Collaborative Review – Bladder Cancer

A Critical Analysis of Orthotopic Bladder Substitutes in Adult Patients with Bladder Cancer: Is There a Perfect Solution?

Wassim Kassoufa,* Richard E. Hautmannb, Bernard H. Bochnerc, Seth P. Lernerd, Renzo Colomboe, Alexandre Zlottaf, Urs E. Studerg

aDivision of Urology, McGill University Health Centre, Montreal, Canada
bDivision of Urology, University of Ulm, Ulm, Germany
cDivision of Urology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
dScott Department of Urology, Baylor College of Medicine, Houston, TX, USA
eDepartment of Urology, University Vita-Salute, Scientific Institute San Raffaele, Milan, Italy
fDivision of Urology, University of Toronto, Toronto, Canada
gDivision of Urology, University of Bern, Bern, Switzerland

Abstract

Context: Orthotopic bladder substitute (OBS) has been popularized over the past 2 decades as a diversion following radical cystectomy for invasive bladder cancer. Various reports, mostly single-center experiences, are published on patients with OBS.

Objective: This study reviews the literature regarding indications, postoperative care, complications, quality-of-life measures, as well as functional and oncologic outcomes that have been published on patients with OBS.

Evidence acquisition: An English-language literature review of the Medline database (1990 to January 2010) of published data on patients with OBS following radical cystectomy for bladder cancer was undertaken. Articles that included surgery for noncancer etiology were excluded.

Evidence synthesis: Indications and patient selection criteria have significantly widened over the past 2 decades. Comparable oncologic data have been reported between patients with OBS versus other diversions. Secondary urethral tumors seem less common in patients with OBS compared with those with conduits or continent cutaneous diversions. Durable daytime and nocturnal continence is achieved in 85–90% and 60–80%, respectively. Continence is inferior in elderly patients with OBS. Urinary retention remains significant in the female patients, ranging from 25% to 50%. Complications including electrolyte disturbances, altered sensorium and drug metabolism, mucus retention, rupture, urinary tract infections, and upper tract deterioration are reviewed.

Conclusions: Indications for OBS following radical cystectomy in patients with invasive bladder cancer have significantly widened over the past 2 decades. An OBS should be offered to both male and female patients in the absence of contraindications. Good long-term functional and oncologic outcomes can be achieved in patients with OBS treated in high-volume institutions by experienced surgeons with specific knowledge in the field. Preoperative patient information, patient selection, surgical techniques, and careful postoperative follow-up are the cornerstones to achieve good long-term results.

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* Corresponding author. Division of Urology, Montreal General Hospital, 1650 Cedar Ave. L8–315, Montreal, Quebec, H3G 1A4, Canada. Tel. +1 514 934 8246; Fax: +1 514 934 8297.
E-mail address: wassim.kassouf@muhc.mcgill.ca (W. Kassouf).

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1. Introduction

Radical cystectomy with lymphadenectomy and urinary diversion is the gold standard for invasive bladder cancer [1–4]. The goals are to provide optimal cancer outcomes, prevent renal deterioration, and maintain functional and anatomic restoration as close as possible to the natural preoperative state. A variety of urinary diversions performed to reconstruct the urinary tract includes urinary conduits, continent cutaneous diversions, and orthotopic bladder substitute (OBS). Ileal OBS has gained increasing popularity as a form of urinary diversion in patients undergoing radical cystectomy for bladder cancer in recent years. In the past, the general default was to recommend an ileal conduit as the preferred diversion. Over the years, there has been a paradigm shift to OBS as the default diversion, and the question has become, “Who is not a suitable candidate for an OBS?” This review focuses on various aspects of OBS including indications, postoperative care, complications, and quality-of-life (QoL) assessment as well as oncologic and functional outcomes.

2. Evidence acquisition

A literature review of the Medline database (primarily focused from 1990 to January 2010) was undertaken to find relevant papers on OBS following radical cystectomy with restrictions to humans and English-language publications. Articles that included surgery for noncancer etiology were excluded. Search terms included bladder cancer, urinary diversion, orthotopic bladder substitute, neobladder, ileum, urinary reconstruction, radical cystectomy, urethral recurrence, cancer outcome, continence, hypercontinence, functional results, and complications.

