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IMPLEMENTATION OF ENHANCED RECOVERY AFTER SURGERY (ERAS) PROTOCOLS IN LIVER TRANSPLANTATION

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Background. Liver transplantation (LT) is one of the most complex surgical procedures, presenting significant challenges in preoperative preparation, intraoperative management, and postoperative rehabilitation. These complexities make it demanding both technically and logistically. The introduction of enhanced recovery after surgery (ERAS) protocols has revolutionized perioperative care across numerous surgical disciplines, leading to improved patient outcomes and reduced healthcare costs. However, the application of ERAS protocols in LT remains limited and inconsistent, with considerable variation in implementation strategies across institutions. **Objective:** to summarize current knowledge and assess an overview of implementation and outcomes of ERAS protocols in LT recipients. **Materials and methods.** A structured literature search was conducted using the keywords "ERAS" and "liver transplantation" across major scientific databases. The review included a range of relevant publications, including review articles, clinical trials, observational studies, and case-control studies. **Conclusion.** ERAS protocols in LT are designed to optimize postoperative recovery, improve clinical outcomes, and minimize the risk of complications. Given the complexity and individuality of each LT case, ERAS pathways must be carefully tailored to the recipient's clinical condition, donor characteristics, and intraoperative variables.

Keywords: liver transplantation, rehabilitation, enhanced recovery after surgery, ERAS.

INTRODUCTION

Perioperative management of liver transplantation (LT) has advanced significantly in recent decades, resulting in improved patient outcomes, reduced morbidity and mortality, and enhanced quality of life [1]. Despite these achievements, the global burden of chronic liver diseases, responsible for approximately 2 million deaths worldwide annually, continues to rise [2]. As indications for LT expand, the demand for this procedure is projected to grow by 10% over the next decade, while the total cost of care is expected to rise by 50% over the next 20 years [3]. These trends underscore the need to implement enhanced recovery after surgery (ERAS) protocols in LT to accommodate the growing patient population and manage escalating healthcare costs.

The ERAS concept emerged in the 1990s [4], facilitated by advancements in minimally invasive surgical techniques, introduction of short-acting anesthetics and muscle relaxants, and the use of regional anesthesia [5]. ERAS represents a comprehensive, evidence-based, multimodal perioperative care program designed to attenuate the body's response to surgery, thereby reducing perioperative and postoperative complications. This approach facilitates shorter hospital stays without increasing readmission rates [6]. The efficacy of ERAS protocols has been well-documented across multiple surgical fields, including colorectal surgery, gynecology, and hepatobiliary surgery [7–11]. A dedicated ERAS protocol for LT was developed in 2022 [12], which was adapted and optimized from a previously developed hepatobiliary surgery protocol [13].

LT poses unique challenges for implementation of ERAS protocols due to several factors, including the severity of preoperative patient conditions [14], presence of hepatic encephalopathy [15], prolonged surgery time, high demand for perioperative blood product transfusions [16], and the need for postoperative immunosuppressive therapy [17]. These complexities have contributed to the limited adoption of ERAS protocols in LT, with most centers relying on individualized approaches that demonstrate variable success rates.

This review examines the core components of ERAS protocols in LT and highlights the key barriers to their implementation. A systematic literature search was conducted using the keywords "ERAS" and "liver transplantation". The review includes relevant clinical evidence, encompassing review papers, clinical trials, observational studies, and case-control studies.

WHICH LIVER RECIPIENTS CAN BE INCLUDED IN THE ERAS PROTOCOL?

Although ERAS protocols are increasingly adopted in liver transplant programs, patient selection criteria remain heterogeneous across centers. Nonetheless, several general considerations can help identify candidates most likely to benefit from ERAS implementation:

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Patient readiness and commitment

Successful participation in ERAS requires active patient involvement, including preoperative education and adherence to postoperative instructions. While hepatic encephalopathy may pose challenges, patients with grade 1–2 encephalopathy can generally be included in ERAS protocols [12]. The social and psychological support available to the patient is often underestimated. These factors must be carefully assessed before surgery.

