	Urethral Dilatations n=3 (23%)
	Percutaneous Nephrostomy n=1 (7%)
	Urethroplasty n=1 (7%)

Demographics	Cohort n=13
Age (average years)	68 (36-77)
Gender	Female n=7 (53.8%) Male n=6 (46.2%)
Malignancy	Prostate Cancer n=6 Cervical Cancer n=4 Anal cancer n=1 Rectal Adenocarcinoma n=1 Rhabdomyosarcoma n=1
Time to urinary diversion from radiotherapy	6 months - 37 years
Symptoms prior to diversion	Pelvic/suprapubic pain n=5 (38.4%) Haematuria n=6 (46.1%) Urinary retention n=2 (15.4%) Recurrent UTI n=5 (38.4%) Urinary Incontinence n=12 (92.3%) Urethrocutaneous fistula n=1 (7.7%) Vesicovaginal fistula n=1 (7.7%)
Prior non-surgical Interventions to manage radiation complications	Indwelling urethral catheter n=7 (54%) Bladder Irrigations n=6 (46%) Hyperbaric oxygen therapy n=1 (7%) Anticholinergic pharmacotherapy n=12 (92%)

Table 1: Patient Characteristics.

Of the thirteen patients, 6 underwent formation of continent neobladder using right colon with either appendix or tailored distal ileum as the channel, 6 patients underwent an ileal conduit formation, and one patient had a ureterostomy formed (history of previous nephrectomy due to renal cell carcinoma). In 4 patients, a concomitant simple cystectomy was performed, one patient had a subsequent simple cystectomy and removal of pubic symphysis due to complications with pyocystitis and chronic pubic bone osteomyelitis. Post-operative complications are summarized in Table 2. No deaths were recorded in the peri-operative period.

Surgical Characteristics	n=13
Diversion	Neobladder formation + Mitrofanoff Catheterizable channel n=6 (46%) Ileal Conduit n=6 (46%) Urostomy n=1 (7%)
Cystectomy	Primary cystectomy n=4 (30%) Subsequent cystectomy n=2 Bladder left in situ n=7 (54%)

Table 2: Surgical Characteristics.

Mean follow up was 27 months (range 6 months to 4 years). 10 patients completed a quality of life questionnaire at time of follow up. This questionnaire consisted of 6 domains of energy levels, general wellbeing, pain, urinary tract infections, physical appearance and overall quality of life. Patients were asked if they were given a choice again would they have urinary diversion and if so, would they elect to have it earlier. Most patients reported improvement in all domains. Pain and urinary tract infections were significantly improved in 7 (70%) of the patients. One patient was not satisfied with the physical appearance of the ileal conduit. 8 patients responded that if given the chance they would choose to have the surgery again and would elect to have it sooner.

Discussion

Radiotherapy is commonly used as first line treatment for management of various pelvic malignancies. Even though newer radiotherapy planning techniques such as image guidance and intensity modulation are enabling clinicians to direct high-energy radiation more directly to the target tumor, adjacent structures such as bladder, urethra and distal ureters inevitably receive some degree of radiation contamination. Newer techniques allow delivery of higher doses of radiation with relative sparing of key adjacent structures, but long-term consequences of these measures remains unknown [2]. In prostate cancer, low grade and high grade Adverse Effects (AE) of radiotherapy based on the National Cancer Institute grading system have been reported 20-43 and 5-13%, respectively, with a median follow up of 60 months. Prostatic radiotherapy results in late severe genitourinary toxicity in 3-20% of the patients. [5] For cervical cancer, the risk of low-grade AEs following radiation can be as high as 28%. High-grade AEs occur in about 8% at 3 years and 14.4% at 20 years or ~0.34% per year. [6] The treatment of choice for stage IIB-IV cervical cancer is chemoradiotherapy. The radiation field for cervical carcinoma treatment classically includes the urinary bladder and distal ureters. [7] Mean latency time between radiotherapy and severe urological sequelae in cervical cancer has been reported 19.4 years [8].

Urologic complications following pelvic radiotherapy are diverse and include radiation cystitis, lower urinary tract dysfunction, stricture disease, fistula formation, and the development of second primary cancers. Radiation cystitis is the most common of these complications, and in its most severe form of haemorrhagic cystitis can be devastating and at times life threatening. Other complications, whilst not immediately life threatening, still convey major morbidity and can often result in multiple hospital admissions and interventions with significant negative impacts on patient's quality of life. Due to the severity and chronicity of these complications, usually patients undergo multiple conservative and surgical interventions before they are considered for urinary diversion or cystectomy. The management of these conditions have evolved during the years, but is difficult to standardize due to the lack of quality randomized studies and the potential toxicities of the various treatment proposed, and diversity of presentations. Comorbidities including age and frailty in this patient population also greatly impact the choice, safety and efficacy of available treatment options.

