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Review article

Early recovery protocol in patients undergoing laparoscopic radical cystectomy

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ABSTRACT

Introduction: The Enhanced Recovery After Surgery program (ERAS), has become the basis of perioperative management after colorectal surgery, vascular, thoracic, and more recently the radical cystectomy. The aim of this study is to show our initial experience using an ERAS protocol.

Materials and methods: A total of 47 laparoscopic radical cystectomies (LRC) were compared in this study. For retrospective data analysis, the patients were divided into two groups: Group A included patients who underwent LRC before the ERAS protocol was implemented; and Group B included patients who underwent LRC after the ERAS protocol was implemented.

Results: Hospital stay was significantly shorter ($p = 0,04$) in Group B with a median of 11.73 days versus 17.53 days in Group A. The paralytic ileus is the most common complication in both groups, and only two complications seem to be lower between groups; central vein catheter infection in Group A was 14.2% versus 5.2% in Group B and paralytic ileus in Group A was 35.7% versus 21.0% in Group B. There was no statistical difference between groups in the appearance of minor or major complications.

Conclusion: The combination of minimally invasive surgery and an ERAS protocol is a feasible multidisciplinary challenge and is useful in the recovery of patients undergoing LRC.

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1. Introduction

Radical cystectomy remains nowadays the treatment of choice for localized muscle-invasive bladder cancer (MIBC). Laparoscopic radical cystectomy (LRC) and robotic-assisted laparoscopic cystectomy have been shown to be feasible both in male and female patients.¹ The benefits of the minimal invasive approaches such as the laparoscopic approach has been demonstrated in decreased length of stay, intraoperative blood loss, postoperative pain, and recovery. However, according to the European Association of Urology in their 2013 edition,² these techniques are still experimental because of the limited number of cases reported, an absence of long-term oncological and functional outcome data, and a possible selection bias.

The Enhanced Recovery After Surgery program (ERAS) or “fast-track” program, has become the basis of perioperative management after colorectal surgery, vascular, thoracic, and more recently the radical cystectomy.^{3,4} These programs attempt to modify the physiological and psychological responses to major surgery contributing in the reduction of postsurgical complications and hospital stays and improving the cardiopulmonary and bowel function after surgery resulting in a faster recovery of patients.^{5,6} The principles of ERAS protocol include: information and advice prior to surgery to the patient, preoperative nutrition, avoiding prolonged fasting, perioperative carbohydrate loading 2 hours prior to surgery, standardized anesthetic and analgesic techniques (epidural analgesia and nonopioid), and early mobilization.

Our department started to perform LRC in 2005⁷ and since then it has been the technique of choice for the treatment of MIBC. In 2012, with collaboration of the Anesthesiology and Reanimation Department and the Nutrition Unit of our hospital, we introduced the application of an ERAS program for patients undergoing LRC

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and urinary diversion. The aim of this study is to show our initial experience.

2. Materials and methods

From January 2011 to December 2012, a total of 47 LRC with ileal conduit urinary diversion or ileal neobladders were performed in our institution. After an exhaustive search of recent literature and with the collaboration of the Department of Anesthesiology and reanimation, nutrition, and nursing staff, a modified ERAS protocol was designed. This protocol was divided into three sections: preoperative, intraoperative, and postoperative. The features of the protocol are shown in Table 1.

LRC was performed by three experienced surgeons using the technique described by Cansino et al.⁷ For retrospective data analysis the patients were divided into two groups; Group A included patients who underwent LRC before ERAS protocol was implemented and Group B included patients who underwent LRC after ERAS protocol was implemented. The main outcome measures were the duration of total hospital stay, and the intraoperative or postoperative complications.

The statistical analysis has been checked by a statistician. Comparative analysis between groups was made using the non-parametric test Mann–Whitney *U* test and Chi-square test with Fisher's exact test used for categorical measures. Statistical analysis was performed using the SPSS 20 system (SPSS Inc., Chicago, IL, USA). Results are expressed as *n* (%) or median \pm standard deviation.

3. Results

The demographic and clinical characteristics of both groups are shown in Table 2. There were no significant differences between them in the demographic and clinical variables assessed in this study.

The hospital length stay was significantly lower ($p = 0.04$) in Group B (ERAS group) with a median of 11.73 days (range 5–19) versus 17.53 days (range 12–22) in Group A (no ERAS group).

Table 1
Modified ERAS protocol.

