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Original Article

Feasibility, safety and effectiveness of the enhanced recovery after surgery protocol in patients undergoing liver resection

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Backgrounds/Aims: The implementation of enhanced recovery after surgery (ERAS) protocols has demonstrated significant advantages for patients by mitigating surgical stress and expediting recovery across a spectrum of surgical procedures worldwide. This investigation seeks to assess the effectiveness of the ERAS protocol specifically in the context of major liver resections within our geographical region.

Methods: Our department conducted retrospective analysis of prospectively collected data, gathered from consenting individuals who underwent liver resections from January 2018 to December 2023. The assessment encompassed baseline characteristics, preoperative indications, surgical outcomes, and postoperative complications among patients undergoing liver surgery.

Results: Among the included 184 patients (73 standard care, 111 ERAS program), the baseline characteristics were similar. Median postoperative hospital stay differed significantly: 5 days (range: 3–13 days) in ERAS, and 11 days (range: 6–22 days) in standard care ($p < 0.001$). Prophylactic abdominal drainage was less in ERAS (54.9%) than in standard care (86.3%, $p < 0.001$). Notably, in ERAS, 88.2% initiated enteral feeding orally on postoperative day 1, significantly higher than in standard care (47.9%, $p < 0.001$). Early postoperative mobilization was more common in ERAS (84.6%) than in standard care (36.9%, $p < 0.001$). Overall complication rates were 21.9% in standard care, and 8.1% in ERAS ($p = 0.004$).

Conclusions: Our investigation highlights the merits of ERAS protocol; adherence to its diverse components results in significant reduction in hospital length of stay, and reduced occurrence of postoperative complications, improving short-term recovery post liver resection.

Key Words: Enhanced recovery after surgery; Postoperative complications; Hepatectomy

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INTRODUCTION

Major abdominal surgeries have the potential to elicit significant physiological disruptions, encompassing a catabolic state, increased oxygen demand, retention of salt and water, prolonged postoperative pain, nausea, vomiting, compromised pulmonary function, delayed restoration of gastrointestinal function, and hindered mobilization [1]. According to the conventional theory of surgical stress, the surgical injury triggers survival reactions in the body, leading to various neuroendocrine responses and the mobilization of functional energy reserves, resulting in a hypermetabolic and hyper functional state [2]. This theory underscores the importance of reducing and regulating the severity of the surgical stress response, rather than outright suppression or blockage. Building upon this concept, enhanced recovery after surgery (ERAS) programs have emerged as a focal point in perioperative management. The fundamental principle of the ERAS concept involves mitigating the severity of the surgical stress response by minimizing the invasiveness of interventions [3]. Originating in the mid-90s, Prof. Henrik Kehlet conceptualized this idea of fast-track surgery, initially applied to patients undergoing colorectal surgery, resulting in significantly shortened postoperative stays [1].

Liver resection has historically been categorized as major abdominal surgery, carrying elevated risks of morbidity and mortality. In contrast to several other abdominal procedures, liver resection has emerged as an intricate surgical intervention, carrying inherent risks, such as extended surgical duration, intraoperative hemorrhage, hemodynamic instability, and significant fluid shifts. Subsequent to the procedure, potential complications may involve coagulopathy, heightened susceptibility to bleeding, pulmonary challenges, biliary leaks, and the occurrence of post-hepatectomy liver failure. The morbidity rates associated with liver resection range (12% to 46%), with mortality reaching 3% [4]. The notion of a fast-track approach in liver surgery was first introduced as early as 2008, antedating the publication of guidelines by the ERAS society that were specifically designed for patients undergoing liver resection. This approach has been deemed safe and effective, resulting in a shortened postoperative stay [5]. While ERAS programs have become the standard of care in colorectal surgery, they have also demonstrated promising outcomes across various other surgical disciplines, like upper gastrointestinal, cardiovascular, urology, gynecology, and orthopedics [6]. In hepatic surgery, individuals administered intrathecal morphine experience decreased perioperative physiological disturbances, and achieve early discharge within a few days [7].

To develop effective postoperative ERAS protocols and consistently diminish surgical complications following liver surgery, our center conducted a study. The objective was to evaluate patient outcomes after liver surgery with the implementation of enhanced recovery care principles.

