Orthotopic urinary diversions after radical cystectomy for bladder cancer: lessons learned last decade

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Purpose of review
Orthotopic urinary diversion (OUD), or neobladder, is believed to be the gold standard for surgical bladder reconstruction following radical cystectomy though it is performed far less often than ileal conduits. As both a continent and intracavitary diversion, OUDs offer unique advantages for patients. Their utilization has decreased overall though, especially with the advent of robotic surgery. In this review, we will cover patient selection for OUD, functional outcomes (i.e., continence, sexual activity, quality of life [QoL]), and robotic orthotopic diversions.

Recent findings
OUDs have seen a proportionally greater decline in utilization compared with ileal conduits as the number of robotic radical cystectomies being performed with intracorporeal diversions increases. Multiple robotic series have demonstrated less perioperative blood loss and shorter hospital stays when compared with the open approach though operative times are longer, the learning curve is steeper, and overall costs may be higher in some settings. Perioperative safety and short-term oncological outcomes appear comparable. Since robotic OUDs are relatively new, functional outcomes are not yet well established. Patient satisfaction with urinary diversion is associated with informed decision-making tailored to the patient. A thorough understanding of expected short and long-term functional outcomes and the care required to maintain an OUD improves QoL and satisfaction with diversion choice.

Summary
Given the potential advantages of OUD, its decreasing use is a remarkable trend. Shared decision-making and a patient-centered approach should be used when selecting the type of urinary diversion.

Keywords
continence, neobladder, orthotopic diversion, quality of life, robotic cystectomy

INTRODUCTION
Radical cystectomy with urinary diversion remains the gold standard for the management of patients with muscle-invasive bladder cancer or high-risk non-muscle-invasive disease refractory to intravesical therapy. The most commonly performed urinary diversion is the ileal conduit followed by orthotopic urinary diversion (OUD). Each has its own advantages in regards to perioperative and functional outcomes that must be taken into account when selecting the diversion. There are few absolute contraindications in choosing an OUD, but most patients undergoing radical cystectomy are eligible for one. Patients with OUD score similarly on long-term quality of life (QoL) metrics when compared with patients with other urinary diversion types. Despite these considerations, several population-based series have demonstrated a decreased number of OUD over time. This

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phenomenon has occurred simultaneously with the increase in robotic-assisted cystectomies. In this review, we discuss patient selection; postoperative continence, sexual activity, and QoL; and discuss the results of recent series on OUD with an emphasis on robotic surgery.

**PATIENT SELECTION**

Though OUDs are not as commonly performed as incontinent diversions, most patients are eligible for this reconstructive procedure [1,2]. Few absolute contraindications exist. Patient selection is key in choosing the appropriate urinary diversion and should take into account each person's unique oncologic, functional, anatomic, and metabolic factors as detailed in Table 1.

It is widely accepted that a positive intraoperative urethral margin is an absolute contraindication for OUD. Historically, prostatic urethral invasion and bladder neck involvement for females have been other deterrents although these patients can still be offered an OUD. In a systematic review and meta-analysis of urethral recurrence after radical cystectomy, out of 6,169 patients included, the incidence of urethral recurrences was low at 4.4% and prostatic urethral involvement at the time of cystectomy did not have a significant effect on urethral recurrences [3]. An earlier study by Labbate et al. found that of the 357 patients who underwent OUD without intraoperative frozen section, 1.6% (or 6 patients) had urethral recurrences by 27 months and overall survival was unchanged in the 15 patients who had a positive urethral margin (HR 0.98, 95% CI 0.24–4.04) [4]. Interestingly, the rate of urethral recurrence for OUD has been reported to be even lower than with other urinary diversions across multiple studies though the reasons for this are unclear [5].

As far as functional contraindications, these include factors that predispose the patient to insufficient self-care that may lead to diversion-related complications. Neobladder training is rigorous and demands frequent timed voiding (i.e., initially every 1–2 h, later every 3–4 h). Approximately 5–10% of male patients and nearly 60% of female patients may need to perform intermittent self-catheterization [6,7]. As an example, an older woman with neurocognitive decline, poor physical condition, and compromised manual dexterity would not be a good candidate for OUD. This patient would be unable to catheterize herself when in retention and may not have the stamina or cognition to adhere to the strict postoperative training needed in order to optimize her expected QoL. For these reasons, younger patients tend to choose OUD, but aside from an inability or refusal to self-catheterize, neither advanced age nor performance status are absolute contraindications [5]. Metabolic concerns are fairly straightforward with renal or liver impairment being absolute contraindications. The degree of liver function necessary is not clear. For renal function, a creatinine clearance of 40 ml/min or higher is recommended [8].

