Original Article

Comparison of postoperative complications of ileal conduits versus orthotopic neobladders

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Background: Radical cystectomy (RC) and urinary diversion (UD), with either an ileal conduit (IC) or an orthotopic neobladder (NB), is a complex surgery, in which various complications can occur. In this study, we compared postoperative complication rates after a RC and UD performed for the treatment of muscle-invasive bladder cancer or recurring high-risk non-muscle-invasive bladder cancer in our center.

Methods: We retrospectively included 604 patients that underwent UDs from December 1996 to August 2015. Complications were classified by type and severity according to the Clavien-Dindo classification (CDC). Univariate and multivariate analyses were performed to identify predictive factors of short-term (≤30 d), intermediate-term (31–90 d), and long-term (>90 d) complications.

Results: Four hundred and forty-five (74%) and 159 (26%) patients received ICs and NBs, respectively. These groups had significantly different long-term complication rates (IC: 39.7% *vs.* NB: 49%, P=0.046), but similar short-term (P=0.319) and intermediate-term complication rates (P=0.397). Short-term complications (CDC I–V) were predicted by male gender, age-adjusted Charlson comorbidity index (aCCI) ≥3, and American Society of Anesthesiologists (ASA) score ≥3. Compared to minor short-term complications (CDC I–II), major short-term complications (CDC III–V) were predicted by male gender and a previous abdominal/pelvic surgery, and long-term major complications were predicted by the type of UD (NB).

Conclusions: The increasing risk of short-term complications with increasing aCCI and ASA score can be used when counseling the patients who are planned to undergo a RC with UD. Patients that receive NBs should be informed of the increased risk of reoperations compared to an IC.

Keywords: Bladder cancer (BC); complication; ileal conduit (IC); neobladder (NB); radical cystectomy (RC)

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Introduction

Bladder cancer (BC) is the 10th most common type of cancer in both sexes worldwide (1,2). A radical cystectomy (RC) with lymph node dissection and urinary diversion (UD) is the treatment of choice for muscle-invasive BC or recurring high-risk non-muscle-invasive BC (3). Complication rates are high with RC plus UDs (RC+UDs), primarily due to the UD (4). The most common UDs are the ileal conduit (IC) and the orthotopic neobladder (NB). However, although the UD type does not affect the long-term oncological outcome, it remains unknown which UD type provides the best overall quality of life (3,5). Comparisons of ICs and NBs have not demonstrated improved quality of life, but NBs might be the best option for carefully selected patients (6,7). Currently, ICs are the most common UD, while the NB is primarily performed in high-volume centers due its technical complexity (8,9). Only motivated patients that understand the new bladder voiding mechanism are candidates for NBs (9).

Here, we compared ICs and NBs in terms of the incidence, severity, and timing of postoperative complications. This information could facilitate decisions regarding RC+UDs. Furthermore, we identified independent risk factors for postoperative complications. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/tau-20-713).

Methods

All procedures performed in this study working on human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of UZ/KU Leuven (No. S59188). For a retrospective study, formal consent was not required. After obtaining Institutional Review Board approval, we reviewed the medical records of patients treated with open RC+UDs performed by two experienced oncologic urologists (H Van Poppel, S Joniau) at the University Hospitals Leuven, between December 1996 and August 2015. Eligible patients received RC+UDs for urothelial carcinoma. Exclusion criteria were RCs for non-oncological disorders (e.g., neurogenic bladder disease, bladder pain syndrome, radiation cystitis, disabling urinary incontinence), palliative RCs, RCs combined with nephroureterectomy, and complete urinary tract extirpations. All IC patients received a Bricker anastomosis, and Leuven N-pouch was performed for the patients who had a NB. The technique for each UD was described previously (10-12). Briefly, Leuven N-pouch was created with a 50-cm segment of preterminal ileum that was folded into four equally long parts. Three parts formed the N-shaped pouch while the most proximal part remained intact to form the afferent isoperistaltic limb onto which the ureters were anastomosed in an end-to-end fashion. UD types were selected in a decision-making process shared between patients and surgeons.

The analyzed preoperative and intraoperative patient characteristics are listed in *Tables 1*,*2*. Perioperative complications were categorized with the modified Clavien-Dindo classification (CDC) as minor (CDC I–II) or major (CDC III–V) (13). Complications were also categorized as short-term (≤ 30 days), intermediate-term (31–90 days), or long-term (>90 days), based on the European Association of Urology (EAU) Guidelines recommendations on reporting surgical complications (14).

The primary endpoint was the incidence of short-, intermediate-, and long-term perioperative complications with ICs compared to NBs. Secondary endpoints were the effects of prognostic clinical and pathological characteristics on complication rates.

Age at surgery was categorized as ≤60, 61–70, and ≥71 years. Comorbidities were categorized based on American Society of Anesthesiologists (ASA) score (≤2 *vs.* ≥3), Charlson comorbidity index (CCI: 0 *vs.* 1 *vs.* 2 *vs.* ≥3), and age-adjusted CCI (aCCI: ≤2 *vs.* 3–5 *vs.* >5).

