# Robot-assisted radical cystectomy with intracorporeal urinary diversion decreases postoperative complications only in highly comorbid patients: findings that rely on a standardized methodology recommended by the European Association of Urology Guidelines

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ORIGINAL ARTICLE

# Robot-assisted radical cystectomy with intracorporeal urinary diversion decreases postoperative complications only in highly comorbid patients: findings that rely on a standardized methodology recommended by the European Association of Urology Guidelines

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## Abstract

**Introduction** The available studies comparing robot-assisted radical cystectomy (RARC) with intracorporeal (ICUD) vs. extracorporeal (ECUD) urinary diversion have not relied on a standardized methodology to report complications and did not assess the effect of different approaches on postoperative outcomes.

**Materials** Two hundred and sixty seven patients treated with RARC at a single center were assessed. A retrospective analysis of data prospectively collected according to a standardized methodology was performed. Multivariable logistic regression models (MVA) assessed the impact of ICUD vs. ECUD on intraoperative complications, prolonged length of stay (LOS), 30-day Clavien Dindo (CD) $\geq 2$ complications and readmission rate. Interaction terms tested the impact of the approach on different patient subgroups. Lowess graphically depicted the probability of CD $\geq 2$ after ICUD or ECUD according to patient baseline characteristics.

**Results** Overall, 162 ICUD vs 105 ECUD (61 vs. 39%) were performed. Intraoperative complications were recorded in 24 patients. The median LOS and readmission rate were 11 vs. 13 ($p=0.02$) and 24 vs. 22% ($p=0.7$) in ICUD vs. ECUD, respectively. Overall, 227 postoperative complications were recorded. The overall rate of CD $\geq 2$ was 35 and 43% in patients with ICUD vs. ECUD, respectively ($p=0.2$). At MVA, the approach type was not an independent predictor of any postoperative outcomes (all $p \geq 0.4$). Age-adjusted Charlson Comorbidity Index (ACCI) was associated with an increased risk of CD $\geq 2$ (OR: 1.2, $p=0.006$). We identified a significant interaction term between ACCI and approach type ($p=0.04$), where patients with ICUD had lower risk of CD $\geq 2$ relative to those with ECUD with increasing ACCI.

**Conclusions** Relying on a standardized methodology to report complications, we observed that highly comorbid patients who undergo ICUD have lower risk of postoperative complications relative to those patients who received ECUD.

**Keywords** Bladder cancer · Robot-assisted radical cystectomy · Intracorporeal urinary diversion · Extracorporeal urinary diversion · Complications

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## Introduction

The reconstructive part of robot-assisted radical cystectomy (RARC) is the major driver of perioperative morbidity [1]. Despite that a trend towards the use of intracorporeal urinary diversion (ICUD) has been observed in the last decade [2, 3], a considerable number of centers are performing extracorporeal UD (ECUD) [4, 5]. Little evidence is available on a head-to-head comparison of these two approaches on perioperative and postoperative morbidity [2, 6–12]. All these comparative reports are limited by the small sample size [6, 8–12] and/or did not rely on [2, 6, 8, 10–12] or did not fulfill all the criteria [7, 9] of a standardized methodology to report complications, as recently proposed by the European Association of Urology (EAU) ad hoc panel [13]. In consequence, this may lead to an underestimation of the complication rates reported [14–16] and unrealistic conclusions on the eventual benefit of one approach relative to the other. Moreover, none of these comparative reports assessed whether specific subgroups of patients might benefit from one approach relative to the other. Furthermore, none of these studies [2, 6–12] have assessed the relationship between the type of approach (ICUD vs. ECUD) and intraoperative complications, length of stay and readmission rate after accounting for multiple confounders.

Based on these considerations, we relied on a large contemporary cohort of patients treated with RARC at a high-volume center to evaluate the feasibility and safety profile of ICUD vs. ECUD, in agreement with a standardized methodology to report complications published in 2012 by a EAU ad hoc panel [13]. We postulated that, despite in general RARC is a procedure associated with non-negligible rates of side effects even when performed at a high-volume center, ICUD might be associated with a lower risk of postoperative complications relative to ECUD and such a benefit might be more evident especially in specific subgroups of patients. In the current manuscript, we also attempted to identify whether the type of approach (ICUD vs. ECUD) is associated with intraoperative complications, length of stay and readmission rate.

## Materials and methods

### Data source and patient selection

The current study relied on a prospectively maintained database which collected data on urothelial carcinoma of the bladder (UCB) patients treated with RARC and extended pelvic lymph node dissection (ePLND) between 2004 and 2018 at Onze-Lieve-Vrouw Hospital (Aalst, Belgium). For the purpose of the current analysis, we focused on patients aged 18 years or older, with histologically confirmed UCB, who underwent RARC with ICUD or ECUD, with or without neoadjuvant chemotherapy. All surgeries were performed by three surgeons (A.M., P.C. and F.D). The choice to perform ICUD or ECUD was based on surgeon's preference and skills.

### Variable definition

The covariates consisted of age at surgery, gender, body mass index (BMI) ($<25$, 25–30, $>30$), comorbid conditions [age-adjusted Charlson Comorbidity Index (ACCI) [17] and American Society of Anesthesiologists (ASA) Physical Status Classification System [18]], previous abdominal surgery, neoadjuvant chemotherapy, clinical T stage ($\leq$T2, T3-T4), clinical N stage (N0, N1-3) and diversion type (ileal conduit, orthotopic neobladder).

