



## Platinum Priority – Bladder Cancer

Editorial by Bernard H. Bochner and Vincent Laudone on pp. 814–815 of this issue

# Standardized Analysis of Frequency and Severity of Complications After Robot-assisted Radical Cystectomy

Bertram E. Yuh\*, Michael Nazmy, Nora H. Ruel, Jason T. Jankowski, Anita R. Menchaca, Robert R. Torrey, Jennifer A. Linehan, Clayton S. Lau, Kevin G. Chan, Timothy G. Wilson

City of Hope National Cancer Center, Duarte, CA, USA

### Article info

#### Article history:

Accepted June 5, 2012  
 Published online ahead of  
 print on June 13, 2012

#### Keywords:

Cystectomy  
 Complications  
 Robotic  
 Bladder cancer

### Abstract

**Background:** Comprehensive and standardized reporting of adverse events after robot-assisted radical cystectomy (RARC) and urinary diversion for bladder cancer is necessary to evaluate the magnitude of morbidity for this complex operation.

**Objective:** To accurately identify and assess postoperative morbidity after RARC using a standardized reporting system.

**Design, setting, and participants:** A total of 241 consecutive patients underwent RARC, extended pelvic lymph node dissection, and urinary diversion between 2003 and 2011. In all, 196 patients consented to a prospective database, and they are the subject of this report. Continent diversions were performed in 68% of cases.

**Outcome measurements and statistical analysis:** All complications within 90 d of surgery were defined and categorized by a five-grade and 10-domain modification of the Clavien system. Univariable and multivariable logistic regression analyses were used to identify predictors of complications. Grade 1–2 complications were categorized as minor, and grade 3–5 complications were categorized as major. All blood transfusions were recorded as grade  $\geq 2$ .

**Results and limitations:** Eighty percent of patients (156 of 196 patients) experienced a complication of any grade  $\leq 90$  d after surgery. A total of 475 adverse events (113 major) were recorded, with 365 adverse events (77%) occurring  $\leq 30$  d after surgery. Sixty-eight patients (35%) experienced a major complication within the first 90 d. Other than blood transfusions given (86 patients [43.9%]), infectious, gastrointestinal, and procedural complications were the most common, at 16.2%, 14.1%, and 10.3%, respectively. Age, comorbidity, preoperative hematocrit, estimated blood loss, and length of surgery were predictive of a complication of any grade, while comorbidity, preoperative hematocrit, and orthotopic diversion were predictive of major complications. The 90-d mortality rate was 4.1%. The main limitation is lack of a control group.

**Conclusions:** Analysis of postoperative morbidity following RARC demonstrates a considerable complication rate, though the rate is comparable to contemporary open series that followed similar reporting guidelines. This finding reinforces the need for complete and standardized reporting when evaluating surgical techniques and comparing published series.

© 2012 European Association of Urology. Published by Elsevier B.V. All rights reserved.

\* Corresponding author. City of Hope National Cancer Center, 1500 E Duarte Road, Duarte, CA 90017, USA. Tel. +1 626 256 4673; Fax: +1 626 301 8285.  
 E-mail address: [byuh@coh.org](mailto:byuh@coh.org) (B.E. Yuh).

## 1. Introduction

Radical cystectomy with extended pelvic lymphadenectomy represents the most effective surgical treatment of muscle-invasive transitional cell carcinoma of the bladder and is a viable alternative for high-risk or refractory superficial disease [1]. Surgery has been traditionally performed with an open approach, but recently the use of laparoscopic and robot-assisted radical cystectomy (RARC) has increased [2–6]. Novel surgical techniques should ideally offer technical, functional, and oncologic enhancements. Minimally invasive surgeons have promoted decreased blood loss and shorter convalescence as benefits of laparoscopic radical cystectomy or RARC. Long-term oncologic and functional outcomes have not been adequately studied.

Despite improvements in surgical technique, technology, and perioperative care, cystectomy with urinary diversion remains a morbid operation with a substantial complication rate. Unfortunately, longitudinal comparative analyses have been difficult to interpret because of differences in reporting and nonstandardization. To objectively assess the full range of adverse events for an operation, a standardized reporting system for complications is required. Martin et al. established 10 criteria to improve the quality of reporting complications [7]. Recent studies examining cystectomy complications using a Clavien grading system have reported complication rates ranging between 48% and 74% [2,3,8–10].

As only limited randomized comparisons of robotic and open cystectomy currently exist [11], objective reporting of complications based on an established system becomes increasingly important. We sought to define the type, incidence, and severity of early postoperative morbidity in a large RARC series using a standardized reporting methodology according to the Martin criteria.

## 2. Patients and methods

Between 2003 and 2011, 241 patients underwent RARC at City of Hope National Cancer Center. Forty-five patients were excluded because they declined participation in our bladder cancer (BCa) database or had concomitant surgery. The remaining 196 patients were consented to our institutional review board–approved cystectomy database. Indications for RARC included muscle-invasive BCa or high-grade refractory or recurrent multifocal bladder tumors not amenable to local therapy. Patients were offered neoadjuvant chemotherapy when indicated and underwent preoperative staging with computed tomography. Patients were offered orthotopic or cutaneous continent diversion or ileal conduit. Contraindications to orthotopic diversion included serum creatinine >2 ng/ml, disease at the urethral margin, or advanced disease. Contraindications to continent cutaneous diversion included poor manual dexterity, creatinine >2 ng/ml, significant comorbidity, symptoms of dementia, or advanced disease. Continent diversions were performed in 68% of cases.

