Update of the ICUD–SIU International Consultation on Bladder Cancer 2018: urinary diversion

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Abstract

Purpose To provide a comprehensive overview and update of the joint consultation of the International Consultation on Urological Diseases (ICUD) and Société Internationale d’Urologie on Bladder Cancer Urinary Diversion (UD).

Methods A detailed analysis of the literature was conducted reporting on the different modalities of UD. For this updated publication, an exhaustive search was conducted in PubMed for recent relevant papers published between October 2013 and August 2018. Via this search, a total of 438 references were identified and 52 of them were finally eligible for analysis. An international, multidisciplinary expert committee evaluated and graded the data according to the Oxford System of Evidence-based Medicine.

Results The incidence of early complications has been reported retrospectively in the range of 20–57%. Unfortunately, only a few randomized controlled studies exist within the field of UD. Consequently, almost all studies used in this report are of level 3–4 evidence including expert opinion based on “first principles” research.

Conclusions Complications rates overall following RC and UD are significant, and when strict reporting criteria are incorporated, they are much higher than previously published. Complications can occur up to 20 years after surgery, emphasizing the need for lifelong follow-up. Progress has been made to prevent complications implementing robotic surgery and fast track protocols. Preoperative patient information, patient selection, surgical techniques, and careful postoperative follow-up are the cornerstones to achieve good results.

Keywords Urinary diversion · Radical cystectomy and complications · MIBC and urinary diversions
Introduction

Radical cystectomy (RC) with urinary diversion (UD) is one of the most challenging procedures in Urological Surgery due to the technical complexity [1]. However, it remains the best surgical option for patients with muscle-invasive bladder cancer (MIBC). The three most common types of UD are incontinent and continent abdominal wall UD (ileal or colonic conduit, ureterocutaneostomy, continent pouches), urethral diversions or neobladders and rectosigmoid diversions. Any form of UD has its specific problems. In this context, surgeons must continue to refine their surgical technique of RC and UD to provide the utmost safety for the patient. Moreover, it is important to constantly work to improve outcomes due to rising healthcare costs. We discuss the 3rd International Consultation on Bladder Cancer recommendations on the reconstructive options after RC, the criteria for selection of the most appropriate procedure, and the outcomes and complications associated with the available UD options.

Materials and methods

This is a non-systematic review to perform an update on UD in bladder cancer (BC). An international, multidisciplinary expert committee evaluated and graded the published data according to the Oxford System of Evidence-based Medicine [2]. The present analysis focused on the following topics (keywords): urinary diversion, radical cystectomy and complications, MIBC and urinary diversions. The preliminary results of this analysis were presented during a joint international consultation of the ICUD and Société Internationale d’Urologie held in Lisbon (Portugal) on October 2017, and its proceedings were later published in electronic book format. For this updated publication, an exhaustive search was conducted in PubMed for recent relevant papers published between October 2013 and August 2018 using upon mentioned topics as keywords. Via this search after further exclusion of records not related to this review, two independent authors (O.R.F and J.P) screened titles and abstracts of a total of 438 references. A total of 386 articles were excluded by to be unrelated articles, articles not fully addressing topics or repeated publications on the same cohort. Fifty-two of them were finally eligible for analysis.

Figure 1 provides the respective CONSORT diagram for the included studies. A summary of conclusions and recommendations is provided in Table 1.
General aspects

Metabolic consequences

The metabolic consequences of UD may vary depending on the different bowel segments used. Loss of bowel length, reducing its absorptive capacity and the contact of urine with the bowel results in shift of electrolytes leading to metabolic changes. These are influenced by co-morbidities such as impaired renal and hepatic function, previous bowel resection, as well as by the patient’s age. Moreover, the movement of water and electrolytes is impacted by the bowel segment used for diversion, the length of the bowel segment, the time that the urine is retained in the reservoir, the concentration of urinary solutes, urinary pH, and osmolality (Table 2).

