https://doi.org/10.31925/farmacia.2026.4.22 **ORIGINAL ARTICLE**

CLINICAL EFFECTIVENESS OF PERIOPERATIVE LOCAL BUPIVACAINE IN MULTIMODAL ANALGESIA IN ERAS PROTOCOL: A PROSPECTIVE COMPARATIVE STUDY

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Abstract

Conventional bupivacaine hydrochloride is widely used in multimodal analgesia because of its prolonged local anesthetic effect, but its role in Enhanced Recovery After Surgery (ERAS) protocols for emergency laparoscopic cholecystectomy remains unclear. This prospective comparative study evaluated the efficacy and safety of perioperative bupivacaine hydrochloride within an ERAS protocol in 130 consecutive patients undergoing emergency laparoscopic cholecystectomy for acute calculous cholecystitis. Sixty-three patients received perioperative bupivacaine hydrochloride by port-site infiltration and intraperitoneal instillation, while sixty-seven received standard perioperative analgesia. Outcomes included postoperative pain, rescue analgesic use, recovery parameters, and adverse events. Compared with controls, the bupivacaine group had significantly lower pain scores during the first 12 postoperative hours, reduced opioid and non-opioid rescue analgesic requirements, earlier mobilization, faster oral intake, shorter hospital stay, and less postoperative nausea and vomiting (all $p < 0.05$). No local anesthetic systemic toxicity or major drug-related complications occurred. Conventional bupivacaine hydrochloride is a safe and effective component of ERAS-based multimodal analgesia for emergency laparoscopic cholecystectomy, improving early recovery while reducing postoperative pain and opioid requirements.

Rezumat

Clorhidratul de bupivacaină convențional este utilizat pe scară largă în analgezia multimodală datorită efectului său anestezic local de lungă durată, însă rolul său în protocoalele *Enhanced Recovery After Surgery* (ERAS) pentru colecistectomia laparoscopică de urgență rămâne insuficient clarificat. Acest studiu prospectiv comparativ a evaluat eficacitatea și siguranța administrării perioperatorii a clorhidratului de bupivacaină în cadrul unui protocol ERAS la 130 de pacienți consecutivi supuși colecistectomiei laparoscopice de urgență pentru colecistită acută litiazică. 63 de pacienți au primit clorhidrat de bupivacaină prin infiltrație la nivelul porturilor și instilație intraperitoneală, iar 67 au beneficiat de analgezie perioperatorie standard. Au fost evaluate durerea postoperatorie, necesarul de analgezice de salvare, parametrii recuperării și evenimentele adverse. Comparativ cu lotul de control, pacienții tratați cu bupivacaină au prezentat scoruri semnificativ mai mici ale durerii în primele 12 ore postoperatorii, necesar redus de analgezice opioide și non-opioide de salvare, mobilizare mai precoce, reluarea mai rapidă a alimentației orale, durată mai scurtă a spitalizării și o incidență mai redusă a grețurilor și vărsăturilor postoperatorii (toate $p < 0,05$). Nu au fost înregistrate cazuri de toxicitate sistemică la anestezicul local sau complicații majore legate de administrarea medicamentului. Clorhidratul de bupivacaină convențional reprezintă o componentă sigură și eficientă a analgeziei multimodale bazate pe protocolul ERAS pentru colecistectomia laparoscopică de urgență, îmbunătățind recuperarea postoperatorie precoce și reducând durerea postoperatorie și necesarul de opioide.

Keywords: bupivacaine hydrochloride, enhanced recovery after surgery (ERAS), laparoscopic cholecystectomy (LC), acute calculous cholecystitis (ACC), multimodal analgesia, postoperative pain

Introduction

Acute calculous cholecystitis is one of the most common causes of emergency hospital admission for biliary disease and remains a frequent indication for urgent laparoscopic cholecystectomy (1, 2). According to current international guidelines, early laparoscopic cholecystectomy is the treatment of choice whenever feasible, as it is associated with reduced morbidity, shorter hospital stays, and lower healthcare costs

compared with delayed surgery (3). Although laparoscopic surgery is less invasive than the open approach, postoperative pain remains an important clinical challenge, adversely affecting early mobilization, oral intake, functional recovery, and hospital discharge.

