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Postoperative pain management in the enhanced recovery after surgery (ERAS) for emergency laparoscopic cholecystectomy

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ABSTRACT

Introduction. Enhanced recovery after surgery (ERAS) is a new patient-centered concept that aims to deliver high-quality perioperative care to surgical patients. This study was performed to compare the effectiveness of the pain management measures in an ERAS-protocol versus the traditional approach of postoperative pain. *Materials and Methods.* A comparative prospective study was performed on 50 patients admitted in the Fourth General Surgery of University Emergency Hospital of Bucharest between 2022 and 2024, with the diagnosis of acute cholecystitis, undergoing emergency laparoscopic cholecystectomy. The patients were randomly assigned into two study groups, an ERAS-group and a Traditional group, according to the type of perioperative care applied. The evaluated outcomes were length-of-stay; preoperative anxiety level, leukocyte count at admission and 24 hours postoperatively, postoperative pain levels quantified using Visual Analog Scale 24 hours after surgery and postoperative nausea and vomiting events. *Results*. The two study subgroups were comparable in terms of demographic and clinical preoperative characteristics. Statistical analysis showed significant lower values of preoperative anxiety level in ERAS group ($p<0.001$), lower levels of postoperative pain (VAS 2.96±0.75 vs 4.65±1.69, $p<0.001$) and earlier resumption of the intestinal transit. However, there were no differences in the total hospital stay between the traditional and ERAS groups. *Conclusions*. Implementing ERAS protocol for emergency laparoscopic cholecystectomy improve postoperative functional outcome and the patients' quality of care.

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Introduction

Laparoscopic cholecystectomy (LC) is one of the most performed surgical procedures in gastrointestinal surgical services worldwide, being the gold standard for the treatment of gallstone disease [1]. It is now an evidence-based practice that LC may be performed safely in emergency clinical scenarios, including acute cholecystitis, and it is recommended that LC be performed as soon as the patient's clinical condition allows intervention [2].

Postoperative pain is one of the most redoubtable clinical scenarios that may complicate the evolution of a surgical patient. Science-proof data support that uncontrolled levels of postoperative pain could significantly impact the patients' clinical evolution after a surgical procedure, exposing them to the risk of further complications and delaying the surgical recovery [3]; furthermore, emergency surgery carries an even higher risk of postoperative pain-related complications [4-6]. Therefore, surgeons must acknowledge that any surgery, and, especially, emergency procedures expose the patients to potentially high levels of postoperative pain, and, thus, apply effective measures in order to control them. Nowadays, alongside pharmacological therapy, surgeons

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can turn to multiple non-pharmacological actions, which were proven to have inconclusive results [6,7].

Enhanced Recovery After Surgery (ERAS) protocols are multimodal strategies that intend to optimize the outcome of a patient undergoing a surgical procedure. With beginnings in the last decade of the 20th century, with the Danish surgeon Henrik Kehlet as one of the pioneers, ERAS protocols add together a variety of perioperative measures intended to diminish the general impact of surgery, and, in the meantime, to improve the recovery after the surgical aggression, in a wide variety of surgical pathologies, including oncologic and emergency surgery [8-10]. One of the key aspects approached in an ERAS-strategy is the improvement of postoperative pain level; the surgeon performing under an ERAS-specific protocol may use a large variety of means in order to gain postoperative pain control [11]. Though, an important aspect depicted by ERAS protocols is avoiding as much as possible the usage of opioids, because of their adverse effects that may exert a negative impact on the postoperative recovery [12,13]. The ERAS society implemented specific protocols in many of the general surgery fields; even that being said, a consensus for a specific ERAS protocol intended to optimize LC has not been met, the ensemble of measures applied being the choice of the surgeon. In order to emphasize the role of analgesia in ERAS protocols, we performed a study that is intended to investigate the results of applying a multimodal postoperative pain control strategy to patients undergoing LC for acute cholecystitis, as part of a complex ERAS protocol; also, the complementary measures that may impact the postoperative pain levels and the related complications were noted.