MATERIALS AND METHODS

This study involves a retrospective examination of a prospectively maintained database conducted within our department, spanning January 2018 to December 2023. Following thorough informed consent procedures, a total of 184 patients were enrolled in this investigation. Ethical clearance was sought from the institutional ethical committee (IEC/SKIMS Protocol no. 248/2023). Standard protocol following liver resection was followed in 73 patients who were evaluated for a period of two years from January 2018 to December 2020. From January 2021 to December 2023, a total of 111 patients were studied after applying ERAS protocol to all these patients post liver resection. We performed all the liver resections by the open method. None of the patients was operated on by minimally invasive technique.

Patients > 18 years age who underwent liver resection for benign, as well as malignant diseases, were included in the study. All tenets of the Helsinki declaration were followed. Patients undergoing emergency surgery were excluded.

The ERAS program encompassed preoperative patient counseling and education providing information regarding the upcoming liver surgery. Cessation of preoperative smoking and alcohol was encouraged at least 4 weeks prior to surgery. The solid orals were allowed up to 6 hours, and liquid orals up to 2 hours, before anesthesia induction. All patients received a commercially available carbohydrate drink (296 mL, providing 200 Cal) two hours before surgery. No patient received any preanesthesia medication. For pain management, epidural block was given at thoracic 7–8 or 8–9 level. Anesthesia was induced with propofol, fentanyl, and rocuronium. Every patient was given antimicrobial prophylaxis (injection Cefazolin 2 g) 60 minutes before skin incision. Skin preparation was made with chlorhexidine–alcohol based solution. Patients were shifted to ward 4–6 hours postoperation from the post anesthesia care unit. Only patients with major liver resections were kept in the intensive care unit for the first 24 hours. All patients were encouraged to drink and eat from postoperation day zero. Laxatives (mainly lactulose) were used routinely from the day of surgery onwards to stimulate bowel movement. Postoperatively pain was assessed individually, and managed by round-the-clock multimodal analgesia (epidural + intravenous). On-demand analgesia was also provided to the patients. Epidural analgesia (ropivacaine 0.5%, six hourly) was used for 0–72 hours after the surgery, and patients were weaned from invasive analgesia. Ibuprofen and paracetamol were the most commonly used oral analgesic drugs, while opioids were avoided in all patients. Postoperative early ambulation defined by ambulation within first 24 hours post-surgery was applied to all patients in the ERAS group. Patients were discharged when pain was controlled with oral analgesics, independent mobilization, and tolerating orals adequately, along with no untreated surgical complications. Table 1 presents a summary of the ERAS protocol. Discharge criteria for patients under the ERAS protocol included normal or decreasing serum bilirubin levels, effective pain control through oral analgesics, the ability to tolerate solid food, and ambulation without support.

The conventional care provided to the non-ERAS group included standard practices, such as routine general anesthesia, tracheal intubation, a standard fluid regimen during surgery, and the use of intravenous opioids in the postoperative period for analgesia.

The non-ERAS cohort received traditional care, which encompassed routine Ryles Tube decompression of the stomach, a standard intraoperative fluid regimen, conventional general

Table 1. Summary of enhanced recovery protocol in liver surgery

Preoperative	Preoperative counseling education and exercise
	Avoidance of bowel preparation
	Avoidance of preanesthesia medications
	Carbohydrate loading up to 2 h before surgery
Perioperative	Antibiotic prophylaxis
	Epidural analgesia
	Short acting intravenous anesthesia drugs
	Avoidance of hypothermia
	Glycaemic control
	Goal directed intravenous fluid therapy
	No nasogastric drainage tube or early removal
	No routine prophylactic abdominal drainage
Postoperative	Avoidance of ICU stay
	Early removal of urinary catheter (within first 24 h)
	Early oral intake
	Early discontinuation of intravenous fluids
	Early ambulation
	Nausea and vomiting prophylaxis
	Multimodal analgesia

ICU, intensive care unit.

anesthesia, and postoperative utilization of intravenous analgesics or intravenous opioids. The key outcome paraments included the duration of hospital stay, the time taken for mobilization, and complications in the first month post-surgery.

