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Urinary Diversion for Incontinence and Voiding Dysfunction in Cancer Survivors: a Critical Review of the Literature

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Abstract
Purpose of Review Urinary diversion (UD) remains the last option for improving quality of life in patients with treatment-refractory urinary incontinence (UI) or voiding dysfunction after cancer treatment. We aim to critically review the utility of UD for UI and voiding dysfunction in patients previously treated for malignancy.
Recent Findings UD patients are at high risk given their oncologic treatment and multiple procedures prior to UD. The severe impact of UI and voiding dysfunction on quality of life is significant. Despite the risk of complications after UD, men reported significant improvement of their urinary symptoms and were confident that they would have sought UD sooner.
Summary UD remains a last option for some men dealing with severe urinary symptoms after treatment of pelvic malignancy in both men and women. Further investigation is needed to better characterize the burden of disease and potential gains surrounding management of these men.

Keywords Urinary diversion · Incontinence · Malignancy · Cancer · Voiding dysfunction

This article is part of the Topical Collection on *Cancer-Associated Voiding Dysfunction*

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Introduction

Management of pelvic malignancies including cervical cancer, prostate cancer, and rectal cancer requires multi modal treatment including surgical resection, chemotherapy, or radiotherapy. Treatment often has unintended deleterious effects on pelvic structures in close proximity. Urinary-related complications including reduction in bladder capacity, fistula formation, and urinary incontinence (UI) from damage to the sphincter with resultant stress urinary incontinence may arise and significantly impact patients' quality of life [1]. Voiding dysfunction and UI may be treated with anticholinergics, intravesical botulinum injections, urethral bulking procedures, urethral sling, or placement of an artificial urinary sphincter. Failure of these less invasive measures or patients with small contracted bladders may leave permanent urinary diversion (UD) as the only feasible option [2, 3].

Typical indications for UD include malignancy involving the bladder, severe urethral stricture disease, or neurogenic bladder. Others undergo UD after failure of conservative therapy to treat infection, bleeding, fistula formation, or pain [4]. UD remains the last option for managing treatment-refractory UI or voiding dysfunction after primary treatment of pelvic malignancy. We aim to critically review the literature about the utility of UD for incontinence and voiding dysfunction in patients who have previously been treated for malignancy.

Indications for Urinary Diversion

Broadly speaking, the indications for UD can be classified into three main categories, per a historical article published by Jacobs: (1) malignant disease-related indications such as bladder cancer, radiation-induced hemorrhagic cystitis, surgical extirpation, and ureteral obstruction due to pelvic malignancy or

scarring; (2) congenital abnormalities such as ectopic viscera or congenital neurologic disorders of the urinary tract; and (3) non-malignancy-related lesions such as severe bladder incompetence due to poor function, significant contraction with limited capacity, severe traumatic injuries to the bladder or urethra and persistent fisutae formation [5]. The indications for UD often relate to treatment-refractory symptoms such as voiding dysfunction, UI, and rectourethral or vesicovaginal fistula associated with incontinence. To better understand the etiology, urinary complaints can be further characterized into storage-related or outlet-related issues (Table 1). Using a similar approach to these patients as is used in patients who present with lower urinary tract symptoms without prior cancer history can aid in characterization of symptom severity. Although several interventions aimed at alleviating morbidity associated with treatment-refractory symptoms may be performed, repeated procedures with limited benefit must ultimately be abandoned in favor of definitive UD. The decision to transition to UD must be made with shared decision-making and careful consideration of the patient's goals and the potential risks and benefits of the procedure.

Quantification of symptoms using validated tools such as the American Urological Association Symptom Index (AUASI) and assessment of bladder function and emptying with urodynamics can provide objective measures of the patients' symptoms [6•]. For example, management of incontinence using a urinary sling or artificial sphincter may be less beneficial in patients with severe overactive symptoms or small capacity bladders. Alternatively, those with overflow incontinence would not benefit from anticholinergic medications or intravesical botulinum injections. Table 2 compares characteristics of patients undergoing UD for UI after treatment for pelvic malignancy.