Clinicopathologic and complications data were collected prospectively. In addition, independent review of all inpatient charts, outpatient notes, outside hospital notes, and correspondence with local physicians for complications was performed by academic urologists. All complications within 90 d of surgery were recorded and graded according to an established five-grade Clavien classification [12]. Clavien grade 1 or 2 complications were categorized as minor

complications, and grade 3–5 complications were considered major. Preoperative comorbidities were computed using an age-adjusted Charlson comorbidity index (CCI) [13].

Presurgical patient preparation included clear liquids and GoLyte<sup>ly</sup> or magnesium citrate the day before surgery. Beginning in 2009, oral alvimopan was administered if there were no contraindications. Sequential compression devices were routinely used, and a second-generation cephalosporin was administered intravenously for 1 d perioperatively. In 2006, initiation of subcutaneous low-molecular-weight heparin began postoperatively with confirmation of stable hematocrit, and patients were also discharged home with a 4-wk supply.

### 2.1. Operative technique

Four experienced surgeons performed >97% of the RARCs. Robotic cystectomy with the da Vinci Surgical System robot was completed using a six-port transperitoneal approach. Bilateral ureters were freed down to the base of the bladder and clipped. Extended pelvic lymphadenectomy was performed bilaterally from the inferior mesenteric artery down to the node of Cloquet. Limits of dissection were the genitofemoral nerve (laterally) and the obturator fossae (posteriorly). Posterior dissection beneath the base of the bladder was performed, followed by dropping the bladder anteriorly. The dorsal venous complex was controlled using an

**Table 1 – Patient demographics**

Gender, no. (%)	
Female	32 (16.3)
Male	164 (83.7)
Age at surgery, yr, median (IQR)	70.4 (62.9–77.0)
BMI, median (IQR)	27.1 (24.1–30.5)
CCI, median (IQR)	5 (4–6)
ASA score, no. (%)	
II	41 (20.9)
III	123 (62.8)
IV	31 (15.8)
Patients with previous abdominal surgery, no. (%)	106 (54.1)
Receipt of neoadjuvant chemotherapy, no. (%)	43 (21.9)
Diversion type, no. (%)	
Ileal conduit	62 (31.6)
Continent cutaneous	48 (24.5)
Orthotopic neobladder	86 (43.9)
Surgery length, min, median (IQR)	432 (384–498)
EBL, ml, median (IQR)	400 (250–525)
Histology, no. (%)	
Transitional cell carcinoma	179 (91.3)
Adenocarcinoma	9 (4.6)
Squamous cell carcinoma	4 (2.0)
Mixed carcinoma	4 (2.0)
Nodal yield, median (IQR)	28 (19–39)
Pathologic T stage, no. (%)	
T0,Tis,Ta,T1	74 (37.7)
T2	52 (26.5)
T3	48 (24.5)
T4	22 (11.2)
Pathologic node status, no. (%)	
N0	152 (77.5)
N1	15 (7.7)
N2	27 (13.8)
N3	1 (0.5)
Positive surgical margins, no. (%)	8 (4.1)
Preoperative hematocrit, %, median (IQR)	39.6 (36.2–42.8)
Preoperative creatinine, median (IQR)	1.0 (0.9–1.2)
Length of stay, d, median (IQR)	9 (7–13)

IQR = interquartile range; BMI = body mass index; CCI = Charlson comorbidity index; ASA = American Society of Anesthesiologists; EBL = estimated blood loss.

endovascular stapler. In females, the posterior vagina was opened for specimen extraction and closed with suturing. In men, the specimen was extracted through a small midline incision concurrently used for urinary diversion.

In 2003, the same surgeon who performed the cystectomy completed the diversion. Beginning in 2004, a two-team approach was used, and a single surgeon from that point forward performed all diversions. Extracorporeal diversion was completed through a midline incision extending 6–8 cm from the camera port. Ileal conduits were constructed with interrupted Bricker ureteroileal anastomoses over 8F feeding tubes using a Turnbull stoma. Continent cutaneous Indiana pouches were constructed using a segment of ascending colon and terminal ileum. The terminal ileum was tapered over a 14F red Robinson catheter, and the pouch was additionally drained with a temporary 24F catheter. Orthotopic neobladders were created using the Studer method; the robot was redocked for the urethra–neobladder anastomosis.

Nasogastric tubes were not routinely left in place or were discontinued by postoperative day 1. Ureteral stents were removed 3 wk postoperatively, as indicated. Cystography was performed after orthotopic neobladder at 3 wk postoperatively, prior to Foley removal. Temporary continent cutaneous pouch catheters were discontinued 3 wk after surgery.