Preoperative	
1.	Preadmission counseling.
2.	Fluid and carbohydrate loading: 2 teaspoons of sugar in clear liquids 8 h and 2 h prior to surgery.
3.	No prolonged fasting: solid food intake up to 8 h prior to surgery and liquids up to 2 h prior to anesthetic induction.
4.	No selective bowel preparation: only a fleet enema is used the day prior to surgery.
5.	Antibiotic prophylaxis: amoxicillin clavulanate 2 g 30 min prior to anesthetic induction.
6.	Thromboprophylaxis: bemparin 3.500 IU subcutaneous 12 h prior to surgery, maintained until 15 d to 1 mo post-surgery.
Intraoperative	
1.	Short-acting anesthetic agents.
2.	Epidural anesthesia/analgesia.
3.	Maintenance of normothermia: body warmer.
4.	Maintenance of normovolemia
Postoperative	
1.	No nasogastric tube.
2.	No parenteral nutrition.
3.	Use of prokinetic agents: metoclopramide 10 mg every 8 h.
4.	Early oral nutrition: the 1 st d or 2 nd d after surgery only water. Then the progression of the diet depends on the evolution of each patient.
5.	Avoid opioid analgesia.
6.	Early mobilization.
7.	Usage of chewing gum.

ERAS = enhanced recovery after surgery.

Table 2
Demographic, surgical, and pathological findings.

	Patients' data		
	Group A	Group B	<i>p</i>
ERAS protocol	No	Yes	—
No.	28	19	—
Age, y; median (SD)	65.82 (10.390)	64.22 (11.058)	0.588
Ileal conduit	22	15	0.365
Neobladder	6	4	0.178
Surgical data (median)			
Surgery time	341 min	340 min	0.652
Estimated blood lost	270 cc	260 cc	0.588
Pathological state			
pT0–pT1	4	3	0.658
pT2	5	4	0.515
pT3	11	8	0.588
pT4	8	4	0.457
pNx	4	3	0.167
pN+	9	6	0.658
pN–	15	10	0.452
M0	0	0	—
M1	0	0	—

ERAS = enhanced recovery after surgery.

The appearance of minor or major complications and the division into intra- and postoperative complications are shown in Table 3. Complications included were: (1) *infectious*: from wound infection to sepsis; (2) *thrombotic*: deep vein thrombosis, pulmonary thromboembolism; (3) *hemorrhagic*: transfusion; (4) *others*: paralytic ileus, evisceration, intestinal dehiscence, urine leak, and fistulae. It is remarkable that the most common complication in both groups is the paralytic ileus, and only two complications seem to be lower between groups: the central vein catheter infection in Group A was 14.2% versus 5.2% in Group B and paralytic ileus in Group A was 35.7% versus 21.0% in Group B, but there was no statistical difference between the groups.

4. Discussion

Nowadays, there are few studies based on the use of ERAS protocol in urological surgery. ERAS protocols or “fast-track” guidelines in urology have been introduced in the past decade. Arumainayagam et al.³ in 2008 implemented an ERAS protocol and it led to a significant reduction in hospital stays and equivalent morbidity in patients undergoing radical cystectomy compared with traditional clinical guidelines or protocols.

Pruthi et al.⁸ reported the introduction of ERAS protocol after radical cystectomy in 262 patients. When compared with historical controls, the most recent 100 patients had better postoperative

Table 3
Complications.

Complications	Group A	Group B	<i>p</i>
Infections			
Wound infection	0	0	—
Central vein catheter infection	4	1	0.1
Pneumonia	0	0	—
Sepsis	1	0	0.5
Thrombotic			
Deep vein thrombosis pulmonary	0	0	—
Thromboembolism	0	0	—
Transfusion	2	1	0.6
Paralytic ileus	10	4	0.2
Evisceration	0	0	—
Intestinal dehiscence	1	0	0.4
Urine leak	0	1	0.4
Fistulae	0	1	0.4

recoveries. Donat et al⁹ combined early nasogastric tube removal with metoclopramide in 27 patients compared with 54 controls. Complication rates were similar in both groups, but the intervention group had an earlier return to bowel sounds and tolerance of diet. These studies support our findings; our study shows a statistically significant shorter hospital stay in the ERAS protocol group.

Current ERAS protocols include >20 items,⁴ in our study we used 17 of them (Table 1). In other ERAS studies^{3,8} no more than 10 items were used. Current standardized ERAS protocol is based on colorectal surgery,¹⁰ this means that some of these interventions cannot be extrapolated into radical cystectomy. For example, we did not use in our protocol the avoidance of suction drainage of the peritoneal cavity. After colorectal procedures this maneuver results in comparable anastomotic leak and overall outcomes rates between groups of patients using or not ERAS protocols, thus the placement of drainage may be safely avoided.¹¹ No specific study to radical cystectomy is available regarding this issue. Due to the added risk of urinary leak, the results from colorectal surgery might not apply to radical cystectomy patients.