A recent study analyzing the Healthcare Cost and Utilization Project Nationwide Inpatient Sample to examine trends in the utilization of conduit UD with concomitant cystectomy for benign indications from 1998 to 2011 reported the majority of patients (73%) appear to undergo the surgery without concurrent cystectomy. Those who underwent concomitant cystectomy were more often older, male, presented with radiation cystitis or bladder dysfunction, and had Medicare. They reported the proportion of patients undergoing concomitant cystectomy increased over time from 20.2% in 1998 to 35.2% by 2011, independent of insurance payer, hospital characteristics, and region within the USA [7].

Faris et al. reported their experience with 30 patients who presented with complications after radiotherapy for prostate cancer and underwent UD [8]. Five patients had undergone prostatectomy prior to radiation and three underwent salvage therapy for biochemical recurrence. The post-treatment UI was significant, with men using an average of 5–7 pads per day and AUASI scores of 12.5–32 at presentation. In attempts to salvage urinary function, men had previously undergone an average of four operative interventions prior to UD. The indications for UD varied, 37% underwent UD for fistula, 20% for end-stage bladder, 27% for devastated outlet, and 17% with a combination of indications. Their findings highlight men's willingness to undergo multiple procedures or interventions to regain urinary continence. Though limited only to post-radiation patients, the authors demonstrate how severe UI and voiding dysfunction continue to be a significant adverse effect of management of prostate cancer.

Mayer et al. reported on urinary adverse sequelae of radiotherapy for treatment of prostate cancer [9]. In a retrospective review, they report the adverse urinary events of 73 men with prostate cancer treated with various radiation therapies. Using the radiation therapy oncology group grading system, they focused primarily on adverse events including hematuria requiring transfusion, hemorrhagic cystitis, contraction of the bladder to less than 100 ml, necrosis, bladder mucosal ulceration, ureteral stenosis, and acute urinary obstruction not attributed to clot obstruction. Patients reported a mean of 3 (0–

Table 1 Indications for UD by diagnosis and patient complaints/symptoms

	Storage/irritative	Voiding/obstructive
Objective findings	Low bladder capacity	Intrinsic sphincter dysfunction
	Decreased bladder compliance	Bladder neck contracture
	Refractory detrusor overactivity or Radiation cystitis	Refractory urethral/prostatic Stricture
	Urethral fistula formation	Post-RP incontinence
		Urethral fistula formation
Symptoms	Frequency	Incomplete emptying
	Urgency	Post-void dribbling
	Urge incontinence	Hesitancy
	Nocturia	Weak stream
	Small volume voiding	Intermittency
	Dysuria/pain with urination	Overflow incontinence
		Straining

Table 2 Characteristics of patients undergoing UD for UI/voiding dysfunction after treatment for pelvic malignancy

	Authors			
	Faris et al.	Sack et al.	Mayer et al.	Bassett et al.
Year	2014	2016	2016	2016
Design	Retrospective	Retrospective	Retrospective	Retrospective
Cohort size	30	15	73	100
Age (years)	67.5 (55–78)[a]	72 (63–82)[a]	73 (59–92)[a]	71 (51–89)
Cancer treatment ([b] of patients)	EBRT (6) BT (11) EBRT + BT (13)	RP+XRT XRT+salvage chemotherapy BT XRT XRT+BT TURP+XRT	RP+EBRT (19) HDR+EBRT (19) LDR+EBRT (5) Any 'other' combination (1)	EBRT (12) HDR (2) LDR (2) RP+EBRT (49) BT+EBRT (17) HDR+boost (12) Proton beam (1) Other combinations (2) Cryoablation post-RT (18)
Pads per day at presentation	5.8 (1–12)[a]	7.3 (1–20)[a]	–	–
Time from treatment to UD	4.6 years (1–13)[a]	29.1 months (5–65)[a]	8 years (0–17)[b]	8 years (0.8–31)[b]
No. Procedures prior to UD	4.4 (2–13)[a]	3.7 (1–12)[a]	3 (0–12)[a]	3.7 (0–15)[a]
Post-UD follow-up (months)	–	28.3 months (5–88)[a]	16 months (0–61)[a]	16.5 months (3–98)

UD urinary diversion, *UI* urinary incontinence, *EBRT*/*XRT* external beam radiation therapy, *BT* brachytherapy, *RP* radical prostatectomy, *HDR* high-dose radiation brachytherapy, *LDR* low-dose radiation brachytherapy

[a] Mean (range)

[b] Median (range)

12) procedures prior to definitive management for their urinary complaints. Roughly one-third underwent UD, 14 with incontinent UD, and nine with catheterizable pouches. The authors propose an algorithm of management in which UD is considered an option only after failure of conservative measures such as artificial urinary sphincter or clean intermittent catheterization. From our experience, additional procedures such as intravesical Botox injection, artificial urinary sphincter placement, or fistula repair may be pursued prior to permanent UD but at the cost of an increased risk of potential complications. A frank discussion of the risks and benefits of each intervention, and which risks outweigh the benefits, should be discussed in detail prior to UD. Further discussion will benefit and educate the patient as well as better elucidate what the patient values most.

