

Clinical-Bladder cancer

Surgical approach as a determinant factor of clinical outcome following radical cystectomy: Does Enhanced Recovery After Surgery (ERAS) level the playing field?

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Abstract

Purpose: To determine whether surgical approach is a determinant of clinical outcomes following radical cystectomy (RC) and urinary diversion when using an Enhanced Recovery After Surgery (ERAS) protocol.

Materials and Methods: We studied all patients undergoing both open radical cystectomy (ORC) and robotic-assisted radical cystectomy (RARC) and urinary diversion with ERAS for bladder urothelial carcinoma from May 2012 to December 2016. Surgical and clinical outcomes within 90 days after surgery were compared between ORC and RARC, including readmission and major complication rates (Clavien-Dindo grade \geq III). Multivariable logistic regression modeling was used to determine factors that predict readmission and major complications.

Results: A total of 345 and 143 patients underwent ORC and RARC, respectively. The ORC group had a greater proportion of continent urinary diversion (71.9 vs. 40.6%, $P < 0.001$), shorter operative time (5.4 vs. 7.3 hours, $P < 0.001$), higher estimated blood loss (500 vs. 200 ml, $P < 0.001$), and higher intraoperative and postoperative transfusion rates (20.9 vs. 9.1%, $P = 0.002$ and 20 vs. 11.9%, $P = 0.04$, respectively). Median length of stay was 4 days for ORC (interquartile range 4–6 days) and 6 days for RARC (interquartile range 4–7 days; $P < 0.001$). There was no significant difference between ORC and RARC groups in major complication rates (20 vs. 23.8%, $P = 0.51$) or readmission rates (32.2 vs. 36.4%, $P = 0.4$) within 90 days after surgery. Multivariable logistic regression analysis showed that surgical approach was not an independent factor predictive of readmission ($P = 0.33$) or major complications ($P = 0.76$).

Conclusions: Surgical approach is not a determinant of readmission or major complications following RC in the context of an ERAS protocol. © 2019 Elsevier Inc. All rights reserved.

Keywords: Urinary bladder neoplasms; Cystectomy; Postoperative complications; Patient readmission

Abbreviations: ERAS, Enhanced Recovery After Surgery; RC, radical cystectomy; ORC, open radical cystectomy; RARC, robotic-assisted radical cystectomy; IQR, interquartile range; LOS, length of stay; IV, intravenous; POD, postoperative day; EBL, estimated blood loss; BMI, body mass index; CCMI, Charlson comorbidity index; ASA, American Society of Anesthesiologists; NAC, neoadjuvant chemotherapy; GI, gastrointestinal; GU, genitourinary; DVT, deep venous thrombosis; OR, odds ratio; CI, confidential interval

1. Introduction

Bladder cancer is a serious urological malignancy in the United States, with more than 81,000 new diagnoses and over 17,200 deaths estimated in 2018 [1]. Although radical

cystectomy (RC) is considered the gold standard treatment for muscle invasive bladder cancer [2,3], it is associated with considerable morbidity [4].

Since its first introduction in 2003 [5], robotic-assisted radical cystectomy (RARC) has quickly gained popularity. The proportion of radical cystectomies performed robotically increased rapidly from 0.6% in 2004 to 12.8% in 2010 [6], and since increased to 28.9% of all RC cases in 2012

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[7]. The 2 surgical approaches continue to be compared and heavily debated in the literature. Retrospective studies and systemic reviews suggest that RARC is associated with shorter length of hospital stay [6,8–11] and less overall or major complications (Clavien-Dindo grade \geq III) [12–17]. However, such results should be interpreted with caution since most of these studies are based on data prior to 2012, when Enhanced Recovery After Surgery (ERAS) protocols were not yet adopted for most urological surgeries.

ERAS protocols are evidence-based multimodal pathways that optimize the perioperative care of patients undergoing complex surgeries. First introduced in patients undergoing colectomy, the goal of ERAS is to improve acute recovery after surgery. In more recent years, ERAS protocols applied to RC have been shown to reduce intraoperative blood loss, transfusion rates [18], time to bowel function, complication rates, length of stay (LOS), and readmission rates [18–20].

In 2012, we adopted an ERAS pathway for all patients undergoing both open and RARC at our institution. Herein, we present the perioperative outcomes of patients undergoing open radical cystectomy (ORC) or RARC in the modern era, focusing on readmission and complication rates within the framework of the institutional ERAS pathway. We hypothesized that ORC patients had similar postoperative complication rates and readmission rates as patients who underwent RARC.

2. Methods

2.1. Study population

Patients undergoing ORC or RARC and urinary diversion with ERAS for primary bladder urothelial carcinoma at our institution from May 2012 to December 2016 were identified from our institutional review board approved intent-to-cure bladder cancer database.