Functional and nutritional status

Sarcopenia and cachexia should be ruled out, and proactive measures must be taken to optimize the patient's nutritional status [17]. Multimodal prehabilitation has emerged as an effective strategy for enhancing the physiological reserves of LT recipients [18].

Absence of cardiopulmonary dysfunction

К Severe cardiopulmonary dysfunction can significantly complicate ERAS implementation due to increased risk of perioperative complications, challenges in the administration of infusion therapy, specific requirements for anesthetic support, and reduced exercise tolerance, which can directly affect surgical outcomes [12]. Whenever feasible, ERAS protocols should be adapted to each patient's needs and risks to optimize outcomes.

Satisfactory graft function

Graft function is a critical determinant of successful LT and directly impacts the feasibility of accelerated postoperative recovery [18]. A graft with low steatosis (<30%), an adequate graft-to-recipient weight ratio (GRWR >0.8), high-quality preservation, and implantation using meticulous surgical techniques forms the foundation for favorable outcomes [18–21]. Postoperatively, adequate graft function should be evidenced by the resolution of metabolic acidosis, normalization of liver enzyme levels, and improvement in both functional and cognitive status [20].

In general, most ERAS principles can be safely applied to most LT recipients, except for patients presenting with acute liver failure. Implementation of ERAS protocols has improved postoperative outcomes in all surgical specialties [12]. The ERAS protocol can be modified or adapted to the patient's clinical condition and tailored to the requirements of the surgical team and attending physicians [12].

ACCELERATED RECOVERY IN LIVER TRANSPLANT RECIPIENTS

Building on the success of ERAS protocols in other surgical specialties, many transplant centers are now incorporating elements of accelerated recovery into perioperative patient management, even during the early stages of their LT programs [22]. Short-term complications – such as ventilator-associated pneumonia, acute kidney injury, postoperative ileus, and biliary complications – are known to worsen graft survival and increase morbidity and mortality [23–28]. Integrating ERAS principles has been shown to reduce the incidence of these early postoperative complications, thereby improving overall liver transplant outcomes [12].

Preoperative preparation

Preoperative evaluation for LT should involve a comprehensive assessment of the patient's comorbidities, both related and unrelated to liver failure. Most patients with chronic liver disease (CLD) are physically weakened by the time of transplantation. Sarcopenia and weakness are observed in approximately 50% of candidates preparing for surgery [29]. Optimizing the patient's nutritional status before surgery is a critical step in reducing postoperative complications and accelerating recovery.

Risk stratification can be supported by validated tools, including the Karnofsky Performance Status Index [30], the Frailty Index [31], and muscle mass indices derived from computed tomography (CT) imaging [32]. The European Association for the Study of the Liver (EASL) recognizes that patients with CLD often face a dual burden of malnutrition and obesity [33].

Although three randomized controlled trials evaluating preoperative nutritional interventions found no significant differences in short-term outcomes between intervention and control groups [34–36], targeted preoperative strategies remain promising. These include vitamin D supplementation and ensuring adequate caloric and protein intake, which may improve postoperative outcomes [36].

Preoperative optimization of the patient's clinical status is crucial in improving surgical outcomes [12]. This process requires the coordinated efforts of a multidisciplinary team, including surgeons, anesthesiologists, hepatologists, and other relevant specialists [12]. Signs of decompensated cirrhosis should be identified and corrected whenever possible before surgery to reduce perioperative risks [18]. Notably, current evidence does not support correction of coagulopathy before surgery unless the patient shows clinical signs of coagulation disorders [12].

Cardiopulmonary screening is particularly important in preoperative assessment of LT recipients. Beyond common cardiovascular conditions such as ischemic heart disease and valvular pathologies, these patients often present with diastolic dysfunction and electrophysiological abnormalities, which may significantly increase perioperative risk under the stress of transplantation [18]. Ultrasound evaluation of the pleural cavities is also recommended to detect hepatic hydrothorax, which commonly develops secondary to impaired liver synthetic function. Management of hydrothorax typically includes diuretic therapy, correction of protein disorders, and, if necessary, thoracentesis or drainage.