Materials and Methods

We performed a single-center prospective study including 50 patients presented in the Emergency Service between January 2022 and August 2024 and admitted in the Fourth General Surgery Department of The Emergency University Hospital of Bucharest for acute cholecystitis. The criteria for admission respected the Tokyo 2018 Guidelines for acute calculous cholecystitis, as depicted in Table 1.

Table 1. Acute cholecystitis diagnosis algorithm used for admission, adapted from Tokyo 2018 Guidelines

• Acute cholecystitis diagnosis requires the presence of local inflammatory signs
• Local signs of inflammation (tenderness, palpable mass in right upper quadrant, positive Murphy's sign)
• For certain diagnosis, both imagistic findings and systemic inflammation markers are required
• Imagistic findings of acute cholecystitis (pericholecystic fluid, gallbladder wall of at least 4 mm thickness, enlargement of the gallbladder)
• Systemic findings of inflammation (elevated leukocyte count, elevated CRP, fever)

The severity of the cholecystitis was also established using the same guideline (Table 2).

Table 2. Acute cholecystitis severity algorithm used at admission, adapted from Tokyo 2018 Guidelines

Mild	• Acute cholecystitis in an otherwise healthy patient with no organ failure and mild inflammatory changes in the gallbladder
Moderate	• Acute cholecystitis associating high WBC count (>18,000/mm3), signs of local inflammation (palpable mass, tenderness in the right upper quadrant, gangrenous cholecystitis, pericholecystic abscess etc.)
Severe	• Acute calculous cholecystitis associated with organ failure (neurological, cardiovascular, respiratory, renal, hepatic)

The study respected medical ethics and was approved by the Emergency University Hospital's Ethics Committee (approval no. 63461/20.10.2023).

The criteria for inclusion in the study were: patients of age between 18-70 years, ASA score of less than III, undergoing LC for acute cholecystitis in emergency settings, with mild to moderate acute cholecystitis. A careful differential diagnosis was carried out to exclude other possible causes of acute abdomen.

The exclusion criteria were: patients that needed conversion from laparoscopic to open surgery, LC performed in another hospitalization than the initial one, presence of acute pancreatitis, cholangitis or choledocholithiasis that required conservative treatment or endoscopic retrograde cholangiopancreatography prior to surgery, organ dysfunction associated with severe acute cholecystitis, patients denying the participation into the study.

Preoperatively, patients were randomly assigned to two distinct groups: a traditional study group, and a ERAS group, respectively. Patients from both groups underwent emergency LC as soon as their general status allowed surgery under general anesthesia, but not later than 72 hours after the admission. Venous blood samples were collected at admission in order to evaluate the severity of cholecystitis as well as the presence of organ dysfunction, while the preoperative pain level was measured using Visual Analogue Scale (VAS).

Postoperatively, venous blood samples were collected 24 hours after surgery and patients were asked to assess their postoperative pain level using Visual Analogue Scale in order to compare postoperative pain levels between groups. First flatus time and postoperative nausea and vomiting events were also noted. Patients were discharged when asymptomatic, with oral feeding and liquid intake reinstated.

The patients were compared in terms of pre and postoperative pain assessed by VAS, preoperative anxiety level, the presence of postoperative nausea and vomiting syndrome, and the postoperative length of stay.

Results

After applying inclusion criteria, 50 patients were enrolled in this study, 26 in the traditional perioperative group and 24 in the ERAS group. The mean age of the traditional group was 52.92 years, while the mean age of the ERAS group was 52.58 years. Baseline data are depicted in Table 3.

