



Reducing post-radical cystectomy complications with enhanced recovery after surgery (ERAS) protocol: is it time to change?

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ABSTRACT

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Radical cystectomy (RC) remains associated with a greater number of postsurgical complications than any urological procedure. Enhanced recovery after surgery (ERAS) protocol is a multimodal perioperative care pathway designed to achieve early postsurgical recovery. We evaluated the perioperative outcome of post-RC patients, comparing the effectiveness of ERAS to conventional recovery protocols. We identified 37 patients who underwent RC for bladder cancer from 2016 to 2018. The characteristics, complication rate and clinical outcomes were evaluated in these groups of patients. In this study, the mortality was 8.1%, and the complications were 37.8%. The most frequent complications were anastomotic leakage (16.2%), wound dehiscence (13.5%), infections/sepsis (8.1%), and paralytic ileus (8.1%). The ERAS protocol significantly reduced operative time ($p=0.001$; OR=216; CI95%: 12.0-3855.2) and reduced overall complications ($p=0.04$; OR= 0.14 CI95%: 0.016-1.132). Extensive complications and mortality develop following the RC procedure. Meanwhile, refinement in perioperative care has been reducing the rate of serious complications. The ERAS protocol distinctly reduces the post-RC complication rate.

ABSTRAK

Radikal sistektomi masih dikaitkan dengan kejadian komplikasi yang lebih tinggi dibandingkan prosedur lainnya. Protokol *enhance recovery after surgery* (ERAS) merupakan metode multimoda preoperatif yang dikembangkan untuk mencapai pemulihan lebih awal pasca bedah. Telah dilakukan evaluasi luaran preoperative pasien post-RC dengan membandingkan antara ERAS dengan protocol pemulihan konvensional. Sebanyak 37 pasien yang menjalani RC karena kanker saluran kemih antara 2016-2018 dievaluasi. Dilaporkan terdapat 8.1% kematian dan 37.8% komplikasi. Kompleksi paling sering terjadi adalah kebocoran pada anastomosis (16,2%), dehisensi luka (13.5%), infeksi/sepsis (8.1%) dan paralisis ileus (8.1%). Protokol ERAS mengurangi komplikasi sebesar 4.1 kali dibandingkan non-eras (OR=4.1; 95% CI: 0.63-27.66). sehingga pada laporan penelitian awal ini menunjukkan bahwa ERAS protocol mengurangi angka komplikasi pada radikal sistektomi.

Keywords:

Bladder cancer;
Radical cystectomy;
ERAS protocol;

INTRODUCTION

Bladder cancer (BC) is known as the 7th most common cancer globally and it is more prevalent in men than in women.¹ Radical cystectomy (RC) remains the standard treatment for patients with muscle-invasive bladder cancer (MIBC).¹ Despite the rapid advances in surgical techniques, anesthesia, and perioperative care, the RC persists to be associated with higher morbidity and longer postoperative day of care compared to any urological procedures.^{2,3} Improvement is necessary in various fields, including surgical techniques for postoperative care, to solve this problem. Several factors that influence morbidity rate and postoperative hospitalization day include patients' physiology, postoperative complications, and intraoperative factors.^{4,5}

An enhanced recovery after surgery (ERAS) protocol was founded in 1990 by Professor Henrik Kehlet and practiced in several major surgical procedures, such as colorectal surgery to radical cystectomy.⁶ The ERAS protocol has 22 policy points aiming to reduce postoperative parameters, such as hospitalization time, complications, and health care costs, using preoperative, perioperative, and postoperative approaches.^{2,4,7-9}

Research on the ERAS protocol by Maffezzini, practicing 6 out of 22 ERAS policy points, has shown morbidity and a reduced length of stay compared to non-ERAS protocol groups.⁸ Several studies on the ERAS protocol application reported favorable outcomes while conducted in different countries and various research methods.^{2,6,7,10}

The purpose of this study was to determine the effect of ERAS protocol application following radical cystectomy at Dr.Sardjito General Hospital, Yogyakarta. Heretofore, the ERAS protocol has not been widely practiced in Indonesia, and studies using this protocol remain small in number. Although many

studies reported the advance of the ERAS protocol, the challenge of further effectiveness evaluation persists due to the distinction of the ERAS protocol implementation in previous studies.