Special attention should be directed toward identifying and managing infections. Prophylactic antibiotics are indicated for bacterial infections, while antiviral therapy is recommended for hepatitis B, C, and D. In the context of rising antibiotic resistance, screening for multidrug-resistant organisms, including carbapenem-resistant *Enterobacteriaceae*, should be an essential component of preoperative evaluation [18].

Renal function assessment is equally critical. Evaluation should include markers of kidney injury, such as cystatin C, NGAL, and KIM-1 (if available), in combination with ultrasound examination and glomerular filtration rate (GFR) estimation using creatinine clearance. In some patients, judicious fluid expansion combined with splanchnic vasoconstrictor therapy may be effective [12, 18].

Psychosocial assessment is a critical component of preoperative preparation, as depression affects 17%–57% of liver transplant candidates and anxiety disorders occur in 19%–55% [37]. Psychological counseling has been shown to improve short-term postoperative outcomes, primarily by enhancing adherence to the treatment plan, which reduces the risk of graft rejection [38]. Additionally, abstinence from alcohol and smoking is strongly recommended [38].

Preoperative fasting requirements for these patients are generally similar to those for other major surgical procedures: six hours for solid food and two hours for liquids. Prolonged fasting is discouraged. There is no strong evidence for or against preoperative carbohydrate loading in liver transplant recipients [12].

Intraoperative measures

Anesthetic measures

An optimal anesthetic regimen is critical for accelerating postoperative recovery and improving short-term outcomes following LT. The primary objectives of intraoperative anesthesia are facilitating early extubation, providing effective postoperative analgesia, and minimizing the risk of respiratory depression. LT recipients typically require lower doses of anesthetic agents than the general surgical population [12].

Intraoperative monitoring of anesthetic depth, using tools such as the bispectral index (BIS) or equivalent monitors, allows for precise titration of inhalation anesthetics and opioids. Short-acting opioids, when used in dose-optimized regimens, have been shown to facilitate rapid recovery. Evidence suggests that dose reduction strategies improve recovery outcomes regardless of the opioid chosen [12].

Traditionally, benzylisoquinoline muscle relaxants have been the agents of choice for LT due to their extrahepatic metabolism [39]. However, the introduction of sugammadex [40] has made vecuronium or rocuronium suitable alternatives.

Regional anesthesia techniques, particularly neuraxial approaches, were previously used with caution due to the high risk of coagulopathy in patients with chronic liver disease. Recently, there has been renewed interest in regional anesthesia in this patient group due to its potential advantages in terms of reducing opioid consumption, improving hemodynamic stability, and alleviating postoperative pain [41, 42]. In some centers, transversus abdominis plane (TAP) blocks are now routinely used in liver recipients without significant coagulation disorders. TAP blocks provide high-quality intraoperative analgesia and facilitate early extubation [41].

Adequate intraoperative volume management is critical for preventing postoperative complications in LT. Sustained hypervolemia and elevated central venous pressure (CVP) should be avoided [12]. The assessment of volemia should rely on dynamic and minimally invasive cardiac output monitoring and adjusted tailored to the patient's needs and the experience of the anesthesiology team. Empirical correction of coagulopathy should be avoided; instead, blood substitutes should be prescribed based on viscoelastic tests and clinical assessment [43].

Every patient who has undergone LT should be assessed for early extubation ideally within 3–8 hours postoperatively. The decision should be individualized, based on the patient's clinical condition and the availability of close postoperative monitoring. Numerous studies have shown that early extubation after LT improves short-term outcomes [44].

Although there are no strict recommendations regarding contraindications for early extubation, several factors are considered relative exclusions for early extubation in many centers: need for high-volume blood transfusion (>2 units/hour), severe vasoplegia, severe preoperative hepatic encephalopathy, acute liver failure, preoperative mechanical ventilation, concerns about graft function, such as persistent hyperlactatemia [44].

Surgical measures

Surgical techniques should be optimized to reduce operating time, minimize blood loss, and decrease cold ischemia time [12]. Routine use of veno-venous bypass is generally not recommended [45]. However, the creation of a temporary portocaval shunt may be indicated in cases where prolonged interruption of hepatic blood flow is anticipated.