Table 2. Base line demographics of patients

Variable	Standard protococl (n = 73)	ERAS protocol (n = 111)	*p*-value
Mean age (range), yr	49.3 (17–74)	48.6 (16–78)	0.15
Mean BMI, kg/m^2	24.7	25.3	
Sex			
Male	46 (63.0)	64 (57.7)	0.46
Female	27 (37.0)	47 (42.4)	0.47
Comorbidity			
HTN	25	31	0.36
DM	29	24	0.007
Obesity	3	4	0.86
COPD	34	37	0.07
Chronic liver disease	16	21	0.61
ASA			
1	13	19	0.9
2	48	74	0.89
3	12	18	0.96

Values are presented as number (%) or number only, unless otherwise indicated.
ERAS, enhanced recovery after surgery; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists.

Table 3. Diagnosis

Diagnosis	Standard protocol (n = 73)	ERAS protocol (n = 111)	*p*-value
Left lateral OCH	34 (46.5)	36 (32.4)	0.05
Left OCH	7 (9.5)	9 (8.1)	0.36
Right OCH	3 (4.1)	5 (4.5)	0.44
Right posterior OCH	1 (1.3)	4 (3.6)	0.18
Right anterior OCH	0 (0)	3 (2.7)	NA
Perihilar cholangiocarcinoma	4 (5.4)	6 (5.4)	0.49
Alveolar hydatid	7 (9.5)	9 (8.1)	0.36
Carcinoma gallbladder	17 (23.3)	39 (35.1)	0.09

Values are presented as number (%).
ERAS, enhanced recovery after surgery; OCH, oriental cholangiohepatitis; NA, not applicable.

We defined the duration of hospital stay as the time from the day of surgery to the day of discharge from the hospital. Any adverse events occurring from the time of surgery to one month post-discharge were classified as per Clavien–Dindo classification for postoperative complications.

Statistical analysis

We compared continuous variables by using the Mann–Whitney U test, while utilizing the chi-square test for the comparison of categorical data, as appropriate. Statistical significance was acknowledged when two-tailed *p*-values were below 0.05, computed using SPSS, version 28.0 (IBM Corp.).

RESULTS

The study encompassed a total of 184 patients, with 73 individuals receiving standard care, and 111 patients undergoing the ERAS program. All patients underwent liver resections by the open method. The baseline characteristics of the included

Table 4. Type of hepatic resection

Type	Standard protocol (n = 73)	ERAS protocol (n = 111)	*p*-value
Right hepatectomy	9 (12.3)	13 (11.7)	0.44
Left hepatectomy	12 (16.4)	15 (13.5)	0.58
Left lateral sectionectomy	34 (46.5)	36 (32.4)	0.05
Right anterior sectionectomy	0 (0)	3 (2.7)	NA
Right posterior sectionectomy	1 (1.3)	4 (3.6)	0.18
Central hepatectomy	0 (0)	1 (0.9)	NA
Segment 4B-5 resection/Wedge resection	17 (23.3)	39 (35.1)	0.08

Values are presented as number (%).
ERAS, enhanced recovery after surgery; NA, not applicable.

Table 5. ERAS implementation rates

Variable	Standard protocol (n = 73)	ERAS protocol (n = 111)	*p*-value
Postoperative oral intake on POD 1	35 (47.9)	98 (88.2)	< 0.001
Early ambulation (within 24 h)	27 (36.9)	94 (84.6)	< 0.001
Prophylactic drains	63 (86.3)	61 (54.9)	< 0.001
Nasogastric tube drainage	46 (63.0)	11 (10.0)	< 0.0001
Postoperative nausea vomiting	59 (80.8)	24 (21.6)	< 0.0001

Values are presented as number (%).
ERAS, enhanced recovery after surgery; POD 1, postoperative day 1.

patients in the two groups were similar, and are detailed in Table 2. Table 3, 4 present information regarding the preoperative diagnosis and type of liver resection, respectively.

