

# The application of enhanced recovery after surgery (ERAS) protocol in radical cystectomy and urinary diversion using bowel segment reduces the length of stay: A multicenter comparative study in Indonesia

Agus Rizal Ardy Hariandy Hamid<sup>1\*</sup>, Adhitama Alam Soeroto<sup>1</sup>,  
Ahmad Zulfan Hendri<sup>2</sup>, Sawkar Vijay Pramod<sup>3</sup>, Faurisky Febrian Prapiska<sup>4</sup>,  
Dita Aditiansih<sup>5</sup>, Nurul Ratna<sup>6</sup>, Chaidir Arif Mochtar<sup>1</sup>, Rainy Umbas<sup>1</sup>

<sup>1</sup>Department of Urology, Cipto Mangunkusumo Hospital, Faculty of Medicine, Universitas Indonesia;

<sup>2</sup>Division of Urology, Department of Surgery, Sardjito Hospital, Faculty of Medicine, Universitas Gadjah Mada;

<sup>3</sup>Department of Urology, Hasan Sadikin Hospital, Faculty of Medicine, Universitas Padjadjaran;

<sup>4</sup>Division of Urology, Department of Surgery, Adam Malik Hospital, Faculty of Medicine, Universitas Sumatera Utara;

<sup>5</sup>Department of Anesthesiology and Intensive Care, Cipto Mangunkusumo Hospital, Faculty of Medicine, Universitas Indonesia;

<sup>6</sup>Department of Nutrition, Cipto Mangunkusumo Hospital, Faculty of Medicine, Universitas Indonesia.

\*Corresponding author:

Agus Rizal Ardy Hariandy Hamid;  
Department of Urology, Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia;

rizalhamid.urology@gmail.com

Received: 2023-04-12

Accepted: 2023-05-28

Published: 2023-09-05

## ABSTRACT

**Introduction:** Radical cystectomy is one of the most invasive urological procedures, with high difficulty and various complications. The Enhanced Recovery After Surgery (ERAS) protocol was created to improve patient outcomes after such surgery, including radical cystectomy. This study aims to evaluate the application of ERAS on radical cystectomy in Indonesia.

**Methods:** This was a multicenter study (Jakarta, Yogyakarta, Bandung, and Medan) from July 2016 to April 2021. This study compared the postoperative length of stay, diet intake, bowel movement, and mobilization pattern of the subject receiving ERAS protocol with the non-ERAS subject. Curtailed, fast preoperative carbohydrate loading was administered to patients. There was no mechanical bowel preparation except one day before in selected cases. Postoperative patterns after surgery and the length of stay were analyzed.

**Results:** We collected 128 subjects in this study, with 74 (60 %) subjects enrolled with ERAS protocol and 54 (40 %) with non-ERAS. There were statistically significant differences in length of stay with a median of 11 days vs. 16 ( $p$ : 0.001), intensive care unit admission duration with a median of 2 days vs. 3 ( $p$ : 0.004) and time to sit after radical cystectomy with a mean of 2.14 days vs 2.89 ( $p$ :-: 0.004) in subject with ERAS protocol compared to non-ERAS protocol.

**Conclusion:** This multicenter study found that ERAS was demonstrated to be efficacious in decreasing the duration of hospital stay, the duration of intensive care unit admission, and the time for the subject to sit after the radical cystectomy.

**Keywords:** radical cystectomy, bladder cancer, ERAS.

**Cite This Article:** Hamid, A.R.A.H., Soeroto, A.A., Hendri, A.Z., Pramod, S.V., Prapiska, F.F., Aditiansih, D., Ratna, N., Mochtar, C.A., Umbas, R. 2023. The application of enhanced recovery after surgery (ERAS) protocol in radical cystectomy and urinary diversion using bowel segment reduces the length of stay: A multicenter comparative study in Indonesia. *Bali Medical Journal* 12(3): 1897-1900. DOI: 10.15562/bmj.v12i3.4530

## INTRODUCTION

According to data from GLOBOCAN 2018, bladder cancer is the 10<sup>th</sup> most common cancer worldwide, including in Indonesia. Radical cystectomy (RC) with lymph node dissection and urine diversion (UD) is the gold standard treatment for muscle-invasive bladder cancer. Radical cystectomy remains one of the most difficult and invasive urological procedures.<sup>1</sup> Radical cystectomy (RC), which involves a large surgical resection, has a greater risk of bleeding, perioperative transfusion, urine diversion, and a high rate of postoperative

sequelae. Furthermore, patients requiring major urologic surgery are typically elderly, with a variety of comorbidities such as cardiovascular events, anemia, infection, and malnutrition.<sup>2</sup> The postoperative morbidity and mortality rates of individuals who undergo RC with UD have been studied up to 70%. The mortality rate was 0.3 percent in a retrospective evaluation of 304 patients using a care pathway, while overall major and minor complication rates were 4.9% and 30.9%, respectively.<sup>1,2</sup> Another major trial with 1142 patients found mortality and early complication rates of 2.7 and