## 2.2. Statistical analysis

Statistical Analysis System software was used to conduct all statistical analyses. Demographic, clinical, and pathologic variables were summarized using descriptive statistics, with medians and interquartile ranges reported for continuous variables and proportions for categorical variables. Variables were further stratified by type of diversion, transfusion status, length of stay (LOS), and mortality and then tested across the various strata using the Pearson  $\chi^2$  test and the Student *t* test to compare categorical and continuous data, respectively. For data not normally distributed, the Fisher exact test and the Wilcoxon test were used to compare categorical and continuous variables, respectively. Univariable and multivariable logistic regression were used to analyze the effect of demographic, preoperative, surgical, and pathologic factors on the incidence of complications following RARC.

## 3. Results

Patient clinical and pathologic characteristics are summarized in Table 1. Of 196 patients, 156 patients (80%) experienced one complication or more within 90 d of surgery; 475 total complications were captured, for an average of three adverse events per patient; 365 complications (77%) occurred in  $\leq 30$  d, with the remaining 110 complications (23%) occurring between 31 and 90 d postoperatively.

Complications were grouped and analyzed in a systems-based manner (Fig. 1 and Table 2). Most common were hematologic complications (20.4%), followed by infectious complications (16.2%), gastrointestinal complications (14.1%), and procedural complications (10.3%). Anemia was the most common hematologic disorder, though 98% of events were classified as minor. Minor urinary tract infections represented 42% of the infectious complications. Gastrointestinal complications mostly consisted of ileus or small bowel obstruction (67%), with the majority (84%) being minor. Ureteral or urethral anastomotic leaks made up 71% of the procedural complications captured.

Sixty-eight patients (35%) experienced a major complication during the first 90 d after surgery. Ureteral stricture occurred in 14 patients (7%), requiring percutaneous nephrostomy drainage; 38% of all infectious complications were major. The incidence of complications for patients who underwent RARC from 2003 to 2007 ( $n = 67$ ) was higher than for patients who underwent RARC in 2008 and later ( $n = 129$ ) (88.1% compared with 75.2%,  $p = 0.03$ ). However, no significant change was seen in the incidence of major complications (35.8% compared with 34.1%).

Four patients (2%) died in  $\leq 30$  d, and eight patients (4.1%) died  $\leq 90$  d after surgery; two patients each died of

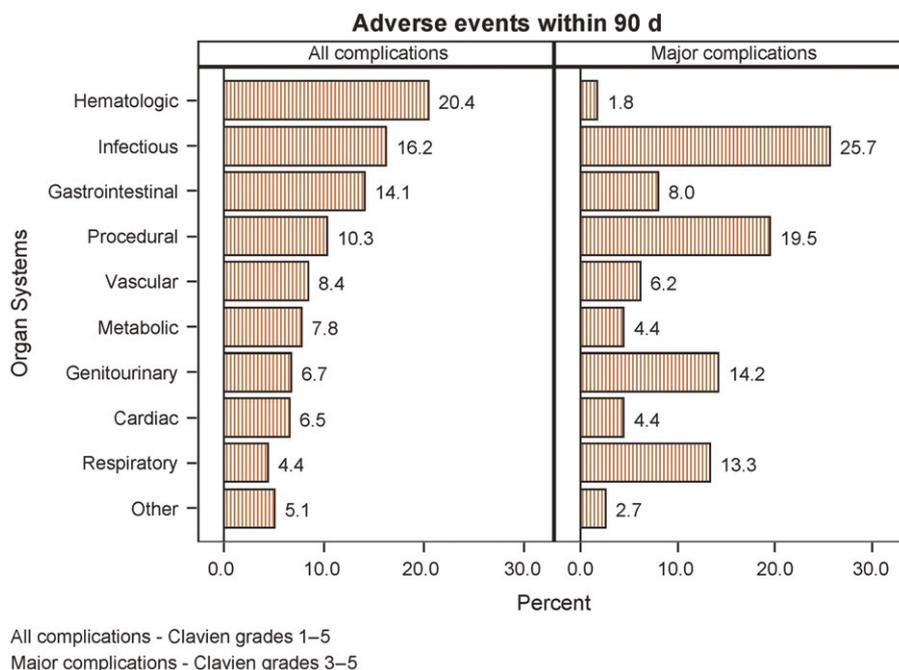


Fig. 1 – Breakdown of all grades and major complications by system.