2.2. Surgical procedure

Open surgeries were performed by 1 of 3 fellowship-trained surgeons extensively experienced in ORC and urinary diversion. Similarly, all RARC procedures were performed by 1 of 3 fellowship-trained surgeons with extensive experience and robotic volume ($>2,000$ cases each). At our institution, RARC typically involves an extended pelvic lymph node dissection up to the aortic bifurcation or inferior mesenteric artery, along with a completely intracorporeally performed urinary diversion. Surgical technique for open and robotic radical cystectomy at our institution has been reported prior [21,22].

2.3. ERAS protocol

Preoperatively, the protocol is highlighted by the absence of bowel preparation and inclusion of high-protein high-

carbohydrate liquid drinks. Intravenous (IV) antibiotics start just before surgery and continue for 24 hours postoperatively, at which time the patient is transitioned to oral suppressive antibiotics at a prophylactic dose that is continued until ureteral stent removal. Intraoperatively, fluid intake is minimized after clipping the ureters, with careful monitoring of intravascular fluid volume. If a nasogastric or orogastric tube was placed preoperatively, it is removed at the end of surgery. On the night of the surgery, postoperative patients are started on a clear liquid diet. If tolerated well, they proceed to regular diet on postoperative day (POD) 1. If patients do not tolerate oral food by POD 6 or 7, parenteral feeding is initiated [19,23]. Patients receive a cholinergic drug (neostigmine) and μ -opioid receptor antagonist (alvimopan) until the first bowel movement [19].

2.4. Discharge and follow-up

Discharge criteria include adequate oral intake (over 1 l/day), bowel movement, pain control with oral medication, and expected laboratory values. Patients are discharged with oral prophylactic antibiotics until stent removal, deep vein thrombosis prophylaxis. All patients are discharged home after placement of midline intravenous catheter for administration of 1 l of lactated ringers solution given by home health nurses every other day for 2 weeks. Postoperative visits are scheduled at 1, 3, 6, and 12 to 16 weeks [19].

2.5. Data collection and analysis

Patient data were captured prospectively, including surgical approach and diversion type, LOS, 30-day and 90-day complications according to the Clavien-Dindo postoperative complication classification system and readmission rates. Patients readmitted to an outside hospital were captured by outside medical records. Continuous variables were compared between ORC and RARC groups using Kruskal-Wallis test. Categorical variables were compared using Chi-squared and Fisher's exact test. Rate of complications and readmission were analyzed by Chi-squared test. Multivariable logistic regression analysis was performed to identify independent predictors for readmission and major complications. Variables that showed significant difference were entered into a multivariable analysis. The variables entered into the model for major complications prediction were surgical approach, patient age, preoperative hematocrit level, and LOS. The variables entered into the model for readmission prediction were surgical approach, patient age, diabetes, and blood transfusion. Data were analyzed using SAS 9.0 software.

3. Results

3.1. Patient characteristics

We identified a total of 488 patients with primary urothelial carcinoma who underwent RC and urinary

diversion with ERAS at our institution from May 2012 to December 2016, of which 345 patients underwent ORC, and 143 patients underwent RARC. Table 1 lists the demographics and disease characteristics of the 2 studied cohorts. No significant difference in age or comorbidity existed between the 2 groups. A greater proportion of patients in the ORC group underwent neoadjuvant chemotherapy (32.2 vs. 23.1%, $P=0.05$). Patients in the ORC group had lower baseline hemoglobin (11.9 vs. 12.5 g/dl, $P=0.03$) and hematocrit level (36 vs. 37.8, $P=0.03$) prior to surgery.

3.2. Surgical data, LOS, readmission, and complications

Surgical data, LOS, readmission, and complications are listed in Table 2. The ORC group had shorter operative time (5.4 vs. 7.3 hours, $P<0.001$), higher estimated blood loss (500 vs. 200 ml, $P<0.001$), and higher intraoperative and postoperative transfusion rates (20.9 vs. 9.1%, $P=0.002$ and 20 vs. 11.9%, $P=0.04$, respectively). A greater proportion of patients in the ORC group had orthotopic neobladder as urinary diversion (67.3 vs. 38.5%, $P<0.001$). There was no significant difference in surgical pathology between the 2 groups (Table 2).

Median LOS following ORC was 4 days (interquartile range 4–6 days) vs. 6 days (interquartile range 4–7 days) following RARC ($P<0.001$). No significant difference was observed in readmission rate within 30 days (18.3%, ORC vs. 21.7%, RARC, $P=0.38$) and 90 days (32.2%, ORC vs. 36.4%, RARC, $P=0.38$) after surgery. There was no significant difference in minor or major complication rates except for wound complications (7.8%, ORC vs. 2.8%, RARC, $P=0.04$).