Statistical analysis

Descriptive statistics were expressed as the mean ± standard deviation (SD) or the percentage for continuous and non-numeric variables, respectively. Continuous and categorical variables were compared with the students' *t*-test and chi-squared test, respectively. Significance was set at $P<0.05$. Univariate and multivariate analyses were performed to identify independent predictors of complications. After performing a Pearson's correlation test, significant factors in univariate analyses were included in multivariate logistic regression models. Statistical analyses were performed with MedCalc version 16.2.1 (MedCalc Software bvba, Oostende, Belgium).

Table 1 Preoperative characteristics according to type of UD

Variables	IC (n=445)	NB (n=159)	P value
Gender, N (%)			0.106
Male	361 (81.1)	138 (86.8)	
Female	84 (18.9)	21 (13.2)	
Age at surgery (years), N (%)			<0.0001
≤60	51 (11.5)	102 (64.2)	
61–70	165 (37.1)	50 (31.4)	
≥71	229 (51.5)	7 (4.4)	
Continuous, mean ± SD	70.7±8.2	58.1±8.2	
CCI, N (%)			<0.0001
0	182 (40.9)	108 (67.9)	
1	105 (23.6)	25 (15.7)	
2	85 (19.1)	18 (11.3)	
≥3	73 (16.4)	8 (5.0)	
aCCI, N (%)			<0.0001
0 [≤2]	103 (23.1)	109 (68.6)	
1 [3–5]	281 (63.1)	47 (29.6)	
2 [>5]	61 (13.7)	3 (1.9)	
ASA, N (%)			<0.0001
≤2	315 (71.1)	136 (86.6)	
≥3	128 (28.9)	21 (13.4)	
BMI (kg/m^2), mean ± SD	25.5±3.9	26.1±4.8	0.127
Neo-adjuvant chemotherapy, N (%)	69 (15.5)	33 (20.8)	0.130
Previous abdominal/pelvic surgery, N (%)	226 (50.8)	54 (34.0)	<0.0001
Previous abdominal/pelvic irradiation (excluding any primary RT with curative intent to the bladder), N (%)	31 (7.0)	2 (1.3)	0.007
Clinical T stage, N (%)			0.376
T0	4 (0.9)	5 (3.1)	
Ta	15 (3.4)	5 (3.1)	
CIS	27 (6.1)	10 (6.3)	
T1	76 (17.1)	39 (24.5)	
T2	231 (51.9)	85 (53.5)	
T3	50 (11.2)	11 (6.9)	
T4	34 (7.6)	1 (0.6)	
Unknown	8 (1.8)	3 (1.9)	
High-grade disease, N (%)	411 (92.4)	143 (89.9)	0.204
Clinical node-positive disease, N (%)	40 (9.0)	9 (5.7)	<0.0001
Active smoker, N (%)	102 (22.9)	55 (34.6)	0.013
Pre-op serum creatinine (mg/dL), mean ± SD	1.20±0.68	1.04±0.22	0.0039

CCI, Charlson comorbidity index; aCCI, age-adjusted Charlson comorbidity index; ASA, American Society of Anesthesiologists physical status classification system; BMI, body mass index; RT, radiotherapy; CIS, carcinoma in situ.

Table 2 Intraoperative characteristics related to the type of UD

Variables	IC (n=445)	NB (n=159)	P value
Operation time (min), mean ± SD	209.2±50.5	223.6±45.7	0.002
Estimated blood loss (mL), mean ± SD	1,297±1,014	1,224±703	0.423
Extent of lymphadenectomy, N (%)			0.141
Limited	35 (8.2)	15 (9.6)	
Extended	221 (51.5)	80 (51.3)	
Super-extended	150 (35.0)	60 (38.5)	
Intraoperative adhesiolysis, N (%)	106 (23.9)	17 (10.8)	0.001
Small bowel injury, N (%)	4 (0.9)	1 (0.6)	0.752
Colon injury, N (%)	2 (0.4)	0 (0.0)	0.399
Rectal injury, N (%)	10 (2.3)	0 (0.0)	0.057
Major vascular injury, N (%)	30 (6.8)	9 (5.7)	0.642
Length of hospital stay (days), mean ± SD	21.0±11.2	23.7±10.9	0.009

UD, urinary diversion; SD, standard deviation.

Results

Clinical characteristics

Of 927 patients that received RC+UDs, 604 were included after exclusion criteria; 445 had ICs and 159 had NBs (*Table 1*). The patients with ICs were significantly older and had higher CCI, aCCI and ASA scores (all: P<0.0001), and more frequent previous abdominal and/or pelvic surgery (P=0.001) than the patients with NBs. Neoadjuvant chemotherapy (NAC) rates were similar between groups (P=0.130).

Due to technical complexity, NBs required longer operation times than ICs (P=0.002; *Table 2*). Blood loss was similar between groups (P=0.423). Due to more frequent previous abdominal/pelvic surgery, ICs required intraoperative adhesiolysis more frequently than NBs (P=0.001).