While as any novelty, regarded initially with reluctances, Enhanced Recovery After Surgery (ERAS) programs have transformed perioperative management by integrating evidence-based interventions that attenuate surgical stress response, preserve physiological function, and accelerate postoperative recovery (4, 5). A fundamental component of ERAS pathways is multimodal analgesia, which combines systemic non-opioid analgesics with regional and local anesthetic techniques to improve pain control while minimizing opioid consumption and opioid-related adverse effects. Although ERAS protocols are well established in elective surgery, their implementation in emergency laparoscopic cholecystectomy remains less standardized because of the acute inflammatory setting and the limited opportunity for preoperative optimization (6).

Bupivacaine hydrochloride is a long-acting aminoamide extensively used for surgical wound infiltration and regional anesthesia because of its prolonged analgesic effect and favorable pharmacological profile (7). It produces reversible blockade of voltage-gated sodium channels in peripheral nerve fibers, thereby inhibiting the initiation and propagation of nociceptive impulses. Its high lipid solubility and extensive plasma protein binding promote sustained tissue retention and prolonged sensory blockade (7, 8). Following local administration, bupivacaine diffuses through the surgical wound, fascial layers, muscle, and peritoneal surfaces, providing analgesia by reducing both somatic and visceral nociceptive transmission (8, 9). These pharmacological properties make bupivacaine an attractive component of multimodal ERAS protocols, with the potential to reduce postoperative pain intensity, decrease opioid requirements, facilitate early mobilization, and improve functional recovery after laparoscopic surgery.

Previous clinical studies and meta-analyses have demonstrated that local administration of bupivacaine can improve postoperative analgesia following laparoscopic cholecystectomy (8, 9). However, the available evidence remains heterogeneous with respect to the timing of administration, concentration, dose, infiltration technique, and outcome measures. Moreover, relatively few studies have specifically evaluated the integration of bupivacaine into standardized ERAS pathways in the emergency surgical management of acute calculous cholecystitis.

Therefore, the present prospective comparative clinical study aimed to evaluate the effectiveness of a bupivacaine-based local anesthetic strategy incorporated into a standardized ERAS protocol in patients undergoing emergency laparoscopic cholecystectomy for acute calculous cholecystitis. The primary objective was to assess postoperative pain intensity, while secondary objectives included postoperative analgesic consumption, time to first mobilization, time to oral intake, incidence of postoperative nausea and vomiting, and length of hospital stay.

Materials and Methods

Study design and setting

This prospective, single-center comparative clinical study was conducted in the Fourth General Surgery Department, Emergency University Hospital Bucharest, during January 2024 and January 2026. Consecutive adult patients diagnosed with acute calculous cholecystitis (ACC) and undergoing emergency laparoscopic cholecystectomy were prospectively enrolled during the study period. The study was conducted in accordance with the ethical principles of the Declaration of Helsinki and was approved by the Ethics Committee of the Emergency University Hospital Bucharest (Approval no. 63461/20.10.2023). Written informed consent was obtained from all participants before enrollment.

The study evaluated the effectiveness of a bupivacaine-based local anesthetic strategy incorporated into a standardized Enhanced Recovery After Surgery (ERAS) protocol. The primary objective was to compare postoperative pain intensity and recovery outcomes between patients receiving perioperative bupivacaine infiltration as part of the ERAS pathway and those managed with standard perioperative analgesia.

Patient selection

Eligible patients were adults aged 18 - 75 years with a diagnosis of acute calculous cholecystitis established based on clinical presentation, laboratory investigations, and abdominal ultrasonography or computed tomography. All patients were classified as American Society of Anesthesiologists (ASA) physical status I - III and were considered suitable candidates for emergency laparoscopic cholecystectomy under general anesthesia. Written informed consent was obtained from all participants before study inclusion, after reasonable disclosure (10).

Patients were excluded if they were unable to reliably assess postoperative pain because of cognitive impairment, severe psychiatric disease, or neurological disorders. Additional exclusion criteria included chronic opioid therapy (> 30 days), chronic pain syndromes, alcohol or substance abuse, known hypersensitivity to amide-type local anesthetics, severe hepatic dysfunction (Child-Pugh class B or C), severe renal insufficiency, clinically significant coagulopathy, pregnancy, or breastfeeding. Patients requiring conversion to open cholecystectomy, common bile duct exploration, extensive adhesiolysis,

abdominal drainage because of intraoperative findings, or those with major intraoperative complications were also excluded from the final analysis.