Rectourethral and vesicovaginal fistulae are well-known potential complications of radiotherapy [4]. Prior genitourinary procedures or instrumentation may be further predisposed to fistula formation. Patients with symptomatic fistulae may present with UI or urine leakage per rectum, unresponsive to conservative and less invasive therapies. Objective and subjective success in resolution of these symptoms may only be achieved with UD in this specific group of patients. UD also remains a potential option for patients wishing to avoid staged procedures [10]. For those with larger, more complex fistulae or impaired wound healing, fistula repair may have a higher risk of failure. The risk of failure is increased in those patients with prior pelvic radiation [2, 11, 12].

Life After Urinary Diversion

Patients may undergo creation of an incontinent or continent UD, often using ileum or colon (less common). For those patients that choose UD for non-oncologic indications, the possibility of bladder preservation and whether to perform a concurrent cystectomy remains a decision point [3]. The choice of UD type remains a product of informed decision-making by physician and patient. From a provider standpoint, additional factors may play a role in the decision-making process including operative time, patient health and functional

status, and surgeon's preference as well as the complication risk profile for each UD type [13, 14].

From a patient standpoint, creation of a conduit or neobladder can have significant impact on body image. This remains a viable option for a patient without known contraindications to continent UD. Absolute indications include long-standing urinary obstruction, chronic renal failure, and severe hepatic dysfunction with or without mental status changes; relative contraindications include the presence of compromised bowel function by processes such as inflammatory bowel disease [15] and urethral involvement by tumor during oncologic management. Though some patients may prefer a neobladder over creation of a conduit, the bladder outlet may be significantly damaged or strictured after prior cancer treatment and additional procedures that this may not be a feasible option. Interestingly, previous work has shown that the magnitude of impact of body image on quality of life (QoL) was not found to be important in patients with bladder cancer who underwent radical cystectomy and UD [16].

Complications

After UD, complications range in severity from superficial skin infection to death. The risk of complications ranges from 17 to 88% with patients experiencing an average of two complications post-UD within a median of 1.1 years after UD in some series. The most common complications are infectious in nature or wound-related [12, 14]. By 20 years after UD, 80% will experience at least one complication attributed to their surgery [4, 9, 13, 17•, 18–20]. Many who have experienced complications also grapple with malnutrition; nutrition is an integral protective factor which is often difficult to manage [18]. In addition to nutritional concerns, metabolic derangements and osteomalacia with resulting bone disease are other potential sequelae of UD [21]. In patients who undergo UD for treatment-refractory fistulae, we see that prior pelvic radiation is significantly associated with an increased risk of complications such as anastomotic leak, fistula recurrence, conduit revision, and delayed resolution of their preoperative urologic conditions [2, 12].

From the study by Mayer et al., men who underwent UD were noted to have the most significant complications (nine in total) as well including three deaths, two Clavien-Dindo grade 4 complications and eight readmissions within 6 weeks of UD. The authors emphasize that UD is an option of last resort, as it is not without reported risk of complications (39%) and death (13%) [9].

A recent multi-institutional retrospective study reported predictors for postoperative complications after UD in men who underwent UD with urinary conduit or continent catheterizable pouch for severe urinary adverse events after prostate radiation [18]. The authors report the majority (81%) underwent multimodal radiation therapy for treatment and later presented with urinary complaints at a median of 8 years (interquartile range, IQR 5–12) post-treatment. The mean number of procedures prior to presentation was 3.7 (SD 2.2). Half (51%) had undergone RP + EBRT while 10% had a combination of cryotherapy and radiotherapy (RT).

