

# Enhanced Recovery Protocol After Radical Cystectomy for Urinary Bladder Cancer at The Prince Hussein Urology Center.

*Dr.Ashraf AL-Majali MD\*, Tareq AL-Nasser, MD\*, Dr. Bilal Abu-Naja MD\*, Dr.Mohammad AL-Qudah MD\*, Mutaz AL-Atoum MD\*, Motasem Smadi, MD\*, Dr. Firas Khorri MD\*, Dr. Ahmad AL-Hiari MD\*, Dr.Mohammad Abd AL-Dyeam MD\*, Anees AL-Hjazeen RN\*\*, Dr.Mohanad Naser MD\**

## ABSTRACT

**Objectives:** The main objective of this study was to evaluate the effect of Enhance Recovery After Surgery (ERAS) on radical cystectomy for muscle invasive bladder cancer, including hospital stay, the early mobilization, and the complications.

**Methods and materials:** Retrospectively, 400 medical files were reviewed for patients who underwent radical cystectomy with ileal conduit in the Prince Hussein Urology Center between May 2011 and March 2020. These files were divided into two teams (group-1: 187 patients underwent radical cystectomy with application of the ERAS protocol; group-2: 213 patients underwent radical cystectomy without the ERAS protocol. Pre, peri and postoperative parameters of both teams were compared. The ERAS elements were bowel preparation, carbohydrate loading, body warming and regional anesthesia, the decrease of drains use, early postoperative mobilization, early oral feeding with nasogastric tube removal. Follow-up amount was from 1<sup>st</sup> day to 90-days postoperatively.

**Results:** concerning the demographic data of both groups (age, gender, and body mass index), there have been no vital variations (The P value was greater than “0.05”). On the opposite hand, there have been significant differences in respect to the categorical data (hospital stay, early mobilization, the quality of hospital stays, postoperative complications, readmission rates, operative time, blood transfusion rates, and hospitalization costs) (The P-value was lower than “0.05”)

**Conclusion:** The ERAS protocol plays an effective role in decreasing patients’ hospital stays and costs, complication rates, readmission rates, operative time, and blood transfusion rates. Also, it increases the early mobilization rate and the quality of hospital stays.

**Keywords:** Radical cystectomy, Enhanced Recovery after Surgery, hospital stay, post-operative complications.

**RMS December 2023; 30 (3): 10.12816/0061655**

## Introduction

Radical cystectomy has proved to be the most suitable choice for muscle invasive bladder cancer; this kind of cancer mainly occurs in the elderly comorbid patients with a mean age of sixty-eight years. The early complications of this surgery (during hospitalization or within the period of the thirty days of surgery) accounts for 20-57% (1). Also, bladder cancer patients are exposed to extend the danger of specific nutrients deficiencies on account of the cancer itself (2); therefore, patients at a nutritional process risk are increasingly susceptible to complications upon major urological procedures (3).

From the Departments of:

\*Nephrology and urology.

\*\*registered nurse.

Correspondence to be addressed to Dr Mohand Naser.M Mohandnaser1970@gmail.com Tel +962772048848

Consequently, wonderful perioperative management could contribute to the interference of morbidity and mortality of RC (4). This results in the employment of enhanced recovery after surgery (the ERAS) protocols which are multimodal perioperative care pathways which are designed to attain early recovery after surgical procedures by maintaining preoperative organ function and reducing the profound stress response following surgery. The key elements of the ERAS protocols include: preoperative counselling, the improvement of nutrition, standardized analgesic and anesthetic regimens and early mobilization (5).

Due to the best morbidity that are related to the RC among all urological surgical procedures, enhanced recovery after surgery (the ERAS) protocols will facilitate to reduce the surgical stress response which is caused by radical cystectomy (6). With time, there have been several enhancements in the ERAS protocols to boost the first recovery hospital keeping the post major abdominal procedures (7, 8). Moreover, the use of the ERAS protocols pre, intra and postoperative for radical cystectomy patients was suggested (9). Finally, the ERAS protocols for radical cystectomy were found cost-effective in 30-days prices which are relative to straightforward management (10).