### Outcomes

The primary end point of our study was to analyze 30-day postoperative complications between ICUD vs. ECUD and to identify whether specific subgroups of patients might benefit from one approach relative to the other. Postoperative complications were collected based on patient chart review done by a dedicated data manager and medical doctors and were graded according to the Clavien–Dindo (CD) classification system [19]. From February to June 2018, a retrospective collection system for 30-day postoperative complications was performed based on patient interview done by four medical doctors. The quality criteria for accurate and comprehensive reporting of surgical outcomes recommended by the European Association of Urological (EAU) Guidelines on reporting and grading of complications were fulfilled (Table 1) [13].

The secondary end point was to identify independent predictors of intraoperative complications, prolonged length of stay (LOS) and readmission. Intraoperative complications were categorized according to the Satava classification [20]. Prolonged LOS was defined as any in-hospital stay prolongation over the 75th percentile (16 days in our patient population).

### Statistical analysis

Statistical analyses as well as reporting and interpretation of the results were conducted according to established guidelines [21] and consisted of four analytical steps. First, medians and interquartile ranges, as well as frequencies and proportions were reported for continuous and categorical variables, respectively. The Mann–Whitney and Chi-square

**Table 1** Quality criteria for accurate and comprehensive reporting of surgical outcome to collect data on postoperative complications

| Criteria | |
|---|---|
| 1. Define the method of accruing data[a] | Retrospective data collection based on chart review and a patient interview conducted by telephone |
| 2. Define who collected the data | Data were collected by dedicated data manager and medical doctors who were not involved in the treatment |
| 3. Indicate the duration of follow-up[a] | 30 days |
| 4. Include outpatient information[a] | Outpatient information was collected |
| 5. Include mortality data and causes of death[a] | Mortality data and cause of death were collected |
| 6. Include definitions of complications[a] | Complications were defined as any deviation from the ideal postoperative course |
| 7. Define procedure-specific complications[a] | Procedure-specific complications were defined and collected |
| 8. Report intraoperative and postoperative complications separately | Intraoperative and postoperative complications were reported separately |
| 9. Use a severity grading system for postoperative complications[a] | The Clavien–Dindo system was used |
| 10. Postoperative complications should be presented in a table either by grade or by complication type | Postoperative complications were presented in a table by complication type |
| 11. Include risk factors[a] | The age-adjusted CCI and the ASA were prospectively collected for all patients |
| 12. Include readmissions and causes | Data on readmissions were collected |
| 13. Include reoperations, types and causes | Data on reoperation, types and causes were collected |
| 14. Include the percentage of patients lost to follow-up | 23 patients were excluded due to incomplete information on 30-day complications |

*CCI* Charlson Comorbidity Index, *ASA* American Society of Anesthesiologists Physical Status Classification System

[a]Outcomes in common with the Martin criteria

tests were applied to compare the statistical significance of differences in the distribution of continuous or categorical variables, respectively.

Second, four separate sets of multivariable logistic regression models were fitted to assess the impact of the type of approach (ICUD vs. ECUD) on intraoperative complications, prolonged LOS, 30-day CD ≥ 2 complications and readmission rate, after adjusting for several confounders. Predictors included were gender, ACCI, BMI, neoadjuvant chemotherapy, previous abdominal surgery, clinical T stage, clinical N stage and diversion type. All multivariable analyses were fitted after adjustment for clustering at single surgeon level, using generalized estimation equation (GEE) functions [22].

Third, to test the hypothesis that the impact of the type of approach was different in specific patient subgroups, an interaction term between type of approach (ICUD vs. ECUD) and each individual covariate in predicting primary and secondary outcomes was used.

Fourth, logistic regression derived coefficients were used to estimate the 30-day CD ≥ 2 probability. The locally weighted scatter plot smoothing method [23] was used to graphically explore the probability of 30-day CD ≥ 2 after ICUD or ECUD according to patient baseline characteristics. Analyses were performed using the R software v.3.5.1 and all tests were two-sided with significance level set at $p < 0.05$.

## Results

### Patient characteristics

Overall, 267 patients were included in the study (Table 2). 162 (61%) and 105 (39%) patients received ICUD and ECUD, respectively. Patients treated with ICUD had lower rate of previous abdominal surgery relative to those treated with ECUD (67.3 vs. 85.7%, $p = 0.001$). No statistically significant differences in terms of age at surgery (median: 71 vs 68 years old, $p = 0.05$), BMI (median 26.3 vs 25.4, $p = 0.6$), ACCI (median 4 vs 3, $p = 0.07$), and neoadjuvant chemotherapy use (24.1 vs 25.7%, $p = 0.8$) were recorded between ICUD and ECUD. On pathological report, patients undergoing RARC with ECUD were more frequently ≥ pT3 (40 vs 26%, $p = 0.006$) or pN1 (22 vs 12%, $p = 0.07$) compared to those treated with RARC with ICUD.

### Intraoperative complications, length of stay and readmission

Overall, 24 intraoperative complications occurred in 267 patients. The most common were bleeding ($n = 14$), ureteral injury ($n = 2$) and bowel injury ($n = 2$). According to Satava classification, the highest grade of complication recorded was grade 1 in 6.7% of patients (18/267), grade 2 in 1.8% of patients (5/267) and grade 3 in 0.7% of patients (1/267).