Postoperative complications

Short-term (≤30 days) complications

Overall, minor and major short-term complications occurred at similar rates with ICs and NBs (P=0.319, *Table 3*). One patient with a NB died perioperatively, due to a perforation of the small intestine, which resulted in septic shock and acute myocardial infarction.

The most common minor complications were urinary tract infection (UTI) with fever, pneumonia, superficial wound dehiscence, blood transfusion, and ileus (defined as no sign of bowel transit for >5 days). The most common major complications were intestinal anastomotic leakage that required a reoperation, urosepsis, re-laparotomy due to evisceration, and pulmonary infection. Among the most common complications, pulmonary, and wound-related complications occurred significantly more frequently with ICs than with NBs (*Table 3*).

Intermediate-term (31–90 days) complications

In the intermediate term, data were missing for 33 patients (27 ICs and 6 NBs), due to loss to follow-up or death. Overall, minor and major intermediate-term complications occurred at similar rates with ICs and NBs (P=0.397, *Table 4*).

Most complications in both groups were of genitourinary origin, and the most common were UTIs. The most common minor complications were gastrointestinal complications in both groups, and herniations and stoma problems in the IC group. In both groups, the most common major complications were upper urinary tract (UUT) obstructions that required ureteral stenting or a nephrostomy tube insertion and fistulas that required re-operations. Total gastrointestinal, genitourinary and wound complications, and herniations were more common with NBs than with ICs.

Table 3 Short-term (≤30 days) complications in patients after RC with IC or NB

Complications	CDC	IC (n=445)	NB (n=159)	Total (n=604)	P value
Short-term (≤30 days) complications	0	163 (36.6)	64 (40.3)	227 (37.6)	0.319
	1–2	220 (49.4)	80 (50.3)	300 (49.7)	
	3–5	62 (13.9)	15 (9.4)	77 (12.7)	
	Total	445 (73.7)	159 (26.3)	604 (100.0)	
Complication category					
1. Gastrointestinal		128 (28.8)	39 (24.5)	167 (27.6)	0.50
Ileus		117 (26.3)	32 (20.1)	149 (24.7)	0.27
	II	116 (26.1)	31 (19.5)	147 (24.3)	0.22
	IIIb	1 (0.2)	1 (0.6)	2 (0.3)	1.00
Leakage from uretero-intestinal anastomosis	II	0 (0)	1 (0.6)	1 (0.2)	0.59
Intestinal anastomotic leakage		4 (0.9)	4 (2.5)	8 (1.3)	0.27
Need for nasogastric catheter	II	1 (0.2)	2 (1.3)	3 (0.5)	0.36
Need for re-surgery	IIIb	3 (0.7)	2 (1.3)	5 (0.8)	0.86
Closed loop syndrome	IIIb	2 (0.5)	0 (0)	2 (0.3)	0.97
Acute cholecystitis	IIIb	1 (0.2)	0 (0)	1 (0.2)	1.00
Infected intraabdominal hematoma	IIIb	1 (0.2)	0 (0)	1 (0.2)	1.00
Intraabdominal bleeding	IIIb	1 (0.2)	0 (0)	1 (0.2)	1.00
Intra- & retroperitoneal hematoma + ischemic intestine	IIIb	1 (0.2)	0 (0)	1 (0.2)	1.00
Fistula between neobladder and intestine	IIIb	0 (0)	1 (0.6)	1 (0.2)	0.59
Small intestine perforation	IIIb	1 (0.2)	0 (0)	1 (0.2)	1.00
Small intestine perforation with subsequent septic shock & AMI	V	0 (0)	1 (0.6)	1 (0.2)	0.59
2. Genitourinary		61 (13.7)	24 (15.1)	86 (14.2)	0.81
Fistula	II	0 (0)	1 (0.6)	1 (0.2)	0.59
Ureteral stenting	IIIa/b	1 (0.2)	2 (1.3)	3 (0.5)	0.36
UTI with fever		54 (12.1)	16 (10.1)	71 (11.8)	0.63
	II	53 (11.9)	16 (10.1)	70 (11.6)	0.68
	IVa	1 (0.2)	0 (0)	1 (0.2)	1.00
Urosepsis		6 (1.3)	5 (3.1)	11 (1.8)	0.28
	II	3 (0.7)	3 (1.9)	6 (1.0)	0.40
	IVb	3 (0.7)	2 (1.3)	5 (0.8)	0.86
3. Cardiovascular		14 (3.1)	1 (0.6)	15 (2.5)	0.16
Atrial fibrillation	II	6 (1.3)	0 (0)	6 (1.0)	0.32
Supraventricular tachycardia	II	0 (0)	1 (0.6)	1 (0.2)	0.59

Table 3 (*continued*)