Table 2 – Total complications by system

Adverse event	Clavien grade		Total	% total	
	Minor (1–2)	Major (3–5)			
Hematologic	Anemia	90	2	92	20.4
	Other	5	0	5	
Infectious	Urinary tract infection	32	6	38	16.2
	Abdominopelvic abscess	0	12	12	
	Sepsis	3	3	6	
	Lung infection	3	2	5	
	Wound infection	4	1	5	
	Kidney infection	0	3	3	
	Other	6	2	8	
		48	29	77	
Gastrointestinal	Ileus/small intestinal obstruction	38	7	45	14.1
	Colitis	8	0	8	
	Diarrhea	5	0	5	
	Gastritis	1	1	2	
	Gastrointestinal bleed	0	1	1	
	Other	6	0	6	
		58	9	67	
Procedural	Urethral anastomotic leak	18	6	24	10.3
	Ureteral anastomotic leak	1	10	11	
	Wound seroma or superficial breakdown	7	0	7	
	Wound dehiscence	1	2	3	
	Intraoperative gastrointestinal injury	0	2	2	
	Intraoperative arterial injury	0	1	1	
	Other	0	1	1	
Vascular	Thromboembolic event	27	22	49	8.4
	Hypertension	13	3	16	
	Hypotension	16	0	16	
	Lymphocele	4	1	5	
Metabolic	Dehydration	0	3	3	7.8
	Electrolyte imbalance	33	7	40	
	Acidosis	21	5	26	
	Other	5	0	5	
Genitourinary	Urinary tract obstruction	4	0	4	6.7
	Renal failure	2	0	2	
	Urinary fistula	1	0	1	
	Other	3	0	3	
Cardiac	Arrhythmia	16	16	32	6.5
	Myocardial infarction	25	1	26	
	Cardiomyopathy	0	2	2	
	Other	0	1	1	
Respiratory	Respiratory failure	1	1	2	4.4
	Pleural effusion	1	1	2	
	Dyspnea	0	1	1	
	Aspiration	4	2	6	
	Other	6	15	21	
Other		21	3	24	5.1
	Total	362	113	475	

*Ileus* was defined as the inability to tolerate oral intake by postoperative day 10, need for reinsertion of a nasogastric tube, or initiation of total parenteral nutrition. *Dehydration* was defined as the need for an intravenous fluid bolus after a regular diet was tolerated. *Kidney infection* was defined as fever with flank pain and/or radiographic evidence of pyelonephritis. *Sepsis* was defined as clinical evidence of infection with similar bacterial species present in both urine and blood cultures. *Thromboembolic events* included deep vein thrombosis and pulmonary embolism.

sepsis, respiratory insufficiency, and BCa progression; one patient died of cardiac arrest; and one patient died of unknown causes. Patients with early mortality were older and had higher CCI ( $p \leq 0.03$ ).

In univariable analysis, American Society of Anesthesiologists (ASA) score, preoperative hematocrit  $\leq 35\%$ , estimated

blood loss (EBL), operative time, and being a candidate for continent diversion were predictive of complications of any grade within 90 d of surgery (Table 3). In multivariable analysis looking at only presurgical indicators, ASA score, preoperative hematocrit, and being a candidate for continent diversion were significant predictors of any complications.

**Table 3 – Predictors of all complications**

Predictor	Univariable		Multivariable (presurgical indicators) <sup>†</sup>		Multivariable (presurgical and postsurgical indicators) <sup>**</sup>	
	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)
Age	0.3	1.02 (0.98–1.05)			0.03	1.05 (1.004–1.094)
ASA score (4 vs ≤3)	0.05	4.34 (0.99–19.02)	0.03	5.63 (1.19–26.59)	0.009	10.4 (1.8–60.2)
Receipt of neoadjuvant chemotherapy	0.7	1.16 (0.49–2.74)				
Preoperative HCT ≤35%	0.01	6.27 (1.44–27.24)	0.006	8.50 (1.88–38.5)	0.008	8.6 (1.8–42.1)
Indication for urinary diversion						
Continent cutaneous diversion (vs ileal conduit)	0.0006	4.15 (1.30–13.32)	0.003	6.40 (1.88–21.74)		
Orthotopic diversion (vs ileal conduit)	0.02	1.33 (0.63–2.84)	0.04	2.40 (1.03–5.58)		
Operative time	0.001	1.59 (1.20–2.10)			0.006	1.71 (1.17–2.50)
EBL	<0.0001	1.005 (1.003–1.008)			0.0003	1.006 (1.003–1.009)

OR = odds ratio; CI = confidence interval; ASA = American Society of Anesthesiologists; HCT = hematocrit; EBL = estimated blood loss; BMI = body mass index.  
<sup>†</sup> Age, gender, BMI, smoking status, receipt of neoadjuvant chemotherapy, previous abdominal surgery, and clinical stage were also tested in the multivariable model, with negative statistical results.  
<sup>\*\*</sup> Gender, BMI, smoking status, receipt of neoadjuvant or adjuvant chemotherapy, previous abdominal surgery, clinical and pathologic stage, urinary diversion type, and nodal yield were also tested in the multivariable model, with negative statistical results.

In multivariable analysis of all presurgical and postsurgical indicators, age, ASA score, preoperative hematocrit, EBL, and operative time remained predictors of complications of any grade.

For prediction of major complications (Table 4), preoperative hematocrit ≤35% and EBL were significant on univariable analysis. In multivariable analysis of presurgical and all indicators, CCI, preoperative hematocrit, and orthotopic neobladder diversion were significant predictors of major complications.

Stratifying complications by diversion type, 45 of 62 patients with an ileal conduit (73%), 44 of 48 patients with a continent cutaneous pouch (92%), and 67 of 86 patients with an orthotopic neobladder (78%) experienced a complication. The respective rates for major complications were 17 of 62 patients (27%), 15 of 48 patients (31%), and 36 of 86 patients (42%). Patients with ileal conduits were older and

had higher CCI, higher ASA score, and lower body mass index (BMI) (all  $p \leq 0.03$ ) (Tables 5 and 6). Patients receiving an ileal conduit had a worse pathologic stage than other patients; 50% of these patients were found to be  $\geq pT3$  ( $p < 0.01$ ).

