Efficacy of the Addition of Robot-assisted Radical Cystectomy with Extracorporeal Urinary Diversion after an Enhanced Recovery Protocol

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Purpose: It is unclear if robotic radical cystectomy with extracorporeal urinary diversion (eRARC) provides additional benefit when performed along with enhanced recovery after surgery (ERAS). We assessed the additional efficacy of eRARC in terms of perioperative outcomes.

Materials and Methods: We retrospectively assessed 143 patients undergoing radical cystectomy with urinary diversion between June 2010 and December 2021 at a single center. The patients were assigned to three groups: open radical cystectomy (ORC) with conventional recovery after surgery (CRAS) [Group A], ORC with ERAS [Group B], and eRARC with ERAS [Group C]. A propensity score-matched analysis was performed to evaluate how ERAS and eRARC affected outcomes respectively. Meanwhile, multivariable analysis was used to detect the predictors of prolonged length of hospital stay (LOS).

Results: The median LOS was shorter after ERAS and eRARC. In the propensity score-matched analysis, ERAS was linked to a significantly shorter median LOS (28.0 vs. 20.0 days, $P < .001$), but eRARC was not associated with a shorter LOS (19.0 vs. 17.5 days, $P = .21$). Neither ERAS nor eRARC were connected with a reduce in complication rate. Following multivariable analysis, ERAS was found to be independently associated with shorter LOS (OR=0.23, $P < .001$), but eRARC demonstrated no such correlation (OR=0.29, $P = .096$).

Conclusion: ERAS had strong association with shorter LOS, although eRARC did not contribute to additional efficacy. Neither ERAS nor eRARC decreased the complication rate.

Keywords: radical cystectomy; enhanced postsurgical recovery; robot-assisted surgery; urinary diversion; ileal conduit; length of stay; postoperative complication

INTRODUCTION

Radical cystectomy (RC) is the standard of care for muscle-invasive bladder cancer and non-muscle-invasive bladder cancer refractory to bladder-instillation therapy[1]. The complex procedures of RC include organ extirpation and urinary tract reconstruction, which are associated with relatively high morbidity[2]. Enhanced recovery after surgery (ERAS) is a multimodal program that aims to hasten postoperative recovery and improve perioperative outcomes. After gradual uptake, ERAS is commonly observed in RC[3,4]. ERAS provides the advantage of a shortened length of hospital stay (LOS); however, lower complication rates and faster bowel recovery have also been reported[4,5]. In addition, robot-assisted radical cystectomy (RARC) is widely used as a minimally invasive surgery and is recognized as comparable to open radical cystectomy (ORC) for oncologic and perioperative outcomes[3, 6-8]. Similar to ERAS, RARC provides the advantage of shortened LOS, faster bowel recovery, and less intraoperative blood loss[7,9].

Given the initial findings, the individual efficacy of ERAS and RARC have been demonstrated. However, concurrent analyses of those techniques remain scarce. A previous study that analyzed both considered only RARC with intracorporeal urinary diversion (iRARC)[10]. Other studies evaluated the benefits of iRARC after ERAS, but none evaluated RARC with extracorporeal urinary diversion (eRARC) in a similar setting[11-13]. The learning curve for the complicated surgical skills of urinary reconstruction in iRARC suggests that the surgeon and hospital volume might be associated with complication rates[2,14]. Hence, adopting iRARC is challenging in non-high-volume centers, and eRARC might play an indispensable role in the transition from ORC to RARC.

Recently, we sequentially introduced the use of both ERAS and eRARC. Subsequently, we assessed whether eRARC provided additional efficacy in postoperative patient outcomes when added to ERAS.

MATERIALS and METHODS

Study design

We retrospectively identified 143 patients who underwent RC with ileal conduit creation between June 2010 and December 2021 at a single institution. We excluded patients who underwent neobladder and other additional procedures related to concomitant malignancies, such as upper tract urothelial carcinoma and colorectal

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Table 1. The change points of perioperative protocol from CRAS to ERAS