MATERIALS AND METHODS

Subjects

The data were collected retrospectively. All patients undergoing RC in Dr.Sardjito General Hospital, Yogyakarta between January 2016 and January 2018 were included. The patients rejecting the ERAS protocol were offered to the conventional protocol. Patients refusing RC for their BC and candidating trimodal therapy were excluded.

Protocol

In this study, the ERAS protocol implementation in the preoperative phase was related to several nutritional status assessments, including fluid and carbohydrate intake, no premedication, bowel preparation, antibiotic prophylaxis, and thromboprophylaxis. Protocols in the intraoperative phase included short-duration anesthetics preferring epidural injection at the level of 5-6th thoracic vertebrae, no drainage tube installation, and body temperature monitoring. Protocols at the postoperative stage included early mobilization, normal diet, and as early as possible catheter withdrawal.^{1,3,5} Nasogastric tube (NGT) installation and opioid usage for painkillers were avoided.^{1,3,5} In this study, the observed compliance rate was 100%, and neither of the groups refused our protocol. Meanwhile, the conventional protocol was promoting delayed oral intake, mobility, and postoperative conservative approach. This study was approved by the Medical and Health Research Ethics Committee, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito General Hospital, Yogyakarta with approval number KE/0976/08/2019.

Statistical analysis

The comparison of the patients experiencing postoperative complications by age, nutritional status, comorbidity, ERAS/conventional protocol application, surgical duration, amount of bleeding, and urinary diversion types was performed using SPSS 22.0. The statistical test was performed using the Chi-square test. The risk ratio (RR) with a p value <0.05 was considered significant.

RESULTS

In this study, from January

2016 to December 2018, the data of 37 samples undergoing radical cystectomy were collected. The majority of the patients were male. Transitional cell carcinoma was the most common pathological finding, as shown in TABLE 1. There was an 81-year-old geriatric patient undergoing a radical cystectomy procedure. From these data, only nine patients underwent the ERAS protocol. Considering that the implementation of the new ERAS protocol was carried out in January 2018, all patients undergoing the ERAS protocol were prospectively observed with a 2-month follow-up duration.

TABLE 1. The Clinical and Pathological Characteristics

Characteristics	Value	p
Age (mean ± SD years)		
• ERAS	60.78 7.3	0.915
• Conventional	61.11 9.8	
Gender [n (%)]		
• Male	33 (89.1)	<0.05
• Female	4 (10.8)	
Pathological diagnosis [n (%)]		
• Transitional cell carcinoma	29 (78.3)	<0.05
• Squamous cell carcinoma	4 (10.8)	
• Adenocarcinoma	4 (10.8)	
Urine Diversion [n (%)]		
• Ileal conduit	28 (75.6)	<0.05
• Orthotopic neobladder	3 (8.1)	
• Cutaneous ureterostomy	6 (16.2)	

The mortality rate in this study was relatively high, at 8.1%. There was a patient who passed away 24 hours postoperation. The patient was classified as ASA 3 with sepsis as the comorbid, the 3-hour operation went smoothly, and 500 cc bleeding occurred.

In this study, we found that the patients undergoing the ERAS protocol had a significantly shorter operation time compared to the conventional protocol (p=0.001; OR=216; CI95%: 12.0-3855.2).

Bleeding, leakage, sepsis, morbidity, and postoperative complications showed no statistical significance.

Regarding the complications in this study, one patient had to undergo reoperation on the second postoperative day due to general peritonitis caused by ileo-ileal anastomosis leakage. Following re-surgery, the patient's condition continued to improve and was discharged on the 12th postoperative day.

