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The Implementation of Modified ERAS Protocol in Laparoscopic Radical Cystectomy: An Outcome at Universitas Gadjah Mada Urological Institute

Said Alfin Khalilullah [1*], Ahmad Zulfan Hendri [2]

[1] Division of Urology, Department of Surgery, Universitas Syiah Kuala, Aceh, Indonesia

[2] Division of Urology, Department of Surgery, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada - Dr. Sardjito Hospital, Yogyakarta, Indonesia

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*Corresponding author:
Said Alfin Khalilullah
Division of Urology, Department of Surgery, Universitas Syiah Kuala, Aceh, Indonesia
saidalfink@gmail.com
Trisnukamajaya@aol.com

ABSTRACT

Background: Enhanced recovery after surgery (ERAS) protocol is multimodal perioperative care designed to achieve enhanced postoperative outcomes. Unfortunately, all these elements are not always fully applied due to each center's limitations. In this study, the ERAS protocol was modified and implemented in patients with bladder cancer who underwent laparoscopic radical cystectomy (LRC). This study aimed to evaluate the outcomes of the modified ERAS protocol in LRC surgery.

Methods: The retrospective study design was used to evaluate 35 patients (27 males and 8 females) who underwent LRC with the application of the perioperative modified ERAS protocol. All information relating to perioperative, intraoperative, and postoperative patient data was obtained from medical records. All complications that occurred were classified according to the Clavien-Dindo classification.

Results: The mean age in this study was 58.3 ± 9.2, and the most common pathological finding was urothelial carcinoma. Intraoperative blood loss was 318.5 ± 112.5 cc with those requiring intraoperative blood transfusion of 4.8 ± 2.0 patients. The mean first diet was 2.1 ± 1.2 days. For bowel activities, the first flatulence was 1.6 ± 0.8 days. The mean mobilization with first sitting was 1.8 ± 0.9 days. Seventeen percent of patients experienced intraoperative complications and postoperative complications were encountered in 28.6% of patients. According to the Clavien-Dindo classification, most complications were grades 1-2 (17.1%). There was no incidence of mortality in this study.

Conclusions: These promising results, including the postoperative recovery and complications rates, require validation with multi-center and randomized studies to confirm the benefits of the modified ERAS protocol in minimally invasive procedures, especially LRC surgery.

INTRODUCTION

Since being popularized by Professor Henrik Kehlet in 1990, the ERAS protocol has immediately become a major focus in perioperative management [1]. After giving promising results in the field of colorectal surgery, nowadays, ERAS protocol is widely applied in the field of urologic surgery, especially radical cystectomy [2].

The focus that differentiates the ERAS procedure from the usual standard care is in treatments designed to restore physiological function after surgery and minimize postoperative over responsiveness by improving cardiopulmonary function, restoring digestive function, and returning to normal activities [3].

ERAS protocol involves multidisciplinary teamwork in optimizing patient care [4]. In addition, the ERAS protocol has been shown to have an important clinical value in the management of the health system in general, including a shorter length of stay, reduced incidence of complications, and early recovery [5].

Several studies have shown satisfactory results by implementing the ERAS protocol in minimally invasive

surgeries, such as laparoscopic procedures [6,7]. However, implementing the ERAS protocol is still a clinical challenge at our center since there is no agreement in the multidisciplinary team, and it is necessary to modify the ERAS protocol to be simpler. This study aimed to evaluate the implementation of the ERAS protocol in our center.

METHODS

Data collection

A retrospective study was conducted in the Urology Department, Universitas Gadjah Mada, Dr. Sardjito General Hospital on 35 patients who underwent LRC due to bladder cancer between 2015 until 2020. We excluded (a) patients with ethnic non-Indonesian, (b) patients with non-LRC surgery and non-ERAS perioperative management, and (c) patients with incomplete medical record data. In our center, open procedures on radical cystectomy were also performed. However, only the laparoscopic procedures were included in this study to minimize bias because there are two different procedures.