Elements	CRAS	ERAS
Mechanical bowel preparation	Take magnesium citrate orally on the day before the operation	Omit any mechanical bowel preparation
Preoperative carbohydrates loading	Fasting from 24 hours before the operation	Taking liquid containing carbohydrates 2 hours before the surgery
Preoperative fasting	Fasting from 24 hours before the operation	Take a meal by the night before surgery
Resection site drainage	Indwell perianastomotic and pelvic drains Removal of drain decided by attending surgeon	Indwell only pelvic drain Drain was principally removed in postoperative day 2Preoperative
fluid management	Loading two litter electrolyte solution from 48 hours before the operation	Omit preoperative hydration
Nasogastric intubation	Removal of the nasogastric tube at postoperative day 1	Remove nasogastric tube at the end of the operation
Early oral diet	Resumption of oral intake decided by the surgeon	Resumption of liquid taking in postoperative day 1 and taking meal on postoperative day 2

Abbreviations: CRAS, conventional recovery after surgery; ERAS, enhanced recovery after surgery

cancer, and those with surgical complications. ERAS was adopted in July 2017, and eRARC in June 2018[15]. ERAS was used in all patients undergoing eRARC. Figure 1 depicts the timing of the changes in perioperative protocol and surgical approach.

We allocated the patients to the following three groups: Group A comprised 75 patients who underwent ORC with conventional recovery after surgery (CRAS) between June 2010 and June 2017, Group B comprised 47 patients who underwent ORC with ERAS starting in July 2017, and Group C comprised 21 patients who underwent eRARC with ERAS starting in June 2018. The institutional review board approved the study (approval number 712).

Surgical procedures

ORC

After a suprapubic to infraumbilical skin incision, a retrograde and retroperitoneal approach was taken, with the peritoneum being opened just before specimen removal. The prostate and seminal vesicles in men and the uterus and anterior vaginal wall in women were also extracted. Pelvic lymph node dissection, whose extent was determined at the surgeon's discretion, was ordinarily performed below the level of the common iliac artery. The surgeon's experience varied from fellowship to expert, but at least one well-experienced surgeon attended each operation.

RARC

RARC was performed with a da Vinci Si, X, or Xi surgical robot (Intuitive Surgical, Sunnyvale, CA, USA) and six ports. The surgical maneuvers were identical to those in ORC, but an antegrade and transperitoneal approach was used. Before attempting RARC, every surgeon had performed over 30 robot-assisted radical prostatectomies. All patients were operated on consecutively starting with the initial implementation of RARC.

Urinary diversion

To construct an ileal conduit, a 60 mm Endo GIA stapler (Covidien, Dublin, Ireland) was used to isolate a 15–20 cm segment of the ileum 10–15 cm from the oral side of the cecum valve. The stapler was also used to create the functional end-to-end ileal–ileal anastomosis; the Nesbit or Wallace method with ureteral stents was used to create the ureteroileal anastomosis. In RARC, an extra 5 cm skin incision was added to extirpate the specimen and construct the ileal conduit.

Perioperative protocol

ERAS was formally introduced in July 2017[15]. However, parts of its preoperative counseling, education, and medical optimization had been applied before that. No anesthesiologist was dedicated to RC procedures; therefore, intraoperative anesthesia was managed by the attending anesthesiologist in each case. Table 1 lists the changeover from CRAS to ERAS.

Data extraction

The demographic data collected for patients included age, sex, body mass index (BMI), American Society of Anesthesiologist physical status (ASAPS), Barthel In-

Table 2. Patient characteristics and operative parameters

Variables [a]	Group A (CRAS+ORC) (n = 75)	Group B (ERAS+ORC) (n = 47)	Group C (ERAS+eRARC) (n = 21)	*P*-value
Age, year	70.0 (66.5–74.5)	73.0 (69.0–76.0)	75.0 (73.0–78.0)	.005
Gender (male)	61(81.3)	37 (78.7)	18 (85.7)	.79
BMI, kg/m²	22.8 (21.2–24.8)	22.9 (21.3–25.1)	24.3 (22.3–26.6)	.28
ASAPS 1	24 (32.0)	16 (34.0)	6 (28.6)	.50
ASAPS 2	39 (52.0)	22 (46.8)	8 (38.1)	
ASAPS 3≤	12 (16.0)	9 (19.1)	7 (33.3)	
Barthel Index<60	1(1.3)	2(4.3)	1(4.8)	.30
NAC	27 (36.0)	20 (42.6)	6 (28.6)	.52
Prior abdominal surgery	23 (30.7)	12 (25.5)	2 (9.5)	.15
Prior pelvic radiotherapy	7 (9.3)	3 (6.4)	0 (0.0)	.33
Operation time, minutes	469.0 (424.0–512.5)	429.0 (352.0–453.0)	407.0 (375.0–501.0)	.003
Intraoperative transfusion	23 (30.7)	11(23.4)	0(0.0)	.014