Forty patients (20%) had a preoperative hematocrit <35%. Of 196 patients, 86 (43.9%) required a blood transfusion perioperatively. Patients requiring blood transfusion had lower preoperative hematocrits (36.9 compared with 42.1), lower BMI, higher preoperative serum creatinine, higher CCI or ASA score, and female gender (all  $p \leq 0.03$ ). Patients with higher pathologic stage required transfusion more frequently ( $p = 0.02$ ). Transfusions were significantly associated with an increased LOS (9 d compared with 11.5 d,  $p < 0.01$ ). Patients with increased age, higher CCI, or higher pathologic stages also had a longer LOS ( $p \leq 0.03$ ). There was a trend toward longer LOS in the continent cutaneous and ileal conduit groups ( $p = 0.06$ ).

**Table 4 – Predictors of major complications**

Predictor	Univariable		Multivariable (presurgical indicators) <sup>†</sup>		Multivariable (presurgical and postsurgical indicators) <sup>††</sup>	
	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value	OR (95% CI)
CCI	0.09	1.18 (0.97–1.43)	0.01	1.34 (1.07–1.69)	0.007	1.39 (1.10–1.76)
Receipt of neoadjuvant chemotherapy	0.07	1.90 (0.95–3.79)	0.2	1.70 (0.80–3.63)	0.2	1.70 (0.78–3.69)
Preoperative HCT ≤35%	0.004	2.84 (1.40–5.76)	0.009	2.83 (1.29–6.20)	0.02	2.62 (1.19–5.78)
Indication for urinary diversion						
Continent cutaneous diversion (vs ileal conduit)	0.7	1.20 (0.53–2.75)	0.3	1.70 (0.67–4.30)	0.7	1.24 (0.43–3.60)
Orthotopic diversion (vs ileal conduit)	0.07	1.91 (0.94–3.85)	0.002	3.70 (1.59–8.58)	0.02	3.01 (1.21–7.52)
Operative time	0.08	1.20 (0.98–1.46)			0.4	0.5
EBL	0.02	1.001 (1.00–1.002)			0.1	0.1

OR = odds ratio; CI = confidence interval; CCI = Charlson comorbidity index; HCT = hematocrit; EBL = estimated blood loss; BMI = body mass index; ASA = American Society of Anesthesiologists.  
<sup>†</sup> Age, gender, BMI, smoking status, ASA score, previous abdominal surgery, and clinical stage were also tested in the multivariable model, with negative statistical results.  
<sup>††</sup> Age, gender, BMI, smoking status, receipt of adjuvant chemotherapy, ASA score, previous abdominal surgery, clinical and pathologic stage, and nodal yield were also tested in the multivariable model, with negative statistical results.

**Table 5 – Comparison of urinary diversion type and incidence of transfusion**

	Diversion type			p value	Transfusion incidence		p value
	Ileal conduit, n = 62	Continent cutaneous, n = 48	Orthotopic neobladder, n = 86		No transfusion, n = 110	Transfusion, n = 86	
Gender, no. (%)							
Female	15 (24.2)	17 (35.4)	0 (0.0)	<0.01	11 (10.0)	21 (24.4)	<0.01
Male	47 (75.8)	31 (64.6)	86 (100.0)		99 (90.0%)	65 (75.6)	
Age at surgery, yr, median (IQR)	75.9 (70.8–82.2)	70.7 (62.9–76.8)	64.8 (59.0–71.6)	<0.01	68.9 (61.7–75.7)	72.2 (65.7–79.4)	0.07
BMI, median (IQR)	25.6 (23.2–29.4)	26.7 (24.4–32.0)	27.8 (24.3–31.4)	0.03	28.1 (25.2–32.0)	25.6 (23.1–28.7)	0.03
CCI, median (IQR)	6 (5–7)	5 (4–6)	4 (3–5)	<0.01	5 (4–6)	5 (5–7)	<0.01
ASA score, no. (%)							
II	7 (11.3)	9 (18.8)	25 (29.1)		31 (28.2)	10 (11.6)	
III	37 (59.7)	31 (64.6)	55 (64.0)	<0.01	65 (59.1)	58 (67.4)	0.02
IV	17 (27.4)	8 (16.7)	6 (7.0)		13 (11.8)	18 (20.9)	
Diversion type, no. (%)							
Ileal conduit					30 (27.3)	32 (37.2)	
Continent cutaneous					19 (17.3)	29 (33.7)	<0.01
Orthotopic neobladder					61 (55.5)	25 (29.1)	
Surgery length, h, median (IQR)	6.0 (5.3–6.9)	8.0 (7.4–9.3)	7.4 (6.9–8.5)	<0.01	7.2 (6.4–8.0)	7.3 (6.5–8.5)	0.3
EBL, ml, median (IQR)	300 (200–400)	450 (300–650)	400 (300–550)	0.03	350 (250–500)	450 (250–700)	<0.01
Nodal yield, median (IQR)	23 (15–32)	28 (19–41)	31.5 (21–40)	0.01	28.5 (19–39)	27 (17–39)	0.4
Pathologic T stage, no. (%)							
Tis,T0,Ta,T1	12 (19.3)	14 (29.2)	48 (55.8)		51 (46.4)	23 (26.7)	
T2	19 (30.6)	18 (37.5)	15 (17.4)	<0.01	28 (25.5)	24 (27.9)	0.02
T3	18 (29.0)	11 (22.9)	19 (22.1)		24 (21.8)	24 (27.9)	
T4	13 (21.0)	5 (10.4)	4 (4.7)		7 (6.4)	15 (17.4)	
Positive surgical margins, no. (%)	7 (11.3)	0 (0.0)	1 (1.2)	0.01	3 (2.7)	5 (5.8)	0.4
Preoperative hematocrit, % , median (IQR)	37.1 (33.6–40.5)	39.2 (36.9–42.8)	41.2 (37.6–44.0)	<0.01	42.1 (38.7–44.3)	36.9 (33.3–39.7)	<0.01
Length of hospital stay, d, median (IQR)	9.5 (8–14)	10 (8–14.5)	9 (7–12)	0.03	9 (7–11)	11.5 (8–17)	<0.01