This study was approved by the Medical and Health Research Ethics Committee of Universitas Gadjah Mada with certificate number KE/FK/1388/EC/2020**.** All patient data were obtained from medical records. Perioperative details included age, gender, pathological finding, staging, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and urinary diversion type. Information relating to intra-operative findings included estimated blood loss, requiring intraoperative transfusion, and intraoperative complications if any. Additionally, postoperative information included the day of diet, mobilization, bowel movement, drain removal, length of stay, re-operation, and re-admission. We also included the data of postoperative complications according to the Clavien-Dindo classification.

The modified ERAS protocol

Until now, there has been no multidisciplinary agreement at our center in implementing the ERAS protocol, and this made us unable to implement all points of the ERAS protocol. The modified ERAS protocol was designed to be simpler. Modifications of the ERAS protocol that we applied are described in **Table 1**. The fundamental differences from the modified ERAS protocol are low molecular weight heparin (LMWH) for thrombosis prophylaxis, carbohydrate loading before surgery, multimodal analgesia, and early postoperative oral intake.

In this modified ERAS, we did not always give LMWH preoperative to prevent thrombosis prophylaxis as implemented in the ERAS protocol. However, we consulted with the haemato-oncology division to evaluate the needed LMWH administration. We also modified the preoperative carbohydrate loading to 4 hours before surgery with 400 mg of glucose water, and fluid intake can be started 12 hours after surgery. We do this modification as there is no agreement in multidiscipline.

Table 1. Modified ERAS protocol

Item	Component
Preoperative	Diet: Fasting 6 h before surgery (according to anesthesia), carbohydrate loading 4 h before surgery (water with glucose 400 mg).
	No bowel preparation.
	Consultation with hemato-oncology division for the evaluation of LMWH heparin for the prevention of DVT.
Intraoperative	Goal-directed intraoperative fluid therapy.
Postoperative	Non-opioid analgesia.
	If good tolerance, a fluid diet can be started 12 hours after surgery.
	Consider diet through NGT if patient unable to take diet after 3-4 days but bowel activity is present. If there is no bowel activity, begin total parenteral nutrition.
	Post-operative gradual mobilization (since H-0 start to sitting)
	Giving gastrointestinal prophylaxis with ranitidine until bowel function returns to normal.
	Administration of anti-emetic, Metoclopramide if needed.

LMWH = Low molecular weight heparin; NGT = Naso gastric tube DVT = Deep venous thrombosis.

RESULTS

This research's results were obtained after analyzing 29 samples of patients diagnosed with ovarium malignancy from the Obstetrics and Gynecology Polyclinic register in Mangusada Badung Regional Public Hospital in January-December 2019 by matching the register data and medical record numbers stored in the hospital. It aimed to know the characteristic profile of patients with ovarian cancer at Mangusada Badung Regional Public Hospital. **Table 1** explains that more than 60% of patients were diagnosed in the end-stage (stadium III malignancy).

This research found about 65.5% of patients with serous tumor subclassification, with the lowest percentage being mixed germ cell tumors. This study predominantly uncovered that ovarian cancer was diagnosed at the age of 51–60 years, but then decreased in the age group of 60 years, and fewer patients were diagnosed with ovarian cancer in the age group less than 30.

The most highly diagnosed ovarian cancer was in patients with obesity (BMI > 25 kg/m2). The percentage increases in line with the increase in the BMI of the age group. In addition, nullipara was found dominantly in patients with ovarian cancer than primipara and multipara**.** This research also reviewed the overall contraceptive use in patients with ovarian cancer. **Table 1** displays that almost half of the patients with ovarian cancer admitted to having early menarche at the age of 12 years, while the percentage at the later age of menarche was minor.