Reported events ranged from intractable incontinence (55%) and urethral stricture/bladder neck contracture (52%) to necrosis of the lower urinary tract (25%). Eighty-three percent of men underwent creation of a urinary conduit (93% ileal, 7% colon) with cystectomy. Short-term (within 90 days) postoperative complications included death in four men, ICU admission in 13, and early reoperations in 13 men, with a total of 16 operations between them. Eighty-five percent had long-term follow-up of a median of 16.5 months (range 3–98). Twenty-two percent underwent additional operations (27 in total) for indications related to long-term complications. In this high-risk subset of patients, the complication rates peaked at 38%, though UD offered potential relief from crippling incontinence, voiding dysfunction, recurrent infections, and fistula formation.

With regard to nutrition status, normal weight men had higher odds of short-term complications included Clavien ≥3a categories relative to overweight men (OR 4.9, 95% CI 1.3–23.1, $p = 0.02$) and obese men (OR 6.3, 95% CI 1.6–31.1, $p = 0.009$). Interestingly, there was a reduction in odds of short-term complications for each 1 point increase in BMI (OR 0.91, 95% CI 0.83–0.99, $p = 0.031$). Roughly one-third (38%) were readmitted for short-term postoperative complications; only BMI was associated with readmission (OR 0.89, 95% CI 0.8–0.97, $p = 0.009$). The authors attributed the observed association between BMI and decreasing odds of complications to improved nutrition status. They postulated that this could alternatively be explained by the obesity "paradox" in which a higher BMI has a protective effect in the setting of physiologic stressors such as post-surgical recovery [22]. In these men, "normal" weight may have in fact reflect malnutrition at rates higher than their overweight or obese counterparts.

Comparison of Diversion Types

A previous study by Nazmy et al. evaluated how complications differ by type of UD (ileal conduit, Indiana pouch, orthotopic bladder substitute) for patients treated for bladder cancer [20]. The majority were continent UDs (68%) with an overall complication rate of 78% at 90 days after UD. Hematologic complications such as postoperative anemia and transfusion were the most frequent in all three groups. At 90 days, the rate of major complications reached 40%, highest in the orthotopic bladder substitution group. Patients with an Indiana pouch had the highest rate of late complications (54.9 vs 29.1%, $p = 0008$) compared to ileal conduit and orthotopic bladder substitution combined. Compared to ileal

conduit, Indiana pouch was also a significant predictor of both urinary tract infections (OR 7.3, 95% CI 2.3–23.7, $p = 0009$) and 90-day major complications (OR 6.6, 95% CI 2–21.8, $p = 0.002$).

Monn et al. published their institution's experience with short-term morbidity and mortality for patients with bladder cancer managed with cystectomy with ileal conduit, Indiana pouch, or neobladder UD. They noted that patients with Indiana pouch UD more frequently experienced complications (67% for Indiana pouch, 49% for ileal conduits, and 35% for neobladder, $p = 0.009$). Complication rates differed significantly for three Clavien I–II complications and were most common in those with an Indiana pouch UD: deep incisional (15%) or organ space (10%) surgical site infections and fascial dehiscence (8%). Interestingly, major Clavien III–V complication rates did not differ significantly across all UD types (12–13% for all types, $p = 0.884$) and UD type was not associated with increased odds of major complications [14].

Another study compared ileal conduit, Indiana pouch, neobladder, and sexuality-preserving cystectomy with neobladder; we see no significant difference in complication rates despite complications being common (44% within 30 days of surgery, 51% for later complications). Similar to other studies, infectious minor complications such as urinary tract infections were most common. Approximately 24% experienced a metabolic acidosis: 17% in ileal conduits, 24% Indiana pouch, and 26% in orthotopic UDs. Twenty-eight percent experienced a late major complication. Type of UD was not significantly associated with early or late complications on multivariate analysis [23].

One study of 24 patients with prior prostatectomy and later underwent radical cystectomy with orthotopic neobladder creation for bladder cancer reported a similar rate of early major complications (33%). Half of the patients experienced early complications postoperatively and eight experienced complications categorized as Clavien III or greater. The authors emphasized the impact of scarring and anatomic alteration after prior cancer treatment, as well as the severe pelvic adhesions, on the operative difficulties of UD in these patients. Continence after neobladder creation is also of concern, with a continence rate of 57.9% reported in this cohort. They postulate the dissection of the external sphincter can often be difficult to appreciate given the prior surgeries, which increases the risk of postoperative incontinence and is specific to this patient population [24].