3. Evidence synthesis

Most publications were based on retrospective single-institutional experiences with nonstandardized reporting of complications and varying duration of follow-up. Randomized prospective studies evaluating urinary diversions are sparse. As such, most of the data presented is of level 3 or 4 evidence. Due to these limitations, this review provides suggestions based on everyday clinical practice in addition to evidence-based medical recommendations.

3.1. Selection criteria for bladder cancer patients

As the understanding of bladder cancer biology and physiologic changes post-OBS increases, the contraindications for OBS has significantly narrowed. An absolute contraindication to OBS is overt involvement of disease within the urethra distal to the prostate. Additional contraindication for OBS or any form of continent diversion is severely compromised renal function (serum creatinine levels >150 μmol/l or glomerular filtration rate <50 ml/min). Compromised renal function secondary to ureteral obstruction by cancer may normalize following percutaneous drainage and allow additional patients to proceed with an OBS. Severe hepatic dysfunction is also a contraindication to OBS because the risk of hyperammoniogenic encephalopathy is increased. Other relative contraindications include intestinal dysfunction (eg, Crohn’s disease, short bowel syndrome), urinary stress incontinence, sphincter dysfunction, and recurrent/multiple urethral strictures. Mental or physical impairment that precludes the motor hand or intellectual skills to self-catheterize should it become necessary was historically another contraindication for OBS. However, recent reports demonstrate that the need to catheterize is rare provided the reservoir has no outlet obstruction or is treated when it occurs [5]. Although feasible, previous abdominal/pelvic radiation is associated with an increased risk of complications including urethral strictures and incontinence [6,7]. With regard to age, a differentiation between physiologic age and chronologic age should be made. Chronologic age should not be a contraindication to OBS. However, in general, elderly patients (particularly octogenarians) have prolonged recovery of continence and increased risk of long-term incontinence (particularly nocturnal) when compared with younger patients, and OBS is typically not encouraged for them. Although physicians may be less inclined to perform OBS in obese patients, studies have shown that OBS is feasible and can have similar functional outcomes in patients with a higher body mass index [8]. OBS may in fact be desirable in select individuals to avoid the considerable high rate of stoma-related complications with any cutaneous diversions performed in the obese patients. Some investigators consider OBS as a relative contraindication in patients with multifocal disease, extensive carcinoma in situ (CIS), involvement of the distal prostatic urethra and/or prostatic stroma in men, or tumor located at the bladder neck in women because these scenarios are associated with a significantly increased risk of developing secondary urethral tumors [9]. However, large series documenting urethral recurrence risk with long-term follow-up have demonstrated that if the intraoperative distal urethral margin is negative, an OBS can still be performed in patients who strongly desire it even if the high-risk features just listed are present.

3.2. Bowel segment considerations

The three important properties for OBS include configuration, accommodation, and compliance. A good capacity OBS under low pressure (highly compliant) without significant high-pressure reflux is the desired outcome. Detubularized and folded segments provide these characteristics using shorter length of bowel needed compared with non-detubularized segments [10]. Ileum is the preferred bowel segment because it has less contractility and better compliance compared with colon and cecum [11,12]. Reservoirs constructed with colonic segments have higher storage pressures compared with ileum segments and may be associated with lower continence rates in patients with OBS [13,14]. Finally, as a result of mucosal atrophy over the long term, ileal segments have less reabsorption of urinary
wastes and electrolytes in patients with OBS compared with colonic segments [15].