Abbreviations: ASAPS, American Society of Anesthesiologist physical status; BMI, body mass index; IQR, interquartile range; NAC, neoadjuvant chemotherapy; CRAS, conventional recovery after surgery; ERAS, enhanced recovery after surgery; ORC, open radical cystectomy; eRARC, robotic assisted radical cystectomy with extracorporeal urinary diversion

[a] Data are presented as median (interquartile range: IQR) for continuous variables and number (percent) for categorical variables.

Table 3. Patient characteristics and operative parameters in post-propensity score matched cohorts in Group A and B, and Group B and C

Variables[a]	Group A (CRAS+ORC) (n = 40)	Group B (ERAS+ORC) (n = 40)	*P*-value
Age, year	72.0 (69.8–75.0)	72.5 (68.8–76.0)	.62
Gender (male)	32 (80.0)	32 (80.0)	1.00
BMI, kg/m²	22.3 (21.1–23.7)	22.9 (21.1–24.7)	.74
ASAPS 1	13 (32.5)	10 (25.0)	.95
ASAPS 2	22 (55.0)	21 (52.5)	
ASAPS 3≤	5 (12.5)	9 (22.5)	
NAC	18 (45.0)	16 (40.0)	.82
Prior abdominal surgery	11 (27.5)	12 (30.0)	1.00
Prior pelvic radiotherapy	3 (7.5)	3 (7.5)	1.00
Operation time, minutes	444.0 (390.3–473.2)	436.5 (379.0–468.8)	.59
Intraoperative transfusion	11 (27.5)	10 (25.0)	1.00
Variables [a]	**Group B (ERAS+ORC) (n = 14)**	**Group C (ERAS+eRARC) (n = 14)**	***P*-value**
Age, year	72.0 (70.3–76.8)	75.0 (70.0–75.0)	.93
Gender (male)	12 (85.7)	11 (78.6)	1.00
BMI, kg/m²	24.1 (22.3–25.9)	24.0 (22.4–26.5)	.77
ASAPS 1	7 (50.0)	4 (28.6)	.51
ASAPS 2	4 (28.6)	6 (42.9)	
ASAPS 3≤	3 (21.4)	4 (28.6)	
NAC	5 (35.7)	3 (21.4)	.68
Prior abdominal surgery	0 (0.0)	1 (7.1)	1.00
Prior pelvic radiotherapy	0 (0.0)	0 (0.0)	NaN
Operation time, minutes	438.0 (424.0–463.5)	430.5 (389.5–495.0)	.73
Intraoperative transfusion	0 (0.0)	0 (0.0)	NaN

Abbreviations: ASAPS, American Society of Anesthesiologist physical status; BMI, body mass index; NAC, neoadjuvant chemotherapy; NaN, not a number
[a]Data are presented as median (interquartile range) for continuous variables and number (percent) for categorical variables

dex, prior abdominal surgery, prior pelvic radiotherapy, and neoadjuvant chemotherapy (NAC). Operation time and use of transfusion were also extracted as operative parameters.

Complications were graded using the Clavien–Dindo classification version 2.0, with a complication greater than grade 3 defined as a major complication. All patients were followed postoperatively for at least 90 days.

Outcome measures

The primary endpoint was LOS. The secondary endpoint was the 90-day postoperative complication rate, including overall complications, major complications, paralytic ileus, and miscellaneous gastrointestinal (GI) complications, such as bowel obstruction and anastomosis failure.

Statistical analysis

The Chi-squared test was used to compare categorical variables, whereas, the Kruskal–Wallis test was used to compare continuous variables. Categorical variables are reported as frequencies and percentages, and continuous variables are reported as medians with interquartile range (IQR).

In outcome analyses, LOS and complication rates were first compared between the groups. Next, pairs of groups were compared (Group A vs. Group B and Group B vs. Group C) to estimate the outcome improvement resulting from ERAS and eRARC individually. A propensity score-matched (PSM) analysis was performed to correct for differences in patient characteristics between the two groups. The propensity scores were calculated with a logistic regression model using the following variables: age, sex, BMI, ASAPS, prior abdominal surgery, prior pelvic radiotherapy, and NAC. The caliper was set at 0.2 and matched to obtain a 1:1 patient ratio between the two groups by nearest neighbor matching. Finally, univariate and multivariable analyses were performed to assess the contributions of ERAS and eRARC to outcomes.