**Table 2** Baseline and perioperative characteristics of 267 patients treated with RARC

| Variables | Overall ($n=267$) | Intracorporeal urinary diversion ($n=162$, 61%) | Extracorporeal urinary diversion ($n=105$; 39%) | $p$ value |
|---|---|---|---|---|
| Age, years | | | | |
| Median | 71 | 71 | 68 | 0.05 |
| IQR | 62–77 | 64.2–78 | 61–76 | |
| Gender, *n* (%) | | | | |
| Male | 224 (83.9) | 135 (83.3) | 89 (84.8) | 0.8 |
| Female | 43 (16.1) | 27 (16.7) | 16 (15.2) | |
| BMI, score | | | | |
| Median | 26.2 | 26.3 | 25.4 | 0.6 |
| IQR | 23.2–28.4 | 23.4–28.3 | 22.9–29.3 | |
| A-CCI, score | | | | |
| Median | 4 | 4 | 3 | 0.07 |
| IQR | 2–5 | 3–5 | 2–5 | |
| ASA score, *n* (%) | | | | |
| 1 | 20 (7.5) | 11 (6.8) | 9 (8.6) | 0.5 |
| 2 | 153 (57.3) | 99 (61.1) | 54 (51.4) | |
| 3 | 89 (33.3) | 49 (30.2) | 40 (38.1) | |
| ≥4 | 5 (1.9) | 3 (1.8) | 2 (1.9) | |
| Neoadjuvant chemotherapy, *n* (%) | | | | |
| No | 201 (75.3) | 123 (75.9) | 78 (74.3) | 0.8 |
| Yes | 66 (24.7) | 39 (24.1) | 27 (25.7) | |
| Previous abdominal surgery, *n* (%) | | | | |
| No | 199 (74.5) | 109 (67.3) | 90 (85.7) | 0.001 |
| Yes | 68 (25.5) | 53 (32.7) | 15 (14.3) | |
| cT stage, *n* (%) | | | | |
| CIS | 13 (4.9) | 9 (5.6) | 4 (3.8) | 0.2 |
| T1 | 76 (28.5) | 50 (30.9) | 26 (24.8) | |
| T2 | 127 (47.6) | 79 (48.8) | 48 (45.7) | |
| T3 | 36 (13.5) | 17 (10.5) | 19 (18.1) | |
| T4 | 15 (5.6) | 7 (4.3) | 8 (7.6) | |
| cN stage, *n* (%) | | | | |
| N0 | 225 (84.3) | 140 (86.4) | 85 (81) | 0.06 |
| N+ | 42 (15.7) | 22 (13.6) | 20 (19) | |
| pT stage, *n* (%) | | | | |
| pT0 | 64 (24) | 48 (29.6) | 16 (15.2) | 0.009 |
| pT1 | 68 (25.5) | 45 (27.8) | 23 (21.9) | |
| pT2 | 50 (18.7) | 26 (16) | 24 (22.9) | |
| ≥pT3 | 85 (31.8) | 43 (26.5) | 42 (40) | |
| pN stage, *n* (%) | | | | |
| pN0 | 197 (73.8) | 124 (76.5) | 73 (69.5) | 0.07 |
| pN1 | 42 (15.7) | 19 (11.7) | 23 (21.9) | |
| pNx | 28 (10.5) | 19 (11.7) | 9 (8.6) | |
| Nodes removed | | | | |
| Medina | 15 | 16 | 14 | 0.2 |
| IQR | 11–20 | 12–21 | 9–18 | |
| Surgical margins, *n* (%) | | | | |
| Negative | 247 (92.5) | 150 (92.6) | 97 (92.4) | 0.8 |
| Positive | 20 (7.5) | 12 (7.4) | 8 (7.6) | |
| Diversion type, *n* (%) | | | | |
| Ileal conduit | 241 (90.3) | 146 (90.1) | 95 (90.5) | 0.9 |
| Neobladder | 26 (9.7) | 16 (9.9) | 10 (9.5) | |

**Table 2** (continued)

| Variables | Overall ($n=267$) | Intracorporeal urinary diversion ($n=162$, 61%) | Extracorporeal urinary diversion ($n=105$; 39%) | $p$ value |
|---|---|---|---|---|
| 30-d CD ≥ 2, *n* (%) | | | | |
| Overall | 102 (38.2) | 57 (35.2) | 45 (42.9) | 0.2 |
| During hospitalization | 40 (14.9) | 18 (11.1) | 22 (21.0) | |
| After discharge | 62 (23.3) | 39 (24.1) | 23 (21.9) | |
| Intraoperative complications, *n* (%) | | | | |
| No | 243 (91) | 149 (92) | 94 (89.5) | 0.6 |
| Yes | 24 (9) | 13 (8) | 11 (10.5) | |
| LOS | | | | |
| Median | 12 | 11.5 | 13 | 0.02 |
| IQR | 10–16 | 9–16 | 11–16 | |
| LOS > 75th percentile, *n* (%) | | | | |
| No | 195 (73) | 118 (72.8) | 77 (73.3) | 0.9 |
| Yes | 72 (27) | 44 (27.2) | 28 (26.7) | |
| Readmission, *n* (%) | | | | |
| No | 205 (76.8) | 123 (75.9) | 82 (78.1) | 0.8 |
| Yes | 62 (23.2) | 39 (24.1) | 23 (21.9) | |
| Operative time, min | | | | |
| Median | 350 | 350 | 350 | 0.1 |
| IQR | 300–400 | 300–400 | 300–400 | |
| Estimated blood loss, mL | | | | |
| Median | 325 | 300 | 350 | 0.02 |
| IQR | 200–500 | 150–500 | 300–500 | |
| Transfusion rate, n (%) | | | | |
| No | 244 (91.4) | 150 (92.6) | 94 (89.5) | 0.05 |
| Yes | 23 (8.6) | 12 (7.4) | 11 (10.5) | |

*IQR* interquartile range; *BMI* body mass index; *ACCI* age-adjusted Charlson Comorbidity Index; *ASA* American Society of Anesthesiologists; *CD* Clavien–Dindo; *LOS* length of stay

The overall rate of intraoperative complications was 8 and 10.5% in patients with ICUD vs. ECUD, respectively ($p=0.6$; Table 2).