Table 3. Baseline data of patients included in the study

Variable	Traditional group (n=26)	ERAS group (n=24)	p value
Mean age (years)	52.92±12.528	52.58±14.685	0.93
Sex (M/F%)	15/11 (57.69%)	13/11 (54.16%)	0.80
Duration of symptoms (days)	3.19±2.698	3.19±2.698	0.128
Peritoneal irritation	17 (65.4%)	16 (66.7%)	0.926
Echographic data of cholecystitis	22 (84.6%)	20 (83.3%)	0.659
Sepsis	3 (11.5%)	1 (1.4%)	0.339
TG grade • Mild • Moderate • Severe	13 (50%) 10 (38.4%) 3 (11.5%)	13 (50%) 11 (45.8%) 1(4.1%)	0.6

No statistically significant differences were found between the ERAS group and traditional group in the matters of sex ratio, age, duration of symptoms, presence of peritoneal irritation signs.

Preoperative anxiety levels after specific counseling for both groups was measured using the Amsterdam Preoperative Anxiety Scale [14]. Patients underwent LC in emergency under the specific protocols of the group they were assigned into.

Surgical approach and perioperative care for the two study groups

Surgery was performed using the American approach, with four trocars (2 10-mm trocars, one inserted at the umbilicus, one placed in epigastric region, used for instruments and extraction of the gallbladder specimen; 2 5-mm trocars, one 2 cm below the right lower costal margin, one placed half the distance between the umbilical and the right flank one); the surgeon and camera assistant were placed at the left of the patient, with, if required, a second assistant at the right of the patient, which had the task of grasping and lifting the gallbladder fundus with an atraumatic forceps in order to offer better exposure of the Calot triangle's anatomy. Pneumoperitoneum was induced using Veress needle or, for patients with prior surgery, which had the risk of postoperative adhesions, Hasson technique was used. If stomach air distension was discovered intraoperatively, a nasogastric tube was inserted for decompression, with removal at the end of the surgery. After the surgery, patients were directed to the postoperative intensive care unit for 2 hours in order to monitor their vital signs, therefore being returned to the Department when hemodynamically stable.

The traditional perioperative group received perioperative care as depicted in our unit's protocol; preoperative counseling presented the benefits and risks of laparoscopic surgery and general anesthesia, but did not depict interactive measures. Patients fasted for solids and liquids since admission is surgery was performed in the same day, or since 8 pm in the evening before the surgery if performed the next day. Pneumoperitoneum was created and maintained at a pressure of at least 12mmHg. Drainage of the liver bed was routinely practiced and kept in place as long as the volume collected per 24 hours was higher than 50 ml, but not shorter than 24 hours postoperatively.

Regarding analgesia, they received conventional postoperative intravenous analgesic therapy with the scheme used in our hospital, using Paracetamol 1 g each 8 hours, Metamizole 5 ml each 8 hours, and, if pain still uncontrolled, the therapy was supplemented with Tramadol 100 mg each 8 hours. Patients fasted for liquids for 12 hours after surgery and for solids until first postoperative flatus occurred, but not more than 24 hours after surgery, and were allowed to get out of their bed 12 hours after the surgery.

Patients in the ERAS group, in the meantime, received an enhanced protocol in order to speed up the postoperative recovery. Preoperatively, they were informed about the risks and benefits of both surgery and ERAS protocols, using interactive means, with the surgical team involved in answering the patients' questions in order to reduce the preoperative anxiety levels. Patients were required to fast for solids for solids and liquids 8 and, respectively, 6 hours prior to surgery. LC was performed using a lower pneumoperitoneum pressure, starting at 8-10mmHg, with the possibility for the surgeon to increase the pressure only if the view was unsatisfying. Drainage tube was also routinely placed and removed less than 24 hours after the surgery, unless the volume was higher than 50 ml. Postoperative pain control was gained using the same conventional scheme, but opioids were not used; also, patients could receive postoperative injections with ropivacaine at the trocar sites. Patients were required to get off bed 6-8 hours after surgery. Liquid intake was resumed 6 hours after surgery and solid food was allowed 8 hours after surgery.