Secondary tumors

Secondary tumors can be developed in 0.18–15% of patients after UD; Their frequency is higher after ureterosigmoidostomies (UST) and cystoplasties. The risk of colon tumor following UST is increased 8–550-fold compared to the general population, depending on the patient’s age at the time of operation [3]. The latency period is shorter if the operation is performed because of malignant disease. It can be speculated that an adenoma–adenocarcinoma sequence exists for the secondary tumors similar to that observed in normal colon carcinogenesis [4]. Most experts suggest that a regular endoscopic control in UST and cystoplasties is mandatory from the 5th postoperative year onward, whereas in the case of neobladders, conduits, and pouches it seems sufficient to perform endoscopy in the presence of symptoms such as hematuria or new onset of hydronephrosis.

Pelvic radiation and urinary diversion

Pelvic radiation may produce a damaging exposure of the cecum, appendix, and terminal ileum. Intraoperative inspection of the small and large intestine plays an important role in the selection of appropriate bowel segments for the desired reconstruction.

Bowel that shows thickening or fibrotic changes from prior radiation exposure should be avoided as the use of such segments may lead to poor healing and urinary leaks.

Initial recommendations for UD in patients who have received pelvic radiation included the preferred use of the transverse colon as a conduit [5]. Nevertheless, recent evidence suggests that ileum could be used safely with a similar complication risk to that observed with colonic conduits in the setting of prior pelvic radiation treatment [6]. It would seem from the cumulative evidence published to date that in properly selected patients orthotopic reconstruction can be performed with reasonable functional outcomes assuming 66–77% overall complications [7]. Although the follow-up was limited, it would appear that the neobladder can tolerate moderate levels of radiation (39.6–65 Gy) [8]. Salvage cystectomy after failed bladd ersparing therapy for MIBC is associated with acceptable morbidity, although complication rates are slightly higher than for other RC series [9].

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**Table 1** Summary of conclusions and recommendations for urinary diversion

**RARC** robot-assisted radical cystectomy, **LE** level of evidence, **GR** grade of recommendation
Pregnancy/sexual dysfunction after radical cystectomy and urinary diversion

The etiology of sexual dysfunction after UD is multifactorial, and although effective management options are available, broad awareness of the importance of these long-term consequences of cystectomy and UD have gained a firm footing only over the last several years. Nerve-sparing and organ-preserving approaches to surgery are the most effective strategies to avoid the constellation of complications that negatively affect sexual function and pregnancy [10].

Enhanced recovery after surgery (ERAS)

Originally described in the 1990s [10, 11], enhanced recovery after surgery (ERAS) pathways are standardized interdisciplinary protocols that are aimed at improving outcomes after surgery by minimizing variation in preoperative, perioperative, and postoperative best practice [11]. Key elements in the preoperative pathway include education to ensure compliance, nutritional optimization, smoking cessation, functional rehabilitation, and carbohydrate loading. In the perioperative setting, some common elements include the prevention of hypothermia, judicious fluid management, venous thromboembolism prophylaxis (compression stockings, pneumatic compression, and prophylactic heparin), use of Alvimopan, and avoidance of opioid-based analgesics. Postoperatively, this includes avoidance of nasogastric tube decompression, early oral feeding, early drain removal, early ambulation, avoidance of narcotics through the use of Ketorolac, Acetaminophen, or regional blocks, and continued use of Alvimopan.

While there are several theoretical explanations for why ERAS protocols would improve outcomes, the evidence supporting their use in cystectomy patients is not consistently rooted in robust experimental data. This may explain why there is striking variation in both the magnitude and the direction of the effect of ERAS protocols on perioperative