Figure 1 reveals that patients with IB were dominantly subclassified as mucinous and serous tumors. Meanwhile, patients with IC stadium diagnoses were predominantly subclassified as serous and endometrioid. Hence, one patient was with a serous, mucinous, yet mixed germ cell tumor, diagnosed with IIB stadium. Stadium IIIA and IIIB were found only with a serous subclassification, whereas stadium IIIC was dominated with serous subclassification followed by endometrioid subclassification. Meanwhile, serous subclassification was found in all stadiums of patients with ovarian cancer. As described in **Figure 2**, serous subclassification was found in all age groups and was the most dominant tumor subclassification group in ovarian cancer.

As shown by **Table 2**, the earlier stage was commonly seen at an earlier age, and the later stages were seen in the older age groups.

From 2015 to 2010, a total of 35 patients (27 males and 8 females) underwent the LRC procedure with the application of the perioperative modified ERAS protocol. The demographic data for this study are presented in **Table 2**. Most patients had an ASA score of 2 (n = 29) and extravesical disease (n = 19). There was one patient with metastatic disease who underwent LRC because of uncontrolled hematuria and anemia that was not corrected by blood transfusion.

The mean of intraoperative blood loss was 318.5 ± 112.5 cc, and the mean of those requiring intraoperative blood transfusion was 4.8 ± 2.0 cc. More than 17% of patients experienced intraoperative complications, including intestinal injury and right internal iliac vein injury (**Table 3**). One patient required re-operation caused by peritonitis due to intestinal ileo-ileal leakage and uretero-conduit leakage.

The mean functional recovery including clear water diet and solid diet was 318.5 ± 112.5 cc and 4.0 ± 2.1 days, respectively. For bowel activities, the mean first flatulence and defecation were 1.6 ± 0.8 days and 4.7 ± 2.0 days, respectively. The mean mobilization, sitting, standing, and walking was 1.8 ± 0.9 days, 4.2 ± 2.4 days, and 5.6 ± 3.0 days, respectively (**Table 4**). In addition, two patients needed readmission within 30 days due to surgical site infection and fever with electrolyte imbalance.

Post-operative complications were encountered in 28.6 % of patients within 30 days of surgery with wound dehiscence as the most common finding. According to Clavien-Dindo classification, most complications were grades 1-2 (**Table 5**). There was no incidence of mortality in this study.

Table 2. Clinical characteristics of the samples

Characteristics	n (%)
Age (years), Mean ± SD	58.3 ± 9.2
Gender	
Male	27 (77.1)
Female	8 (22.8)
Pathological finding	
Urothelial cell carcinoma	32 (91.4)
Squamous cell carcinoma	2 (5.7)
Adenocarcinoma	1 (2.8)
Staging	
Organ-confine disease (≤pT2, pN0)	15 (42.8)
Extravesical disease (>pT2 or >pN0)	19 (54.3)
Metastatic disease	1 (2.8)
Body mass index	
Underweight	19 (54.2)
Norm weight	15 (42.8)
Overweight	1 (2.8)
ASA score	
2	29 (82.8)
3	6 (17.1)
Urinary diversion	
Ileal conduit	12 (34.3)
Transureterocutaneostomy	23 (65.7)

Table 3. Intra and postoperative finding

Variable	n (%)
Blood loss (cc), Mean ± SD	318.5 ± 112.5
Requiring blood transfusion (cc), Mean ± SD	4.8 ± 2.0
Overall complications	10 (28.6)
Intraoperative complications	
Rectal injury	3 (8.7)
Sigmoid injury	1 (2.8)
Internal right ileac vein rupture	1 (2.8)
Ileal injury	1 (2.8)
Postoperative complication	
Ileus	3 (8.6)
Infections/Sepsis	3 (8.5)
Wound dehiscence	5 (14.2)
Anastomotic leak	1 (2.8)