We tend to hypothesize that the ERAS protocols would improve the nutritional status of radical cystectomy patients, and therefore, patients' care, and decreasing complications beside the hospital stays.

## **Materials and methods**

The Enrollment of four hundred patients who underwent between May 2011 and March 2020 in the Prince Hussein Urology Center. Among these patients, 187 patients underwent the RC with the ERAS protocol being applied starting from the year 2014 till March 2020 (the ERAS was initially applied in our center in June 2014), while the other 213 patients underwent the RC starting from May 2011 to August 2019 without undergoing the ERAS protocol.

The ages of these patients were between (38 and 76 years), whereas the inclusion criteria were: patients with correctable clotting profile, normal kidney function tests, controlled diabetes mellites and hypertension; The exclusion criteria were: the existence of another malignancy either urological or gastrointestinal, inflammatory bowel disease (IBD), previous major abdominal surgery or radiotherapy that prevent the establishment of the ileal conduit and patients with advanced bladder cancer.

All patients got antibiotics like cephalosporins (second or third generation) to cover gram +ve and -ve bacteria plus metronidazole for anaerobes or ertapenem (Invanz) preoperatively. The follow-up amount of all patients was between the primary day to ninety days postoperatively.

The hospital stays and the times of early ambulation postoperatively, quality of hospital stays, postoperative complications, readmission rates, operative times, blood transfusion rates and hospitalization prices between each team were all compared.

### *The ERAS protocol*

There have been three components of this protocol:

- 1- Preoperatively: the data was given to the patients regarding surgical and anesthetic procedures, stoma siting education, mechanical bowel preparation ( preoperative mechanical bowel preparation including a clear liquid diet, and an enema before surgery), medical optimization (albumin level), smoking cessation four weeks before assigned time of surgery, anticoagulation like: Clexan was given one day before surgery (at

6 p.m.) and stocking application. Within the day of surgery; fasting to food before six hours. However, to water before two hours. Carbohydrate loading and antibiotics before one hour. Before the skin incision (ertapenem (Invanz) 1 gr intramuscularly or intravenously) was applied.

- 2- Intraoperatively: epidural anesthesia, body warming, drains, ileal conduit catheter, and wound infiltration.
- 3- Postoperatively: On Day "0": observing nausea and vomiting, epidural anesthesia, parenteral analgesia, oral analgesia, oral fluids, set outside bed in two hours. Gum chewing and NG tube removal. On Day One: observing nausea and vomiting, blood count and kidney function tests, oral fluid, then soft gastric diet, early walk for six hours., chest physiotherapy, oral analgesia, non-oral analgesia (PCA; patient control analgesia, IM, IV), lactulose 15 ml x 2, ileal conduit catheter and energy drink (Ensure) 50 ml x 2. On Day Two: regular diet, stop non-oral analgesia, notice if patient passed flatus or stool and encourage a lot of ambulation. On Day Three: noticing flatus or stool and discharge to home if patient ingestion and drinking are well, walking, passed flatus or stool, no pain and no fever. On Day Four: the same as Day-3. (Criteria for discharge are: no fever, no vomiting, normal white blood count, tolerating diet, good urine output and passed flatus).

The non-ERAS group protocol includes the following: -

- 1- Preoperative measures consisted of a liquid diet and 12 hours fasting the day before surgery,
- 2- An oral mechanical bowel preparation was performed in the day before surgery.
- 3- The NGT was kept in place normally at least 3 days or until return of bowel function.
- 4- The liquid intake was normal during surgery.
- 5- Intraoperative antimicrobial prophylaxis was made with cephalosporin before surgery and at least 7 to 10 days after surgery. After surgery.
- 6- Patients received no fluids by oral intake; pain medication was administered intravenously (I.V.) using mostly non-opioid drugs.
- 7- Mobilization was mostly started after pain relief from surgery, after at least 2 to 3 days.
- 8- A normal diet was started after return of bowel movement.

