

# Application of enhanced recovery after surgery in patients undergoing radical cystectomy

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## Abstract

**Objective:** This study was performed to evaluate the application of enhanced recovery after surgery (ERAS) in patients undergoing radical cystectomy (RC).

**Methods:** The clinical data of 192 patients who underwent RC were collected in this retrospective cohort study. Among them, 91 patients who underwent ERAS were allocated to the ERAS group, and the remaining 101 patients who underwent traditional postoperative care procedures were allocated to the non-ERAS group. Perioperative indexes in the two groups were compared. The ERAS components included rehabilitation exercise, carbohydrate fluid loading, cessation of nasogastric tubes, omission of oral bowel preparation, regional local anesthesia, body-warming procedures, reduced drainage use, and early postoperative drinking and eating.

**Results:** The times from RC to first water intake, first ambulation, first anal exhaust, first defecation, and pelvic drainage tube removal were significantly shorter and the hospitalization costs were significantly lower in the ERAS than non-ERAS group. The intraoperative blood loss volume, blood transfusion rate, readmission rate, and incidence of postoperative complications were also significantly lower in the ERAS than non-ERAS group.

**Conclusion:** ERAS may effectively accelerate patient rehabilitation and reduce the length of stay, incidence of postoperative complications, readmission rates, and hospitalization costs for patients undergoing RC.

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**Keywords**

Application, enhanced recovery after surgery, radical cystectomy, traditional postoperative care, rehabilitation, postoperative complications, readmission rate, hospitalization cost

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**Introduction**

Radical cystectomy (RC) with pelvic lymph node dissection is the gold standard treatment for muscle-invasive bladder cancer or high-risk localized non-muscle-invasive bladder cancer.<sup>1,2</sup> However, RC remains a challenging surgical procedure with a long operation time and severe trauma, especially for older patients with coexisting cardiopulmonary disease. The postoperative complications and morbidity associated with RC limit the use of this effective operative method.<sup>3,4</sup>

Enhanced recovery after surgery (ERAS) was first reported by the Danish surgeon Kehlet.<sup>5</sup> ERAS involves evidence-based optimization of a series of perioperative treatment procedures that aim to reduce the physical and psychological stress of surgical trauma and thus accelerate the patient's rehabilitation. In colorectal surgery, the use of ERAS regimens has reduced the length of stay (LOS) and postoperative morbidity.<sup>6</sup> However, the application of many ERAS components in RC has no confirmed evidence of effectiveness despite the obvious benefit in patients undergoing abdominal surgery.<sup>7</sup> RC involves surgery of the gastrointestinal and urinary tracts; therefore, the ERAS components are applicable. Several cohort studies have involved the use of ERAS in RC.<sup>8-10</sup>

We herein report our single-center study to evaluate the effectiveness and safety of ERAS in patients undergoing RC. ERAS may serve as a new therapy pattern for patients undergoing RC that can improve

the clinical outcomes of surgery and reduce the economic pressure of patients in many developing countries, including China.

**Methods****Patients**

We retrospectively collected the clinical data of consecutive patients who underwent RC and urinary reconstruction from June 2010 to December 2017 at our hospital (Table 1). Among them, patients who underwent ERAS during the perioperative period from November 2015 to December 2017 were allocated to the ERAS group, and patients who underwent traditional postoperative care procedures from June 2010 to October 2015 were allocated to the non-ERAS group (ERAS was first implemented in our hospital in November 2015). All patients undergoing RC during this period were included in the study.

The times from RC to first water intake, first ambulation, first anal exhaust, first defecation, and pelvic drainage tube removal; LOS; LOS in patients without complications; hospitalization costs; intraoperative blood loss; postoperative complication rate; readmission rate; and 90-day mortality rate were analyzed and compared between the two groups.

This study was approved by the Yantai Yuhuangding Hospital Ethics Committee. All patients provided informed consent to participate.