The median intraoperative time and blood loss were 350 min (IQR: 300–400 min) and 300 cc (IQR: 150–500 cc) in ICUD and 350 min (IQR: 300–400 min) and 350 cc (IQR: 300–500 cc) in ECUD ($p=0.1$ for OT; $p=0.02$ for blood loss). The median length of stay was 11 vs. 13 in ICUD vs. ECUD, respectively ($p=0.02$). Overall, the transfusion rate was 8.6% (ICUD: 7.4%, ECUD: 10.5%; $p=0.5$) and the readmission rate was 23.2% (ICUD: 24.1%, ECUD: 21.9%; $p=0.7$).

At multivariable logistic regression analyses, the type of approach (ICUD vs. ECUD) was not an independent predictor of intraoperative complications (OR: 0.60, 95% CI 0.11–3.06, $p=0.5$), prolonged LOS (OR 0.82, 95% CI 0.38–1.75, $p=0.6$) and readmission (OR 1.31, 95% CI 0.62–2.76, $p=0.4$) after adjusting for multiple confounders (Table 4). Interestingly, BMI > 30 (OR 7.37, 95%CI 2.62–20.67, $p<0.001$), cN + (OR 3.86, 95%CI 1.47–10.12, $p=0.006$) and orthotopic neobladder diversion (OR 4.54, 95%CI 1.34–15.38, $p=0.01$) were all associated with increased risk of intraoperative complications. The interaction tests for the hypotheses that the impact of type of approach on intraoperative complications, readmission and prolonged LOS varies according to BMI, ACCI, gender, neoadjuvant chemotherapy use, previous abdominal surgery and diversion type were all not statistically significant ($p>0.05$).

## Postoperative complications

Table 3 depicts the postoperative complications that were collected according to the standardized criteria published by the EAU guidelines [13]. Table 1 shows the criteria satisfied and defines the quality of our complications collection analysis (14 out of 14 criteria satisfied). Overall, 227 postoperative complications occurred in 267 patients (Table 3). The most common were gastrointestinal (26.2%), infectious (22.5%), genitourinary (7.8%), neurological (6.7%) and cardiac (6.7%) complications (Table 3). According to CD classification, the highest grade of complication recorded was grade 1 in 11% of patients (29/267), grade 2 in 20% patients (55/267), grade 3 in 8.6% (23/267), grade 4 in 7.1%

**Table 3** Summary of 30-day postoperative complications in 267 patients treated with RARC

| Overall complications ($n=227$) | | | |
|---|---|---|---|
| Category | Type of complication | *n* | % |
| Gastrointestinal ($n=70$, 26.2%) | Paralytic ileus[a] | 43 | 16.1 |
| | Mechanical ileus[b] | 6 | 2.2 |
| | Bowel anastomotic leakage | 4 | 1.5 |
| | Pseudomembranous colitis[c] | 4 | 1.5 |
| | Gastric ulcer | 3 | 1.1 |
| | Bowel ischemia | 2 | 0.7 |
| | Gastrointestinal bleeding | 4 | 1.5 |
| | Abdominal compartment syndrome | 1 | 0.4 |
| | Enterocutaneous fistula | 1 | 0.4 |
| | Fecal peritonitis | 1 | 0.4 |
| | Diarrhea | 1 | 0.4 |
| Infectious ($n=60$, 22.5%) | Pyelonephritis/Urosepsis | 23 | 8.6 |
| | Urinary tract infections | 11 | 4.1 |
| | Fever requiring antibiotics | 12 | 4.5 |
| | Intra-abdominal abscess | 4 | 1.5 |
| | SIRS | 4 | 1.5 |
| | Septic shock | 4 | 1.5 |
| | MRSA | 1 | 0.4 |
| | Epididymitis | 1 | 0.4 |
| Genitourinary ($n=21$, 7.8%) | Intra-abdominal leakage of urine | 11 | 4.1 |
| | Acute renal failure | 5 | 1.9 |
| | Ureteral stricture | 2 | 0.7 |
| | Hydronephrosis | 2 | 0.7 |
| | Scrotal hematoma | 1 | 0.4 |
| Neurological ($n=18$, 6.7%) | Delirium | 9 | 3.4 |
| | Peripheral neuropathy | 6 | 2.2 |
| | CVA | 2 | 0.7 |
| | TIA | 1 | 0.4 |
| Cardiac ($n=18$, 6.7%) | Atrial fibrillation | 12 | 4.5 |
| | Heart failure | 1 | 0.4 |
| | Myocardial infarction | 5 | 1.9 |
| Pulmonary ($n=10$, 3.7%) | Pneumonia | 8 | 3.0 |
| | Bronchitis | 1 | 0.4 |
| | Atelectasis | 1 | 0.4 |
| Hematologic/vascular ($n=13$, 4.9%) | Anemia due to postoperative bleeding | 10 | 3.7 |
| | Pulmonary embolus | 2 | 0.7 |
| | Deep venous thrombosis | 1 | 0.4 |
| Wound/skin ($n=5$, 1.9%) | Fascial dehiscence | 3 | 1.1 |
| | Wound infection | 1 | 0.4 |
| | Peristomal cellulitis | 1 | 0.4 |
| Metabolic ($n=4$, 1.5%) | Severe hypoglycemia | 2 | 0.7 |
| | Acidosis | 1 | 0.4 |
| | Gout crisis | 1 | 0.4 |
| Others ($n=8$, 3.0%) | Lymphocele[d] | 4 | 1.5 |
| | Perioperative death | 3 | 1.1 |
| | Compartment syndrome of the leg | 1 | 0.4 |