67 percent, respectively.<sup>1,2</sup> The lack of uniform definitions of perioperative mortality and postoperative complications could explain the disparity. Furthermore, because most of these investigations were retrospective, preoperative comorbidity and minor postoperative problems may have been underreported.<sup>1</sup>

The ERAS protocol was created to change the physiological and psychological response to the impact of major surgery. Enhanced recovery after surgery (ERAS) was first introduced by Henrik Kehlet, a Denmark surgeon, in 1990.<sup>2,3</sup> In urology, there is a surge of interest in the

applicability of ERAS protocols, including radical cystectomy. The ERAS protocol in urological surgeries was initially described in Arumainayagam in 2008. The study observed a shorter median time of 4 days in patients undergoing radical cystectomy procedures.<sup>4</sup> Similar studies with larger sample sizes also reported high reduction variability of the length of stay from 0.8-5 days.<sup>5</sup> The application of ERAS protocol in Indonesia started in 2016, mostly on urological procedure and colorectal surgery.<sup>6,7</sup> An Initial study by Zulfan *et al.*, 2021, showed that ERAS protocol in radical cystectomy patients improves the perioperative outcome.<sup>6</sup> This study aims to evaluate the application of ERAS on radical cystectomy in multicenter in Indonesia.

## METHODS

This was a multicentre prospective cohort study to analyze the difference between a patient who underwent radical cystectomy with ERAS protocol and without ERAS protocol. All muscle-invasive bladder cancer patients who were able to have a radical cystectomy and urinary diversion using a bowel segment from July 2016 to April 2021 were enrolled in this study. All the patients received written informed consent for the study and data publishing and agreed to enroll on their behalf or from their respective family members. Patients with ERAS protocol (EP) had a regular diet until the night before surgery. We gave the patients high protein and carbohydrate supplements the day before surgery, with carbo-loading the morning before surgery. The carbo-loading that we used is 12 grams of sugar in 100 ml of water (sugar water). There were no mechanical bowel preparations except in selected cases, i.e., chronic constipation. The mechanical bowel preparation was performed only one day before the surgery. The prophylactic antibiotic was also given 1 hour before surgery. We used intravenous acetaminophen as an analgesic; narcotic analgesic was avoided. We also compiled the data from the patients who underwent radical cystectomy with the standard of care (without ERAS protocol) as control. We analyzed the diet intake pattern (liquid dan regular diet), bowel movement pattern (flatulence and defecation), and

mobilization pattern (sitting, standing, walking). All patients followed the protocol according to the intended group and were maintained until discharge. All confidential subject data was guaranteed, and Health Research Ethical Committee Universitas Indonesia approved ethical clearance. All the statistical data were analyzed using SPSS software version 22.

## RESULTS

In total, 128 patients were included in this study from 4 National Health centers across Indonesia (Jakarta, Yogyakarta, Bandung, and Medan). The data were divided into two groups: 74 patients were included in the intervention (ERAS) group, and 54 patients were gathered as control (non-ERAS).

The mean time to onset of sitting, the median length of ICU stays, and the length of hospital stay were statistically significantly faster and shorter in the ERAS group. There was no significant difference between both groups in terms of mean time to onset of standing, walking, the median time to onset of starting the liquid diet, starting the regular diet, flatulence, and defecation ( $p > 0.05$ ). (Table 1).

## DISCUSSION

Enhanced recovery after surgery protocols has been widely demonstrated to be beneficial in reducing postoperative complications and the duration of hospital stay in colorectal surgeries for more than two decades.

In our study, most of the pre, peri, and postoperative procedures of ERAS were incorporated, based on a study by Cerantola Y *et al.* in 2013.<sup>8</sup> The application of the ERAS protocol was still limited in Indonesia, which only started in 2016. This study is the first to evaluate the initial application of the ERAS protocol in a multicenter setting in Indonesia. Our study found a significant reduction in length of stay as the primary outcome. In the ERAS group, the median LOS was 11 days, while in the non-ERAS group was 16 days. ( $p: 0.001$ ). Several studies also suggested a similar number in LOS reduction favoring the ERAS protocol group over standard protocol, even in patients with higher tumor staging.<sup>5,9-11</sup> ERAS also reduce LOS