**Table 1.** Characteristics of the ERAS and control groups

Characteristic	ERAS (n = 91)	Control (n = 101)	p
Age, years	69.3 (52–84)	67.4 (48–81)	0.537
Sex			0.724
Female	6	8	
Male	85	93	
BMI (kg/m <sup>2</sup> )	20.3 ± 1.5	20.4 ± 1.4	0.633
Tumor phenotype			0.454
Low-risk NMI cancer	4	6	
High-risk NMI cancer	11	18	
Muscle-invasive BC	76	77	
Operation time, min	302.7 (240–420)	315.9 (210–480)	0.047
Blood loss, mL	368 (245–1800)	425 (330–2600)	<0.001
Transfusion rate	4 (4.4)	15 (14.9)	0.015
Reconstruction			0.805
Ileal conduit	82	91	
Studer pouch	3	2	
Cutaneous ureterostomy	6	8	
Margin status			0.567
Positive	3	5	
Negative	88	96	
Clinical stage			0.82
T1–T2c	6 (6.6)	8 (7.9)	
T3a	36 (39.6)	43 (42.6)	
T3b–T4	49 (53.8)	50 (49.5)	

Data are presented as n, n (%), mean ± standard deviation, or mean (range).

ERAS, enhanced recovery after surgery; BMI, body mass index; NMI, non-muscle-invasive; BC, bladder cancer.

### ERAS protocol

**Preoperative.** Patients in the ERAS group were given an information booklet regarding their expected recovery, including the specific preoperative and postoperative nutritional advice according to the ERAS protocol (Supplementary Table 1). The patients were advised to maintain a normal diet and two nutritional drinks (BOOST™ 1.5; Nestlé Health Science, Epalinges, Switzerland) the evening before surgery and to reduce alcohol intake and cigarette smoking. No preoperative bowel preparation was initiated. Low-molecular-weight heparin (5000 IU subcutaneously twice daily) was administered 12 hours before surgery and prescribed for 2 weeks

to prevent deep venous thrombosis, and compression stockings were prescribed for the duration of the hospital stay.

**Intraoperative.** During RC, epidural analgesia was used if not contraindicated. Intraoperative fluids were limited by real-time monitoring of cardiac output using vascular pressure. Typically, only 1000 to 2000 mL of an intravenous crystalloid was administered for rehydration prior to bladder removal. Laparoscopy, small incisions, an ultrasound knife, vessel sealers (e.g., LigaSure Impact™; Minneapolis, MN, USA), and clips were used to reduce surgical trauma. Standard lymphadenectomy of the obturator, internal iliac, and external

iliac lymph nodes was performed in all patients, and the Bricker and Studer techniques were used for the neobladder. Postoperative analgesia was commenced with application of rectus sheath local anesthetic blocks (20 mL of 0.25% ropivacaine). The surgical incisions were closed using Histoacryl adhesive (TissueSeal, Ann Arbor, MI, USA) instead of intradermal sutures.

**Postoperative.** On the first postoperative day (POD), the patients were advised to ingest 10 to 30 mL of clear fluids per hour. Chewing gum was encouraged, but not for patients who were feeling nauseous. Patients were encouraged to sit and stand up 2 to 4 hours postoperatively. Additional analgesia was allowed on demand through patient-controlled analgesic intravenous opiates. On POD 2, the patients aimed to walk 10 to 20 m and were allowed clear fluids if tolerated. Nausea and vomiting were treated with reduced fluid intake and rest. A light diet was introduced when the patient passed flatus or had a bowel movement. For patients without flatus or a bowel movement by POD 3, an abdominal and pelvic computed tomography (CT) scan was performed to check the patient's recovery progress and any signs of intra-abdominal complications.

### Statistical analysis

Statistical analysis was performed using the SPSS 19.0 software program (IBM Corp., Armonk, NY, USA). The mean and standard error of the mean (SD) are reported for continuous variables assumed to be normally distributed. Continuous variables with a non-normal distribution are summarized by their median values and interquartile ranges and were analyzed using a group *t*-test and a *p* value cutoff of significance. The chi-square test or Fisher's exact test was conducted to assess differences in

covariate distributions between protocols. In all tests, a two-sided *p* value of  $<0.05$  was considered to indicate statistical significance.