TABLE 2. Postoperative complications in patients undergoing radical cystectomy on ERAS and conventional

Variable	ERAS	Conventional	p	OR (CI 95%)
Intraoperative complication				
• Operative time (> 3 h)	1	27	0.001	216 (12.0-3855.2)
• Bleeding (> 500 cc)	6	26	0.460	6.5 (0.88- 47.89)
Post-operative complication				
• Overall	4	9	0.550	0.63 (0.13-2.91)
• Post-operative ileus	3	6	0.470	0.55 (0.10–2.85)
• Leakage	0	4	0.230	N.A
• Sepsis	1	2	0.704	0.615 (0.05-7.71)
• Morbidity	3	5	0.330	0.435 (0.80-2.36)

This study tried to evaluate several factors' roles in the postoperative outcome. Statistical analysis was performed to identify factors' roles in the occurrence of postoperative complications (TABLE 3). Although there were differences in the number of complications in some groups, for example, the short operation time (<3 h) group had fewer complications but showed no statistical significance. In

the operation protocol group, the ERAS protocol showed fewer postoperative complications than the conventional protocol, and the difference was statistically significant (p = 0.04) (TABLE 3). Furthermore, the incidence of complications was reduced to 4 times in the ERAS protocol group compared to the conventional protocol (RR: 4.1; 95%CI: 0.63-27.66; p = 0.04).

TABLE 3. The comorbid and overall complications

Category	Complication		p
	Yes (%)	No (%)	
Comorbidity			
• Yes	40.6	59.4	0.36
• No	20.0	80.0	
ERAS protocol			
• Yes	11.1	88.9	0.04
• No	46.4	53.6	
Nutritional Status			
• Good	33.3	66.7	0.49
• Malnutrition	40.0	60.0	
Total blood loss			
• < 500 cc	20.0	80.0	0.36
• ≥ 500 cc	37.8	62.2	
Age			
• < 60 years	29.4	70.6	0.33
• ≥ 60 years	45.0	55.0	
Urinary diversion			
• Neobladder	50.0	50.0	0.43
• Ileal conduit	58.6	41.4	
• Cutaneous ureterostomy	83.3	16.7	

DISCUSSION

The fundamental finding from this study was that the implementation of the ERAS protocol in patients undergoing radical cystectomy significantly decreased the incidence of postoperative complications. We believe that this study has important clinical implications and can be a scientific basis for ERAS protocol implementation in the future. Several theoretical bases explain why the ERAS protocol can improve perioperative outcomes. First, the principle of the ERAS protocol is to restore physiological functions immediately. For example, perioperative carbohydrate loading can increase insulin sensitivity, causing preserved body mass and muscle strength¹, and goal-directed fluid management has shown a decrease in ileus events by maintaining splanchnic perfusion,^{1,2} monitoring body temperature, maintaining normothermic conditions, early mobilization, and per-oral dietary intake reduces complications by maintaining body homeostasis.^{11,12} Second, the ERAS protocol is very adaptive, with a theoretical basis that can be applied at each center.

Radical cystectomy remains the standard treatment in muscle-invasive bladder cancer (MIBC) patients and is still considered a major surgical procedure with high morbidity and mortality.⁵ In this study, 30-day follow-up was conducted with a postoperative complication rate of 37.8% and a mortality rate of 8.1%. The postoperative complications included anastomosis leakage, surgical wound dehiscence, sepsis, deep vein thrombosis, paralytic ileus, and peritonitis.

The ERAS protocol is an integrated strategy to provide better perioperative outcomes. A previous study showed that implementing the ERAS protocol is not only more adaptive and can be feasibly applied but also improves the patient's peri-operative outcome.⁷ In the surgical

literature series, the ERAS protocol has demonstrated increased perioperative outcomes in several surgical procedures, such as colorectal, vascular, and orthopedic surgery.^{7,12-15}

There are several limitations of this study. First, due to the nature of the observational and design retrospective study, there was potential bias in the data. Second, conducted in a short timeframe (30 days postoperatively), even though acute postoperative complications are the focus of this protocol, further studies need to confirm long-term periods. Despite these limitations, this study has clinical relevance for improving perioperative quality in patients undergoing radical cystectomy. The data from this study have important clinical implications as a scientific basis for ERAS protocol implementation in other protocol implementation centers. Extensive complications and mortality occur following RC. Meanwhile, refinement in perioperative care has reduced serious complications. The ERAS protocol clearly reduced the complication rate after RC.

In this study, ERAS showed significance in reducing intraoperative complications. Additionally, several postoperative complications showed a lower trend in the ERAS protocol, which indicates that the protocol may reduce postoperative complications. The future direction of this study is to continue the observation in a longer time frame and larger samples. 100% compliance also indicated that ERAS protocols are applicable as amenable protocols and need to be applied as peri-operative standards nationally.

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