All statistical analyses were performed using the EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R software (The R Foundation for Statistical Computing, Vienna, Austria)[16]. All P values are two-sided, and $P < 0.05$ was considered statistically significant.

Figure 1. The time sequence of the changes in perioperative protocol and surgical approach

Table 4. Comparison of LOS and complications in post-propensity score matched cohorts in Group A and B, and Group B and C

Variables [a]	Group A (CRAS+ORC) (n = 40)	Group B (ERAS+ORC) (n = 40)	*P*-value
LOS, days	28.0 (23.0–35.0)	20.0 (16.0–24.5)	< 0.001
Overall complication	22 (56.4)	24 (60.0)	.92
Major complication	12 (30.0)	8 (20.0)	.44
Paralytic ileus	6 (15.0)	4 (10.0)	.74
Miscellaneous GI complication	4 (10.0)	2 (5.0)	.67
Variables [a]	**Group B (ERAS+ORC) (n = 14)**	**Group C (ERAS+eRARC) (n = 14)**	***P*-value**
LOS, days	19.0 (14.0–40.0)	17.5 (12.0–25.0)	.21
Overall complication	9 (64.3)	8 (57.1)	1.00
Major complication	4 (28.6)	2 (14.3)	.65
Paralytic ileus	2 (14.3)	1 (7.1)	1.00
Miscellaneous GI complication	0 (0.0)	2 (14.3)	.46

Abbreviations: LOS, length of hospital stay; GI, gastrointestinal

[a]Data are presented as median (interquartile range: IQR) for LOS and number (percent) for each complication.

RESULTS

Table 2 presents the patient characteristics; median age was the only difference between the groups (Group A vs. Group B vs. Group C: 70.0 vs. 73.0 vs. 75.0 years). Table 2 also presents the operative parameters, where the median operation time was the shortest in Group C, (Group A vs. Group B vs. Group C: 469.0 vs. 429.0 vs. 407.0 min). During eRARC, none of the patients received an intraoperative transfusion. However, 27.9% of patients (34/122) were transfused intraoperatively during ORC.

Figure 2 presents a box plot of LOS for each study group. Median LOS declined with the introduction of ERAS and eRARC (Group A vs. Group B vs. Group C: 28.0 vs 20.0 vs 17.0 days).

Table 3 presents the patient characteristics after PSM. The differences in patient characteristics between groups were modified, with each 40 patients matched in Group A and B, whereas each 14 patients corresponded to Group B and C.

Table 4 shows the perioperative outcomes in comparison among cohorts after PSM. LOS was significantly decreased after implementing ERAS (Group A vs. Group B: 28.0 vs. 20.0 days), but the implementing eRARC did not demonstrate the decrease (Group B vs. Group C: 19.0 vs. 17.5 days). In complications, no significant improvements were evident after implementing either ERAS or eRARC, although favorable trends were observed. Thus, no additional benefit of eRARC over ERAS was observed for LOS and complications.

We aimed to identify LOS predictors using univariate and multivariable analysis. In this study, the median LOS was 23 days. Therefore, this number was used as a cut-off. Table 5 presents the results of the relevant analyses. In univariate analysis, major complications and paralytic ileus were factors associated with longer LOS (major complications 95% CI: 1.99–10.3, OR = 4.54; paralytic ileus 95% CI: 1.24–9.31, OR = 3.40), and ERAS and eRARC were factors associated with shorter LOS (ERAS 95% CI: 0.077–0.34, OR = 0.16; eRARC 95% CI: 0.038–0.49, OR = 0.14). In multivariable analysis, the major complication was an independent factor predicting longer LOS, and ERAS was an independent factor predicting shorter LOS (major complication 95% CI: 1.83–12.3, OR = 4.74; ERAS 95% CI: 0.098–0.53, OR = 0.23). Contrastingly, eRARC was not an independent predictor of either longer or shorter LOS (95% CI: 0.21–2.96, OR = 0.29).