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Complications	CDC	IC (n=445)	NB (n=159)	Total (n=604)	P value
Ventricular tachycardia	II	2 (0.4)	0 (0)	2 (0.3)	0.97
Cerebrovascular incident		4 (0.9)	0 (0)	4 (0.7)	0.53
	II	3 (0.7)	0 (0)	3 (0.5)	0.71
	IVa	1 (0.2)	0 (0)	1 (0.2)	1.00
AMI (requiring PTCA)	IVa	2 (0.4)	0 (0)	2 (0.3)	0.97
4. Hematological and vascular		67 (15.1)	18 (11.3)	85 (14.1)	0.38
Postoperative ES transfusion	II	56 (12.6)	12 (7.6)	68 (11.3)	0.16
Fresh frozen plasma transfusion	II	4 (0.9)	1 (0.6)	5 (0.8)	1.00
Pulmonary embolism	II	4 (0.9)	3 (1.9)	7 (1.2)	0.58
Deep venous thrombosis	II	3 (0.7)	2 (1.3)	5 (0.8)	0.86
5. Pulmonary		52 (11.7)	5 (3.1)	56 (9.3)	0.006
Dyspnea	II	1 (0.2)	0 (0)	1 (0.2)	1.00
Pulmonary infection		43 (9.7)	3 (1.9)	46 (7.6)	0.005
	II	34 (7.6)	3 (1.9)	37 (6.1)	0.02
	IVa	8 (1.8)	0 (0)	8 (1.3)	0.20
	IVb	1 (0.2)	0 (0)	1 (0.2)	1.00
Pleural infection	II	2 (0.4)	0 (0)	2 (0.3)	0.97
Desaturation		2 (0.4)	0 (0)	2 (0.3)	0.97
	I	1 (0.2)	0 (0)	1 (0.2)	1.00
	IVa	1 (0.2)	0 (0)	1 (0.2)	1.00
Pneumothorax	IIIa/b	0 (0)	2 (1.3)	2 (0.3)	0.12
Acute pulmonary edema	IVa	1 (0.2)	0 (0)	1 (0.2)	1.00
Acute respiratory failure	IVa	3 (0.7)	0 (0)	3 (0.5)	0.71
6. Lymphatic system		8 (1.8)	0 (0)	8 (1.3)	0.20
Symptomatic lymphocele	II	6 (1.3)	0 (0)	6 (1.0)	0.32
Lymphedema	I	2 (0.4)	0 (0)	2 (0.3)	0.97
7. Wound		82 (18.4)	14 (8.8)	96 (15.9)	0.019
Infection	II	25 (5.6)	3 (1.9)	28 (4.6)	0.10
Superficial wound dehiscence	II	46 (10.3)	9 (5.7)	55 (9.1)	0.14
Evisceration	IIIb	11 (2.5)	2 (1.3)	13 (2.2)	0.57

CDC, Clavien-Dindo classification; AMI, acute myocardial infarction; UTI, urinary tract infection; PTCA, percutaneous transluminal coronary angioplasty; ES, erythrocyte suspension.

Table 4 Intermediate-term (31–90 days) complications in patients after RC with IC or NB

Complications	CDC	IC (n=418)	NB (n=153)	Total (n=571)	P value
Intermediate-term (31–90 days) complications	0	302 (72.2)	107 (70.0)	409 (71.6)	0.397
	1–2	88 (21.1)	36 (23.5)	124 (21.7)	
	3–5	28 (6.7)	10 (6.5)	38 (6.7)	
	Total	418 (73.2)	153 (26.8)	571 (100.0)	
Complication category					
1. Gastrointestinal		15 (3.6)	13 (8.5)	28 (4.9)	0.04
Paralytic ileus	I	0 (0)	1 (0.7)	1 (0.2)	0.60
Persistent tenesmus	I	0 (0)	1 (0.7)	1 (0.2)	0.60
Diarrhea	II	3 (0.7)	9 (5.9)	12 (2.1)	0.0008
Constipation	II	10 (2.4)	2 (1.3)	12 (2.1)	<0.0001
Small intestine resection	IIIb	2 (0.5)	0 (0)	2 (0.4)	0.96
2. Genitourinary		41 (9.8)	18 (11.8)	59 (10.3)	0.65
Renal function decline	I	1 (0.2)	1 (0.7)	2 (0.4)	1.00
Hematuria	I	1 (0.2)	0 (0)	1 (0.2)	1.00
Stone disease (spontaneous passage)	I	1 (0.2)	0 (0)	1 (0.2)	1.00
Penile wound	I	4 (1.0)	0 (0)	4 (0.7)	0.52
UTI with fever	II	12 (2.9)	8 (5.2)	20 (3.5)	0.29
Balanitis (circumcision)	IIIa	1 (0.2)	0 (0)	1 (0.2)	1.00
Orchitis	II	1 (0.2)	0 (0)	1 (0.2)	1.00
UUT obstruction		11 (2.6)	5 (3.3)	16 (2.8)	0.91
Conservative (mild HUN)	I	3 (0.7)	0 (0)	3 (0.5)	0.69
Need for surgery	IIIa/b	8 (1.9)	5 (3.3)	13 (2.3)	0.53
LUT obstruction (urethrotomy)	IIIb	N/A	2 (1.3)	2 (0.4)	N/A
Fistula	IIIb	8 (1.9)	2 (1.3)	10 (1.8)	0.90
Acute renal failure	IVa	1 (0.2)	0 (0)	1 (0.2)	1.00
3. Wound		18 (4.3)	2 (1.3)	20 (3.5)	0.16
Chronic wound problems	I	7 (1.7)	2 (1.3)	9 (1.6)	1.00
Decubitus wound	I	1 (0.2)	0 (0)	1 (0.2)	1.00
Superficial dehiscence	II	2 (0.5)	0 (0)	2 (0.4)	0.96
Evisceration	IIIa/b	4 (1.0)	0 (0)	4 (0.7)	0.52
Wound infection	IIIb	4 (1.0)	0 (0)	4 (0.7)	0.52