in other surgery beside radical cystectomy, it also reduced the LOS in colorectal surgery, as shown in study by Suryadi AS, *et al.*<sup>7</sup> It is thought that the most significant contributor to this number is the delayed return of bowel function and infections in the gastrointestinal and urinary tract.<sup>5</sup> In several initial non-randomized studies applying ERAS protocol for radical cystectomy, a reduction of 3-3.5 days on patient admission time has been demonstrated, with most patients discharged before the 5<sup>th</sup> postoperative day mainly due to the better and earlier return of bowel function.<sup>5</sup> A systematic review of randomized control trials showed no statistically significant difference between a patient who receives mechanical bowel preparation before surgery and a patient with no bowel intervention. However, further study is needed to strengthen this finding.<sup>5-12</sup> A systematic review of randomized control trials showed that there was no statistically significant difference between a patient who receives mechanical bowel preparation before surgery with a patient with no bowel intervention. However further study is needed to strengthen this finding.<sup>13</sup> Preoperative carbohydrate loading was also found to improve perioperative insulin sensitivity, maintain lean body mass, and accelerate the recovery of bowel function.<sup>14</sup> The carbohydrate loading before surgery and shorter fasting duration, not only decrease insulin resistance but also reduce loss of protein and improve muscle function. We use simple sugar water as the preoperative carbohydrate loading solution in our study because of the limitation of medical fees in our centers. The ERAS protocol is believed to attenuate the body's catabolic response to surgery induced by stimulation of the Hypothalamus-Pituitary-Axis (HPA) or autonomic nerve response and the injured tissue.<sup>15</sup>

Several parameters significantly differed between the intervention and control groups other than the length of stay. These parameters are ICU stay and time to sit after the surgery. The median ICU stay was shorter in the ERAS group (median of 2 days) than in the control group (median of 3 days). This finding is similar to the study by Mukhtar *et al.*, 2013 and Karl *et al.*, 2014.<sup>9,16</sup> Both studies found

**Table 1. Subject Characteristics and Feeding and Activity Patterns**

	ERAS (N = 74)	NON - ERAS (N = 54)	p-value
Age (years) (median – range)	59 (18 - 78)	58 (43-81)	0.549 <sup>m</sup>
Bmi (kg/m <sup>2</sup> ) (mean – range)	21.66 (14-31)	20.4 (15-32)	0.31 <sup>m</sup>
Gender			0.383 <sup>m</sup>
male (n = 102)	57 (77%)	45 (83%)	
female (n = 26)	17 (23%)	9 (17%)	
Histopathology			0.295 <sup>m</sup>
tcc (n = 109)	65 (87.8%)	44 (81.5%)	
adeno ca (n = 10)	4 (5.4%)	6 (11.1%)	
scc (n = 9)	5 (6.8%)	4 (7.4%)	
Feeding, activity pattern, and los (days)			
Sitting (mean – range)	2.14 (1-6)	2.89 (1-9)	<b>0.004<sup>m</sup></b>
Standing (median – range)	4 (1-10)	4(2-10)	0.310 <sup>t</sup>
Walking (median – range)	5(1-11)	5(1-12)	0.055 <sup>t</sup>
Icu (median – range)	2 (0-10)	3 (0-4)	<b>0.004<sup>m</sup></b>
Liquid diet (median – range)	1 (0-4)	2 (1-3)	0.098 <sup>m</sup>
Regular diet (median – range)	6 (2-30)	6 (3-16)	0.086 <sup>m</sup>
Flatulence (median – range)	2 (1-6)	3 (1-6)	0.332 <sup>m</sup>
Defecation (median – range)	5 (2-10)	5 (2-13)	0.772 <sup>m</sup>
Length of hospital stay (median – range)	11 (3-43)	16 (6-50)	<b>0.001<sup>m</sup></b>

<sup>m</sup> Mann-Whitney test; <sup>t</sup> independent t-test; <sup>BMI</sup> Body Mass Index; <sup>TCC</sup> Transitional Cell Carcinoma; <sup>SCC</sup> Squamous Cell Carcinoma; <sup>ICU</sup> Intensive Care Units

a shorter ICU stay for the ERAS group. In the study by Mukhtar et al., the mean ICU stay dropped from 2.4 days to 1.0 days ( $p=0.01$ ), and in Karl et al. study, the median ICU stay was 1.8 days vs 2.6 days ( $p<0.001$ ). These results show that with the implementation of the ERAS protocol, the patient will have earlier recovery than the non-ERAS groups, and the faster ICU stay correlates with faster patient discharge from the hospital (shorter length of stay). Also, in our study, the median time to sit was more straightforward in the ERAS group than in the control group. However, comparing time to stand and time to walk showed no significant difference. One possible explanation for these findings might have related to the wide variability of ambulatory time in the non-ERAS group since several patients might stand/walk faster than patients in the ERAS group. We suggest that the mechanisms contributing to this result might rely upon patients' characteristics and general conditions. In another similar setting, Wei et al. reported that the ambulation of patients treated using ERAS protocol tends to be shorter, 8.7 hours after surgery, compared to 3 days if patients were treated with standard protocol.<sup>17</sup> However, the definition of ambulation was not clearly defined and

has only been described as reducing the risk of decubital ulcers. Although the lower mean time to stand and time to walk between both groups were also observed in this study, this difference has not shown any significance.