3.3. Specific postoperative management of orthotopic bladder substitutes

Objectives of postoperative care following radical cystectomy are to minimize complications because rates can be significantly high when using standardized reporting methodology [16,17], educate patients, and provide cost-effective care. Specifics regarding postoperative management following OBS are well reviewed by Varol and Studer [18]. Briefly, we recommend two single J stents that are exteriorized through the OBS. If there is suspected blockage, the ureteral catheters can be irrigated with 2 ml of normal saline. The routine use of a nasogastric or gastrostomy tube is optional [19]. Manual irrigation and aspiration of the OBS is initiated immediately after surgery every 6–12 h. Although a suprapubic tube provide a safety mechanism in the event of urethral catheter blockage, its use is optional if the patient has the more rigid urethral catheter. Duration of urethral catheter is individualized but, in general, lasts for 2–3 wk. Some advocate the routine use of antibiotics at the time of urethral catheter removal to ensure sterile urine [18]. After removal of the urethral catheter, the patient is instructed to void every 2 h during the day (every 3 h at night) and gradually increase the interval up to every 4 h. Pelvic floor muscle exercises must be taught and should be performed several times per hour. Patients must also be taught how to void properly with an OBS: namely, relaxation of the pelvic floor, followed by slight abdominal straining. This can be assisted with gentle hand pressure on the lower abdomen and by bending forward. Patients are taught clean intermittent catheterization (CIC) if unable to adequately empty the OBS to ensure voiding without residual urine. A regular and long-term follow-up is essential for all patients with OBS and is required for optimal reservoir function and to prevent potential complications. Most experts agree that optimal outcomes in patients are preferably achieved in high-volume institutions and treated by experienced surgeons with specific knowledge in the field. Details with regard to metabolic complications, continence, voiding dysfunction, upper tract obstruction, and urethral recurrence are discussed further later in this paper.

3.4. Metabolic disturbances

3.4.1. Electrolyte abnormalities

Metabolic acidosis is more commonly seen in patients with compromised renal function. It is also associated more commonly with ileal or colonic OBS than with ileal conduit diversions. This is due to the longer contact of urine with the bowel mucosa. An initial salt-loss syndrome and acidosis as a result of ammonium reabsorption are the most frequently observed complications but may be prevented if patients are supplemented with sodium chloride and sodium bicarbonate [20]. The clinical significance of minor acidosis remains unknown. However, if severe, symptoms of fatigue, lethargy, weakness, anorexia, and vomiting can develop along with hypokalemia and hypocalcemia. Treatment is commonly effective with the administration of fluid (intravenous Ringer lactate) and alkalinization therapy with oral sodium bicarbonate (2–6 g/d) for small bowel reservoirs or potassium citrate for large bowel reservoirs (particularly if the patient cannot tolerate excess sodium supplementation due to cardiac or renal disease). If acidosis persists, chloride transport blockers (chlorpromazine 25 mg three times per day or nicotinic acid 400 mg three times per day) can be used to limit the development of further acidosis or decrease the need of alkalinizing therapy [21]. Importantly, one must ensure the absence of urinary tract infection or sepsis and that the patient is completely emptying to minimize further absorption. If severe acidosis is refractory to the measures just described, one may consider catheter reinsertion and rehydration with Ringer lactate.

Hypokalemia is more common with colonic OBS than ileal OBS because the ileum reabsorbs some of the potassium and thus is capable of blunting potassium loss by the kidney [22]. Because colon reservoirs have a tendency to lose potassium, potassium citrate is often most appropriate for colonic reservoirs. Severe hypocalcemia and/or hypomagnesemia (due to nutritional depletion and excessive renal wasting) do occur but are infrequent with OBS.

3.4.2. Altered sensorium and drug metabolism

Magnesium deficiency, drug intoxication, or abnormalities in ammonium metabolism are causes of altered mental status specific to patients with OBS. Hyperammonemic encephalopathy in patients with OBS has been reported, particularly in those with cirrhosis or altered liver function. Patients who have hyperammoniogenic coma with clinically normal liver function may have a significant infection with urease-producing bacteria. Treatment of the encephalopathy includes drainage of the OBS with a Foley catheter and oral neomycin to reduce the ammonia load. Abnormal drug metabolism can occur with drugs that are secreted unchanged in the urine and absorbed by the intestinal tract. Toxicity from chemotherapeutic agents such as methotrexate may occur in patients with OBS [23]. To minimize risk of toxicity, patients with OBS should be well hydrated and the reservoir preferably drained during treatment by frequent voiding or placement of a temporary indwelling catheter. Other drugs that can be absorbed from the intestinal tract include phenytoin, theophylline, and antibiotics.