Table 4 (*continued*)

Table 4 (*continued*)

Complications	CDC	IC (n=418)	NB (n=153)	Total (n=571)	P value
4. Herniation		16 (3.8)	3 (2.0)	19 (3.3)	0.42
Incisional herniation	I	6 (1.4)	3 (2.0)	9 (1.6)	0.95
Parastomal herniation		10 (2.4)	N/A	10 (1.8)	N/A
Conservative	I	9 (2.2)	N/A	9 (1.6)	N/A
Surgical repair	IIIb	1 (0.2)	N/A	1 (0.2)	N/A
5. Hematological and vascular		3 (0.7)	0 (0)	3 (0.5)	0.69
Deep venous thrombosis	II	2 (0.5)	0 (0)	2 (0.4)	0.96
Vaginal bleeding	I	1 (0.2)	0 (0)	1 (0.2)	1.00
6. Infectious (other)		4 (1.0)	2 (1.3)	6 (1.1)	1.00
FUO	II	2 (0.5)	0 (0)	2 (0.4)	0.96
Abscess (requiring drainage)	IIIa	2 (0.5)	2 (1.3)	4 (0.7)	0.63
7. Pulmonary		1 (0.2)	0 (0)	1 (0.2)	1.00
Pneumonia (with MOF)	V	1 (0.2)	0 (0)	1 (0.2)	1.00
8. Lymphatic system		2 (0.5)	0 (0)	2 (0.4)	0.96
Lymphedema	I	2 (0.5)	0 (0)	2 (0.4)	0.96
9. Miscellaneous		22 (5.3)	3 (2.0)	25 (4.4)	0.16
Stoma problems (irritation, etc.)		12 (2.9)	N/A	12 (2.1)	N/A
	I	11 (2.6)	N/A	11 (1.9)	N/A
	IIIb	1 (0.2)	N/A	1 (0.2)	N/A
Skin irritation	I	1 (0.2)	0 (0)	1 (0.2)	1.00
Skin necrosis		3 (0.7)	0 (0)	3 (0.5)	0.69
	I	2 (0.5)	0 (0)	2 (0.4)	0.96
	IIIa	1 (0.2)	0 (0)	1 (0.2)	1.00
Dyspareunia	I	1 (0.2)	0 (0)	1 (0.2)	1.00
Depression	II	1 (0.2)	0 (0)	1 (0.2)	1.00
Acute gout attack	II	1 (0.2)	0 (0)	1 (0.2)	1.00
Neuropathic pain	II	2 (0.5)	0 (0)	2 (0.4)	0.96
Electrolyte imbalance	I	1 (0.2)	1 (0.7)	2 (0.4)	1.00
Rise in alkaline phosphatase	I	0 (0)	1 (0.7)	1 (0.2)	0.60
Iron depletion	I	0 (0)	1 (0.7)	1 (0.2)	0.60

CDC, Clavien-Dindo classification; UTI, urinary tract infection; UUT, upper urinary tract; HUN, hydroureteronephrosis; LUT, lower urinary tract; FUO, fever of unknown origin; MOF, multiple organ failure; N/A, not applicable.

Table 5 Long-term (>90 days) complications in patients after RC with IC or NB

Complications	CDC	IC (n=378)	NB (n=143)	Total (n=521)	P value
Long-term (>90 days) complications	0	228 (60.3)	73 (51.0)	301 (57.8)	0.046
	1–2	85 (22.5)	32 (22.4)	117 (22.5)	
	3–5	65 (17.2)	38 (26.6)	103 (19.8)	
	Total	378 (72.6)	143 (27.4)	521 (100.0)	
Complication category					
1. Gastrointestinal		15 (4.0)	14 (9.8)	29 (5.6)	0.027
Diarrhea	II	8 (2.1)	13 (9.1)	21 (4.0)	0.0015
Ileus	IIIb	7 (1.9)	0 (0)	7 (1.3)	0.23
Ischemic intestine perforation	IIIb	0 (0)	1 (0.7)	1 (0.2)	0.62
2. Genitourinary		96 (25.4)	72 (50.3)	168 (32.2)	0.00026
Ureterolithiasis	IIIb	11 (2.9)	5 (3.5)	16 (3.1)	0.96
Pouch calculi	IIIb	N/A	7 (4.9)	7 (1.3)	N/A
UTI	II	50 (13.2)	28 (19.6)	78 (15.0)	0.16
UUT obstruction		34 (9.0)	23 (16.1)	57 (10.9)	0.06
Nephrostomy or stenting	IIIa/b	33 (8.7)	17 (11.9)	50 (9.6)	0.41
Ureteral reimplantation	IIIb	1 (0.3)	6 (4.2)	7 (1.3)	0.0029
LUT obstruction (urethral dilatation)	IIIa/b	N/A	8 (5.6)	8 (1.5)	N/A
Fistula	IIIb	1 (0.3)	1 (0.7)	2 (0.4)	1.00
3. Herniation		85 (22.5)	29 (20.3)	114 (21.9)	0.75
Incisional hernia		41 (10.8)	29 (20.3)	70 (13.4)	0.022
Conservative	I	29 (7.7)	14 (9.8)	43 (8.3)	0.59
Repair	IIIb	12 (3.2)	15 (10.5)	27 (5.2)	0.0034
Parastomal hernia		36 (9.5)	N/A	36 (6.9)	N/A
Conservative	I	28 (7.4)	N/A	28 (5.4)	N/A
Repair	IIIb	8 (2.1)	N/A	8 (1.5)	N/A
Both		8 (2.1)	N/A	8 (1.5)	N/A
Conservative	I	5 (1.3)	N/A	5 (1.0)	N/A
Repair	IIIb	3 (0.8)	N/A	3 (0.6)	N/A