[a]Postoperative nausea or vomiting with associated abdominal distension requiring stoppage of oral intake and intravenous fluid and/or nasogastric tube placement

[b]Defined as clinical and radiographic findings of bowel obstruction requiring intervention

[c]Inflammation of the colon associated with an overgrowth of the bacterium *Clostridium difficile*

[d]Lymphocele was defined as any clearly definable fluid collection and was considered clinically significant when requiring treatment. Ultrasound examination was used to detect lymphoceles

of patients (19/267) and grade 5 in 1.1% of patients (3/267). The overall rate of CD ≥ 2 was 35.2 and 42.9% in patients with ICUD vs. ECUD, respectively ($p = 0.2$). At the last follow-up (median 48 months, IQR 20–63 months), 65 and 46 patients died of cancer-related causes and other cause mortality, respectively.

Twelve patients with CD 3a required radiological intervention for drainage of hematoma ($n = 4$) or drainage of lymphocele or abscess ($n = 8$). Eleven patients had CD 3 b for reoperation due to mechanical obstruction ($n = 6$), drainage of hematoma or abscess ($n = 3$) or evisceration due to fascial dehiscence ($n = 2$). The reasons for admission to intensive care unit (CD 4) were urosepsis ($n = 7$), cardiac infarction ($n = 3$), anemia due to postoperative bleeding ($n = 3$), pneumonia ($n = 3$), delirium ($n = 2$) and peritonitis ($n = 1$). The reasons for perioperative death (CD 5) were multi-organ failure associated with liver metastases ($n = 1$), respiratory failure for pulmonary embolism ($n = 1$) and heart failure ($n = 1$).

At multivariable logistic regression analyses, the type of approach (ICUD vs. ECUD) was not an independent predictor of CD ≥ 2 (OR 1.20, 95% 0.61–2.35, $p = 0.5$), after adjusting for multiple confounders (Table 4). Of note, ACCI was associated with an increased risk of CD ≥ 2 (OR: 1.22, 95%CI 1.06–1.42, $p = 0.006$). The interaction tests for the hypotheses that the impact of type of approach on postoperative CD ≥ 2 complications varies according to BMI, gender, neoadjuvant chemotherapy use, previous abdominal surgery and diversion type were all not statistically significant ($p > 0.05$). Conversely, the interaction test for the hypothesis that the impact of type of approach on postoperative CD ≥ 2 complications varies according to the baseline ACCI was statistically significant (p = 0.04). Specifically, with the increase of the baseline ACCI, patients with ICUD had lower risk of CD ≥ 2 relative to those with ECUD (Fig. 1). For example, in patients with ACCI of 0, the probability of CD ≥ 2 was 23.3 vs 22.9% in ICUD vs ECUD, while in patients with ACCI of 7, the probability of CD ≥ 2 was 44.6 vs 63.0% in ICUD vs ECUD.

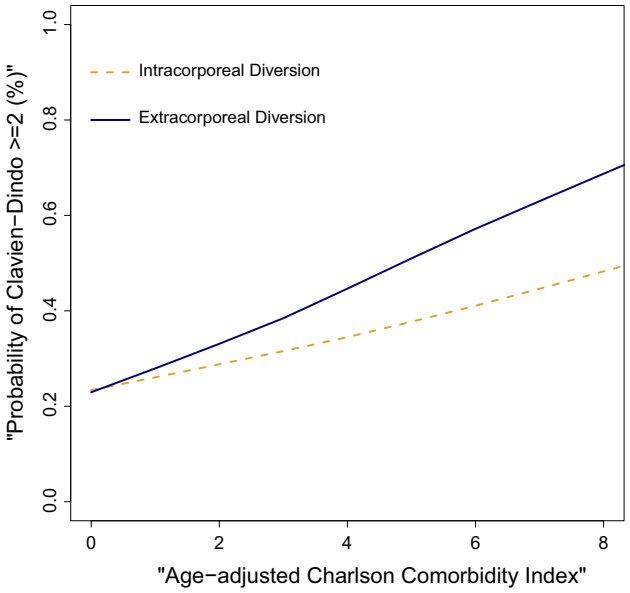


**Fig. 1** Locally weighted scatterplot smoothed exploring the probability of 30-day CD ≥ 2 after testing for interaction term between urinary diversion type (ICUD vs. ECUD) and patient baseline age-adjusted Charlson comorbidity index

## Discussion

In the current study, we hypothesized that, relying on the standardized methodology to report postoperative complications proposed by the EAU ad hoc panel [13], RARC with ICUD might be associated with a lower risk of postoperative complications relative to ECUD and such a benefit might be more evident especially in specific subgroups of patients [24]. Moreover, we also attempted to identify whether the type of approach (ICUD vs. ECUD) is associated with intraoperative complications, length of stay and readmission rate.