Another item that we did not use in our protocol is the early removal of the transurethral bladder catheter. In this aspect, Mattei et al¹² randomized patients with orthotopic ileal bladder substitution and patients with ileal conduit in two groups. Patients in Group 1 had their urethral stents removed between Day 5 and Day 10, whereas patients in Group 2 had the stents removed directly after completion of the uretero-ileal anastomosis. Stenting resulted in improved drainage of the upper urinary tract, improved bowel recovery, and reduced occurrence of metabolic acidosis. The optimal duration of urethral stenting has not been investigated. In our study, after the discharge of patients the urethral stent was maintained during the 1st month in the case of heterotopic urinary diversion and the bladder catheter was maintained for 15 days in the case of orthotopic urinary diversion.

We have not found any studies in urology surgery using ERAS protocol in laparoscopic or robotic approaches. The usage of minimally invasive approaches is included in the 22 items of the ERAS society recommendations.¹¹ Minimally invasive pelvic surgery has been shown to decrease the inflammatory response when compared to the open approach. Recently, laparoscopic and robotic radical cystectomy has been increasingly performed in the treatment of bladder cancer and merits special consideration. While open radical cystectomy and pelvic lymph node dissection remains the gold standard in treating nonmetastatic muscle invasive bladder cancer,² this major surgery is still associated with high morbidity close to 70% in some series.¹³ Numerous centers have reported in recent years their experience with the laparoscopic or robotic approach.^{7,14–17} Unfortunately, most of these studies report retrospective data or prospective comparative data, and high quality randomized controlled trials are lacking. Despite these limitations, laparoscopic and robot-assisted radical cystectomy seems to be associated with lower overall perioperative complications, shorter hospital stay, with equivalent short term oncological safety. Future high quality, high volume controlled studies should help in reaching definitive conclusions.

One of the reduced complications seen in the ERAS protocol group in our study is the paralytic ileus (Group A = 35.7% vs. Group B = 21.0%); intestinal complications are one of the most common problems after radical cystectomy.¹⁸ The etiology of ileus is multifactorial, with a combination of central and peripheral nervous systems, hormonal influences, neurotransmitter, and local inflammatory pathways. Surgical stress, bowel manipulation, opioids, and intraoperative fluids can break the standard homeostasis in the gastrointestinal tract and produce postoperative ileus and impaired function of gastrointestinal absorption. Factors that help to reduce this are epidural anesthesia,¹⁹ minimally invasive surgery, fine

tissue manipulation, avoiding fluid overload, and early oral feeding.^{8,9} In addition, the routine use of nasogastric tube decompression should be avoided after surgery by the higher incidence of fever, atelectasis, and pneumonia in patients who carry it, and any nasogastric tube used during surgery should be removed prior to extubation.⁸

Chewing gum has been used with the intention of improving the recovery of bowel motility. The usage of chewing gum in the postoperative period has been described as a form of “false feeding”.²⁰ We hypothesized that chewing gum increases vagal stimulation leading to increased gastric motility and reducing inhibitory impulses of the sympathetic nervous system. As a result of the vagal stimulation the secretion of gastrointestinal hormones (gastrin, neurotensin, cholecystokinin, and pancreatic polypeptide) increases, producing vagal stimulation of the smooth muscle. Gum chewing is a simple, inexpensive, and harmless intervention for early recovery of bowel function after radical cystectomy.²¹

There are important and noteworthy limitations in our current study. Our cohort is small, and although there is a difference in some complications such as paralytic ileus, it is not statistically significant. Larger cohorts with the open approach have helped to confirm our findings, but this is the first study describing an ERAS protocol in LRC, and we certainly expect ongoing modifications to the current ERAS protocol as novel evidence-based studies are reported and validated, and we hope to stimulate other surgeons to help improving the experience in this field.²²

5. Conclusion

The combination of minimally invasive surgery and an ERAS protocol is a feasible multidisciplinary challenge and is useful in the recovery of patients undergoing LRC, demonstrated by a shorter hospital stay without increasing the risk of postoperative complications. The proposal of the usage of ERAS protocol will allow for future multicenter collaborations evaluating prospective cohorts of urological patients following identical standardized care pathways.

Conflicts of interest

None.

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