CDC, Clavien-Dindo classification; UTI, urinary tract infection; UUT, upper urinary tract; LUT, lower urinary tract; N/A, not applicable.

Long-term (>90 days) complications

Overall, long-term minor complications occurred at similar rates between groups. However, major long-term complications occurred more frequently with NBs than with ICs (P=0.046; *Table 5*).

UTIs were the most common minor complication in both groups. Diarrhea was more common with NBs than with ICs.

After 3 months, major complications increased in both groups, due to UUT obstructions (CDC IIIa/b). NBs were prone to neovesicourethral anastomotic stricture (5.6%), which required urethral dilatation due to high postvoiding residual urine volume or difficulty in voiding. Ureterolithiasis rates were comparable between groups.

Table 6 Univariate and multivariate analysis of patients' characteristics for postoperative complications occurring on short-, intermediate- and long-term (only the significant multivariate analysis is mentioned)

Characteristics	No *vs.* any complication (CDC I–V)						Major complications (CDC ≥ III)					
	Univariable analysis			Multivariable analysis			Univariable analysis			Multivariable analysis		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Short term (≤30 d)												
Gender (men)	1.61	1.05–2.46	0.028	1.64	1.06–2.51	0.025	4.26	1.52–11.93	0.006	4.66	1.66–13.12	0.004
Age at surgery	1.02	0.85–1.23	0.818	–	–	–	1.02	1.00–1.05	0.086	–	–	–
ASA[1] ≥3	1.38	1.07–1.78	0.012	1.36	1.05–1.75	0.018	1.47	0.87–2.49	0.155	–	–	–
aCCI ≥3	1.45	1.03–2.05	0.032	1.49	1.05–2.11	0.024	1.48	0.87–2.53	0.138	–	–	–
Previous abdominal or pelvic surgery	1.25	0.90–1.74	0.189	–	–	–	2.05	1.25–3.35	0.005	2.19	1.33–3.60	0.002
NB *vs.* IC	0.79	0.55–1.14	0.220	–	–	–	0.60	0.32–1.10	0.084	–	–	–
NAC	1.22	0.78–1.90	0.391	–	–	–	0.81	0.41–1.60	0.549	–	–	–
Intermediate (31–90 d)												
Gender (men)	1.02	0.60–1.33	0.946	–	–	–	0.99	0.40–2.45	0.980	–	–	–
Age at surgery	1.00	0.98–1.02	0.871	–	–	–	1.01	0.96–1.05	0.924	–	–	–
ASA[1] ≥3	1.18	0.69–1.81	0.414	–	–	–	1.07	0.68–1.47	0.253	–	–	–
aCCI ≥3	1.36	0.90–2.07	0.149	–	–	–	1.21	0.52–2.84	0.659	–	–	–
Previous abdominal or pelvic surgery	0.99	0.67–1.47	0.973	–	–	–	1.99	0.89–4.47	0.094	–	–	–
NB *vs.* IC	0.93	0.60–1.44	0.740	–	–	–	1.46	0.63–3.34	0.375	–	–	–
NAC	0.67	0.38–1.16	0.154	–	–	–	0.62	0.18–2.10	0.414	–	–	–
Long term (>90 d)												
Gender (men)	1.21	0.76–1.96	0.406	–	–	–	1.22	0.67–2.24	0.506	–	–	–
Age at surgery	1.70	0.97–1.00	0.153	–	–	–	0.98	0.96–1.02	0.078	–	–	–
ASA[1] ≥3	1.04	0.91–1.35	0.658	–	–	–	1.17	0.70–1.44	0.258	–	–	–
aCCI ≥3	0.87	0.61–1.26	0.468	–	–	–	0.75	0.48–1.16	0.195	–	–	–
Previous abdominal or pelvic surgery	1.44	0.98–2.12	0.065	–	–	–	0.98	0.64–1.52	0.938	–	–	–
NB *vs.* IC	1.46	0.99–2.15	0.057	–	–	–	1.74	1.10–2.75	0.017	–	–	–
NAC	0.96	0.60–1.53	0.861	–	–	–	0.98	0.55–1.76	0.953	–	–	–

[1], ASA: ASA 1–2 vs. ASA 3–4. ASA, American Society of Anesthesiologists physical status classification system, aCCI, age-adjusted Charlson comorbidity index; NAC, neoadjuvant chemotherapy; NB, neobladder; IC, ileal conduit; OR, odds ratio; CI, confidence interval.