Our results failed to confirm the first statement of our hypothesis. Indeed, no difference was observed between ICUD and ECUD with respect to 30-day CD ≥ 2, after adjustment for several confounders. Similarly, secondary end points (intraoperative complications, length of stay and readmission rate) were not different between the two approaches. However, we interestingly reported potential interaction between the type of approach and ACCI and identified strong predictors of intraoperative complications. Overall, the following noteworthy findings are highlighted.

First, our data showed that RARC is a complex procedure that is not devoid of complications, even in expert hands. Specifically, we reported an overall rate of 38.2% of CD ≥ 2. This finding is in line with those previously reported by historical series of RARC from centers of excellence [7] and confirms that, even after an initial learning curve phase [25], the rate of complication is still not negligible in the RARC setting. As such, strict postoperative follow-up and careful management of these patients are mandatory. Moreover, it is important to remark that, differently from previous analyses [2, 6, 8, 10–12], our data provide strong evidences that are based on a standardized methodology for complication reporting [13]. This should be mandatory to avoid underestimation of the rate of complications reported [14–16]. Other analyses that attempted to report data using a similar methodology failed in reporting complications in a complete standardized fashion. For instance, Ahmed et al. [7] and Lenfant et al. [9] used a similar approach, but they did not fulfill all the 14-item criteria of the EAU guidelines. In consequence, our analysis represents the strongest study in terms of quality of complications reported after RARC.

**Table 4** The following procedures are considered as procedure related: paralytic ileus, mechanical ileus, bowel anastomosis leakage, enterocutaneous fistula, fecal peritonitis, pyelonephritis/urosepsis, urinary tract infections, intra-abdominal abscess, intra-abdnominal leakage of urine, ureteral strictures, hydronephrosis, lymphocele, peristomal cellulitis

| | Clavien–Dindo ≥ 2 | | | | Intraoperative complications | | | | LOS > 75% | | | | 30-days after discharge Readmission | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | OR | 95% CI | | *p* value | OR | 95% CI | | *p* value | OR | 95% CI | | *p* value | OR | 95% CI | | *p* value |
| Reconstruction | | | | | | | | | | | | | | | | |
| Intracorporeal | Ref | | | | Ref | | | | Ref | | | | Ref | | | |
| Extracorporeal | 1.20 | 0.61 | 2.35 | 0.5 | 0.60 | 0.11 | 3.06 | 0.5 | 0.82 | 0.38 | 1.75 | 0.6 | 1.31 | 0.62 | 2.76 | 0.4 |
| Age-adjusted CCI | 1.22 | 1.06 | 1.42 | **0.006** | 1.13 | 0.85 | 1.50 | 0.4 | 1.44 | 1.22 | 1.71 | **< 0.001** | 1.01 | 0.82 | 1.23 | 0.9 |
| Gender | | | | | | | | | | | | | | | | |
| Male | Ref | | | | Ref | | | | Ref | | | | Ref | | | |
| Female | 0.78 | 0.42 | 1.50 | 0.4 | 0.73 | 0.17 | 3.09 | 0.7 | 1.40 | 0.64 | 3.05 | 0.4 | 1.35 | 0.43 | 4.28 | 0.6 |
| Neoadjuvant chemotherapy | | | | | | | | | | | | | | | | |
| No | Ref | | | | Ref | | | | Ref | | | | Ref | | | |
| Yes | 0.85 | 0.38 | 1.87 | 0.7 | 0.61 | 0.16 | 2.35 | 0.5 | 1.40 | 0.63 | 3.14 | 0.4 | 0.52 | 0.23 | 1.15 | 0.1 |
| BMI | | | | | | | | | | | | | | | | |
| < 25 | Ref | | | | Ref | | | | Ref | | | | Ref | | | |
| 25–30 | 0.98 | 0.50 | 1.95 | 0.9 | 0.98 | 0.32 | 2.92 | 0.9 | 1.24 | 0.68 | 2.27 | 0.4 | 1.31 | 0.72 | 2.39 | 0.3 |
| > 30 | 1.54 | 0.65 | 3.65 | 0.3 | 7.37 | 2.62 | 20.67 | **< 0.001** | 1.53 | 0.51 | 4.59 | 0.4 | 1.33 | 0.53 | 3.33 | 0.5 |
| Previous abdominal surgery | | | | | | | | | | | | | | | | |
| No | Ref | | | | Ref | | | | Ref | | | | Ref | | | |
| Yes | 0.93 | 0.50 | 1.72 | 0.8 | 0.36 | 0.11 | 1.21 | 0.09 | 1.31 | 0.60 | 2.88 | 0.4 | 0.59 | 0.24 | 1.43 | 0.2 |
| cT stage | | | | | | | | | | | | | | | | |
| ≤ cT2 | Ref | | | | Ref | | | | Ref | | | | Ref | | | |
| cT3-4 | 1.13 | 0.51 | 2.51 | 0.7 | 0.60 | 0.16 | 2.24 | 0.4 | 1.45 | 0.62 | 3.40 | 0.3 | 0.48 | 0.18 | 1.29 | 0.1 |
| cN stage | | | | | | | | | | | | | | | | |
| N0 | Ref | | | | Ref | | | | Ref | | | | Ref | | | |
| N + | 0.99 | 0.45 | 2.21 | 0.9 | 3.86 | 1.47 | 10.12 | **0.006** | 1.05 | 0.41 | 2.68 | 0.9 | 1.15 | 0.46 | 2.90 | 0.7 |
| Diversion | | | | | | | | | | | | | | | | |
| Bricker | Ref | | | | Ref | | | | Ref | | | | Ref | | | |
| Neobladder | 1.69 | 0.72 | 3.96 | 0.2 | 4.54 | 1.34 | 15.38 | **0.01** | 4.93 | 1.92 | 12.63 | **< 0.001** | 4.18 | 1.57 | 11.14 | **0.004** |