BMI = body mass index; IQR = interquartile range; CCI = Charlson comorbidity index; ASA = American Society of Anesthesiologists; EBL = estimated blood loss.

**Table 6 – Comparison of length of hospital stay and 90-d mortality**

	Length of stay, d			p value	90-d mortality		p value
	1–7, n = 55	8–14, n = 104	≥15, n = 37		Alive at 90 d, n = 188	Died within 90 d, n = 8	
Gender, no. (%)							
Female	5 (9.1)	22 (21.2)	5 (13.5)	0.1	30 (16.0)	2 (25.0)	0.6
Male	50 (90.9)	82 (78.8)	32 (86.5)		158 (84.0)	6 (75.0)	
Age at surgery, yr, median (IQR)	65.3 (59.5–74.1)	70.8 (63.8–77.5)	73.9 (67.9–79.5)	0.01	69.9 (62.3–76.8)	78.4 (72.4–80.1)	0.03
BMI, median (IQR)	28.3 (24.1–32.7)	26.7 (23.8–29.8)	26.1 (24.2–30.9)	0.3	27.1 (24.1–30.5)	27.5 (21.1–33.1)	0.9
CCI, median (IQR)	5 (3–6)	5 (4–6)	6 (5–7)	<0.01	5 (4–6)	6.5 (5.5–8)	0.006
ASA score, no. (%)							
II	16 (29.1)	21 (20.2)	4 (10.8)		41 (21.9)	0 (0.0)	
III	31 (56.4)	68 (65.4)	24 (64.9)	0.3	118 (63.1)	5 (62.5)	0.1
IV	8 (14.5)	14 (13.5)	9 (24.3)		28 (15.0)	3 (37.5)	
Diversion type, no. (%)							
Ileal conduit	13 (23.6)	34 (32.7)	15 (40.5)		57 (30.3)	5 (62.5)	
Continent cutaneous	10 (18.2)	26 (25.0)	12 (32.4)	0.06	47 (25.0)	1 (12.5)	0.2
Orthotopic neobladder	32 (58.2)	44 (42.3)	10 (27.0)		84 (97.7)	2 (25.0)	

IQR = interquartile range; BMI = body mass index; CCI = Charlson comorbidity index; ASA = American Society of Anesthesiologists.

#### 4. Discussion

Radical cystectomy remains the gold standard surgical therapy for locally aggressive urothelial carcinoma. Awareness of the significant associated morbidity is important for patients and clinicians to establish realistic expectations. Complications are related to the technical complexity of the

operation, as well as the increased age of patients, preexisting comorbidities, and perioperative metabolic and fluid shifts. We report a prospective comprehensive complication analysis of a consecutive series of RARCs. All complications within 90 d were recorded and graded according to the Clavien system by urologic oncologists. Our series demonstrates that RARC can be performed with

oncologic prudence in regard to surgical margin status and lymph node yields, two important factors related to recurrence and long-term survival [14,15]. The positive margin rate (4.1%) was low despite 36% of patients with extravesical disease, and the median lymph node yield (28) was consistent with other academic centers [16] and representative of an oncologic template dissection.

Most studies evaluating morbidity of radical cystectomy do not use a formal grading system, account for comorbidities, or clearly define various complications [17]. These factors likely lead to an underestimation of the true morbidity for the procedure. To standardize reporting, complication grading systems [12] and criteria for reporting surgical outcomes have been adopted [7].