3.3. Univariate and multivariable analysis of major complications and readmission

Demographics and surgical data of patients with and without major complications are demonstrated in Table 3. Patients having major complications after surgery had older age (73 vs. 70, $P=0.01$) and lower baseline hemoglobin (11.5 vs. 12.2 g/dl, $P=0.05$) and hematocrit (36 vs. 36.8, $P=0.04$). From a surgical perspective, patients with major complications had higher postoperative transfusion rate (32.3 vs. 13.7%, $P<0.001$), longer LOS (5 vs. 4 days, $P=0.001$), and greater proportion of extravesical disease (38.2 vs. 28.2%, $P=0.05$). Demographics and surgical data of patients with and without readmission are presented in

Table 1
Patient demographics and disease profile

	ORC with ERAS <i>N</i> = 345	RARC with ERAS <i>N</i> = 143	<i>P</i> value
<i>Characteristics</i>			
Age, y, median, (IQR)	70 (63–76)	72 (63–76)	0.390
Gender, <i>n</i> (%)			0.040
Male	273 (79.1)	125 (87.4)	
Female	72 (20.9)	18 (12.6)	
BMI, median, (IQR)	27.1 (23.5–29.9)	27 (23.8–31.2)	0.600
Race			0.070
AA	10 (2.9)	4 (2.8)	
Asian	30 (8.7)	4 (2.8)	
Caucasian	305 (88.4)	136 (94.4)	
Charlson comorbidity index, <i>n</i> (%)			0.200
CCMI 0	153 (44.3)	51 (35.6)	
CCMI 1	92 (26.7)	42 (29.4)	
CCMI ≥2	100 (29)	50 (35)	
ASA score, <i>n</i> (%)			0.900
1–2	71 (20.6)	30 (21)	
3–4	274 (79.4)	113 (79)	
<i>Baseline laboratory work, median, (IQR)</i>			
Albumin	42.0 (39–44)	42 (40–44)	0.980
Hematocrit	36.0 (30.5–41.3)	37.8 (33.1–40.7)	0.030
Hemoglobin	11.9 (10.1–13.7)	12.5 (10.9–13.7)	0.030
<i>Clinical T stage, n (%)</i>			
≤T2	289 (83.8)	128 (89.5)	0.120
≥T3	56 (16.2)	15 (10.5)	
<i>Clinical positive lymph nodes, n (%)</i>			
NAC, <i>n</i> (%)	25 (7.2)	12 (8.4)	0.710
NAC, <i>n</i> (%)	111 (32.2)	33 (23.1)	0.050
Prior pelvic radiation, <i>n</i> (%)	3 (0.9)	1 (0.7)	1.000

ASA = American Society of Anesthesiologists; BMI = body mass index; CCMI = Charlson comorbidity index; ERAS = enhanced recovery after surgery; IQR = interquartile range; NAC = neoadjuvant chemotherapy; ORC = open radical cystectomy; RARC = robotic-assisted radical cystectomy.

Table 2
Surgical data, hospital stay, readmission, and complications of ORC and RARC

	ORC with ERAS N = 345	RARC with ERAS N = 143	P value
<i>Surgical data</i>			
Operative time, hours, median, (IQR)	5.4 (4.6–6.4)	7.3 (6.4–8.1)	<0.001
EBL, ml, median, (IQR)	500 (300–700)	200 (150–300)	<0.001
Intraoperative transfusion, n (%)	72 (20.9)	13 (9.1)	0.002
Postoperative transfusion, n (%)	69 (20)	17 (11.9)	0.040
Diversion type, n (%)			<0.001
Orthotopic	232 (67.3)	55 (38.5)	
Continent	16 (4.6)	3 (2.1)	
Incontinent	97 (28.1)	85 (59.4)	
Total No. of dissected lymph nodes (IQR)	43 (30–54)	42 (31–53)	0.580
<i>Surgical pathology</i>			
Positive surgical margin, n (%)	16 (4.6)	8 (5.6)	1.000
Positive soft tissue margin, n (%)	4 (1.2)	1 (0.7)	1.000
Pathological T stage, n (%)			0.160
≤T2	247 (71.6)	93 (65)	
≥T3	98 (28.4)	50 (35)	
Pathological N stage, n (%)			0.380
N0	280 (81.2)	111 (77.6)	
≥N1	65 (18.8)	32 (22.4)	
<i>Hospital stay</i>			
Day, median, (IQR)	4 (4–6)	6 (4–7)	<0.001
Extended hospital stay			<0.001
No (≤4 days), n (%)	185 (53.6)	36 (25.2)	
Yes (>4 days), n (%)	160 (46.4)	107 (74.8)	
<i>Readmission</i>			
Within POD 30, n (%)	63 (18.3)	31 (21.7)	0.380
Within POD 90, n (%)	111 (32.2)	52 (36.4)	0.400
<i>Complications</i>			
Within POD 30, n (%)			0.090
Minor (Clavien grade I–II)	162 (47)	60 (42)	
Major (Clavien grade III–V)	37 (10.7)	26 (18.1)	
Within POD 90, n (%)			0.510
Minor (Clavien grade I–II)	192 (55.7)	72 (50.3)	
Major (Clavien grade III–V)	69 (20)	34 (23.8)	
Cardiac	39 (11.3)	19 (13.3)	0.540
Pulmonary	10 (2.9)	7 (4.9)	0.280
GI	87 (25.2)	39 (27.3)	0.650
GU	96 (27.8)	39 (27.3)	1.000
DVT	22 (6.4)	10 (7)	0.840
Infection	116 (33.6)	49 (34.3)	0.920
Neurological	16 (4.6)	10 (7)	0.380
Bleeding	55 (15.9)	13 (9.1)	0.060
Surgical complications	36 (10.43)	12 (8.4)	0.620
Wound complications	27 (7.8)	4 (2.8)	0.040
Other complications	54 (15.6)	21 (14.7)	0.890