DISCUSSION

After the sequential implementation of ERAS and eRARC, we assessed whether eRARC, when added to ERAS, provided additional efficacy in terms of patient outcomes. To our knowledge, this is the first study to evaluate both eRARC and ERAS concurrently. The results revealed that LOS was shorter in patients receiving ERAS (Groups B and C) than in those receiving CRAS (Group A). Moreover, ERAS was found to be an independent predictor of shorter LOS.

Recent meta-analyses evaluating the utility of ERAS for RC also reported shortened LOS[4,5]. ERAS implementation has not been standardized and has differed between institutions. However, some theoretical advantages of each element of ERAS have been suggested. For instance, early resumption of oral intake can promote faster bowel function recovery and maintain metabolism, preoperative carbohydrate loading might

Table 5. Univariate and multivariable analysis for predictors of LOS ≤ 23days

Variables	Univariate (OR, 95%CI)	*P*- value	Multivariable (OR, 95%CI)	*P*-value
Age	1.03 (0.98–1.09)	.19		
BMI	1.02 (0.92–1.12)	.73		
ASAPS 3≤	0.50 (0.12–2.09)	.34		
Barthel Index<60	1.06 (0.15–7.76)	.95		
Major complication	4.54 (1.99–10.3)	< 0.001	4.74 (1.83–12.3)	.001
Miscellaneous GI complication	1.95 (0.55–7.01)	.30		
Paralytic ileus	3.40 (1.24–9.31)	.017	2.35 (0.72–7.61)	.16
eRARC	0.14 (0.038–0.49)	.002	0.29 (0.21–2.96)	.096
ERAS	0.16 (0.077–0.34)	< 0.001	0.23(0.098–0.53)	< 0.001

Abbreviations: ASAPS, American Society of Anesthesiologist physical status; BMI, body mass index; ERAS, enhanced recovery after surgery; eRARC, robotic assisted radical cystectomy with extracorporeal urinary diversion; GI, gastrointestinal; LOS, length of hospital stay; OR, odds ratio

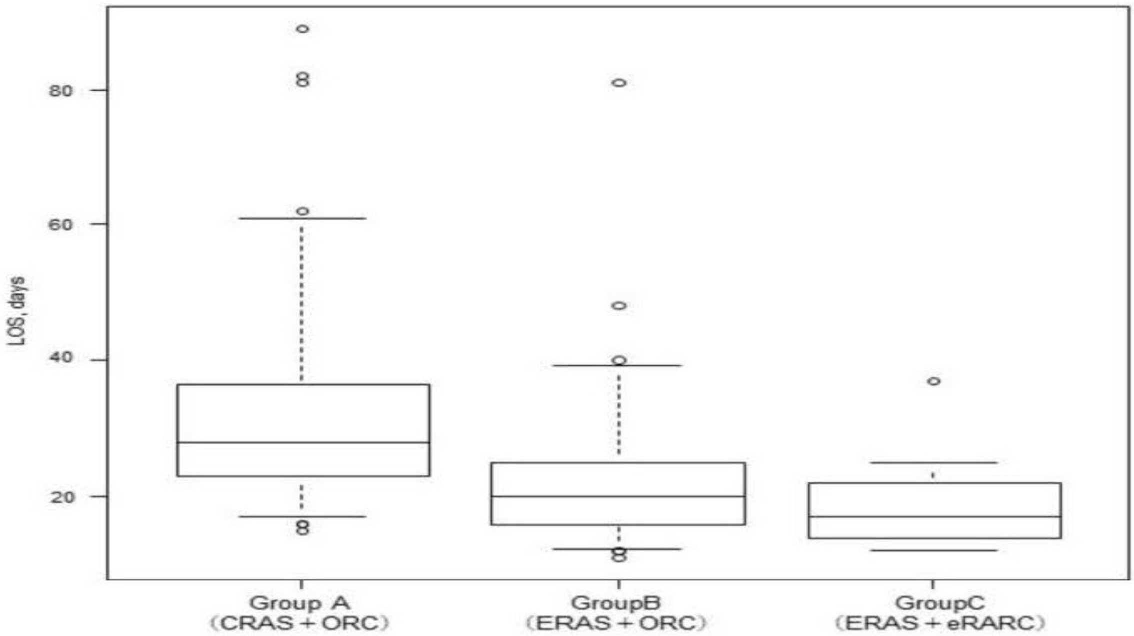

Figure 2. The box plot of the median LOSs of the groups

improve insulin resistance and maintain muscle mass, and omitting a nasogastric tube might facilitate faster pulmonary recovery and early mobilization[4,5,17]. By acting synergistically, these practices might contribute to shortened LOS.