In the ERAS group, a noteworthy 88.2% of patients initiated enteral feeding on postoperative day 1 (POD 1), exclusively through the oral route. This percentage was significantly higher than the corresponding figure in the standard protocol group, where only 47.9% began enteral feeding on POD 1 ($p < 0.001$). Prophylactic nasogastric intubation was avoided in a substantial majority of the ERAS group (Group 2), with only 10.0% undergoing this procedure, compared to 63.0% in the standard protocol group (Group 1) ($p < 0.0001$). Similarly, the use of prophylactic abdominal drainage was less prevalent in the ERAS group (54.9%), in comparison to the standard protocol group (86.3%), with a significant difference noted ($p < 0.001$). Likewise, a higher proportion of patients in the ERAS group (84.6%) commenced early postoperative mobilization (which was defined as of bed ambulation within the first 24 hours post-surgery), a significant contrast to the standard protocol group, where only 36.9% of patients engaged in early mobilization ($p < 0.001$). Table 5 gives the application rates of the ERAS protocol.

Specific to liver surgery, complications like post-hepatectomy hemorrhage and post-hepatic liver failure were not seen in any of the patients in either group. Postoperative bile leak was present in three and four patients in the ERAS and standard groups, respectively, which was not significant statistically. The overall complication rate in the standard and ERAS group was 21.9% and 8.1%, respectively ($p = 0.004$). In the ERAS group, the median postoperative hospital stay was 5 days (range: 3–13 days), whereas in the standard group, it was 11 days (range: 6–22 days), revealing a significant difference ($p < 0.001$). Summary of postoperative complications is depicted in Table 6.

In terms of readmissions, one patient in the ERAS group was readmitted for abdominal collections, while none in the standard care group experienced readmission; however, this difference was not statistically significant ($p > 0.05$). There was one death in the standard protocol group due to postoperative sepsis, while there was no mortality in the ERAS protocol group.

Table 6. Postoperative outcome and complications

Complication	Standard protocol (n = 73)	ERAS protocol (n = 111)	*p*-value
Post-hepatectomy haemorrhage	0 (0)	0 (0)	NA
Post-hepatectomy liver failure	0 (0)	0 (0)	NA
Intra-abdominal collection	4 (5.5)	2 (1.8)	0.08
Sepsis	5 (6.8)	2 (1.8)	0.04
Atelectasis/pneumonia	13 (17.8)	4 (3.6)	0.0006
SSI	14 (19.2)	8 (7.2)	0.007
Bile leak	4 (5.5)	3 (2.7)	0.16
Complication Clavien–Dindo ≥ 3	9 (12.3)	11 (9.9)	0.30
Over all complication	16 (21.9)	9 (8.1)	0.004
Length of stay, day	11 (6–22)	5 (3–13)	0.02
Mortality	1 (1.4)	0 (0)	NA

Values are presented as number (%) or median (range).
ERAS, enhanced recovery after surgery; SSI, surgical site infection; NA, not applicable.

DISCUSSION

The current study illustrates that incorporating an evidence-based multimodal enhanced recovery program after liver resection accelerates postoperative recovery, leading to a markedly reduced hospital stay. Individuals undergoing the ERAS protocol demonstrated the capacity to ingest fluids within 4 hours of liver resection, and resumed a regular diet on the first POD. The majority of patients regained full mobility within 3 days, resulting in the discharge of nearly half of the patients from the hospital within a 5 days timeframe. The observed decrease in the length of stay consistently correlated with a reduction in postoperative complications. Furthermore, our study emphasizes the beneficial effects of ERAS in mitigating postoperative complications following liver resection. These findings align with previous studies that suggest that ERAS facilitates recovery and yields improved perioperative outcomes across various parameters [8-10]. Consistent with the discoveries by Koea et al. [7], the reduction of perioperative fasting durations and the administration of carbohydrate drinks up to 2 hours before surgery played a role in preserving normal blood glucose levels, and alleviating sensations of thirst, hunger, and anxiety. Additionally, the meticulous control of intravenous fluids and the avoidance of bowel preparation proved effective in averting delayed gastrointestinal function, interstitial edema, compromised pulmonary compliance, and cardiac overload, ultimately mitigating stress responses and the associated complications. In theory, ERAS program encompasses three distinct phases. Considering the patient's viewpoint, comprehensive education assumes a pivotal role in preoperative care, serving as an effective strategy to aid patients and their families in understanding the cost-to-benefit ratio associated with major liver resection. In the surgical setting, goal-directed fluid therapy is indispensable, serving to maintain hemostasis, while also reducing blood loss through the regulation of central venous pressure. Postoperative care centers around the core concept of pain control [11]. The achievement of early mobilization is contingent upon effective multimodal pain management. In contrast to the conventional notion advocating rest after major hepatectomy, the ERAS program promotes early activity. This approach aims to stimulate metabolic processes, hasten gastrointestinal recovery, and reduce the risks of venous thrombosis and lung infections [12]. Our study aligns with the notion that proficient pain control facilitates early mobilization, hastens recovery, and shortens hospital stays. Early initiation of enteral nutrition postoperatively, as opposed to the traditional 'nil by mouth' approach, enhances clinical outcomes [13]. In our investigation, the ERAS group demonstrated well-tolerated oral intake of water within 4 hours after surgery, with the introduction of normal nutrition on the day following the operation. The prompt resumption of a regular diet, in conjunction with other components of the enhanced recovery program, seeks to alleviate delayed gastrointestinal function post-surgery, and may even stimulate appetite. Savikko et al. [14] studied 134 patients with open and laparoscopic liver resections. In their study, 79.1% patients were discharged by POD 5 after the implementation of the ERAS protocol the median postoperative stay was 4 days in the ERAS group, as compared to 6 days in the control group. In our study, the median postoperative hospital stay in the ERAS group was 5 days, whereas in the standard group, it was 11 days. A similar conclusion was reported by Li et al. [15] in their meta-analysis published in 2017, wherein they analyzed 524 patients, of whom 254 where in the ERAS group, and 270 in the traditional care group. This analysis also verified that the ERAS group exhibited significantly improved postoperative recovery and reduced hospital stay, and decreased complication rates, compared to the control group.