This study is the first multicentre study in Indonesia that analyze subjects who received ERAS protocol compared to non-ERAS before radical cystectomy. There are some limitations and barriers found in this study. First, this study is a national-wide multicentre study of four major national hospitals in Indonesia. Not all hospitals in Indonesia have already implemented the ERAS protocol as the standard care before the radical cystectomy procedure because there is considerable doubt in the application of ERAS protocol and the need for a multidisciplinary team. Multidisciplinary collaboration is an important point that would affect the success of ERAS Protocol implementation.<sup>18</sup> Collaboration between specialty, nurse, and other supporting areas is essential, and good communication is needed to ensure there is no mistake in ERAS protocol patient care. This is also supported by Springer JE et al., 2019,<sup>19</sup> where this study stated that good communication in the institution is the solution for good ERAS protocol

implementation. Supporting from another department, i.e., Anaesthesiology Department, Clinical Nutrition Department, and the nurse, is crucial in implementing the ERAS Protocol. Pickens et al. study in 2021 analyzes that an excellent routine multidisciplinary audit for ERAS protocol significantly reduces the length of stay and ensures a good clinical outcome post-operatively, and this is one of the reasons why good interdisciplinary collaboration is one of the keys to success in implementing ERAS protocol.<sup>20</sup> Another limitation of our study is we did not analyze the complication rate and the cost-effectiveness of the ERAS group compared to the non-ERAS group. Parallel with the shorter length of stay in the ERAS group, the medical cost of the patient should be cheaper. Also, the shorter length of stay will correlate with lower postoperative complications in the patients. Nabhani J et al. study in 2016 concluded that the ERAS protocol, besides clinical benefits, also saved significant medical costs, especially intensive care unit costs, surgical costs, ancillary treatment costs, and supplies costs.<sup>21</sup> This could be the basis for the next study to analyze whether ERAS protocol correlates with lower complication rates and lower medical care costs.

## CONCLUSION

This study found that ERAS was efficacious in decreasing the duration of hospital stay, intensive care unit admission, and the time for the subject to sit after the radical cystectomy.

## CONFLICT OF INTEREST

We declare that there were no conflicts of interest in this study.

## FUNDING

We thank Universitas Indonesia for funding this study under PUTI 2022 grant program. Project number NKB-129/UN2.RST/HKP.05.00/2022.

## ACKNOWLEDGEMENTS

We are thankful to all the staff for helping with the data retrieval.

## AUTHOR CONTRIBUTION

All authors contributed equally from conception, design, data extraction, and statistical analysis to interpretation of data. They also took part in the drafting of the manuscript and final approval for submission.

## ETHICAL CLEARANCE

This study has obtained ethics approval from the Ethics Committee of The Faculty of Medicine, University of Indonesia - Cipto Mangunkusumo Hospital No. KET-881/UN2.F1/ETIK/2017 before the study was conducted.