Bold indicate *p* values < 0.05

Second, when applying this standardized methodology for reporting complications, no difference in complication rates was reported between ICUD and ECUD (OR 1.20, $p = 0.5$). These data suggest that each type of urinary reconstruction is relatively safe in the hands of expert surgeons who are confident with a specific urinary diversion technique. Previous analyses based on multi-institutional data showed similar findings [7, 9]. This assumption is also confirmed by the absence of differences between the type of approach and secondary outcomes, such as intraoperative complications (OR: 0.60, $p = 0.5$), readmission rates (OR 1.31, $p = 0.4$) and prolonged LOS (OR 0.82, $p = 0.6$).

Subsequently, when looking at multiple factors that may interact with postoperative complication rates, we reported a differential effect of urinary diversion approach according to baseline comorbidity patient profile. Specifically, in patients with low ACCI grade, no clinically meaningful differences in complication rates were recorded between ICUD and ECUD. Conversely, in patients with high ACCI grade, ICUD patients had lower CD ≥ 2 complication rates compared to ECUD patients. Indeed, it may be argued that most of the postoperative CD ≥ 2 complications, such as fever due to urinary infection, wound infection, fascial dehiscence, paralytic bowel urinoma requiring drainage or bowel injury, are often related to the reconstructive part of the procedure. As such, the benefit of a complete intracorporeal urinary diversion approach may be greater in higher comorbid patients who are more exposed to develop postoperative complications.

Third, we identified BMI and orthotopic neobladder diversion as independent predictors of intraoperative complications. These data confirm what has been previously observed in retrospective studies [7, 8]. Indeed, obese patients are known to have higher risk of complications even in other robot-assisted surgical procedures [26]. Our data

confirm this finding. Moreover, to the best of our knowledge, we are the first to provide evidence that cN + is an independent predictor of intraoperative complications in the setting of RARC. It is of note that LND is the surgical phase of the procedure where the risk of injuring important anatomical structures is higher. As such, it is plausible that the detection of positive nodes at CT scan associated with reactive or even metastatic tissue involving vascular and nerve structures is an important risk factor for intraoperative complications. This finding may also play a crucial role during preoperative counseling to properly inform patients on their risk of potential intraoperative complications during the surgical procedure.

Taken together, our analysis represents the first study that reports complications after RARC according to the 14-item standardized reporting tool proposed by the EAU guidelines and that attempts to assess whether, relying on this methodology, there are differences between one urinary diversion reconstruction approach relative to the other (ICUD vs. ECUD). Moreover, after testing for multiple interaction terms, we reported for the first time that higher comorbid patients are less exposed to CD $\geq$ 2 complications, when ICUD is proposed. In consequence, we believe that these data may help to counsel clinicians in selecting the urinary diversion approach type that best fits with specific patient comorbidity profile.

Despite its strengths, our analysis is not devoid of limitations. Of note, as for previous analyses that reported perioperative RARC outcomes, our study is based on a retrospective analysis with all of its inherent limitations. However, to the best of our knowledge, none of the data from prospective trials on RARC have been used for secondary analyses of the effect of diversion type on perioperative outcomes according to the different comorbidity profiles. Additionally, no pre-established criteria were used to define which patients should have undergone ECUD or ICUD. Indeed, the decision to perform a specific urinary diversion approach was based on surgeon preference and this point may have introduced a bias in the reported results.

## Conclusions

RARC is associated with a non-negligible rate of complications, even when performed at a high-volume center. Relying on the standardized methodology proposed by the EAU guidelines to report complications, we observed that highly comorbid patients who undergo ICUD have lower risk of postoperative complications relative to those patients who received ECUD. These findings should be considered to improve patient counseling and clinical decision making.

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## Compliance with ethical standards

**Conflict of interest** Elio Mazzone certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (e.g., employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: none.