We found that 80% of patients experienced an adverse event in the first 90 d, with the majority of these complications (76%) being minor. Most complications (77%) occurred  $\leq 30$  d after surgery. Mortality at 90 d was 4.1%. These results are comparable to recently published series that used a similar reporting methodology [2,3,8]. Smaller series reviewing initial perioperative outcomes of RARC report complication rates ranging from 34% to 63% [3–5]. Shabsigh et al. used a standardized reporting methodology in a series of 1142 open radical cystectomy patients [9]. At 90 d postoperatively, 64% of patients experienced a complication; 13% of the complications were major, the mortality rate was 2.7%, and the blood transfusion rate was 66%. In a series of 156 RARC patients, Hayn et al. identified 52% of patients having experienced a complication within 90 d of surgery [5]. In contrast to these studies, our study defined any blood transfusion as a complication, which could explain our increased complication rate. We also recorded a higher major complication rate, though direct comparison is challenging, as ileal conduit was performed in 63% [9] and 93% [5] of patients in these respective studies. The majority of our major complications (62%) were secondary to urinary diversion and often warranted higher Clavien classification because of procedural intervention (percutaneous drain or nephrostomy).

Transfusion rates for contemporary open cystectomy series range between 38% and 66% [9,18]. Our perioperative transfusion rate was 44%. Although EBL at the time of RARC is reduced, many patients ultimately require a transfusion. Possible reasons include patient comorbidity, frequent baseline anemia, and suppression of intraoperative EBL through pneumoperitoneum. In our study, transfused patients were older and had more comorbidities, higher pathologic stage, and lower preoperative hematocrit compared with nontransfused patients.

Median operative time of 432 min is longer than many open series and could affect postoperative morbidity. The time difference may be explained by the learning curve and the fact that the majority of patients underwent a continent diversion that took 80–120 min longer, on average ( $p < 0.01$ ). Our median LOS of 9 d is similar to most published open series, which range from 6 to 11 d [9,18–20]. Our 23% incidence of ileus or small bowel obstruction is also similar to the incidence in open series [9,18].

Most surgical complications and major complications were urinary diversion related. This finding may be partly

explained by the high percentage of continent diversions performed. Other reporters have given similar complication rates when comparing continent and conduit diversions [21,22]; however, no randomized controlled studies exist, and historical results may be influenced by a selection bias that favored continent diversion in healthier patients. In our study, patients with continent diversions were younger and healthier, and they had higher baseline hematocrit and lower pathologic stage. We believe that complex urinary diversions lend themselves to a slightly higher rate of diversion-related complications. Another reason may be that the urinary diversion is created through a minilaparotomy and then placed back inside the abdomen. Inadvertent kinking or twisting of the ureters and/or diversion may occur, leading to the aforementioned complications.

Multivariable analysis showed that age, ASA score, preoperative anemia, operative time, and EBL were statistically significant predictors of complications of any grade. However, when predicting major complications, only preoperative anemia, increased comorbidity, and orthotopic neobladder diversion were significant. Age [9,23], ASA score [8,10], and EBL [3] have previously been identified as significant predictors of complications. Other reports have also demonstrated that blood transfusion increases postoperative morbidity, specifically infectious complications [24,25]. The underlying reason is debated. Some evidence suggests that transfusion leads to direct immunosuppression [26]. Other evidence suggests that transfusion merely identifies individuals with greater underlying comorbidities, who are therefore at increased risk for complications. The predisposition for major complications in orthotopic diversion is possibly related to procedural intervention for ureteral and urethral neobladder anastomotic leaks.

The main limitations of our study include lack of randomization and smaller sample size compared with large open series [27]. Although to our knowledge this study represents the largest single-institution analysis of RARC, the statistical results may still be underpowered. Additionally, while the Clavien system represents an objective and graded method of measurement, the system remains intervention-based, and reproducibility biases may exist. While our data were prospectively collected, analysis was performed retrospectively. Finally, our patient population represents the experience of a tertiary cancer center and may not coincide with the experience of community hospitals. Although complication rates are high, we did demonstrate a decrease in incidence of total complications over time. As robotic technology improves, so will the ability to safely and efficiently perform intracorporeal diversions that may help lower complication rates. Also, with randomized comparative studies, we may better understand which patients are best suited for RARC.

## 5. Conclusions

When a standardized reporting methodology is used, RARC is associated with a high complication rate, though this rate is comparable to that of contemporary open series that used similar reporting guidelines. Our study reinforces the need

for accurate and standardized reporting when scrutinizing surgical techniques and comparing published series.

**Author contributions:** Bertram E. Yuh had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Yuh, Wilson, Jankowski, Lau, Chan.

**Acquisition of data:** Yuh, Wilson, Nazmy, Jankowski, Menchaca, Torrey, Linehan, Lau, Chan.

**Analysis and interpretation of data:** Yuh, Wilson, Ruel.

**Drafting of the manuscript:** Yuh, Wilson, Nazmy, Jankowski.

**Critical revision of the manuscript for important intellectual content:** Yuh, Wilson, Nazmy, Jankowski, Torrey, Linehan, Lau, Chan.