Organ perfusion techniques are critical for protecting the liver graft during the phases of explantation, preservation, and reperfusion. Mechanical perfusion methods also help prevent ischemic reperfusion syndrome and early transplant dysfunction [46, 47]. Whenever feasible, such methods should be considered for all deceased donor grafts, particularly expanded-criteria donors [46].

In cases of massive intraoperative hemorrhage, the use of autologous blood reinfusion systems may be appropriate [48].

Postoperative rehabilitation of liver recipients

Postoperative management of LT recipients is a highly complex and multidisciplinary process aimed at optimizing graft function, preventing complications, and facilitating recovery [12]. Successful care requires continuous monitoring of liver graft function, tailored immunosuppressive therapy, and timely detection and management of vascular, biliary, and infectious complications, while supporting the patient's overall physical rehabilitation.

A multidisciplinary team – including transplant surgeons, anesthesiologists, hepatologists, infectious disease specialists, physical therapists, and dietitians – plays a critical role in ensuring optimal postoperative outcomes.

The implementation of ERAS protocols in LT remains challenging due to a number of factors, such as optimization of infusion therapy, selection of immunosuppression regimens, complex multimodal anesthesia, early removal of catheters and postoperative drains.

Patients with end-stage liver disease have increased susceptibility to infections, which directly affects the effectiveness of accelerated recovery protocols [12]. In addition to these clinical challenges, entrenched surgical and postoperative practices ("clinical dogmas") in some transplant centers may slow the adoption of ERAS protocols [11–13]. These factors will be discussed further below.

ERAS protocols have traditionally emphasized the careful management of fluid therapy, particularly the prevention of hypervolemia. Despite this, many transplant centers continue to favor relative hypervolemia in the early postoperative period to mitigate the risk of vascular complications that may be triggered by hypovolemia [49]. However, recent evidence challenges this approach, indicating that a positive cumulative fluid balance is associated with an increased risk of hepatic artery thrombosis [50]. Notably, even attempts to maintain normovolemia may inadvertently result in fluid overload in this patient population [50]. In light of these findings, some researchers advocate for routine echocardiographic assessment of all liver transplant recipients upon admission to guide and individualize infusion therapy [12, 50].

Unlike other surgeries, post-op pain management in LT recipients is often underestimated, largely due to the standard practices of delayed extubation and delayed mobilization [12]. However, adoption of ERAS protocols requires a multimodal analgesic regimen that not only improves patient comfort but also facilitates early mobilization and accelerates overall recovery [11–13]. Importantly, the requirement for postoperative opioids in LT patients is generally significantly lower than in other surgical populations, particularly in those with high MELD scores and severe hypoalbuminemia [51]. While some centers recommend paracetamol as a first-line analgesic in the postoperative setting [51], others contraindicate its use in LT patients [22]. Moreover, the use of subcostal TAP blocks has been shown to effectively reduce morphine consumption and facilitate earlier weaning from mechanical ventilation [52].

Early removal of catheters and surgical drains remains a significant challenge in LT recipients, largely influenced by the severity of the patient's condition and graft function. Factors such as ongoing bleeding, the need for vasopressor support, management of biliary complications, and postoperative lymphorrhea. However, evidence suggests that LT patients are at high risk of catheter-associated infections, which can negatively impact short-term outcomes [53]. To mitigate this risk, strict adherence to aseptic and antiseptic protocols is essential, along with the use of central venous catheters coated with antimicrobial agents [12]. Although current literature lacks clear consensus or guidelines regarding the optimal timing for catheter and drain removal, early removal may be justified if the patient's condition is stable.

LT recipients are particularly vulnerable to postoperative infections due to the combined effects of pre-existing immunodeficiency and immunosuppressive therapy. Infections not only increase the risk of sepsis but may also contribute to graft dysfunction. Opportunistic pathogens, especially cytomegalovirus (CMV), can lead to significant complications, including vascular and biliary damage. Antibiotic prophylaxis against bacterial infections should be guided by local antimicrobial resistance patterns. Prevention of CMV infection is largely dependent on the serological compatibility between donor and recipient [53]. In some transplant centers, in addition to serological tests, polymerase chain reaction (PCR) testing for CMV is mandatory [22]. Antifungal prophylaxis is also strongly recommended for liver recipients identified as high-risk for invasive fungal infections [54].