3.4.3. Vitamin B12 deficiency

Absorption of vitamin B12 occurs primarily in the terminal ileum. Deficiency in vitamin B12 has been reported in varying degrees in patients with OBS constructed with ileum or ileocecal segment, and if deficiency persists, irreversible neurologic and hematologic sequelae may occur. Incidence and prevalence of vitamin B12 deficiency in patients with OBS remains unknown, although some report up to a third of patients may develop vitamin B12 deficiency over long-term follow-up [24]. Vitamin B12 loss seems to be more frequent either in patients whom >60 cm of ileum is resected or if the terminal ileum and ileocecal valve are resected [24,25]. Depletion of body stores of vitamin B12 requires 3–5 yr.
Although there is no consensus with regard to routine monitoring of vitamin B₁₂ levels in patients with OBS, one study reported that regular administration of vitamin B₁₂ every 6 mo have been shown to prevent development of B₁₂ deficiency at 10-yr follow-up [24].

3.4.4. Osteomalacia
Osteomalacia occurs when mineralized bone is reduced and the osteoid component becomes excessive. Over the long term, patients with OBS may develop osteomalacia due to persistent acidosis, vitamin D resistance, exchange of bone calcium against protons, and stimulation of osteoclasts. With normal renal function, severe bone defects are uncommon after OBS; the risk is higher with colonic OBS because metabolic acidosis is more frequent and calcium reuptake is less efficient than with ileal OBS. Symptoms include lethargy, pain in weight-bearing joints, and proximal myopathy. Serum calcium and phosphate are usually reduced in patients with osteomalacia, and alkaline phosphatase is elevated [26]. Treatment involved correction of acidosis along with calcium and active vitamin D supplementation.

3.5. Urinary tract infection
Unlike ileal conduits, urine cultures from OBS are typically sterile. Mixed cultures generally do not require treatment as long as the patient is asymptomatic. However, patients with Proteus or Pseudomonas in the urine should be treated regardless of symptoms because there is a risk for deterioration of the upper tracts in this setting. One should ensure adequate emptying of the reservoir because bacterial colonization is strongly correlated with postvoid residual urine in patients with OBS. Although the clinical significance of bacteriuria in asymptomatic patients with OBS is controversial, its presence has been associated with worsening incontinence [27]. Others have also reported that patients with OBS have a significant increased risk of bacteriuria (around 50%); half of these patients will develop a urinary tract infection (UTI), and 18% will develop septic episodes over a 5-yr period [28]. In asymptomatic and continent patients with OBS who adequately empty their reservoir and develop recurrent bacteriuria despite antibiotic therapy, many investigators do not recommend routine prophylactic antibiotics to reduce risk of drug-resistant bacteria and drug-related adverse effects.

3.6. Mucus production
In the early postoperative period while the indwelling catheter is still in place, it is recommended to irrigate regularly to avoid mucus buildup and blockage [18]. Mucus accumulation occurs more frequently in patients with incomplete emptying of the reservoir and those performing CIC. Increased mucus production may be an early sign of UTI or irritation of the OBS. Early and late mucus retention develops in 0.6–2% and 3% of patients, respectively [29,30]. In the rare situation when significant mucus retention develops, patients are recommended to irrigate periodically with sterile water via a catheter and evacuate mucus from the reservoir as well as a trial of medical therapy (N-acetylcysteine or urea). Importantly, the cause of residual urine must be identified and treated.

3.7. Rupture
Rupture can occur due to acute (cather trauma, mucus retention) or chronic overdistention of the OBS [31,32]. To decrease risk of rupture due to chronic overdistention, one should emphasize to the patient with OBS not to retain urine for long periods and void regularly every 3–4 h, and residual urine must be removed at regular intervals. An additional risk factor is overdistention of the OBS during hydration for cisplatin chemotherapy. In this setting, we recommend placing a temporary urethral catheter that can be removed the following day. Rupture can present with acute onset of abdominal pain in a patient with OBS. Patients with rupture who have uncontrollable pain, peritoneal signs, or sepsis require prompt surgical exploration and repair because delayed intervention can lead to life-threatening sepsis with necrosis of the reservoir and gangrene of the abdominal wall. However, if a patient is hemodynamically stable with uninfected urine and no peritoneal signs, conservative management with indwelling catheter drainage, broad-spectrum antibiotics, and close surveillance is the preferred option.