### Results

In total, 192 patients were included in this study (ERAS group,  $n=91$ ; non-ERAS group,  $n=101$ ). The times from RC to first water intake, first ambulation, first anal exhaust, first defecation, and pelvic drainage tube removal were significantly shorter and the hospitalization costs were significantly lower in the ERAS than non-ERAS group ( $t=-20.38$  hours,  $-123.05$  hours,  $-8.57$  hours,  $-16.74$  hours,  $-34.23$  days, and  $-41.51$  thousand USD, respectively;  $p<0.05$ ). The blood loss volume in the ERAS group (245–1800 mL; mean, 368 mL) was significantly lower than that in the non-ERAS group (330–2600 mL; mean, 425 mL) ( $p<0.001$ ), and a significantly lower blood transfusion rate was observed in the ERAS than non-ERAS group (4.4% vs. 15.0%, respectively;  $p=0.015$ ). According to the Clavien–Dindo classification of surgical complications, 5 grade I and 9 grade II postoperative complications occurred in the ERAS group and 8 grade I and 21 grade II postoperative complications occurred in the non-ERAS group; according to these findings, the incidence rate of postoperative complications was significantly lower in the ERAS than non-ERAS group (15.4% vs. 28.7%, respectively;  $p<0.05$ ). The ERAS group also had a significantly lower incidence rate of readmissions than the non-ERAS group (6.6% vs. 16.0%, respectively;  $p=0.045$ ). The tumor stage, margin status, and survival outcomes were not significantly different between the two groups. The LOS was significantly shorter for patients treated with than without ERAS ( $4.8 \pm 1.7$  vs.  $11.2 \pm 2.7$  days,  $p<0.001$ ). At a median follow-up time of 46 (range, 4–88) months, 121 (63%) patients

**Table 2.** Surgery recovery parameters in the ERAS and control groups

Parameter	ERAS	Control	<i>p</i>
First intake of clear liquid, hours	2.5 ± 0.6	30.1 ± 12.9	<0.001
First ambulation, hours	8.7 ± 2.2	73.1 ± 4.7	<0.001
First anal exhaust, hours	8.8 ± 7.1	30.6 ± 23.3	<0.001
First defecation, hours	17.0 ± 5.0	81.1 ± 36.2	<0.001
Drainage tube removal, days	3.5 ± 0.5	7.8 ± 1.1	<0.001
LOS, days	4.8 ± 1.7	11.2 ± 2.7	<0.001
LOS in patients without complications, days	4.3 ± 0.4	10.7 ± 0.8	<0.001
Hospitalization cost (thousand USD)	6.3 ± 0.5	9.1 ± 0.5	<0.001
Postoperative complications	14 (15.4)	29 (28.7)	0.027
Vomiting	5 (5.5)	8 (7.9)	
Urine leakage	1 (1.1)	2 (2.0)	
Intestinal obstruction	4 (4.4)	7 (6.9)	
Pneumonia	0 (0.0)	2 (2.0)	
Urinary tract infection	3 (3.3)	7 (6.9)	
Deep venous thrombosis	0 (0.0)	1 (1.0)	
Other*	1 (1.1)	2 (2.0)	
Readmission	6 (6.6)	16 (16.0)	0.045
30 days	4 (4.4)	11 (11.0)	
90 days	2 (2.2)	5 (5.0)	
90-day mortality	3 (3.3)	4 (4.0)	0.806

Data are presented as mean ± standard deviation or n (%).

ERAS, enhanced recovery after surgery; LOS, length of stay; USD, United States dollars.