## Statistics

Statistical analysis in relevance to the previously mentioned variables between every team was done by using the SPSS computer program version-24; the results were expressed as mean  $\pm$  SD (standard deviation) or number, the comparison between the mean values of both groups continuous clinical variables was carried out by using Mann-Whitney U test. The Comparison between both groups regarding the categorical data (N (%)) was performed by the chi-square test. The P-value  $< 0.05$  was considered statistically significant.

We have attained approval from our institution in the Royal Medical Services ethical committee for publication.

## Results

In total, 400 patients were enclosed during this study (the ERAS group n= 187; non- the ERAS group n=213). The demographic data (ages, genders, and body mass indexes) between both had of no significant differences; (the P value is worth = 0.065, 0.073, 0.096, respectively). Cluster one ages (38- 72 years), whereas group-2 (41-76 years). Body mass indexes in the ERAS group (24-31 kg/m<sup>2</sup>), while within the different groups it was (23.4-32.1 k/m<sup>2</sup>). Table I. The significant P value under 0.05.

**Table I:** demographic data.

Variables	Group-1 (the ERAS)	Group-2 (the non-ERAS)	the “P” value
Ages (mean± SD©)	(54.64±7.76)	(57.27±8.94)	0.0653
Gender (N*\%) male	101(54%)	108(51%)	0.0733
Gender (N *\%) female	86(46%)	105(49%)	
Body mass index (BMI) (mean± SD)	(26.87±1.37)	(26.89±1.81)	0.0962

N\*: stands for the number of the patients

SD©: stands for standard deviation

In Table II, the comparison was created between each team concerning the hospital stays, the time of early mobilization, the quality of hospital stays, the postoperative complications; vomiting, urine leak, intestinal obstruction, urinary tract infection, deep venous thrombosis (according to Clavien-Dindo classification of surgical complications), readmission rates, operative times and the blood transfusion rates). The significant P value was lower than 0.05. Concerning hospitalization costs, we estimated it to be lower from over all stay length in hospital but exact numbers is not available as military hospital. The ERAS group used dramatically less opioids overall and on each postoperative day. Overall complication rates were lower the ERAS group compared to the historical control group.

Fever was the most common reason for readmission, accounting for 57% of all readmissions. Other causes were abdominal pain and/or gastrointestinal symptoms (25%), dyspnea or chest pain and flank pain

**Table II:** the categorical data of both groups and the comparison.

Variables	Group-1 (the ERAS)	Group-2 (the non-ERAS)	the “P” value
The time for early ambulation \hrs. (mean± SD*)	(10±1.4)	(56.2±4.8)	0.012
Hospital stays\ days (mean ± SD)	(4.5±1.6)	(7.8±2.1)	0.033
Quality of hospital stays (Without complications) (n©\%)	(166\89%)	(170\80%)	0.009
Readmission rates (n\%)	(16\8.5%)	(43\20.1%)	0.026
30 days	(10\5.3%)	(28\13.1%)	
90 days	(6\3.2%)	(15\7%)	
Blood transfusion rates (n\%)	(18\9.6%)	(35\16.4%)	0.0153
Operative times \min. (mean ± SD)	(266 ±27.8)	(283± 32.3)	0.021
Complication rates (regarding Clavien-Dindo classification) (n\%)			0.031
Grade I			
Grade II			
Grade III a, b	(8\4.2%)	(15\7%)	
Grade IV a, b	(13\6.9%)	(27\12.7%)	
Grade V	(2\1%)	(6\2.8%)	
	-	-	

## DISCUSSION

There have been significant differences between patients who underwent ERAS and those who did not had the ERAS in terms of the time of early ambulation, hospital stays, the quality of hospital stays, operative times, the blood transfusion rates, readmissions, the hospital costs and the complication rates were all in favor of group-1 (the ERAS) (the P value lower than 0.05). In our study, median length of stay decreased from 8 days in the historical control group to 5 days in the ERAS group, to the benefit of patients who would rather be at home and to the benefit of the healthcare system in terms of cost and resource utilization.