**Statistical analysis:** Yuh, Wilson, Ruel.

**Obtaining funding:** None.

**Administrative, technical, or material support:** Menchaca, Ruel.

**Supervision:** Yuh, Wilson.

**Other (specify):** None.

**Financial disclosures:** Bertram E. Yuh 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 (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

**Funding/Support and role of the sponsor:** None.

**Acknowledgment statement:** The authors thank Nicola Solomon, PhD, for editorial assistance and critical review.

## References

- [1] Herr HW, Sogani PC. Does early cystectomy improve the survival of patients with high risk superficial bladder tumors? *J Urol* 2001;166:1296–9.
- [2] Ng CK, Kauffman EC, Lee M-M, et al. A comparison of postoperative complications in open versus robotic cystectomy. *Eur Urol* 2010;57:274–82.
- [3] Sung HH, Ahn JS, Seo SI, et al. A comparison of early complications between open and robot-assisted radical cystectomy. *J Endourol*. In press.
- [4] Khan MS, Elhage O, Challacombe B, Rimington P, Murphy D, Dasgupta P. Analysis of early complications of robotic-assisted radical cystectomy using a standardized reporting system. *Urology* 2011;77:357–62.
- [5] Hayn MH, Hellenthal NJ, Hussain A, Stegemann AP, Guru KA. Defining morbidity of robot-assisted radical cystectomy using a standardized reporting methodology. *Eur Urol* 2011;59:213–8.
- [6] Murphy DG, Challacombe BJ, Elhage O, et al. Robotic-assisted laparoscopic radical cystectomy with extracorporeal urinary diversion: initial experience. *Eur Urol* 2008;54:570–80.
- [7] Martin II RC, Brennan MF, Jaques DP. Quality of complication reporting in the surgical literature. *Ann Surg* 2002;235:803–13.
- [8] Hautmann RE, de Petroni RC, Volkmer BG. Lessons learned from 1,000 neobladders: the 90-day complication rate. *J Urol* 2010;184:990–4, quiz 1235.
- [9] Shabsigh A, Korets R, Vora KC, et al. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. *Eur Urol* 2009;55:164–76.
- [10] Novara G, De Marco V, Aragona M, et al. Complications and mortality after radical cystectomy for bladder transitional cell cancer. *J Urol* 2009;182:914–21.
- [11] Nix J, Smith A, Kurpad R, Nielsen ME, Wallen EM, Pruthi RS. Prospective randomized controlled trial of robotic versus open radical cystectomy for bladder cancer: perioperative and pathologic results. *Eur Urol* 2010;57:196–201.
- [12] Clavien PA, Sanabria JR, Strasberg SM. Proposed classification of complications of surgery with examples of utility in cholecystectomy. *Surgery* 1992;111:518–26.
- [13] Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
- [14] Herr HW, Lee C, Chang S, et al. Standardization of radical cystectomy and pelvic lymph node dissection for bladder cancer: a collaborative group report. *J Urol* 2004;171:1823–8, discussion 1827–8.
- [15] Karl A, Carroll PR, Gschwend JE, et al. The impact of lymphadenectomy and lymph node metastasis on the outcomes of radical cystectomy for bladder cancer. *Eur Urol* 2009;55:826–35.
- [16] Dhar NB, Klein EA, Reuther AM, Thalmann GN, Madersbacher S, Studer UE. Outcome after radical cystectomy with limited or extended pelvic lymph node dissection. *J Urol* 2008;179:873–8, discussion 878.
- [17] Donat SM. Standards for surgical complication reporting in urologic oncology: time for a change. *Urology* 2007;69:221–5.
- [18] Lowrance WT, Rumohr JA, Chang SS, Clark PE, Smith Jr JA, Cookson MS. Contemporary open radical cystectomy: analysis of perioperative outcomes. *J Urol* 2008;179:1313–8, discussion 1318.
- [19] Lee CT, Dunn RL, Chen BT, Joshi DP, Sheffield J, Montie JE. Impact of body mass index on radical cystectomy. *J Urol* 2004;172:1281–5.
- [20] Clark PE, Stein JP, Groshen SG, et al. Radical cystectomy in the elderly: comparison of clinical outcomes between younger and older patients. *Cancer* 2005;104:36–43.
- [21] Parekh DJ, Clark T, O'Connor J, et al. Orthotopic neobladder following radical cystectomy in patients with high perioperative risk and comorbid medical conditions. *J Urol* 2002;168:2454–6.
- [22] Hautmann RE. Urinary diversion: ileal conduit to neobladder. *J Urol* 2003;169:834–42.
- [23] Konety BR, Allareddy V, Herr H. Complications after radical cystectomy: analysis of population-based data. *Urology* 2006;68:58–64.
- [24] Braga M, Vignali A, Radaelli G, Gianotti L, Di Carlo V. Association between perioperative blood transfusion and postoperative infection in patients having elective operations for gastrointestinal cancer. *Eur J Surg* 1992;158:531–6.
- [25] Vamvakas EC, Carven JH, Hibberd PL. Blood transfusion and infection after colorectal cancer surgery. *Transfusion* 1996;36:1000–8.
- [26] Vamvakas EC, Blajchman MA. Deleterious clinical effects of transfusion-associated immunomodulation: fact or fiction? *Blood* 2001;97:1180–95.
- [27] Stein JP, Lieskovsky G, Cote R, et al. Radical cystectomy in the treatment of invasive bladder cancer: long-term results in 1,054 patients. *J Clin Oncol* 2001;19:666–75.