\*One case of atrial fibrillation in the ERAS group; one case of irritability allergy and stress ulcer each in the control group.

were still alive and 22 patients had been lost to follow-up. The 90-day mortality rate was 3.3% (3 patients) in the ERAS group and 4.0% (4 patients) in the non-ERAS group patients. There was no significant difference in overall or BC-specific survival when stratified by ERAS use (Table 2).

## Discussion

Since the introduction of ERAS into colorectal surgery, several preoperative, intraoperative, and postoperative steps have been implemented to improve patient rehabilitation.<sup>11</sup> ERAS is currently used in many surgeries with similar benefits, including esophageal cancer surgery,<sup>12</sup> bariatric surgery,<sup>13</sup> and other types of gastrointestinal surgery.<sup>14</sup> The application of ERAS in urological practice is still limited despite the growing evidence of its efficacy for patients

undergoing RC.<sup>15–17</sup> Many patients undergoing RC may benefit from refinements in perioperative management. Our data indicate that ERAS significantly reduced the times from RC to first water intake, first ambulation, first anal exhaust, first defecation, and pelvic drainage tube removal as well as the hospitalization costs compared with traditional perioperative treatment, demonstrating excellent improvements in postoperative recovery. However, patients' survival outcomes did not differ between the two groups. Compliance with the protocol is the most important element in ERAS. Pędziwiatr et al.<sup>18,19</sup> and Pisarsaka et al.<sup>20</sup> described their experience with ERAS in colonic and rectal cancer surgery and indicated that we should improve compliance with the ERAS protocol.

Implementation of ERAS represents not only the development of a single discipline

but also, and more importantly, the collaboration of surgical departments, anesthesiologists, and nurses. Encouraging patients' active participation in ERAS and promoting cooperation among patients and doctors are the foundation for application of ERAS because they not only increase patient compliance with ERAS but also improve clinical outcomes of surgery. In this study, lower intraoperative blood loss volumes and transfusion rates were found in the ERAS than non-ERAS group. The incidence rates of postoperative complications and readmission were also significantly lower in the ERAS group, which is consistent with previous reports.<sup>8,21-23</sup>

ERAS promotes the use of a rapid- and short-acting anesthesia to reduce the intraoperative stress rate, accelerate recovery, promote early ambulation, and restore gastrointestinal peristalsis.<sup>8,23</sup> During the intraoperative period, reducing the patient's body exposure time, raising the operating room temperature, or preheating the intravenous transfusion fluids prevent hypothermia, which may cause intraoperative and postoperative complications such as incision wound infection and hemorrhage.<sup>24</sup> In a previous study of intraoperative hemodynamic management in non-cardiac surgery, sufficient uptake of liquid and energy before the operation ensured effective perioperative tissue perfusion, which, in combination with controlling the intraoperative fluid transfusion volume, prevented edema caused by fluid overload.<sup>25</sup> In addition, prolonged bed rest after surgery is likely to cause deep vein thrombosis. Therefore, with the ERAS protocol, physicians encourage patients to undertake ambulation earlier than the time conventionally suggested for ambulation after RC to both avoid formation of deep vein thrombosis and stimulate bowel movement.<sup>26</sup> The omission of oral bowel preparation and cessation of nasogastric tubes can also effectively enhance bowel

movement. Daneshmand et al.<sup>8</sup> and Arumainayagam et al.<sup>23</sup> found that ERAS could shorten the LOS. We drew the same conclusion in the present study, which was probably the most inspiring outcome. In most developed countries, patients' medical costs are largely covered by insurance. However, in many developing countries, including China, the cost of the operation is a huge financial burden for most families. Therefore, reducing the LOS and hospitalization costs through the implementation of ERAS can reduce the economic pressure and benefit patients undergoing RC.

This study has two main limitations. First, it was not a prospective randomized controlled trial. Second, the data were derived from a single center, which may have influenced the results.

## Conclusion

The application of ERAS in patients undergoing RC may effectively accelerate patient rehabilitation and reduce the LOS and hospitalization costs. These changes will not increase the rates of postoperative complications or readmission.

## Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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