In this study, no difference in LOS between Group B and C was observed. Moreover, eRARC was not a significant predictor of shortened LOS in multivariable analysis. Chen et al. and Schiavina et al. demonstrated additive efficacy for RARC after ERAS, but their analyses were limited to patients undergoing iRARC [12,13]. The evidence for the superiority of iRARC compared with eRARC has emerged mainly from the large-scale studies performed in academic centers[18,19]. Furthermore, hospital and surgeon volume correlations with postoperative outcomes have been reported[2,14]. Notably, Kimura et al., in LOS, reported that the randomized study group did not show RARC superiority in contrast to the nonrandomized study group[20]. Considering the preceding findings, the contribution of RARC to LOS remains uncertain, but any potential positive efficacy might not be observed in a non-high-volume community center and a retrospective study, such as in this study.

In this study, a major predicted complication was longer LOS. A meta-analysis evaluating morbidity in RC reported a range of 36%–86% for 90-day overall complications and 8.6%–35% for major complications—comparable to our results[20]. With ERAS and eRARC, we observed a favorable trend in major complications, although there were no significant improvements. Concerning the potential advantages of ERAS, Feng et al. suggested that ERAS can promote early GI function recovery, thus, facilitating wound healing, which might help avoid severe morbidity[21]. Some results were favorable but controversial in terms of the actual contribution of ERAS to the decrease in complications[5,17]. The lack of a universal protocol in ERAS may have caused variability in the results. Regarding RARC, the avoidance of intra-abdominal exposure and evaporative fluid loss could have diminished complications[9]. However, inconsistent results have been reported[20]. Indeed, multiple factors, such as surgical experience, specific operative procedures, and patient characteristics could affect perioperative outcomes[14,22,23]. Therefore, the surgical approach might not be the definitive factor for reducing complications[12].

Our study has several limitations. First, it is a retrospective, nonrandomized study conducted at a single center with a small patient sample. Second, the LOS for patients in our study was much longer than those in European and American studies (roughly 7–14 days), regardless of the surgical approach[20]. This finding might reflect the universal health reimbursement provided through employee- and community-based social health insurance in Japan and the existing local traditions[24]. In previous Japanese studies, Muto et al. reported median LOSs of 25.5 days with ORC and 19.0 days with RARC (comparable to the results of the present study), and Gondo et al. reported even longer median LOSs (ORC: 35.0 days; RARC: 39.0 days)[25,26]. Third, ERAS implementation at our institution involved only a few potential ERAS elements. The ERAS protocol has not yet been standardized, so the number of elements to be performed and the method of performing them have not yet been established[5]. However, previous studies suggest that at least 15 elements should be implemented to maximize the benefit[27]. Our simplified ERAS implementation might have left room for further improvement. Nevertheless, our limited implementation was found to yield a consistent effect. Fourth, the present study focused on only eRARC. Currently, iRARC might be superior to eRARC regarding postoperative outcomes[28,29]. However, those favorable results have been reported from large-scale studies[14,29]. Therefore, our study would not have yielded similar results even if iRARC had been conducted. Finally, the study comparisons spanned different eras, with differences in maturity between the surgical team and the individual surgeon, thus potentially influencing outcomes.

Considering the preceding limitations, further prospective investigation in a larger population with adjustments for patient and surgeon characteristics will be needed. Identification of the optimal implementation of the ERAS protocol will also be desirable.

CONCLUSIONS

To summarize, we assessed whether eRARC, when added to ERAS, provided additional efficacy in patient outcomes. The implementation of ERAS was associated with a significant shortening of LOS, but no significant shortening of LOS was observed with the implementation of eRARC. Multivariable analysis revealed that ERAS was a significant predictor of shorter LOS but that eRARC had no significance as a LOS predictor. With respect to complications, neither ERAS nor eRARC was associated with any significant improvement.

SUMMARY

The impact of robotic surgery on perioperative outcomes in addition to the use of early postoperative programs for radical cystectomy has been proved. These programs reduced the length of hospital stay but with minimal effect of additional robotic surgery.

CONFLICTS OF INTEREST

The authors have no relevant financial or non-financial interests to disclose.

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