Pouch calculi occurred in 4.9% of NBs.

Although total herniation rates were similar between groups, incisional hernias occurred significantly more frequently with NBs than with ICs (P=0.022). In addition, ICs were prone to parastomal hernias (*Table 5*).

Predictors of complications

Male gender, ASA score ≥3, and aCCI ≥3 were independent risk factors for any short-term complications (CDC I–V) (*Table 6*, *Figure 1*). Major short-term complications were associated with male gender and previous abdominal/pelvic

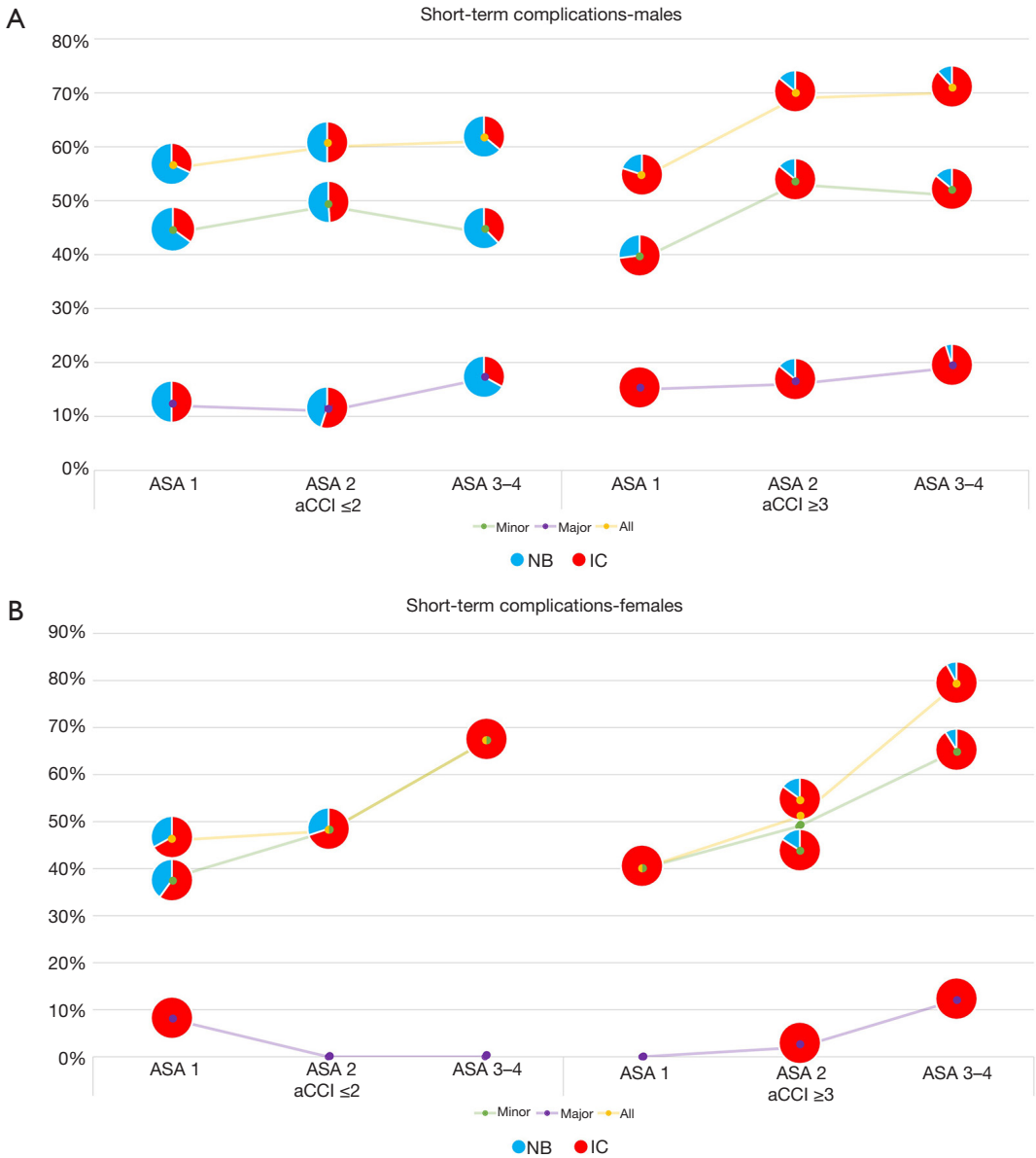

Figure 1 Short-term complication rates in males (A) and females (B) according to grouping with regard to age-adjusted Charlson comorbidity index (aCCI) and American Society of Anesthesiologists (ASA) scores. NB, neobladder; IC, ileal conduit.

surgery. None of the studied factors were associated with minor or major intermediate-term complications. Major long-term complications were associated with the NB. NAC administration did not impact the complication risk at any time.