After the surgery, the specific recovery protocols were pursued and multiple indicators were measured in order to establish the difference between the two groups. The results of our measurements are depicted in Table 4.

Statistical analysis showed significant differences between the 2 study subgroups in terms of functional outcomes. The patients in ERAS group presented a lower preoperative anxiety level ($p<0.001$). Although the 2

groups were comparable in terms of preoperative characteristics, including TG severity grading of acute cholecystitis and VAS for pain at admission, the patients in ERAS group presented lower levels of postoperative pain (VAS at 24 hours after surgery 2.96 vs 4.65, p<0.001), earlier resumption of intestinal transit, and a lower rate of POVN events (8.3% vs 19.2%, p<0.001). There were however, no differences in total hospital stay between the 2 study groups.

Table 4. Preoperative characteristics in patients included in the study.

Variable	Traditional group (n=26)	ERAS group (n=24)	p value
Preoperative anxiety level*	21.08±3.261	13.67±2.548	<0.001
WBC at admission (x10/mm3)	12.44 ± 3.72	13.13 ± 3.56	0.5
WBC 24 hours after surgery (x10/mm3)	10.75 ± 3.04	9.64 ± 2.48	0.39
VAS at admission	7.73 ± 1.18	7.42 ± 1.14	0.17
VAS 24 hours after surgery	4.65 ± 1.69	2.96 ± 0.75	<0.001
First flatus (hours)	18.17 ± 8.62	14.46 ± 6.1	0.001
PONV (number of events)	5 (19.2%)	2 (8.3%)	<0.001
LOHS (days)	5.85 ± 2.32	5.33 ± 2.2	0.43
Intraoperative complications	0	0	n/a

Footnote: WBC - white blood cell count; VAS - Visual Analogue Scale; PONV - postoperative nausea and vomiting; LOHS - length of hospital staying; * - measured using Amsterdam preoperative anxiety scale, after counseling the patients as depicted in the two protocols

Discussions

While elective cholecystectomy is one of the most frequent conditions that are operated on a daily basis [15], emergency presentation require a more extensive preoperative assessment. In emergency presentations, the challenges are not related solely in the surgical attitude, but in establishing the correct indication for surgery in conditions of discrete or discordant symptoms compared to laboratory data [16,17]. The severity of preoperative inflammation was found to be correlated with the intra and postoperative complications [18-21]. A careful preoperative preparation is mandatory to optimize the outcomes.

Several studies evidenced that postoperative pain management is a major indicative of patients' satisfaction [22].

ERAS protocols depict perioperative strategies intended to fasten the recovery process after a surgical procedure while minimizing the risk for further complications. Postoperative pain management in ERAS protocols uses multiple means in order to gain control over the pain level. Surgeons must acknowledge that, by definition, an optimal postoperative pain management strategy should not be granted to a single measure, but to an assembly of issues that make up an ERAS protocol. We performed our study in order to evaluate the impact of applying ERAS measures in patients undergoing emergency LC, a setting where postoperative pain could gain higher levels than elective settings, consecutively raising the risk for postoperative complications. Multiple mechanisms are involved in wound healing, including inflammation, cell proliferation, angiogenesis, epithelialization, wound contraction, and matrix remodeling [23,24]. Several studies found a significant correlation between postoperative pain, wound healing and patient's stress [25,26].

Controlling preoperative anxiety may prove to be a challenge for the surgeon performing emergency LC. It was shown in a paper of the American Society of Anesthesiologists, analyzing the results of 3,661 anesthesiologists, that preoperative anxiety may directly influence the postoperative pain level [27]. Thus, in the emergency setting, higher levels of anxiety may be experienced by the patient [28,29]; also, due to insufficient time or resources, surgeons cannot always perform preoperative counseling at ERAS standards, possibly exposing the patient to the risk of a persistent high preoperative anxiety level and consequent surgical stress. In order to perform this study, we managed to create a friendly environment, using interactive means to present the risks and benefits of both LC and ERAS protocols, and allowing patients to ask questions and get answers about every query they had in order to raise their compliance with the performed procedures. We managed to measure preoperative anxiety using the Amsterdam scale, showing that preoperative anxiety level was statistically significantly lower in the ERAS group, thus emphasizing the need for appropriate counseling especially in difficult settings, such as emergency admissions.