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<th>Bowel segment</th>
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<th>Disadvantages</th>
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<td>Least water permeability</td>
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<td>PPIs or H2 blockers, Irrigation of the bladder with bicarbonate, Vitamin B12 supplementation, Fluid intake, carbonic acid, intravenous saline</td>
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<td>No malabsorptive sequelae</td>
<td>Higher water permeability than the colonic wall</td>
<td>Dilute urine: hypovolemic, hypochloremic, hyperkalemic acidosis</td>
<td>Oral sodium bicarbonate, catheter drainage, Ringer lactate infusion</td>
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<td>Terminal ileum</td>
<td>Length of the mesentery</td>
<td>Higher water permeability than the colonic wall</td>
<td>Vitamin B12 deficiency, Dilute urine: hypovolemic, hypochloremic, hyperkalemic acidosis</td>
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<td>Colon</td>
<td>Less water-permeable than the ileal wall</td>
<td>Storage function of right-sided colon</td>
<td>Steatorrhea, Vitamin B12 deficiency, Bile salt loss, Diarrhea</td>
<td>Cholestyramine 3 × 4 g per day, Vitamin B12 supplementation, Oral sodium bicarbonate, catheter drainage, Ringer lactate infusion</td>
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PPIs proton pump inhibitors

aLifelong supplementation required

bMainly in cases of concomitant resection of the ileocecal valve and use of the right-sided colon

cOr potassium citrate, in cases of hypokalemic acidosis

Pregnancy/sexual dysfunction after radical cystectomy and urinary diversion

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outcomes [12]. Nevertheless, in a recent meta-analysis, ERAS reduced the length of the index hospitalization, lowered the rate of low-grade complications, and improved the time to bowel function without impacting overall readmission rates [12]. While these findings are compelling and seem to support the implementation of ERAS for cystectomy patients, they must be contextualized within the obvious limitation that most of these studies constituted low-level evidence. In lieu of a clinical trial, a natural experiment employing a difference-in-differences approach may be the next logical step as it would similarly offer relatively unbiased effect estimates while mitigating the confounding effect of contemporaneous changes to clinical care.

**Quality of life (QoL) following urinary diversion**

“Quality of life” is a construct that encompasses the physical, psychosocial, and functional health and reflects a patient satisfaction with various aspects of his/her life. To minimize bias, quality of life is most commonly assessed by standardized patient-reported survey instruments. Valid, reliable, longitudinal measurement of quality of life has important implications for research comparing treatment options as well as for delivery of patient-centered clinical care.

While there is little variation in general or disease-specific quality of life outcomes by urinary diversion type historically, emerging evidence from high-quality publications in the last few years has suggested that some important differences may exist. Whereas incontinent diversions have demonstrated greater improvement in physical health compared to continent diversions, continent diversions have shown superior emotional function and body image compared to cutaneous diversion [13, 14]. While there is sparse information regarding the effect of gender on quality of life after cystectomy, male patients seem to show better scores in the neobladder subgroup [13] and female patients exhibit no difference between ileal conduits and neobladders [15].

With respect to sexual function, some evidence has suggested improved outcomes with neobladders compared to ileal conduits [16]. Informed decision making remains the key factor for choice of diversion for patients undergoing cystectomy. Future patient-centered research is needed and has been identified as a priority for funding agencies.

**Types of urinary diversion**

**Ileal conduit (IC)**

Urinary conduit using ileum is the most commonly performed conduit procedure [17]. IC is indicated in patients who do not qualify for a continent diversion or do not want to comply with the inconveniences of a continent diversion. In this context the physical and mental status, age, body habitus (obesity, malformations), extent of disease, prognosis, urethral involvement, kidney and liver function, and the patient’s expectations and preferences, as well as the surgeon’s experience and preference, often play an important role in the decision. A short-term complication highly relevant to IC is urine leak at the ureteroileal anastomosis, which occurs in 2–5.5% of patients [18].

This problem can be obviated by proper surgical technique and placement of ureteral stents. Two studies showed that stenting reduced the risk of early upper tract dilatation and was associated with improved bowel function [19, 20]. Madersbacher et al. analyzed all conduit-associated complications in 131 patients occurring later than 3 months after surgery. Sixty-six percent of patients had conduit-associated complications [21]. The most frequent complications were renal insufficiency (27%), problems with the stoma (24%), intestinal problems (24%), symptomatic upper urinary tract infections (23%), conduit and ureter anastomotic stenosis/strictures (14%), and urolithiasis (9%). In the first 5 years of their analysis, 45% of patients developed complications. This percentage increased over time to 50%, 54%, and 94% among patients who survived 10, 15, and over 15 years, respectively.