Early initiation of enteral nutrition and early patient mobilization are critical components of any enhanced recovery protocols following LT [12]. These measures are particularly important for patients with chronic liver disease, who often present with pre-existing nutritional deficiencies and reduced physical function [12, 55]. In some centers, nasogastric tubes are removed during the immediate postoperative period, sometimes while the patient is still coming out of anesthesia. However, caution is advised in patients with hepaticojejunostomy, where early removal may compromise adequate intestinal decompression.

Oral feeding can be initiated within 12 to 24 hours after transplantation. Parenteral nutrition should be reserved for cases in which enteral feeding fails to meet the patient's caloric and nutritional needs [55]. Early mobilization should begin as soon as clinically feasible

[11–13]. Particular emphasis should also be placed on respiratory physiotherapy and exercises, which play a vital role in preventing pulmonary complications.

Length of hospital stay following LT is widely recognized as a key indicator of treatment quality and effectiveness. A review of six studies assessing optimal discharge timing revealed that, under specific conditions, patients can be safely discharged as early as postoperative day 8 [56–61]. This early discharge is generally appropriate for low-risk patients and in transplant centers equipped with robust outpatient monitoring and follow-up systems.

To support earlier discharge and ensure long-term success, transplant centers are encouraged to implement comprehensive patient education programs. These programs should focus on raising patient awareness of the need to adhere to immunosuppression regimens and awareness of potential complications. In addition, systematic clinical audits have been shown to enhance adherence to medical recommendations and contribute to improved clinical outcomes across transplant populations [62].

IS IT POSSIBLE TO APPLY ERAS PROTOCOLS IN PEDIATRIC LIVER TRANSPLANTATION?

Traditionally, pediatric LT recipients were placed on mechanical ventilation for several days postoperatively. The primary reasons for this prolonged ventilation included a higher GRWR and a greater incidence of vascular complications [63, 64]. However, advances in surgical techniques – such as graft size reduction and monosegmental transplantation – along with improvements in anesthesiology and pediatric intensive care, have enabled some centers to adopt early extubation practices after pediatric LT [65].

Although no meta-analyses have yet evaluated the overall effectiveness of ERAS protocols in this specific patient population, multiple reports in the literature indicate that early extubation is associated with a reduced length of stay in the intensive care unit (ICU) [65].

Fullington et al. [66] reported a series of observations involving 84 pediatric patients who underwent LT. Over the last three years of their study, the authors documented a twofold increase in the number of intraoperative extubations, which correlated with improved short-term outcomes, namely, a reduced length of stay in the ICU and a lower frequency of reintubations. However, the publication did not provide detailed descriptions of the specific surgical or anesthetic techniques employed in their center.

A later report by Sahinturk et al. [67] found that early extubation was achieved in 48% of pediatric liver recipients, also demonstrating a decrease in the length of stay in the ICU. The authors presented a series of cases involving 16 patients under two years of age who were extubated immediately after LT. In all cases, a right-sided TAP block was combined with a bilateral rectus abdominis block after wound closure, resulting in reduced postoperative opioid consumption [68].

ERAS protocols in LT can be effectively adapted for pediatric patients. Recent advances in pediatric anesthesiology, such as adoption of myofascial blocks, together with improvements in pediatric intensive care, have contributed to shorter durations of postoperative ventilation. Additional measures that may further support the successful implementation of ERAS in pediatric transplantation include optimized preoperative nutritional support, use of bedside ultrasound for postoperative monitoring, and active parental participation in the child's care [65].

CONCLUSION

Although many centers remain unfamiliar with, or have yet to adopt, ERAS protocols, their introduction has the potential to improve perioperative outcomes in LT significantly. This procedure presents unique challenges and risks that can hinder implementation of ERAS protocols; however, perioperative teams can develop tailored accelerated recovery strategies that align with institutional resources and individual patient needs. The success of any transplant program – including ERAS integration – relies on a multidisciplinary approach supported by a skilled, collaborative team. Ultimately, application of enhanced recovery protocols reduces early postoperative complications and ultimately improves overall treatment outcomes.

The authors declare no conflict of interest.

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