DVT = deep venous thrombosis; EBL = estimated blood loss; ERAS = enhanced recovery after surgery; GI = gastrointestinal; GU = genitourinary; IQR = interquartile range; ORC = open radical cystectomy; POD = postoperative day; RARC = robotic-assisted radical cystectomy.

Table 4. Patients readmitted to hospital after surgery had older age (73 vs. 70, $P=0.007$), greater incidence of diabetes (32.7 vs. 17.5%, $P<0.001$), and higher postoperative transfusion rate (31.5 vs. 10.7%, $P<0.001$). Multivariable logistic regression modeling showed that, after adjusting for age, postoperative transfusion rate, baseline hematocrit, diabetes, and LOS, surgical approach was not an independent factor predictive of major complications ($P=0.516$) or readmission ($P=0.312$) after RC (Table 5).

4. Discussion

The primary goal of this study is to investigate whether surgical approach is a determinant factor predictive of major complications and readmission after RC in the era of ERAS. Several studies have implicated RC and urinary diversion by open approach to be associated with longer LOS [6,8–11] and more complications [12–17]. Leow et al. reviewed 34,672 ORC and 2,101 RARC patients

Table 3
Demographics and surgical data of patients with and without major complications within postoperative day 90

	With major complications N = 102	Without major complications N = 386	P value
<i>Characteristics</i>			
Age, year, median, (IQR)	73 (64–78)	70 (62–76)	0.010
Gender, n (%)			0.570
Male	81 (79.4)	317 (82.1)	
Female	21 (20.6)	69 (17.9)	
BMI, median, (IQR)	26 (23–29.2)	27.4 (23.9–30.3)	0.190
Race			0.160
African American	2 (2)	12 (3)	
Asian	3 (3)	31 (8)	
Caucasian	97 (95)	343 (89)	
Charlson comorbidity index, n (%)			0.200
CCMI 0	35 (34.3)	169 (43.8)	
CCMI 1	30 (29.4)	104 (26.9)	
CCMI ≥2	37 (36.3)	113 (29.3)	
Diabetes	30 (29.4)	80 (20.7)	0.080
ASA score, n (%)			0.890
1–2	20 (19.6)	81 (21)	
3–4	82 (80.4)	305 (79)	
<i>Baseline laboratory work, median, (IQR)</i>			
Alb	42 (40–45)	42 (39–44)	0.830
HCT	36 (30–39.8)	36.8 (32–41.4)	0.040
HGB	11.5 (10–13.3)	12.2 (10.6–13.8)	0.050
Clinical T stage, n (%)			1.000
≤T2	87 (85.3)	330 (85.5)	
≥T3	15 (14.7)	56 (14.5)	
Clinical N stage, n (%)			0.670
N0	93 (91.2)	358 (92.8)	
≥N1	9 (8.8)	28 (7.2)	
NAC, n (%)	23 (23)	121 (31)	0.090
Prior pelvic radiation, n (%)	0	4 (1)	0.580
<i>Surgery</i>			
Surgical approach, n (%)			0.460
ORC	69 (20)	276 (80)	
RARC	33 (23.1)	110 (76.9)	
Operative time, h, median, (IQR)	6.1 (4.9–7.3)	5.8 (4.8–7)	0.180
EBL, ml, median, (IQR)	350 (250–550)	400 (250–600)	0.400
Intraoperative transfusion, n (%)	18 (17.6)	67 (17.4)	1.000
Postoperative transfusion, n (%)	33 (32.3)	53 (13.7)	<0.001
Diversion type, n (%)			0.820
Orthotopic	59 (57.8)	228 (59.1)	
Nonorthotopic	43 (42.2)	158 (40.9)	
Total dissected lymph nodes, (IQR)	43 (31–56)	42 (30–54)	0.520
Length of stay, (IQR)	5 (4–9)	4 (4–6)	0.001
<i>Surgical pathology</i>			
Positive surgical margin, n (%)	5 (5)	19 (5)	1.000
Positive soft tissue margin, n (%)	1 (1)	4 (1)	1.000
Pathological T stage, n (%)			0.050
≤T2	63 (61.8)	277 (71.8)	
≥T3	39 (38.2)	109 (28.2)	
Pathological N stage, n (%)			0.130
N0	76 (74.5)	314 (81.3)	
≥N1	26 (25.5)	72 (18.7)	