3.8. Upper tract deterioration
Renal function deterioration in patients with OBS can be caused by several specific factors related to OBS including obstruction (more commonly due to stenosis at the ureteroileal anastomosis or inability to evacuate the reservoir completely), transmission of high-pressure reservoirs to the upper tract, recurrent infections, and stone formation. Other factors that can also cause renal function compromise in general (not specific to OBS) include diabetes, hypertension, and medications. Few long-term studies have evaluated renal function after OBS, and the assessment of renal function in most studies is limited because it relied on suboptimal end points such as serum creatinine and/or radiologic studies. One prospective study followed a cohort of 74 patients with long-term follow-up (mean: 84 mo) treated with OBS and refluxing anastomosis at the afferent limb and demonstrated that only 1% of the renal units developed loss of cortical thickness if kidneys were normal preoperatively [33]. In this study, renal deterioration was seen only in patients with pre- or postoperative ureteral obstruction.

High-pressure reflux may lead to renal damage over long-term follow-up. However, the need for antireflux procedures for low-pressure detubularized OBS is not the same as with ureterosigmoidostomy, continent cutaneous diversion, or a conduit. Long-term randomized studies evaluating the role of antireflux procedures in patients with OBS are sparse. One study randomized patients who received an ileal OBS with a refluxing end-to-side ureteroileal anastomosis at the isoperistaltic limb versus an antirefluxing nipple valve [34]. After a median follow-up of approximately 5 yr, there was no difference in serum
creatinine, incidence of infected urine, and functional reservoir capacity between the two groups. It has been demonstrated that the afferent limb in the refluxing group functions as a dynamic antireflux system that causes minimal ureteral reflux under normal voiding conditions in the absence of an overfilled reservoir. Anastomotic stenosis with upper tract deterioration was significantly higher in patients with antirefluxing nipple valves compared with those with refluxing anastomosis (13.5% vs 3%) [34]. Another randomized study confirmed these findings where patients with nonrefluxing anastomosis had a higher incidence of stenosis compared with those with refluxing anastomosis (16.7% vs 3.3%) [35]. Other studies, albeit nonrandomized, have shown no difference in the rates of pyelonephritis, upper tract stone formation, or serum creatinine in patients with refluxing versus nonrefluxing anastomoses; however, the incidence of ureteroileal stenosis remains higher in the nonrefluxing anastomoses compared with a refluxing one (13% vs 1.7%) [36]. Currently, an ongoing randomized trial at the University of Southern California (USC) is comparing the Studer pouch and the T-pouch (it includes an extraserosal afferent limb that functions as a dynamic antireflux system that causes decreased functional urethral length is associated with higher rates of stress incontinence [48]. Decreased urethral sensitivity at the male membranous urethra has also been shown to be associated with higher rates of incontinence [49]. Older patients may have higher incontinence rates due to decreased tone of the urethral sphincter with advanced age, which may explain the mild increase in daytime incontinence that occurs 4–5 yr after OBS [50,51]. Takenaka et al demonstrated daytime continence rates of 75% in octogenarians following OBS [52]; others reported continence rates of 56% in patients >75 yr of age [53]. Bowel configuration can also influence continence rates in patients following OBS. In one study, elongated ileal OBS had lower early continence rates compared with spherical OBS (41% vs 69% at 3–6 mo); however, the continence rates were the same by 1 yr following surgery (89% vs 87%) [54]. Nerve-sparing cystectomy is significantly associated with better continence rates [55]. Whether this is due to the actual nerves spared or simply a more meticulous dissection around the prostatic apex with less damage to the external sphincter mechanism and membranous urethra remains to be determined. Lastly, there may be an association between gender and daytime continence rates. Most reports of the functional outcomes such as continence are derived from OBS in male patients. However, there are recent data on daytime continence in women following OBS. In a study from the Mayo Clinic on 59 women following OBS, the daytime continence rate defined as no pads per day was 90% [56]. In contrast, the USC experience reported daytime continence rates in women following OBS to be 77% [57].