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**Table 1.** Absolute and relative contraindications for orthotopic urinary diversion

| Absolutes contraindications | Relative contraindications |
|-----------------------------|----------------------------|
| **Oncologic**               |                            |
| Positive intra operative urethral margin | Prostatic urethral involvement (men) |
| Bladder neck involvement (women) |
| **Functional**              |                            |
| Inability or refusal to self-catheterize if needed or adhere to neobladder training | Older age |
| Poor performance status |
| Neurocognitive impairment |
| **Anatomic**                |                            |
| Insufficient bowel length or viable bowel | History of brachytherapy |
| **Metabolic**               |                            |
| Compromised renal or liver function | Prior pelvic radiation |
OUTCOMES

Continence

Compared with an ileal conduit, continence is one distinguishing feature of an orthotopic diversion. Daytime continence tends to be higher than at nighttime with nearly 21–70% of patients reporting continence during the day vs 19–79% at night by 12 months [9]. Over time, daytime continence appears sustainable with one study reporting 92%, 90%, and 79% continence at 10, 15, and 20 years after surgery; nighttime rates were overall less at 70%, 65%, and 55%, respectively [10]. Reporting and definitions of continence are not standardized, which is apparent in the range of rates seen in the literature. In a urinary continence follow up study of 244 patients with ileal OUD, Kretschmer et al. used a stricter definition of continence (no pad or maximum 1 safety pad daily and ≤10 g of urine loss) and found daytime and nighttime continence rates were lower than previously reported at 54.3% and 36.3%, respectively [11,12]. This is important to understand when counseling patients regarding expectations with continence postsurgery. Furthermore, because patients’ degree of bother will also vary, so will the effect of any postoperative incontinence on their QoL. Some will be troubled by a few drops of urine, whereas others will be unbothered with a nightly condom catheter or multiple nighttime awakenings to change pads.

The type of OUD constructed may also play a role in continence though the specifics of this require further research [13]. Preservation of pelvic autonomic nerves likely confers improved continence, which can be readily performed using a robotic approach [14]. It is also important to relay to patients that factors unrelated to the OUD itself can adversely affect their continence after surgery, such as advanced age, surgeon inexperience with OUD, baseline incontinence due to urethral rhahdosphincter insufficiency, poor performance status, and comorbidities like ischemic cardiac disease, obesity, and diabetes [15,16].

Sexual function

Sexual function after radical cystectomy is frequently altered due to injury to pelvic autonomic nerves during the extirpative portion of the procedure. The resulting dysfunction greatly affects the patient’s QoL. In one study assessing outcomes after OUD, investigators found sexual inactivity independently resulted in worse QoL as measured by the EORTC QLQ-C30 [17]. There is mixed data regarding sexual function and diversion type that is confounded by both age and differences in preoperative erectile function. Nerve-sparing (NS) radical cystectomy has been suggested as a means to salvage sexual function while not compromising oncologic outcomes. Furrer et al. reported on 180 patients who underwent cystectomy with OUD over a roughly 20 year time period and found 56% had unilateral and 31% had bilateral NS. Five years after surgery, 52% (75/144) of preoperatively potent patients had erections sufficient for penetration. Potency evaluation only included patients with potent erections preoperatively, and potency rates differed based on NS status with 10% (2/20) potent if no attempts at nerve sparing, 52% (42/81) if unilateral, and 72% (31/43) if bilateral NS [18]. Multiple studies suggest that uterine preservation and sparing the anterior vaginal wall can improve sexual function and is comparable to standard oncologic outcomes for radical cystectomy in well-selected female patients [19,20]. Women with bulky posterior wall tumors and cancer at the bladder base should be excluded from organ-sparing techniques given the higher chance for recurrence.

Quality of life

More than half of OUD patients report high global QoL after surgery with sexual inactivity, cancer recurrence, and stress urinary incontinence associated with worse QoL scores [17]. Pelvic floor muscle training has shown improvement of one’s QoL [12]. In comparison to patients with other urinary diversions, OUD patients fare similarly if not better. An earlier pooled analysis by Yang et al. with 3,754 patients found no difference in QoL between those with a continent vs an incontinent diversion, although a recent longitudinal study by Kretschmer et al. found that after two years, OUD patients had significantly higher general health QoL scores than those with ileal conduits [2,21]. Furthermore, the latter study found more OUD than ileal conduit patients achieved a good general QoL score (61.1% vs 32.4%, P = 0.019). Overall few patients report decision regret regardless of diversion. A recent longitudinal cohort study by Check et al. found no difference in decision regret between patients with an ileal conduit or OUD at both 6 and 18 months after surgery. In both groups at either time points, greater informed decision making was strongly associated with less decision regret [22]. Expectation management is essential in preoperative counseling. Leo et al. found that strong goal alignment occurred when patient-identified goals specific to a diversion aligned with the diversion they received. Patients who chose OUD had goals of avoiding a urostomy bag and maintaining natural bodily functions while those who opted for an ileal conduit had goals of
avoiding bladder training and urinary leakage [23]. Discussing these and other specific goals can help patients navigate their options and feel more favorably about their diversion after surgery.