BMI = body mass index; CCMI = Charlson comorbidity index; IQR = interquartile range; LOS = length of stay; NAC = neoadjuvant chemotherapy.

between 2004 and 2010. Their study suggested that the median LOS was 10.2 days for RARC and 11.8 for ORC ($P=0.008$) [6]. Hu et al. reviewed 7,308 ORC and 439 RARC patients from 2002 to 2012. They observed that the

mean LOS was 10.1 days for RARC and 11.2 for ORC ($P=0.004$) [9]. Ng et al. retrospectively reviewed 104 ORC and 83 RARC patients between 2002 and 2008. They found that the open group had a higher overall complication rate at

Table 4
Demographics and surgical data of patients with and without readmission within postoperative day 90

	With readmission N = 162	Without readmission N = 326	P value
<i>Characteristics</i>			
Age, year, median, (IQR)	73 (64–78)	70 (62–76)	0.007
Gender, n (%)			0.900
Male	133 (82.1)	265 (81.3)	
Female	29 (17.9)	61 (18.7)	
BMI, median, (IQR)	26.9 (23.5–29.8)	27.1 (23.8–30.4)	0.700
Race			0.630
African American	4 (2.4)	10 (3.1)	
Asian	9 (5.6)	25 (7.7)	
Caucasian	149 (92)	291 (89.2)	
Charlson comorbidity index, n (%)			0.170
CCMI 0	58 (35.8)	146 (44.8)	
CCMI 1	49 (30.2)	85 (26.1)	
CCMI ≥2	55 (34)	95 (29.1)	
Diabetes	53 (32.7)	57 (17.5)	<0.001
ASA score, n (%)			0.240
1–2	28 (17.3)	73 (22.4)	
3–4	134 (82.7)	253 (77.6)	
<i>Baseline laboratory work, median, (IQR)</i>			
Alb	42 (39–44)	42 (40–44)	0.690
HCT	36.2 (30.6–40.4)	36.8 (32–41.5)	0.130
HGB	12 (10.1–13.5)	12.3 (10.5–13.8)	0.170
<i>Clinical T stage, n (%)</i>			
≤T2	146 (90.1)	271 (83.1)	0.040
≥T3	16 (9.9)	55 (16.9)	
<i>Clinical N stage, n (%)</i>			
N0	148 (91.4)	303 (92.9)	0.590
≥N1	14 (8.6)	23 (7.1)	
NAC, n (%)	40 (24.7)	104 (31.9)	0.110
Prior pelvic radiation, n (%)	2 (1.2)	2 (0.6)	0.600
<i>Surgery</i>			
Surgical approach, n (%)			0.460
ORC	111 (68.5)	234 (71.8)	
RARC	51 (31.5)	92 (28.2)	
Operative time, hour, median, (IQR)	6.2 (5–7.2)	5.8 (4.8–7.2)	0.100
EBL, ml, median, (IQR)	350 (250–600)	400 (250–600)	0.790
Intraoperative transfusion, n (%)	33 (20.4)	52 (15.9)	0.254
Postoperative transfusion, n (%)	51 (31.5)	35 (10.7)	<0.001
Diversion type, n (%)			0.820
Orthotopic	98 (60.5)	189 (58)	
Nonorthotopic	64 (39.5)	137 (42)	
Total dissected lymph nodes, (IQR)	43 (30–55)	43 (30–54)	0.920
Length of stay, (IQR)	5 (4–6)	5 (4–6)	0.140
<i>Surgical pathology</i>			
Positive surgical margin	4 (2.5)	20 (6.1)	0.120
Positive soft tissue margin	0	5 (1.5)	0.180
Pathological T stage, n (%)			0.600
≤T2	110 (67.9)	230 (70.6)	
≥T3	52 (32.1)	96 (29.4)	
Pathological N stage, n (%)			0.190
N0	124 (76.5)	266 (81.6)	
≥N1	38 (23.5)	60 (18.4)	

BMI = body mass index; CCMI = Charlson comorbidity index; IQR = interquartile range; LOS = length of stay; NAC = neoadjuvant chemotherapy.