The same findings were reported by Chunxiao Wei and colleagues in the year 2018 with significant leads with regard to patients' rehabilitation, readmissions, costs <sup>(11)</sup>, hospital stays <sup>(12)</sup>, and postoperative complications <sup>(13)</sup>. Therefore, the expansion of the idea of the ERAS protocol with a significant variation of surgical procedures was recommended <sup>(14)</sup>.

Regarding Gastrointestinal (GI) complications; the ERAS protocol decreases these complications <sup>(15)</sup> by expedites bowel function recovery <sup>(16)</sup> through a big reduction within the time to the primary flatus, the time of the first stool and the time of a standard diet <sup>(17)</sup>, and so decrease the GI interventionism by reducing the requirement for nasogastric tubing and total parenteral nutrition besides the reduction of orotracheal intubation for mechanical ventilation <sup>(18)</sup>. Reduced paralytic ileus and cardiovascular complications were also noticed <sup>(19)</sup>.

Within the different hand, some studies reported that ERAS have not nevertheless been widely-enforced in urology and the proof for individual interventions is restricted or unavailable <sup>(20)</sup>; therefore, a lot and expanded studies are required to prove the efficacy of the ERAS for patients undergoing Open RC <sup>(21)</sup>. Also, H. Djaladat and associates reported that sadly despite the use of an ERAS protocol, the major and minor complication rates were high. The readmission with infectious complications being the foremost common reason for readmission. Thus, the minimum of during the study of open radical cystectomy with urinary diversion still has high complication and readmission rates even with an ERAS protocol <sup>(22)</sup>.

Robotic radical cystectomy conjointly had an opportunity for the ERAS protocol and it was found that the patient undergoing robotic radical cystectomy is probably going to boost morbidity and mortality, and shorten the hospital keep <sup>(23)</sup>.

Several small studies evaluating elements of the ERAS care pathways in RC found benefits in postoperative morbidity, return to bowel function (Roth et al. 2013; Jensen et al. 2015; Lee et al. 2014). A few studies of early fast track, multimodal, or enhanced recovery programs have also been published, showing improvements in length of stay, time to GI recovery, and post-operative ileus (Maffezzini et al. 2007; Arumainayagam et al. 2008; Pruthi et al. 2010; Bazargani et al. 2017; Daneshmand et al. 2014; Baack Kukreja et al. 2017). Adding anesthesia-related elements to an existing surgical enhanced recovery program reduced transfusions and nausea, while continuing to demonstrate good results in time to GI recovery and length of stay (Patel et al. 2018). Reviews and meta-analyses of these early studies have shown similar improvements in length of stay and return of bowel function with no change or an improvement in complications (Di Rollo et al. 2015; Mir et al. 2015; Tyson and Chang 2016).

Finally, the protocol is not a substitute for major urological surgeries, neither is it a method of imposing patients to be discharged sooner to receive their postoperative care within the home. It is an associate degree evidence-based protocol designed to boost the patients' expertise and recovery from cystectomy <sup>(24)</sup>.

## CONCLUSION

The ERAS protocol once was utilized in major urological procedures like Radical cystectomy; it decreases the hospital stays, the readmission rates, the hospital costs, the post-operative complications and will increase the standard of patients' recovery with early walk and quick come back of bowel habits, and so probably reducing health care expenditure. We tend to advise the employment of the ERAS protocol with major urological procedures because it has been proved based mostly protocol for the enhance recovery upon these surgeries.