Low-pressure pneumoperitoneum has been granted as one of the main measures that a surgeon may apply in an ERAS protocol in order to improve not only the postoperative pain level, but also the overcome of the surgery. Ortenzi et al. showed in their systematic review that a pneumoperitoneum pressure of 6-10mmHg is associated with lower pain levels and a diminished consumption of analgesics, but also with the drawback of a possible unsatisfying view of the anatomical landmarks [30,31]. It is also to note that one may find himself, when operating an acute cholecystitis in emergency settings, in difficult scenarios because of the visceral adhesions, the pericholecystic fluid or the distension of the gallbladder, that may bring difficulties [32,33]. In our protocol, pneumoperitoneum pressure was initially established at 8-10mmHg, but the surgeon had the option to raise the pressure as needed, in order to achieve Critical View of

Safety without exposing the patient to additional risk. No intraoperative complications were noted in both groups.

Postoperative nausea and vomiting are events that may occur in the evolution of almost any surgical procedure, with a close relationship to postoperative pain levels and exerting a certain influence over postoperative recovery. Amirshahi et al., in their study from 2020, show that 27.7% from 22,683 enrolled patients presented postoperative nausea and vomiting, with the subsequent conclusion that their approaches must be effective in order to control them and to avoid consecutive complications [34]. A general principle of ERAS protocols states that postoperative pain and nausea control must be gained not only by prophylactic antiemetic drugs; a holistic approach is required, adding up pharmacological and nonpharmacological means [11,35]. Our study shows that there is a statistically significant difference between the traditional and ERAS group, with a lower number of postoperative nausea and vomiting events in the ERAS group, whose patients received prophylactic antiemetic therapy.

ERAS patients had a shorter length of stay than the traditional group, but not statistically significant in our study. Several studies found that ERAS protocols allow the faster discharging of the patients without exposing them to additional risks [36,37]. It is also to be mentioned that leukocyte count 24 hours after the surgery was not statistically significant between the two groups; this demonstrates that surgical aggression may still exert an important influence over the postoperative recovery.

It's important to acknowledge that our study, like other papers, has its own limits. First of all, this paper depicts the experience of a single surgical center, with a personalized ERAS protocol, that may be subject to change according to the specific needs of every medical unit and the clinician's option. In the meantime, measuring postoperative pain using Visual Analogue Scale, even if known as a standardized tool for quantification of pain levels, may give altered results because of subjectivity, as patients may experience different sensitivities over multiple pain levels. Furthermore, the lack of a standardized ERAS protocol for laparoscopic emergency cholecystectomy urges for precaution and further research into the field in order to establish certain limits and indications.

Conclusions

Postoperative pain is a frequent complication that may occur after a surgical procedure and harden the recovery process. Acute emergency surgery, a key component of every acute care unit, poses an even higher risk of postoperative pain and related complications due to higher levels of pain, increased perioperative anxiety. We managed to prove, in our paper, that applying a personalized ERAS protocol may safely be performed for patients undergoing emergency LC, and improves the general outcome of the surgical procedures, including postoperative pain levels. We used scientific approved tools in order to measure the general impact of the surgery over the patients, including pain levels and related complications, with emerging data showing that ERAS protocols should be taken into consideration even in acute surgery settings.

With the promising results of this paper, we encourage and pursue further research into the field, in order to study the impact of ERAS measures on heterogeneous groups of patients.

Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript. Informed consent was obtained from all subjects involved in the study.

Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

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