POD 30 (59% vs. 41%, $P=0.04$) as well as a higher major complication rate at POD 30 (30% vs. 10%, $P=0.007$) and POD 90 (31% vs. 17%, $P=0.03$). RARC was also an independent predictor of fewer overall and major complications [12]. In reviewing 35 ORC and 104 RARC patients from

2008 to 2011, Sung et al. found that ORC was associated with more grade II or greater complications (68.2% vs. 37.1%, $P=0.001$) as well as multiple complications (37.5% vs. 14.3%, $P=0.014$). In their study, ORC was an independent predictor of grade II or greater complications

Table 5

Multivariable logistic regression analysis of independent predictors of major complications and readmission within 90 days after radical cystectomy

Factors	Major complications OR (95% CI)	P value	Factors	Readmission OR (95% CI)	P value
Surgical approach	1.19 (0.70–1.97)	0.516	Surgical approach	1.25 (0.81–1.94)	0.312
Over 70-year old	1.79 (1.11–2.92)	0.018	Over 70-year old	1.66 (1.11–2.49)	0.014
Hematocrit	0.97 (0.93–1.00)	0.058	Diabetes	2.09 (1.32–3.29)	0.002
Length of stay	1.11 (1.05–1.18)	0.004	Postoperative transfusion	3.74 (2.28–6.19)	<0.001
Postoperative transfusion	2.16 (1.23–3.76)	0.007			

CI = confidential interval; OR = odds ratio.

($P=0.045$) [13]. Kader et al. and Musch et al. also demonstrated that ORC was associated with higher overall complication rates and major complication rates [15,16]. It is important to note that ERAS protocols had not been adopted in any of these studies. Furthermore, many of these studies are flawed in that they compare more modern RARC series (i.e., robotic era starting around 2007–2008) to older ORC series.

Evidence-based ERAS protocols for ORC and urinary diversion decrease LOS, postoperative pain and morbidity, and lower overall health care cost [19,24,25]. Our initial experience with our ERAS protocol applied to ORC and urinary diversion showed reduced LOS from 8 days to 4 days ($P<0.001$) without increase in complication or readmission rates within 30 days [19] and 90 days [26]. We also compared the complication rates in our ERAS cohort with a demographically matched pre-ERAS cohort. Gastrointestinal complications and wound infections were significantly lower in the ERAS group ($P=0.01$ and $P=0.05$, respectively) [26]. It is important to emphasize that the ORC surgical technique as well as the care team remained the same between the two groups. Patients on the ERAS protocol used significantly less opioid analgesics after ORC (20.67 mg vs. 4.9 mg morphine equivalents, $P<0.001$) and experienced a significantly lower incidence of postoperative ileus (22.2 vs. 7.3%, $P<0.001$) [27].

In the present study, we observed that RC performed by either the open or robotic-assisted approach not only achieved equivalent surgical pathology, consistent with the previous studies [28–31], but also similar postoperative clinical outcomes within the framework of the institutional ERAS pathway. It is worth noting that the median LOS of our RARC group was 6 days, shorter than those (8.5–8.9 days) reported in prior, non-ERAS studies [11]. This result is also compatible with the study by Miller et al., which showed LOS of 7 days for RARC within the ERAS protocol [32]. Although LOS was significantly longer in the robotic cohort in this study, we believe that 6 days vs. 4 days was not clinically significant. Complications and readmissions were the more costly outcomes. Infectious, genitourinary, and gastrointestinal complications were the most common for both ORC and RARC groups, which is also consistent with previous studies [12,16]. Although the ORC group had a higher wound complication rate and higher intraoperative

and postoperative transfusion rates (a grade II complication), we failed to identify a significant difference in overall complications between ORC and RARC groups. On multivariate analysis, patients requiring readmission to the hospital were older, more likely to have diabetes and more likely to receive a blood transfusion. While age and diabetes serve as markers of general medical condition, intraoperative transfusion rates may serve as a marker of the difficulty of surgery. Although postoperative transfusion was found to be a significant predictor of major complications and readmission ($P=0.007$ and $P<0.001$, respectively), and patients underwent ORC had higher postoperative transfusion rate ($P=0.04$), we failed to see surgical approach to be a significant predictor of major complications or readmission. Of note, patients in the ORC group had lower preoperative hemoglobin and hematocrit levels. This might be associated with the fact that a greater proportion of patients in this group underwent neoadjuvant chemotherapy.