## References

- 1- Shabsigh A, Korets R, Vora KC, Brooks CM, Cronin AM, Savage C, Raj G, Bochner BH, Dalbagni G, Herr HW, Donat SM. Defining early morbidity of radical cystectomy for patients with bladder cancer using a standardized reporting methodology. *Eur Urol.* 2009 Jan;55(1):164-74. doi: 10.1016/j.eururo.2008.07.031. Epub 2008 Jul 18. PMID: 18675501.
- 2- Michel C, Robertson HL, Camargo J, Hamilton-Reeves JM. Nutrition risk and assessment process in patients with bladder cancer undergoing radical cystectomy. *Urol Oncol.* 2020 Sep;38(9):719-724. doi: 10.1016/j.urolonc.2020.02.019. Epub 2020 Mar 17. PMID: 32192890; PMCID: PMC7438246.
- 3- Cerantola Y, Valerio M, Hubner M, Iglesias K, Vaucher L, Jichlinski P. Are patients at nutritional risk more prone to complications after major urological surgery? *J Urol.* 2013 Dec;190(6):2126-32. doi: 10.1016/j.juro.2013.06.111. Epub 2013 Jun 29. PMID: 23820054.
- 4- Froehner M, Brausi MA, Herr HW, Muto G, Studer UE. Complications following radical cystectomy for bladder cancer in the elderly. *Eur Urol.* 2009 Sep;56(3):443-54. doi: 10.1016/j.eururo.2009.05.008. Epub 2009 May 18. PMID: 19481861.
- 5- Melnyk M, Casey RG, Black P, Koupparis AJ. Enhanced recovery after surgery (ERAS) protocols: Time to change practice? *Can Urol Assoc J.* 2011;5(5):342-348. doi:10.5489/cuaj.11002.
- 6- Mertens E, Zargar H. Enhanced Recovery after Surgery (ERAS) Protocols after Radical Cystectomy: Existing Barriers and Promising new Developments. *SRL Urol.* 2015;1(1): 006-008.
- 7- Koupparis A, Dunn J, & Rowe GE. (2009). Improvement of an enhanced recovery protocol for radical cystectomy. *British Journal of Medical & Surgical Urology*, 3, 237-240.
- 8- Smith J, Meng ZW, Lockyer R, Dudderidge T, McGrath J, Hayes M, Birch B. Evolution of the Southampton Enhanced Recovery Programme for radical cystectomy and the aggregation of marginal gains. *BJU Int.* 2014 Sep;114(3):375-83. doi: 10.1111/bju.12644. Epub 2014 Jul 27. PMID: 24467630.
- 9- Mir MC, Zargar H, Bolton DM, Murphy DG, Lawrentschuk N. Enhanced Recovery After Surgery protocols for radical cystectomy surgery: review of current evidence and local protocols. *ANZ J Surg.* 2015 Jul-Aug;85(7-8):514-20. doi: 10.1111/ans.13043. Epub 2015 Mar 17. PMID: 25781409.
- 10- Nabhani J, Ahmadi H, Schuckman AK, Cai J, Miranda G, Djaladat H, Daneshmand S. Cost Analysis of the Enhanced Recovery After Surgery Protocol in Patients Undergoing Radical Cystectomy for Bladder Cancer. *Eur Urol Focus.* 2016 Apr;2(1):92-96. doi: 10.1016/j.euf.2015.06.009. Epub 2015 Jul 3. PMID: 28723457.
- 11- 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 Dec;46(12):5011-5018. doi: 10.1177/0300060518789035. Epub 2018 Aug 8. PMID: 30088432; PMCID: PMC6300971.
- 12- Pozo C, Shariat SF, D'Andrea D, Fajkovic H, Abufaraj M. Enhanced Recovery after Radical Cystectomy. *Curr Opin Urol.* 2019 May;29(3):227-238. doi: 10.1097/MOU.0000000000000594. PMID: 30950886.
- 13- Tyson MD, Chang SS. Enhanced Recovery Pathways Versus Standard Care After Cystectomy: A Meta-analysis of the Effect on Perioperative Outcomes. *Eur Urol.* 2016 Dec;70(6):995-1003. doi: 10.1016/j.eururo.2016.05.031. Epub 2016 Jun 11. PMID: 27297680; PMCID: PMC5149115.