## REFERENCES

- Hirobe M, Tanaka T, Shindo T, Ichihara K, Hotta H, Takahashi A, et al. Complications within 90 days after radical cystectomy for bladder cancer: results of a multicenter prospective study in Japan. *Int J Clin Oncol*. 2018 Aug 1;23(4):734–41.
- Vukovic N, Dinic L. Enhanced Recovery After Surgery Protocols in Major Urologic Surgery. *Front Med (Lausanne)*. 2018 Apr 9;5:93–93.
- Ljungqvist O, Young-Fadok T, Demartines N. The History of Enhanced Recovery After Surgery and the ERAS Society. *Journal of Laparoendoscopic & Advanced Surgical Techniques*. 2017 Sep 1;27(9):860–2.
- Arumainayagam N, McGrath J, Jefferson KP, Gillatt DA. Introduction of an enhanced recovery protocol for radical cystectomy. *BJU International*. 2008 Mar 1;101(6):698–701.
- Azhar RA, Bochner B, Catto J, Goh AC, Kelly J, Patel HD, et al. Enhanced Recovery after Urological Surgery: A Contemporary Systematic Review of Outcomes, Key Elements, and Research Needs. *European Urology*. 2016 Jul 1;70(1):176–87.
- Hendri AZ, Khalilullah SA, Aditya GA. A preliminary outcome of modified enhanced recovery protocol versus standard of care in radical cystectomy: an Indonesian experience. *African Journal of Urology*. 2021 Aug 12;27(1):111.
- Suryadi AS, Marbun VMG, Lalisang ANL, Jeo WS, Mazni Y, Lalisang TJM. Adjusted enhanced recovery after surgery (ERAS) protocol in colorectal surgery at dr. Cipto Mangunkusumo General Hospital, Jakarta. *Bali Medical Journal*. 2023 Apr 7;12(1):1127–31.
- Cerantola Y, Valerio M, Persson B, Jichlinski P, Ljungqvist O, Hubner M, et al. Guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS®) society recommendations. *Clinical Nutrition*. 2013 Dec 1;32(6):879–87.
- Mukhtar S, Ayres B, Issa R, Swinn M, Perry M. Challenging boundaries: an enhanced recovery programme for radical cystectomy. *annals*. 2013 Apr 1;95(3):200–6.
- Xiao J, Wang M, He W, Wang J, Yang F, Ma X you, et al. Does Postoperative Rehabilitation for Radical Cystectomy Call for Enhanced Recovery after Surgery? A Systematic Review and Meta-analysis. *Current Medical Science*. 2019 Feb 1;39(1):99–110.
- Tyson MD, Chang SS. Enhanced Recovery Pathways Versus Standard Care After Cystectomy: A Meta-analysis of the Effect on Perioperative Outcomes. *European Urology*. 2016 Dec 1;70(6):995–1003.
- Semerjian A, Milbar N, Kates M, Gorin MA, Patel HD, Chalfin HJ, et al. Hospital Charges and Length of Stay Following Radical Cystectomy in the Enhanced Recovery After Surgery Era. *Urology*. 2018 Jan 1;111:86–91.
- Rollins KE, Javanmard-Emamghissi H, Lobo DN. Impact of mechanical bowel preparation in elective colorectal surgery: A meta-analysis. *World J Gastroenterol*. 2018 Jan 28;24(4):519–36.
- Nygren J, Thacker J, Carli F, Fearon KCH, Norderval S, Lobo DN, et al. Guidelines for perioperative care in elective rectal/pelvic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations. *Clinical Nutrition*. 2012 Dec 1;31(6):801–16.
- Kotfis K, Jamioł-Milc D, Skonieczna-Żydecka K, Folwarski M, Stachowska E. The Effect of Preoperative Carbohydrate Loading on Clinical and Biochemical Outcomes after Cardiac Surgery: A Systematic Review and Meta-Analysis of Randomized Trials. *Nutrients*. 2020;12(10).
- Karl A., Buchner A., Becker A., Staehler M., Seitz M., Khoder W., et al. A New Concept for Early Recovery after Surgery for Patients Undergoing Radical Cystectomy for Bladder Cancer: Results of a Prospective Randomized Study. *Journal of Urology*. 2014 Feb 1;191(2):335–40.
- Wei C, Wan F, Zhao H, Ma J, Gao Z, Lin C. Application of enhanced recovery after surgery in patients undergoing radical cystectomy. *J Int Med Res*. 2018/08/08 ed. 2018 Dec;46(12):5011–8.
- Affan MIF, Rahardjo HE, Widia F. Gynecological malignancy with obstructive uropathy patient profile in Cipto Mangunkusumo Hospital: Our 2-year experience. *Bali MedJ*. 2021;10(3):1133–7
- Springer JE, Doumouras AG, Lethbridge S, Forbes S, Eskicioglu C. A Provincial Assessment of the Barriers and Utilization of Enhanced Recovery After Colorectal Surgery. *Journal of Surgical Research*. 2019 Mar 1;235:521–8.
- Pickens RC, Cochran AR, Lyman WB, King L, Iannitti DA, Martinie JB, et al. Impact of Multidisciplinary Audit of Enhanced Recovery After Surgery (ERAS)® Programs at a Single Institution. *World Journal of Surgery*. 2021 Jan 1;45(1):23–32.
- Nabhani J, Ahmadi H, Schuckman AK, Cai J, Miranda G, Djaladat H, et al. Cost Analysis of the Enhanced Recovery After Surgery Protocol in Patients Undergoing Radical Cystectomy for Bladder Cancer. *European Urology Focus*. 2016 Apr 1;2(1):92–6.



This work is licensed under a Creative Commons Attribution