More recently, randomized clinical trials demonstrated similar results with our study. Bochner et al. showed similar grade 2 to 5 complications in RARC and ORC patients (62 vs. 66%, $P=0.7$) at 90-day after surgery [33]. The recently completed RAZOR (randomized open vs. robotic cystectomy) trial showed that ORC group had significantly higher estimated blood loss ($P<0.0001$), higher intraoperative and postoperative blood transfusion rate ($P=0.0002$ and $P=0.0089$, respectively), and shorter operating time ($P=0.005$). No significant differences in overall complications (grades I–V) or major complications (grades III–IV) were identified between the 2 treatment groups [34]. In summary, we believe patients undergoing ORC or RARC both benefit from the ERAS protocol. Surgical approach is not a determinate of major complications or readmission following RC.

Although this was a study with prospectively collected data, standardized protocols within our institution, and dedicated follow-up, there were limitations. Subtle unmeasured variations in protocol adherence may have an unknown effect, as may individual surgeon's determination of patients' readiness for discharge. Although we captured outside facility readmissions through patients' outside medical records, the readmission criteria for outside facilities vary, which could introduce bias in readmission analysis. Also, due to insurance restrictions and patient convenience,

strict ERAS protocol adherence after discharge, especially home IV hydration, might not have been accomplished in all patients. Another limitation of our study was that we failed to take surgical technical skills and the potential effect of learning curve of each surgeon into consideration in this study. Mounting evidence shows that surgical skills directly associated with complication rate, mortality, reoperation rate, and readmission rate [35,36]. The ongoing robot-assisted radical cystectomy with intracorporeal urinary diversion vs. ORC multicenter randomized control trial adjusted the surgeons' competency factor by requiring specific prior RARC and intracorporeal urinary diversion experience and patient postoperative outcome standards. Only those surgeons who met the criteria were included in the study [37]. This trial would provide more comprehensive understanding of factors influencing patient clinical outcomes after RC and urinary diversion.

5. Conclusion

In the framework of an ERAS protocol, surgical approach at our institution was not a determinate factor of major complication rates or readmission rates after RC.