## References

1. Satkunasivam R, Wallis CJ, Nam RK, Desai M, Gill IS (2016) Contemporary evidence for robot-assisted radical cystectomy for treating bladder cancer. Nat Rev Urol 13:533–539
2. Hussein AA, May PR, Jing Z, Ahmed YE, Wijburg CJ, Canda AE et al (2018) Outcomes of intracorporeal urinary diversion after robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium. J Urol 199:1302–1311
3. Collins JW, Adding C, Hosseini A, Nyberg T, Pini G, Dey L et al (2016) Introducing an enhanced recovery programme to an established totally intracorporeal robot-assisted radical cystectomy service. Scand J Urol 50:39–46
4. Parekh DJ, Reis IM, Castle EP, Gonzalgo ML, Woods ME, Svatek RS et al (2018) Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial. Lancet 391:2525–2536
5. Hayn MH, Hussain A, Mansour AM, Andrews PE, Carpentier P, Castle E et al (2010) The learning curve of robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium. Eur Urol 58:197–202
6. Kang SG, Ko YH, Jang HA, Kim J, Kim SH, Cheon J et al (2012) Initial experience of robot-assisted radical cystectomy with total intracorporeal urinary diversion: comparison with extracorporeal method. J Laparoendosc Adv Surg Techn Part A 22:456–462
7. Ahmed K, Khan SA, Hayn MH, Agarwal PK, Badani KK, Balbay MD et al (2014) Analysis of intracorporeal compared with extracorporeal urinary diversion after robot-assisted radical cystectomy: results from the International Robotic Cystectomy Consortium. Eur Urol 65:340–347
8. Bertolo R, Agudelo J, Garisto J, Armanyous S, Fergany A, Kaouk J (2019) Perioperative Outcomes and Complications after Robotic Radical Cystectomy With Intracorporeal or Extracorporeal Ileal Conduit Urinary Diversion: Head-to-head Comparison From a Single-Institutional Prospective Study. Urology 129:98–105
9. Lenfant L, Verhoest G, Campi R, Parra J, Graffeille V, Masson-Lecomte A et al (2018) Perioperative outcomes and complications

of intracorporeal vs extracorporeal urinary diversion after robot-assisted radical cystectomy for bladder cancer: a real-life, multi-institutional french study. World J Urol 36:1711–1718
10. Pyun JH, Kim HK, Cho S, Kang SG, Cheon J, Lee JG et al (2016) Robot-assisted radical cystectomy with total intracorporeal urinary diversion: comparative analysis with extracorporeal urinary diversion. J Laparoendos Adv Surg Techn Part A 26:349–355
11. Tan TW, Nair R, Saad S, Thurairaja R, Khan MS (2019) Safe transition from extracorporeal to intracorporeal urinary diversion following robot-assisted cystectomy: a recipe for reducing operative time, blood loss and complication rates. World J Urol 37:367–372
12. Kingo PS, Norregaard R, Borre M, Jensen JB (2017) Postoperative C-reactive protein concentration and clinical outcome: comparison of open cystectomy to robot-assisted laparoscopic cystectomy with extracorporeal or intracorporeal urinary diversion in a prospective study. Scand J Urol 51:381–387
13. Mitropoulos D, Artibani W, Graefen M, Remzi M, Roupret M, Truss M et al (2012) Reporting and grading of complications after urologic surgical procedures: an ad hoc EAU guidelines panel assessment and recommendations. Eur Urol 61:341–349
14. Hayn MH, Hellenthal NJ, Hussain A, Stegemann AP, Guru KA (2011) Defining morbidity of robot-assisted radical cystectomy using a standardized reporting methodology. Eur Urol 59:213–218
15. Gandaglia G, Bravi CA, Dell'Oglio P, Mazzone E, Fossati N, Scuderi S et al (2018) The impact of implementation of the European Association of Urology Guidelines Panel Recommendations on reporting and grading complications on perioperative outcomes after robot-assisted radical prostatectomy. Eur Urol 74:4–7
16. Cacciamani GE, Medina LG, Tafuri A, Gill T, Baccaglini W, Blasic V et al (2018) Impact of implementation of standardized criteria in the assessment of complication reporting after robotic partial nephrectomy: a systematic review. Eur Urol Focus. https://doi.org/10.1016/j.euf.2018.12.004
17. Koppie TM, Serio AM, Vickers AJ, Vora K, Dalbagni G, Donat SM et al (2008) Age-adjusted Charlson comorbidity score is associated with treatment decisions and clinical outcomes for patients undergoing radical cystectomy for bladder cancer. Cancer 112:2384–2392
18. Saklad M (1941) Grading of patients for surgical procedures. Anesthesiology 2:281–284
19. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
20. Satava RM (2005) Identification and reduction of surgical error using simulation Minimally invasive therapy and allied technologies. MITAT 14:257–261
21. Vickers AJ, Sjoberg DD, European U (2015) Guidelines for reporting of statistics in European Urology. Eur Urol 67:181–187
22. Panageas KS, Schrag D, Riedel E, Bach PB, Begg CB (2003) The effect of clustering of outcomes on the association of procedure volume and surgical outcomes. Ann Intern Med 139:658–665
23. Cleveland WS (1979) Robust locally weighted regression and smoothing scatterplots. J Am Stat Assoc 74(368):829–836. https://doi.org/10.1080/01621459.1979.10481038
24. Williams SB, Kamat AM, Chamie K, Daneshmand S, Froehner M, Thalmann GN et al (2018) Systematic review of comorbidity and competing-risks assessments for bladder cancer patients. Eur Urol Oncol 1:91–100. https://doi.org/10.1016/j.euo.2018.03.005
25. Dell'Oglio P, Mazzone E, Lambert E, Vollemaere J, Goossens M, Larcher A et al (2020) The effect of surgical experience on perioperative and oncological outcomes after robot-assisted radical cystectomy with intracorporeal urinary diversion: evidence from a high-volume center. Eur Urol Focus S2405–4569(20):30035–30043
26. Knipper S, Mazzone E, Mistretta FA, Palumbo C, Tian Z, Briganti A et al (2019) Impact of obesity on perioperative outcomes at robotic-assisted and open radical prostatectomy: results from the national inpatient sample. Urology. https://doi.org/10.1016/j.urology.2019.05.053