The postoperative facets of the ERAS program, implemented in our institution, cultivated a culture that prioritizes early ambulation, timely removal of drains, accelerated advancement of the diet, cessation of intravenous fluids, and heightened reliance on oral multimodal analgesia. Setting pragmatic presuppositions for patients preoperatively, particularly concerning pain management levels and minimizing reliance on opioids, is a crucial step for surgeons considering the adoption of these strategies. Based on our findings, surgeons or institutions aiming to incorporate ERAS components can initiate the process with interventions concentrating on advancing postoperative diet, encouraging activity, and providing guidance on analgesia. Huang et al. [16], in their experience from a tertiary hospital, compared 150 ERAS and 168 non-ERAS patients after hepatectomy. The postoperative hospital stay complication rates were lower in the ERAS group than in the non-ERAS group, which accords with the results in our study. The decrease in complications in the ERAS group in our study was mainly because of decrease in general postoperative complications, like atelectasis, postoperative pneumonia, and surgical site infections.

It is important to recognize several limitations inherent in this study. The retrospective nature of the study design and the relatively modest sample size introduce an inherent risk of selection bias. This concern is particularly noteworthy as all patients were drawn from a single center. The limited scope and historical data collection method may influence the generalizability of the findings, emphasizing the need for cautious interpretation and recognition of the study's inherent limitations. Another limitation of our study may be that the timing of the surgery is different between the two groups, which might have an influence on the final outcome. Additionally, there remains a need for evidence regarding the advantages of ERAS in major hepatectomy for diseased livers, such as those affected by conditions like advanced chronic liver disease, cholestatic liver, and post-chemotherapy steatohepatitis. Additional research is imperative to ascertain the generalizability of the observed results to this specific patient population. This will contribute to a more comprehensive understanding of the implications and potential broader applications of the investigated interventions or protocols.

Conclusion

Our study highlights the significant benefits of implementing an ERAS protocol for major hepatic resections. By closely adhering to the various components of the ERAS program, we observed a notable reduction in hospital stay and post-surgical complications, without compromising patient safety. Our study has unequivocally demonstrated the efficacy of ERAS in liver resection procedures, thereby alleviating any apprehensions surrounding the adoption of this protocol in such surgeries. By highlighting the favorable outcomes and safety profile linked to ERAS implementation, our study offers reassurance and motivation for its broad application in liver resections. These findings underscore the capacity of ERAS to enhance patient outcomes, and advocate its widespread adoption in clinical settings to elevate surgical care standards.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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Conceptualization: MYB. Data curation: SG, MRL. Formal analysis: YA, MJA, MFH. Methodology: MYB. Writing - original draft: MYB, YA, AP. Writing - review & editing: SA, SP.

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