**Orthotopic bladder substitution (OBS)**

Although there is no age cut off for OBS, in practice many patients over the age of 80 years will opt for a conduit. While the reasons are not entirely clear, it is almost certainly related to increased comorbidities and worse overall health status in older patients. The motivation of the patient is the most important factor when considering the suitability for an OBS, although it is difficult to assess this objectively [22]. There are different techniques using ileal segments of OBS [23]. Our committee continues to consider a minimum annual hospital caseload of 25 surgeries, done by not more than two surgeons, to be the definition of a high-volume surgeon’s experience and preference, often play an important role in the decision. A short-term complication highly relevant to IC is urine leak at the ureteroileal anastomosis, which occurs in 2–5.5% of patients [18].

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Retention can occur in the early postoperative period but often appears after an initial phase of good NB function and emptying [27]. In the Ulm series of 116 women, the rate of retention increased steadily over time to approximately 50% by 5 years [28].

**Continent cutaneous diversion (CCD)**

A variety of techniques for construction of a CCD have been described. All use detubularized segments of bowel using either the right colon, ileum, or a combination of the two, folded to form a spherical shape. The advantages of CCD over OBS include immediate continence and, once the reservoir has expanded, ability to void less frequently and often sleep through the night [29]. However, the disadvantages of CCD are a longer, more complex surgical procedure, absolute dependence on catheterization for emptying, and higher rates of late complications related to the efferent continence mechanism that often require surgery to resolve. Continence is usually immediate, though pouch volume will increase and pressure decrease during the initial few months. Because of the routine catheterization, bacterial colonization of the reservoir is the norm, and attempts to sterilize the urine are fruitless.

Many patients receive unnecessary antibiotics from primary care providers. However, febrile infections and even urosepsis do occur, especially in the early postoperative period. Reported rates of early and late febrile infections range from 20 to 40% [30], which is probably higher than with OBS or conduit.

**Anal diversion**

The Mainz pouch II is an adaptation of ureterosigmoidostomy through the addition of rectosigmoid pouch formation [31]. Briefly, the rectosigmoid colon is detubularized and reconfigured into a spherical shape to mitigate the risk of pyelonephritis and anal incontinence. Detubularization of these bowel segments interferes with bowel contractions thereby decreasing storage pressures and increasing capacity, improving urinary continence rates and upper tract preservation. A prerequisite for a successful continent anal diversion is a competent anal sphincter to control continence and allow spontaneous evacuation. Furthermore, coexistent large bowel pathology must be excluded by colonoscopy, computed tomography colonography, or conventional colonography with double contrast prior to surgery.

According to the published literature, daytime urinary continence is achieved in 98% and nighttime continence in 90% [32]. Early postoperative complications include urinary leakage and ileus in up to 30% as well as late complications such as pyelonephritis, ureteral implantation stenosis, and metabolic acidosis in up to 28%, ureter stenosis dilatation/reimplantation in up to 11%, and the need for alkalizing agents in up to 69% [32, 33]. Given the risk of secondary adenocarcinoma formation, indications for Mainz pouch II have over the years become restricted to older patients in whom the latency period until development of a colorectal tumor would exceed their life expectancy and to younger patients who will not accept a stoma for cultural, socioeconomic, or cosmetic reasons and would otherwise have no alternative for UD.

**Robotic diversion**

Globally the indications for robot-assisted radical cystectomy (RARC) with urinary diversion are identical to open radical cystectomy (ORC). Even in the most experienced hands, the rates of overall complications after cystectomy are high, reaching up to 64%, while the rates of Clavien ≥ 3 complications can be as high as 41% [34]. In systematic analyses, meta-analyses and large national health care registries it seems that there is a consistent pattern in complications and outcomes comparing RARC to ORC [35, 36]. RARC shows decreased blood loss, transfusion rates, length of stay (LOS) and overall complications, which may be expected from a minimally invasive procedure (Table 3). On the other hand, the operative times are longer for RARC as compared to ORC.