- 14- Dunkman WJ, Manning MW, Whittle J, Hunting J, Rampersaud EN, Inman BA, Thacker JK, Miller TE. Impact of an enhanced recovery pathway on length of stay and complications in elective radical cystectomy: a before and after cohort study. *Perioper Med (Lond)*. 2019 Aug 22; 8:9. doi: 10.1186/s13741-019-0120-4. PMID: 31440369; PMCID: PMC6704620.
- 15- Bazargani ST, Djaladat H, Ahmadi H, Miranda G, Cai J, Schuckman AK, Daneshmand S. Gastrointestinal Complications Following Radical Cystectomy Using Enhanced Recovery Protocol. *Eur Urol Focus*. 2018 Dec;4(6):889-894. doi: 10.1016/j.euf.2017.04.003. Epub 2017 Apr 25. PMID: 28753885.
- 16- Daneshmand S, Ahmadi H, Schuckman AK, Mitra AP, Cai J, Miranda G, Djaladat H. Enhanced recovery protocol after radical cystectomy for bladder cancer. *J Urol*. 2014 Jul;192(1):50-5. doi: 10.1016/j.juro.2014.01.097. Epub 2014 Feb 8. PMID: 24518775.
- 17- Vlad O, Catalin B, Mihai H, et al. Enhanced recovery after surgery (ERAS) protocols in patients undergoing radical cystectomy with ileal urinary diversions: A randomized controlled trial. *Medicine (Baltimore)*. 2020;99(27): e20902. doi:10.1097/MD.00000000000020902
- 18- Casans-Francés R, Roberto-Alcácer AT, García-Lecina AC, Ferrer-Ferrer ML, Subirá-Ríos J, Guillén-Antón J. Impact of an enhanced recovery after surgery programme in radical cystectomy. A cohort-comparative study. *Rev EspAnesthesiolReanim*. 2017 Jun-Jul;64(6):313-322. English, Spanish. doi: 10.1016/j.redar.2016.12.002. Epub 2017 Feb 14. PMID: 28214097.
- 19- Xiao J, Wang M, He W, Wang J, Yang F, Ma XY, Zang Y, Yang CG, Yu G, Wang ZH, Ye ZQ. Does Postoperative Rehabilitation for Radical Cystectomy Call for Enhanced Recovery after Surgery? A Systematic Review and Meta-analysis. *Curr Med Sci*. 2019 Feb;39(1):99-110. doi: 10.1007/s11596-019-2006-6. Epub 2019 Mar 13. PMID: 30868498.
- 20- Cerantola Y, Valerio M, Persson B, Jichlinski P, Ljungqvist O, Hubner M, Kassouf W, Muller S, Baldini G, Carli F, Naesheimh T, Ytrebo L, Revhaug A, Lassen K, Knutsen T, Aarseth E, Wiklund P, Patel HR. Guidelines for perioperative care after radical cystectomy for bladder cancer: Enhanced Recovery After Surgery (ERAS (®)) society recommendations. *Clin Nutr*. 2013 Dec;32(6):879-87. doi: 10.1016/j.clnu.2013.09.014. Epub 2013 Oct 17. PMID: 24189391.
- 21- Persson B, Carringer M, Andrén O, Andersson SO, Carlsson J, Ljungqvist O. Initial experiences with the enhanced recovery after surgery (ERAS) protocol in open radical cystectomy. *Scand J Urol*. 2015;49(4):302-7. doi: 10.3109/21681805.2015.1004641. Epub 2015 Feb 7. PMID: 25660105.
- 22- Djaladat H, Katebian B, Bazargani ST, Miranda G, Cai J, Schuckman AK, Daneshmand S. 90-Day complication rate in patients undergoing radical cystectomy with enhanced recovery protocol: a prospective cohort study. *World J Urol*. 2017 Jun;35(6):907-911. doi: 10.1007/s00345-016-1950-z. Epub 2016 Oct 12. PMID: 27734131.
- 23- Frith, Clarie &Wakelam, James & Vasdev, Nikhil & Boustead, Gregory & Adshead, James & Lane, Tim & Gowrie-Mohan, Shan. (2014). The role of an enhanced recovery protocol in patients undergoing Robotic Radical Cystectomy. *UROLOGY NEWS VOLUME 18 ISSUE 5 JUNE 2014*.
- 24- Djaladat H, Daneshmand S. Enhanced recovery pathway following radical cystectomy. *CurrOpin Urol*. 2014 Mar;24(2):135-9. doi: 10.1097/MOU.0000000000000027. PMID: 24378979.