Renal function

A recent study by Hautmann et al. found that among its 259 patients who received an OUD over the last 35 years, serum creatinine showed only age-related increase [24**]. Overall, no robust and comparative data exists that shows that OUDs lead to worse renal functional outcomes when compared with other urinary diversions. Multiple factors contribute to post surgical renal function deterioration that can be divided into diversion (i.e., obstruction, recurrent infections) and non-diversion-related causes (i.e., advancing age, comorbidities). Of these, urinary tract obstruction due to ureterointestinal stenosis is more common. Performing an antirefluxing ureteroileal anastomosis has long been thought to lead to increased ureteroenteric stenosis rates, possibly due to the increased dissection and handling of the ureter during surgery which lends itself to ischemic changes [25]. However, neither the more commonly used free-refluxing method nor the antireflux technique have proven superior to the other. Renal function after surgery may also decline naturally due to advanced age but also secondary to patients’ hypertension, diabetes, or obesity.

ROBOT INTRACORPOREAL ORTHOTOPIC URINARY DIVERSION

Robotic radical cystectomy with urinary diversion has transitioned from a novel procedure in urology to a mainstay in treating muscle invasive and bacillus calmette-guérin (BCG) refractory nonmuscle invasive bladder cancer. Over the past decade, there is increasing evidence that robot-assisted radical cystectomy has similar oncological results to open surgery (i.e., positive margin rates, time-to-recurrence) and a similar rate of major and minor complications [26,27]. The robotic approach boasts less operative blood loss and a reduced length of hospital stay by up to 1.5 days although it also comes with a steeper learning curve, is a lengthier operation (1–1.5 h more), and has higher costs [28–30].

Trends and techniques

The clear rise in use of robotics over the last decade has contributed greatly to our understanding and experience with robotic radical cystectomy and OUD. Geographic and institutional differences in use of continent vs incontinent diversions have been widely reported; however, some studies have noted decreased use of OUD over time. Data from a German national database showed a decline in utilization of OUD after cystectomy from 33% in 2006 to 27% in 2014 [30]. In the United States where OUD is already less frequently used than in Europe, OUD accounted for 7.5% of urinary diversions performed from 2001 to 2012 according to National Inpatient Sample data, and a decline in use can be seen from 2008 onwards [1].

Intracorporeal OUD is one of the most technically challenging cases in urology and creating robotic OUD is more complex than creating an ileal conduit. Several techniques for robot-assisted intracorporeal OUD have been developed. The most common methods are the modified Studer ‘U’ neobladder (70%), Hautmann ‘W’ modified (7.5%), ‘V’ neobladder (5%) and the Padua neobladder (5%). To date, there is insufficient data to determine if any of these techniques is superior to others [31]. The steeper learning curve with OUD creation may be responsible for the larger number of robotic ileal conduits and less robotic OUD performed though this may be corrected with time. It is undoubtedly a vicious cycle as lack of trainee access to intracorporeal OUD means less surgeons will be trained in this option for the future. Surgeon ability may also unconsciously influence physicians in counseling patients on their available options. It is important, however, that the choice of urinary diversion does not depend on the surgical approach.

Perioperative results

In the phase 3 non-inferiority trial assessing open vs robotic radical cystectomy (RAZOR), no difference was seen in recurrence, progression-free survival, or overall survival at 3 years. Of the 302 patients enrolled in the trial, 66 (22%) received OUD with comparable rates in the open and robotic groups [26].

In the past, urinary diversions were mostly performed extracorporeal. Over the last decade, this has slowly shifted to more intracorporeal diversions. A few recent studies have highlighted differences in the two approaches. A large multicenter retrospective study by Hussein et al. found mostly similar perioperative results between extracorporeal and intracorporeal diversions. After surgery, intracorporeal diversions had significantly increased total complications (66% vs 58%, P = 0.01) and readmissions (27% vs 17%, P = 0.01) when compared to extracorporeal diversions, but not high-grade complications (21% vs 24%, P = 0.22) [32]. However, in another recent retrospective study, Zhang et al. reported differently. Investigators found lower 90-day Clavien-Dindo Grade 3–5 for intracorporeal vs
extracorporeal diversions (16.9% vs 24.8%, \(P = 0.015\) [33]).

Functional results

It is difficult to accurately describe functional results after robotic-assisted radical cystectomy with intracorporeal OUD creation since there is a paucity of reliable data, and we do not have long-term results to understand if outcomes are sustainable. Nevertheless, of the few studies we have which are observational, continence rates are similar to what has been described previously. In one study just assessing intracorporeal diversion patients, 88% of men and 67% of women reported daytime continence and 74–81% of men and 67% of women reported nighttime continence at 12 months [34]. In a different observational study, patients who underwent robotic intracorporeal OUD (n = 28) reported larger pad size and greater pad wetness than those that had open radical cystectomy with OUD (n = 79) though this study suffered from a small and disproportionate sample size [35].

CONCLUSION

This opinion is an update on OUD after radical cystectomy. Criteria for patient selection and functional outcomes of OUDs have not changed significantly over the past decade. An increase in the use of robotic cystectomy is joined by a slight decrease in the use of OUD. Tailoring diversion type based on patients’ unique needs and not on surgical approach remains the cornerstone of the sustainable QoL outcomes seen with OUD patients.

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Conflicts of interest

There are no conflicts of interest.

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Papers of particular interest, published within the annual period of review, have been highlighted as:

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