Data regarding role of diversion surgery with or without cystectomy in these patients is limited and mostly consists of case series and retrospective cohorts. Sack et al., evaluated quality of life(QoL) in 15 patients undergoing cystectomy with urinary diversion for the management of devastating lower urinary tract issues following prostatic radiotherapy or cryotherapy. Using a

retrospective QoL survey they demonstrated that all patients were satisfied with their QoL after cystectomy and urinary diversion [9].

Another quality of life study evaluated 19 patients undergoing cystectomy and urinary diversion for management of radiation-induced refractory lower urinary tract symptoms. Clinically meaningful improvements were noted in all the physical and mental health domains after cystectomy. Significant improvements were found in certain domains, namely in the level of pain control, general health, role limitations due to emotional problems, and social functioning [10]. The results of our study are in keeping with the previous published reports. Patients reported high rates of satisfaction at time of their follow up after their diversion surgery. Most of patients in our group had significant symptoms of abdominal and suprapubic pain, associated with debilitating lower urinary tract symptoms. In this cohort 70% they had reported complete resolution of pain and reported the ability to return to physical activities as a result of urinary diversion.

Linder et al., describe their experience with 21 patients undergoing cystectomy for refractory haemorrhagic cystitis. [11] These patients had failed various conservative measures before they were considered for cystectomy and urinary diversion. They reported a high rate of complications (42%) and found a trend towards more severe complications in those undergoing emergent cystectomy compared to planned procedures. The overall survival rates were similar in these groups. They concluded that cystectomy for haemorrhagic cystitis is associated with a high risk of perioperative complications as well as mortality, likely reflecting the baseline clinical status of this patient cohort as older with significant comorbidities. Therefore, cystectomy should remain a last resort to control bleeding after failure of conservative measures. In a retrospective report by Faris et al., 30 patients underwent urinary diversion for urological complications related to prostate radiotherapy. Indications for urinary diversion in this cohort included fistula (37%), end-stage bladder (20%), devastated outlet (27%), and a combination of end-stage bladder and devastated outlet (17%). Most common choice for urinary diversion was cystectomy with conduit diversion followed by diversion lone or suprapubic indwelling catheter. They reported that external beam radiotherapy resulted in higher incidence of end-stage bladder dysfunction, whereas brachytherapy seed placement was more commonly associated with a devastated outlet [12].

Neulander et al., in a series of 19 patients describe their technique of simple cystectomy together with urinary diversion for management of severely de-functionalized lower urinary tracts due to various benign pathologies. Simple cystectomy was done concomitantly with urinary diversion in 13 cases and later as a separate procedure in 6, due to complications of a retained nonfunctional bladder. In 9 cases bladder pathology was due to previous radiation for prostate or cervical cancers. They had no per-

operative mortality and complete alleviation of symptoms in their cohort [13]. Patil et al., report a series of 8 patients who underwent salvage cystectomy, orthotopic ileal neobladder formation and urethral pull-through for management of posterior urethral stenosis and defunctionalized bladder. In 6 patients, primary pathology was previous radiotherapy for prostate cancer. Even though this is a small cohort of patients, it describes a unique technique of complete lower urinary tract reconstruction with preservation of continence and storage function [14]. Chrouser et al., describe their experience with urinary fistulas following radiotherapy for prostate cancer. They report simultaneous faecal and urinary diversion to provide the greatest objective and subjective success in their group of patients. Large, symptomatic urinary fistulas after pelvic radiation are associated with significant morbidity. Patients with fistulas larger than 1.5 cm should be considered candidates for immediate urinary and fecal diversion rather than a staged approach [15].

Continent cutaneous diversion can be an appropriate approach in patients with diseased urethra in setting of previous radiation damage. [16] Use of right colon pouch with the tailored distal ileum as the catheterising channel, has multiple advantages. The ileocecal valve provides a natural anti-reflux mechanism. Alternatively, the appendix implanted into submucosa of colon will achieve continence using the Mitrofanoff principal [16,17].

Conclusion

End stage, de-functionalized lower urinary tracts in patients with a background of previous radiotherapy for pelvic malignancies can present in various ways. These patients suffer from long-term debilitating symptoms adversely affecting their quality of life. Guidelines are limited in terms of management of these complex patients. Urinary diversion has a role in management of various forms of radiation damage, and with careful patient selection and knowledge of potential complications can substantially improve quality of life in these patients.

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