3.9. Continence

Objective evaluation of continence with OBS varies across series due to different methodology including subjective and objective definition of degrees of continence determined at different time points from surgery. Multiple factors influence continence including patient age and mental status, an intact and innervated urethral sphincter, urethral length, low-pressure/large-capacity reservoir (>300 ml), absence of bacteriuria, and completeness of voiding. Continence following OBS continues to improve up to 12 mo after surgery. It is preferable to assess continence stratified by daytime versus nocturnal and by gender. Hautmann et al and Thuroff et al provided excellent guidelines for reporting continence after urinary diversion in agreement with the International Continence Society recommendations [30,37].

3.9.1. Daytime continence

Recovery of continence during the day is achieved at an earlier time compared with recovery of nocturnal continence. Analysis of various studies (some reviewed in Hautmann et al. [38]) demonstrated rates of good or excellent daytime continence at 85–90%, defined as totally dry or use of one pad per day after 12 mo from OBS [11,29,30,39–45]. Multicenter experiences have not observed significant deterioration of daytime continence over long-term follow-up [47]. Hautmann reported that decreased functional urethral length is associated with higher rates of nocturnal incontinence [59,60]. In a prospective randomized crossover study comparing 20 male enuretic patients with ileal OBS receiving oxybutynin versus verapamil, both groups showed improved urodynamic parameters and nocturnal continence status in 70% and 55% of patients, respectively [61].
Some studies reported nocturnal continence rates to be inferior in females compared with men. Although studies on nocturnal continence in the female population following OBS are less extensive, rates of 57% and 66% have been reported [56,57]. Similar to daytime continence, higher age also correlated with higher nocturnal incontinence rates (up to 60% in octogenarians) [52]; however, this factor was not consistent across all studies. Lastly, bowel segments may influence nocturnal continence rates. In a recent randomized trial comparing 71 patients who underwent ileal OBS versus ileocolonic OBS, the nocturnal continence rates were superior with ileal OBS compared with ileocolonic OBS (76.3% vs 48.5%; p < 0.05) [62]. In summary, preconditions for obtaining good continence results include good capacity (350–500 ml) of a detubularized ileal cross-folded reservoir, preserved sphincter function (length and its innervations), and sterile urine.

### 3.9.3. Clean intermittent catheterization

In patients with OBS, voiding is initiated by relaxing the pelvic floor while increasing intra-abdominal pressure. Optimum OBS emptying is achieved in the sitting position. Most patients with OBS void spontaneously with adequate emptying of the reservoir. Dysfunctional voiding that requires CIC can occur in approximately 10% of the male population with an OBS, ranging between 4% and 33% depending on various reports and duration of follow-up [11,39,46,63,64]. It is crucial to exclude the presence of a urethral stricture when evaluating patients with voiding dysfunction necessitating CIC. In addition to dysfunctional voiding and stricture of the ileourethral anastomosis, other causes of urinary retention include kinking of the OBS outlet, infraneovesical obstruction due to local recurrence (8.7%), obstructive mucosal prolapse (0.9–7%), cystolithiasis (0.2%), prostatic adenoma (1.7%), and distal urethral strictures (2–3.5%) [25,65]. If a funnel-shaped outlet is avoided and deobstructive surgery is appropriately implemented, excellent long-term results with spontaneous voiding can be observed, and CIC can be avoided in 96% of patients at 10 yr [5,25]. Urinary retention requiring CIC is more common in women, as first described by Hautmann et al. [66], with long-term prevalence rates of 25–50% reported in other series [57,65,67]. It is unclear why the rates of urinary retention are significantly higher in women compared with men. Some investigators believe that this increase is due to changes in the urethral innervations and inability to open the urethra or to relax the pelvic floor. As a consequence of excessive straining, angulation and obstruction of the neobladder-urethral junction and formation of a “pouchocèle” in women is observed. A recommendation that may potentially (but is not necessarily proven to) decrease risk of urinary retention includes placement of omentum posterior to the reservoir, suspension of the vaginal fornices to Cooper ligament, suspension of the vaginal apex to the sacrum, avoidance of excess pouch size (by selecting bowel segment of 40 cm instead of 60 cm), preservation of the autonomic nerve supply to the upper vagina and periurethral area, and avoidance of anastomosis at the end of the funnel-shaped outlet of the reservoir but rather at the most caudal part of the reservoir [48,68–74].