Blood loss and transfusion are classified as grade 2 complications in the Clavien–Dindo classification system and may be downplayed in complication reporting. However, blood loss leading to transfusion is a major predictor of worse oncological prognosis [37–39].

The most important advantages deriving from RARC were a reduction of blood loss and a shorter hospital stay, while operative time was shorter after ORC. Data about long-term functional and oncological outcomes are still lacking, nevertheless a recent randomised, phase III, non-inferiority trial (RAZOR study) concluded that RARC was not inferior to ORC for 2-year progression-free survival; Adverse events occurred in 101 (67%) of 150 patients in the RARC group and 105 (69%) of 159 patients in the ORC group [40].

There is a controversy on whether to perform an intracorporeal (ICUD) or extracorporeal urinary diversion (ECUD). Justifications for ECUD are a shorter operative time and the need for an extraction incision. ICUD presents important challenges included a longer operative time and a steeper learning curve as well as the number of technical challenges. One of the largest series reporting outcomes after ICUD describe a U-shaped neobladder technique and report 80–90% daytime continence rates with complication rates similar to open series [41]. A retrospective analysis of intracorporeal with ECUD including 935 patients who had RARC showed equivalent operative time and no difference.
in the reoperation rates. Patients with ICUD were at lower risk of experiencing postoperative complications [42]. While we are still waiting for stronger scientific evidence RARC with ICUD appears to be a viable alternative to an open operation, offering patients the advantages of a minimally invasive approach.

**Palliative diversion**

Palliative urinary diversion (UD) refers to the insertion of a double J ureteral catheter, a percutaneous nephrostomy (PCN), subcutaneous drainage, ileal conduits or ureterocutaneousostomy. Consensus is lacking as to whether the initial attempt at a palliative UD should be made via ureteral stenting or PCN; however, the need for external urinary drainage devices with PCN may have quality of life implications.

Yet, the insertion of a ureteral double J stent is not always feasible because of extensive pelvic disease, anatomic deformities, bleeding, or ureteral compression. In a series of 186 patients, insertion of a ureteral double J catheter failed in 21% of patients [43].

As an alternative to conventional forms of palliative UD, a subcutaneous pyelovesical bypass was developed more than a decade ago. Desgrandchamps et al. reported on a series of 19 patients who received 27 subcutaneous tubes as a palliative UD [44]. All patients had a PCN as the initial form of diversion. At follow-up of about 6–8 months, the authors observed an improvement of the physical function scale (EORTC QLC-30) as a result of the elimination of the PCN and a parallel worsening of the symptom scale secondary to disease progression [44]. The authors concluded that the subcutaneous pyelovesical bypass provides a better QoL than a standard PCN in terminally ill patients by making them external tube free.

In summary, the survival of a patient undergoing palliative UD is dismal and in the range of 100 days [31, 45]. The decision to perform palliative UD should be approached cautiously in patients with a poor performance status, low serum albumin levels, and other risk factors for rapid decompensation. Since the 6-month survival rate is less than 15%, and in some series even below 5%, the palliative UD in this setting needs to be an individualized decision discussed in a multidisciplinary approach with a medical oncologist.

**Conclusions**

Complications rates overall following RC and UD are significant, and when strict reporting criteria are incorporated, they are much higher than previously published. Complications can occur up to 20 years after surgery, emphasizing the need for lifelong follow-up. Progress has been made to prevent complications implementing robotic surgery and fast-track protocols. Preoperative patient information, patient selection, surgical techniques, and careful postoperative follow-up are the cornerstones to achieve good results. Increased adoption of robotic technology in surgery should lead to future randomised trials across different organ sites to assess the true clinical value provided by novel technology. The International Consultation on Urological Diseases (ICUD) has looked at the published evidence and produced recommendations at various levels.

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**Compliance with ethical standards**

**Conflict of interest** The authors declare that they have no conflict of interest.

**Research involving human participants and/or animals** For this type of study formal consent is not required. This article does not contain any studies with human participants or animals performed by any of the authors.
I informed consent. Informed consent was obtained from all individual participants included in the study.

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