Table 4. Postoperative outcomes of modified ERAS in LRC

Variable	n (%)
Length of stay (days), Mean ± SD	9.8 ± 4.7
Drain removal (days), Mean ± SD	4.8 ± 2.0
Functional recovery (days), Mean ± SD	
First fluid diet	2.1 ± 1.2
First solid diet	4.0 ± 2.1
Bowel activities (days), Mean ± SD	
First flatulence	1.6 ± 0.8
First defecation	4.7 ± 2.0
Mobilization (days), Mean ± SD	
First sitting	1.8 ± 0.9
First standing	4.2 ± 2.4
first walking	5.6 ± 3.0
Readmission within 30 days	2 (5.7)
Reoperation within 30 days	1 (2.8)

Table 5. Postoperative complications based on Clavien-Dindo classification

Grade	n (%)
Grade 1-2	6 (17.1)
Grade 3-4	4 (11.4)
Grade 5	0

DISCUSSION

After we evaluated 35 patients who underwent LRC with the perioperative modified ERAS protocol, we found that the implementation of the protocol showed promising results although not all parts of the protocol were implemented. The data concerning the use of the ERAS protocol for radical cystectomy surgery are still limited. However, several studies have shown good outcomes where the implementation of ERAS can accelerate postoperative recovery reduce the incidence of postoperative complications and the length of stay [8,9,10]. A study by Liu et al. [8] who evaluated the modified ERAS protocol after radical cystectomy has a similar result in this study in terms of length of stay.

We modified the ERAS protocol as listed in **Table 1** and we found that the mean length of stay was 9 days with the mean drain removal of day 4. The bowel movement, functional recovery, and mobilization were also started on day 1. This study also showed the modified ERAS protocol has a lower incidence of overall complications. Previously, there have been several studies that eliminated multiple ERAS protocols [8,9]. These studies found that the modified ERAS can shorten the length of stay with no difference between the incidence of complications.

One meta-analysis evaluated the ERAS protocol in colorectal surgery and concluded that the ERAS protocol could reduce the length of stay by 2.5 days compared with the standard care [10]. Another meta-analysis that evaluated ERAS protocol in radical cystectomy surgery also showed the same results that ERAS protocol enhances postoperative recovery and length of stay.

Several studies also described that another advantage of the ERAS protocol is the positive effect in reducing the incidence of postoperative complications [8,10,11]. Postoperative ileus is one of the most common complications that occur after surgery [8]. The mechanism that contributes to induce postoperative ileus includes prolonged fasting, preoperative bowel preparation, use of the nasogastric tube, opioid analgesic for pain control, restriction of diet, and delayed mobilization [12]. In the ERAS protocol, these risk factors have been eliminated.

There are still limited studies that apply all the ERAS protocols in perioperative management. In our center, we did not fully give thrombosis prophylaxis before surgery and, we used an anti-emetic for preventing nausea and vomiting. This modified ERAS also demonstrated the beneficial effects, which was also seen in one meta-analysis study that eliminated some elements of the ERAS protocol and had the same beneficial effects in enhancing postoperative recovery in terms of reducing the length of stay and overall complication rates [1].

This is not the first study to eliminate several points in the ERAS protocol. For example, eliminating 4 or fewer points in the ERAS protocol also had promising results in enhancing postoperative recovery and reducing overall complications [8,9,12]. Further studies are still needed to validate the effect of individual ERAS components as separate variables.

The limitations of this study are small sample size, single-center, non-randomized control trial, and retrospective design. However, we maintained the accuracy of the data and double-checked all medical records to avoid bias. We believe this preliminary study shows that the modified ERAS protocol is a simpler protocol with equally promising results and provides evidence-based support for the implementation of the modified ERAS protocol in LRC surgery.

CONCLUSIONS

The modified ERAS protocol has promising results in patients with bladder cancer who are undergoing LRC. Further investigations are still needed to confirm the potential advantages of this study. Randomized control studies with multi-center collaborative cohorts are still required to provide more evidence-based support for these promising results.

DECLARATIONS

Ethics Approval

This study was approved by the Medical and Health Research Ethics Committee of Universitas Gadjah Mada with certificate number KE/FK/1388/EC/2020.

Competing of Interest

The author(s) declare no competing interest in this study

Acknowledgment

NA

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