References

- [1] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. *CA Cancer J Clin* 2018;68:7–30.
- [2] Gakis G, Efstathiou J, Lerner SP, et al. ICUD-EAU International Consultation on Bladder Cancer 2012: radical cystectomy and bladder preservation for muscle-invasive urothelial carcinoma of the bladder. *Eur Urol* 2013;63:45–57.
- [3] Stenzl A, Cowan NC, De Santis M, et al. Treatment of muscle-invasive and metastatic bladder cancer: update of the EAU guidelines. *Eur Urol* 2011;59:1009–18.
- [4] 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;55:164–74.
- [5] Menon M, Hemal AK, Tewari A, et al. Nerve-sparing robot-assisted radical cystoprostatectomy and urinary diversion. *BJU Int* 2003;92:232–6.
- [6] Leow J, Reese S, Jiang W, et al. Propensity-matched comparison of morbidity and costs of open and robot-assisted radical cystectomies: a contemporary population-based analysis in the United States. *Eur Urol* 2014;66:569–76.
- [7] Pak J, Lee J, Bilal K, et al. Utilization trends and short-term outcomes of robotic versus open radical cystectomy for bladder cancer. *Urology* 2017;103:117–23.
- [8] Borza T, Jacobs B, Montgomery J, et al. No differences in population-based readmissions after open and robotic-assisted radical cystectomy: implications for post-discharge care. *Urology* 2017;104:77–83.
- [9] Hu J, Chughtai B, O'Malley P, et al. Perioperative outcomes, health care costs, and survival after robotic-assisted versus open radical cystectomy: a national comparative effectiveness study. *Eur Urol* 2016;70:195–202.
- [10] Son S, Lee N, Kang S, et al. Safety and effectiveness of robot-assisted versus open radical cystectomy for bladder cancer: a systematic review and meta-analysis. *J Laparoendosc Adv Surg Tech A* 2017. <https://doi.org/10.1089/lap.2016.0437>.
- [11] Novara G, Catto J, Wilson T, et al. Systematic review and cumulative analysis of perioperative outcomes and complications after robot-assisted radical cystectomy. *Eur Urol* 2015;67:376–401.
- [12] Ng C, Kauffman E, Lee M, et al. A comparison of postoperative complications in open versus robotic cystectomy. *Eur Urol* 2010;57:274–81.
- [13] Sung H, Ahn J, Seo S, et al. A comparison of early complications between open and robot-assisted radical cystectomy. *J Endourol* 2012;26:670–5.
- [14] Knox M, El-Galley R, Busby J. Robotic versus open radical cystectomy: identification of patients who benefit from the robotic approach. *J Endourol* 2013;27:40–4.
- [15] Kader A, Richards K, Krane L, et al. Robot-assisted laparoscopic vs open radical cystectomy: comparison of complications and perioperative oncological outcomes in 200 patients. *BJU Int* 2013;112:E290–4.
- [16] Musch M, Janowski M, Steves A, et al. Comparison of early postoperative morbidity after robot-assisted and open radical cystectomy: results of a prospective observational study. *BJU Int* 2014;113:458–67.
- [17] Li K, Lin T, Fan X, et al. Systematic review and meta-analysis of comparative studies reporting early outcomes after robot-assisted radical cystectomy versus open radical cystectomy. *Cancer Treat Rev* 2013;39:551–60.
- [18] Pang KH, Groves R, Venugopal S, et al. Prospective implementation of enhanced recovery after surgery protocols to radical cystectomy. *Eur Urol* 2017;pii: S0302-2838(17)30660-7.
- [19] Daneshmand S, Ahmadi H, Schuckman A, et al. Enhanced recovery protocol after radical cystectomy for bladder cancer. *J Urol* 2014;192:50–5.
- [20] Tyson M, Chang S. Enhanced recovery pathways versus standard care after cystectomy: a meta-analysis of the effect on perioperative outcomes. *Eur Urol* 2016;70:995–1003.
- [21] Goh AC, Gill IS, Lee DJ, et al. Robotic intracorporeal orthotopic ileal neobladder: replicating open surgical principles. *Eur Urol* 2012;62:891–901.
- [22] Stein JP, Skinner DG. Surgical atlas. Radical cystectomy. *BJU Int* 2004;94:197–221.
- [23] Bazargani S, Djaladat H, Ahmadi H, et al. Gastrointestinal complications following radical cystectomy using Enhanced Recovery Protocol. *Eur Urol Focus* 2017. <https://doi.org/10.1016/j.euf.2017.04.003>.
- [24] Roulin D, Donadini A, Gander S, et al. Cost-effectiveness of the implementation of an enhanced recovery protocol for colorectal surgery. *Br J Surg* 2013;100:1108–14.
- [25] Nabhani J, Ahmadi H, Schuckman A, et al. Cost analysis of the enhanced recovery after surgery protocol in patients undergoing radical cystectomy for bladder cancer. *Eur Urol Focus* 2016;2:97–8.
- [26] Djaladat H, Katebian B, Bazargani S, et al. 90-Day complication rate in patients undergoing radical cystectomy with enhanced recovery protocol: a prospective cohort study. *World J Urol* 2017;35:907–11.
- [27] Xu W, Daneshmand S, Bazargani S, et al. Postoperative pain management after radical cystectomy: comparing traditional versus enhanced recovery protocol pathway. *J Urol* 2015;194:1209–13.
- [28] Yuh B, Wilson T, Bochner B, et al. Systematic review and cumulative analysis of oncologic and functional outcomes after robot-assisted radical cystectomy. *Eur Urol* 2015;67:402–22.
- [29] Parekh D, Messer J, Fitzgerald J, et al. Perioperative outcomes and oncologic efficacy from a pilot prospective randomized clinical trial of open versus robotic assisted radical cystectomy. *J Urol* 2013;189:474–9.
- [30] Ahdoot M, Almaro L, Araya H, et al. Oncologic outcomes between open and robotic-assisted radical cystectomy: a propensity score matched analysis. *World J Urol* 2014;32:1441–6.
- [31] Wang G, Barocas D, Raman J, et al. Robotic vs open radical cystectomy: prospective comparison of perioperative outcomes and pathological measures of early oncological efficacy. *BJU Int* 2008;101:89–93.
- [32] Miller C, Campain NJ, Dbeis R, et al. Introduction of robot-assisted radical cystectomy within an established enhanced recovery programme. *BJU Int* 2017;120:265–72.
- [33] Bochner B, Dalbagni G, Sjoberg D, et al. Comparing open radical cystectomy and robot-assisted laparoscopic radical cystectomy: a randomized clinical trial. *Eur Urol* 2015;67:1042–50.

- [34] Parekh D, Reis I, Castle E, et al. Robot-assisted radical cystectomy versus open radical cystectomy in patients with bladder cancer (RAZOR): an open-label, randomised, phase 3, non-inferiority trial. *Lancet* 2018;391(10139):2525–36.
- [35] Reznick R, MacRae H. Teaching surgical skills—changes in the wind. *N Engl J Med* 2006;355:2664–9.
- [36] Birkmeyer J, Finks J, O’Reilly A, et al. Surgical skill and complication rates after bariatric surgery. *N Engl J Med* 2013;369:1434–42.
- [37] Catto JWF, Khetrpal P, Ambler G, et al. Robot-assisted radical cystectomy with intracorporeal urinary diversion versus open radical cystectomy (iROC): protocol for a randomised controlled trial with internal feasibility study. *BMJ Open* 2018;8(8):e020500.