UD after pelvic exenteration for gynecologic malignancy and evaluation of UD-related complications was previously reported in a retrospective study of 133 women. The majority underwent incontinent UD creation (65%); the remainder continent UD. The majority (59%) underwent UD during management of cervical or vaginal cancer and had radiation prior to UD (90%). Pyelonephritis/urosepsis (36%) and urinary stone formation (14%) were the most common complications observed. Rates of urinary stone formation and bowel obstruction were significantly higher in the continent UD group compared to those with incontinent UDs [25•].

One study of 12 women with UI after neobladder creation highlights additional considerations specific to neobladder creation in women. In their cohort, the majority (58%) had continuous UI after UD while only 33% had intermittent continence. After a careful diagnostic evaluation, neovaginal fistulae were identified in five women and stress UI in another two. The authors stressed the importance of shared decision-making, careful consideration for possible SUI or neovaginal fistula, and the risk of additional procedures including conduit diversion in the counseling of women with neobladder UD [26].

Quality of Life After Diversion

Prior to UD, the health-related QoL is often significantly impaired. Using objective validated surveys, we see the QoL scores are often below the normalized averages of what is expected in domains including mental health, social functioning, and emotional well-being. Systematic reviews of the literature as part of the European Association of Urology guidelines for management of muscle-invasive and mestatatic bladder cancer report that the type of UD had little impact on the overall health-related QoL after cystectomy (level of evidence 2B) [27], a conclusion similarly reached by Porter et al. in a separate review of the literature [28]. After UD, there is a significant improvement in these domains, though these improvements are not associated with specific indications for UD [4, 29]. We feel that this finding remains a motivating factor in pursuing additional procedures or interventions.

One study reported the postoperative complications and quality of life measures in patients previously treated for prostate cancer and subsequently underwent cystectomy and UD for devastating lower urinary tract toxicity [17•]. In this retrospective study, 15 patients were identified who underwent radiotherapy and/or cryotherapy during treatment of prostate cancer; six underwent prostatectomy with adjuvant radiation, five external beam radiotherapy with salvage cryotherapy, and the remainder brachytherapy and/or external beam radiation. UI had been managed conservatively with a mean of 7.3 pads per day. The men subsequently underwent an average 3.7 interventions over 29 months prior to UD with cystectomy (66%) or cystoprostatectomy (33%). The majority (87%) received an ileal conduit. Postoperatively, 11 patients reported early (<30 days after surgery) or late (>30 days) complications. Early complications included abdominal dehiscence (2 patients), bowel leak (1), and *C. difficile* colitis (1) while later complications included pelvic abscess (2), incisional hernia (2), and fistula or stricture formation (2). After discharge, results from the postoperative QoL survey revealed a satisfaction score of 4.3 (Likert scale, 1–5) with many revealing they

would have undergone UD sooner by an average of 13.2 months. The authors emphasized the QoL improvement after UD with recommendations for earlier discussion of UD in patients presenting with treatment toxicities such as those observed in their cohort.

A recent meta-analysis by Cerruto et al. evaluated the health-related quality of life measures of orthotopic neobladder compared to those of patients who underwent ileal conduits for cystectomy and UD for bladder cancer. The authors restricted the review to studies using validated health-related QoL questionnaires. They reported a composite effect of significantly better QoL in patients with an ileal neobladder compared to ileal conduits. Sexual function appeared to be better in orthotopic neobladder patients while urinary function-related QoL was better in the ileal conduit patients. Global health status, physical and cognitive functioning as well as emotional function were better in orthotopic neobladder patients relative to ileal conduit patients [30].

Conclusion

UD remains a last option for some men dealing with severe urinary symptoms after treatment of pelvic malignancy. For a subset of these high-risk patients, the potential documented patient satisfaction benefits of surgical intervention offer relief may outweigh the potential risks. Further investigation is needed to better characterize the burden of disease and potential gains surrounding management of these men.

Compliance with Ethical Standards

Conflict of Interest Drs Washington, Murphy, Awad, Gaither, and Breyer declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent All reported studies/experiments with human or animal subjects performed by the authors have been previously published and complied with all applicable ethical standards (including the Helsinki declaration and its amendments, institutional/national research committee standards, and international/national/institutional guidelines).

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