Our reports fulfilled nine out of ten criteria that have been proposed by Martin *et al.* for accurate and comprehensive reporting of surgical complications (15).

Discussion

Despite recent improvements in perioperative outcomes, RC+UDs remain associated with non-negligible morbidity and mortality (5,16-18). In a comprehensive retrospective review of RC+UDs (n=1,142 patients), Shabsigh *et al.* showed a high overall complication rate (64%), and 13% major complications (18). Currently, due to complexity and morbidity, NBs are performed much less frequently

than ICs (15% *vs.* 85%) (19). Two population-based observational studies showed that ICs and NBs had similar complication rates. However, those studies lacked details on BC characteristics (20,21) and did not give detailed data on complications by using the previously recommended reporting guidelines (18).

Our short-term postoperative minor and major complication rates of 49.7% and 12.7%, respectively, were similar to the 51% and 13%, respectively, reported by Shabsigh *et al.* (18). Our top five short-term complications were gastrointestinal, genitourinary, wound-related, hematologic, and pulmonary in origin, consistent with previous studies (18,22,23).

Figure 1 summarizes many of the important observations from this study. First of all, aCCI ≥3, ASA ≥3, and male gender were independent predictors of any short-term complications. Secondly, rising aCCI and further increasing ASA score show increased risk of complications. Moreover, the age at surgery was not significantly correlated with short-term complications; therefore, aCCI might be more important/useful than biological age in selecting a UD type.

Our results were consistent with the prospective PROMETRICS 2011 study that showed aCCI ≥3 and ASA score ≥3 could independently predict complications after an incontinent UD (24). Although Roghmann *et al.* used slightly different parameters, they found that CCI ≥3 predicted any and high-grade complications and ASA score ≥3 predicted high-grade complications (25). Similarly, Hirobe *et al.* found that CCI ≥2 predicted high-grade complications (26).

Although we expected to observe a difference in the complications between the patients with IC and with NB before our analyses, the UD type did not significantly impact any short- and intermediate-term complications. This can be explained by intuitively the right selection of patients by the surgeon, so that healthier and younger patients underwent a NB, and less healthy and older patients had an IC. However, NBs increased the relative risk of major long-term complications, including UUT obstruction, neovesicourethral stenosis, and pouch calculi (*Table 5*). These findings were partly contrary to previous studies, in which the UD type was not significantly associated with any complications or any major 90-day complications (24,27).

There is an apparent selection bias for UD type when a patient receives preoperative radiotherapy. Only 5.4% of the total patients in this cohort received preoperative irradiation. Moreover, patients were unequally divided between groups (7% *vs.* 1.3% in IC and NB, respectively), impeding comparison between the groups. Our patients have been included in a recent paper which demonstrated that previous radiation increased the relative risk of experiencing any complication after RC (28).

Our relatively high rates of long-term complications could be attributed to dedicated, systematic data registration, performed with a method similar to that recommended by Shabsigh *et al.* (18). A previous abdominal/pelvic surgery increased the relative risk of major short-term complications, possibly due to intraoperative adhesiolysis.

Interestingly, during all three follow-up periods, genitourinary complications were more common with NBs than with ICs. Gastrointestinal complications, particularly diarrhea, were also more common with NBs than with ICs during the intermediate- and long-term follow-ups, but not in the short term.

We recently showed that NAC administration was not associated with short-term postoperative morbidity or mortality (29). In the present study, NAC rates were similar between groups, and they did not affect complication rates in the short, intermediate and long term.

This study had some limitations. Some data on patients and complications (particularly minor complications) might be missing, due to underreporting inherent to retrospective studies and loss to follow-up. The baseline characteristics of the IC and NB populations were quite different. We attempted to perform case-matched analysis and propensity score matching, however, the remaining populations in both groups were too small for reliable statistical analysis. Therefore, we used multivariate analysis correcting for possible confounders. However, we accept that multivariate analysis cannot fully adjust for the differences. Therefore, our results should be interpreted with caution. Ideally a formal matched analysis should be done in a larger multicenter population. The patients included in this analysis date from before the implementation of enhanced recovery after surgery (ERAS) guidelines in our institution, which explains the long hospital stay of the patients. An explicit, detailed history was recorded for all patients that returned to our center for follow-up visits. This approach might have led to more frequent detection of (minor) complications, like UTIs. The relatively long mean time to the last follow-up or death (52.6 months) might partially explain our elevated late complication rate. Moreover, our reports fulfilled 9 out of 10 criteria that have been proposed for reporting of surgical complications. These limitations and strengths should be kept in mind when interpreting the

study results.

Conclusions

Our groups showed significantly different preoperative characteristics; therefore, we could not recommend a particular UD type as the optimal choice for the patients undergoing a RC. However, the increasing risk of short-term complications with increasing aCCI and ASA score, as depicted in *Figure 1*, can be used when counseling the patients who are planned to undergo a RC with UD.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study working on human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of UZ/KU Leuven (No. S59188). For a retrospective study, formal consent was not required.

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