### 3.10. Oncologic outcomes

#### 3.10.1. Secondary urethral tumors

In patients with OBS, early symptoms of secondary urethral tumors may include hematuria (microscopic or gross) and changes in urinary stream. Later symptoms can include urethral bleeding and induration of the periurethral tissue. For patients undergoing the recommended surveillance of the urethra with periodic washes or voided cytology, a secondary urethral tumor can be detected by an abnormal urinary cytology only.

#### 3.10.1.1. Men

Overall, in patients with primary and recurrent bladder cancer, the incidence of urethral tumors is approximately 6% [75]. The incidence of urethral recurrence after radical cystectomy ranges from 0% to 18%, with a meta-analysis in 2002 reporting an incidence of 8.1% [76]. Patients with OBS seem to have a lower risk of secondary urethral tumors compared with those with heterotopic urinary diversions [77,78]. Stein et al reported a 5% risk of secondary urethral tumors with OBS compared with 9% with cutaneous diversions; whether these findings are due to the proximity of the ileum in exerting a protective effect on the retained urethra or due to a patient selection bias remains controversial [79]. Prostatic urethral involvement (superficial and/or stromal invasion) is significantly associated with increased risk of secondary urethral tumors. In the largest reported series of 768 patients by Stein et al, secondary urethral tumors in patients without prostatic urethral involvement, superficial prostatic urethral involvement (mucosal or ductal), and stromal involvement was 6%, 12%, and 18%, respectively, after a median follow-up of 13 yr [79]. Although factors such as multifocal disease and CIS are reported to be associated with an increased risk of concurrent prostatic urethral involvement or secondary urethral tumors [9], studies from USC have demonstrated that they do not appear to significantly increase risk of secondary urethral tumors following radical cystectomy; however these patients reported have not been prospectively followed [77,80]. Selection criteria in the USC series include a negative intraoperative frozen-section analysis of the distal urethral margins at cystectomy. Because the false-negative rates of frozen sections can be as high as 30–50%, other institutions perform routine preoperative paracollicular biopsies to select patients against OBS if CIS is present.

#### 3.10.1.2. Women

Because OBS was first applied to male patients and the incidence of bladder cancer is much lower in women, there is a more extensive experience and longer follow-up in male compared with female patients. Urethral tumor on presentation in women who underwent radical cystectomy for bladder cancer is lower than in men with an incidence of 2–7% [81,82]. In women, tumors at the bladder neck or involvement of the anterior vaginal wall are factors significantly associated with concomitant disease within the urethra [82,83]. Most studies show that almost all
female patients with an uninvolved bladder neck also had an uninvolved urethra; similarly, all female patients with urethral involvement also had concomitant bladder neck involvement. As such, routine preoperative bladder neck biopsies are recommended to rule out the presence of cancer or CIS and help counsel patients. However, because 50% of women with bladder neck and/or anterior vaginal wall involvement do not demonstrate tumor within the urethra, these patients can still be eligible for OBS if they are willing to accept the significant risk of developing secondary urethral tumors. Importantly, there are some case reports of skip lesions where urethral involvement was present in the absence of bladder neck involvement; as such, full-thickness intraoperative frozen section of the distal urethral margin is recommended in all patients who are undergoing an OBS.

3.10.2. Pelvic recurrence

Radical cystectomy with bilateral lymphadenectomy provides excellent local/pelvic control of bladder cancer. In a large series of 1054 patients treated with radical cystectomy, the local recurrence rate was 7% after a median follow-up of 10 yr [1]. Even in women without extensive posterior involvement who were selected to undergo OBS after preservation of the entire vagina, local recurrences were seen in only 5% of the patients [84]. Local recurrence rates remain low but slightly higher in patients with non-organ-confined node-negative disease and node-positive disease compared with organ-confined node-negative disease (13%, 13%, and 6%, respectively) [1]. Similar findings were also observed in a large European series of patients treated with radical cystectomy where local recurrence rates of 13–16% were observed in patients with non-organ-confined disease [2,3]. As such, patients with non-organ-confined disease may still benefit from the advantages of an OBS, particularly because 60% and 30% of patients with extravasal or node-positive disease are alive without evidence of disease at 10 yr after cystectomy. Furthermore, even with local recurrence, most patients (>90%) maintain good OBS function [25,85]. Importantly, the quality of the cystectomy is not compromised in patients receiving an OBS. After adjusting for pathologic stage, several studies demonstrated no difference in cancer-specific survival in patients (male and female) receiving ileal conduit and/or continent cutaneous diversions versus OBS following radical cystectomy [57,86]. OBS appears safe and feasible even in patients with positive nodes and does not affect the ability to receive salvage treatment [87]. However, in the rare situation where patients are found to have intraoperatively gross palpable adenopathy, it is unclear whether they will benefit from the advantages of an OBS because their prognosis remains guarded with limited life expectancy and they commonly die before they attain optimal continence recovery.

3.11. Quality of life

OBS is technically more challenging with slightly longer operative times than ileal conduits. Because longer bowel segments are needed, the risk of bowel dysfunction (diarrhea, vitamin B12 malabsorption) may be higher with OBS than ileal conduit. Early studies comparing ileal conduits with continent cutaneous diversions have shown that patients are satisfied regardless of the type of diversion and adapt well biopsychosocially as long as an adequate and realistic preoperative education is instituted about their type of diversion [88,89]. In a retrospective study, Bjerre et al compared health-related QoL of 38 patients with OBS to 29 with ileal conduits after a median follow-up of 1 yr [90]. Although urinary leakage occurred more frequently in patients with OBS, urinary leakage affected conduit patients more severely, and they scored higher on a leakage distress scale. Sexual and nonsexual physical contacts decreased in most conduit patients but only in the minority of OBS patients. In a recent study, 57 patients who underwent an ileal conduit or ileal OBS were assessed preoperatively with a Karnofsky performance score and followed with a health-related QoL questionnaire [91]. In a similar age-group population, there was no significant difference in most QoL indexes, but body image issues persisted in the conduit group. OBS patients had significantly better physical function and a more active lifestyle. Several other reports have attempted to examine the QoL of patients with various types of diversions and showed inconsistent results among different types of diversions [92–97].

After careful analysis of all the QoL studies, it becomes evident there is a lack of good data evaluating QoL in patients with OBS versus other diversions. Most QoL studies used inappropriate questionnaires. Although some are validated, they were not designed to evaluate specific urologic aspects but rather QoL of patients during chemotherapy (eg, European Organization for Research and Treatment of Cancer C-30, SF-36). Most urologists perform only/mostly one type of diversion. There is a strong bias because patients are subjected preoperatively for selection of a specific diversion and hence patients are prepared for the disadvantages and advantages associated with the different diversions. As such, there is a real risk that patient-led preferences are inappropriately labeled against the OBS. We firmly believe that the QoL of patients with a well-functioning OBS is significantly better than other forms of diversions. However, in agreement with a systematic review in 2005 [98], randomized prospective trials using well-validated disease-specific health-related QoL outcome instruments are warranted to render definitive conclusions regarding QoL measures with different type of diversions.

4. Conclusions

Indications for OBS following radical cystectomy in patients with invasive bladder cancer have significantly widened over the past 2 decades. An OBS should be offered to both male and female patients in the absence of contraindications. Good long-term functional and oncologic outcomes can be achieved in patients with OBS treated in high-volume institutions by experienced surgeons with specific knowledge in the field. Preoperative
patient education, patient selection, surgical techniques, and careful postoperative follow-up are the cornerstones to achieve good long-term results.

**Author contributions:** Wassim Kassouf had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

**Study concept and design:** Kassouf, Hautmann, Bochner, Lerner, Colombo, Zlotta, Studer

**Acquisition of data:** Kassouf.

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**References**