ERAS protocol for emergency laparoscopic cholecystectomy

All patients were managed according to a standardized ERAS protocol adapted for emergency laparoscopic cholecystectomy. Preoperative management included rapid clinical and anesthetic assessment, correction of fluid and electrolyte disturbances when indicated, administration of prophylactic antibiotics within 60 minutes before skin incision, and multimodal preemptive analgesia based primarily on paracetamol, with non-steroidal anti-inflammatory drugs administered when not contraindicated.

General anesthesia was standardized for all patients. Laparoscopic cholecystectomy was performed using a conventional four-port technique by experienced surgeons. Low-pressure pneumoperitoneum was used whenever technically feasible, and intraoperative normothermia was maintained throughout the procedure.

Postoperatively, patients received scheduled non-opioid analgesia, while opioid medications were reserved for rescue analgesia in cases of breakthrough pain (VAS $\geq$ 4). Early oral intake and mobilization were encouraged according to ERAS principles. Hospital discharge was considered when adequate pain control, oral intake, independent mobilization, and the absence of postoperative complications were achieved.

Bupivacaine administration

Patients in the intervention group received combined pre-incisional port-site infiltration and intraperitoneal instillation of bupivacaine hydrochloride. Before skin incision, bupivacaine hydrochloride (0.25 - 0.5%) was infiltrated at each trocar insertion site into the skin, subcutaneous tissue, and fascial layers using incremental injections after careful aspiration to avoid inadvertent intravascular administration.

At the completion of the procedure, diluted 0.25% bupivacaine (20 - 30 mL) was instilled laparoscopically into the subhepatic space and the right subdiaphragmatic region under direct visualization. The total administered dose did not exceed 2 mg/kg body weight.

All local anesthetic administrations were performed according to institutional safety recommendations. Intravenous 20% lipid emulsion was immediately available in the operating room for the management of suspected local anesthetic systemic toxicity (LAST).

Outcome measures

The primary outcome was postoperative pain intensity assessed using the Visual Analog Scale (VAS; 0 - 10) at 2, 6, 12, and 24 hours after surgery. Secondary outcomes included cumulative opioid rescue analgesic consumption during the first 24 postoperative hours, non-opioid rescue analgesic requirements, time to first mobilization, time to oral intake, time to first flatus, incidence of postoperative nausea and vomiting (PONV), and total length of hospital stay.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD), whereas categorical variables were presented as absolute frequencies and percentages. Data distribution was assessed before statistical analysis. Intergroup comparisons were performed using appropriate parametric or non-parametric statistical tests according to data distribution, while categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. A two-sided p-value < 0.05 was considered statistically significant. Statistical analyses were performed using-MedCalc Statistical Software (version 23.1.7; MedCalc Software Ltd., Ostend, Belgium).

Results and Discussion

Patient characteristics

A total of 151 consecutive patients with acute calculous cholecystitis were assessed for eligibility during the study period. Twenty-one patients were excluded after screening because they met one or more predefined exclusion criteria. Consequently, 130 patients were included in the final analysis, with 63 patients allocated to the ERAS plus bupivacaine group and 67 patients to the control group (Figure 1).

No statistically significant differences were observed between the two groups regarding baseline demographic, clinical, or operative characteristics, including age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status, severity of acute calculous cholecystitis according to the Tokyo Guidelines 2018, operative time, or estimated intraoperative blood loss (Table I). These findings indicate that the study groups were comparable before intervention, allowing reliable assessment of postoperative outcomes.

Postoperative pain intensity

Postoperative pain intensity was assessed using the Visual Analog Scale (VAS) at 2, 6, 12, and 24 hours after surgery. Patients in the ERAS plus bupivacaine group experienced significantly lower pain scores than those in the control group during the early postoperative period. The greatest difference between groups was observed at 2 hours after surgery, with progressively decreasing pain intensity in both groups thereafter.

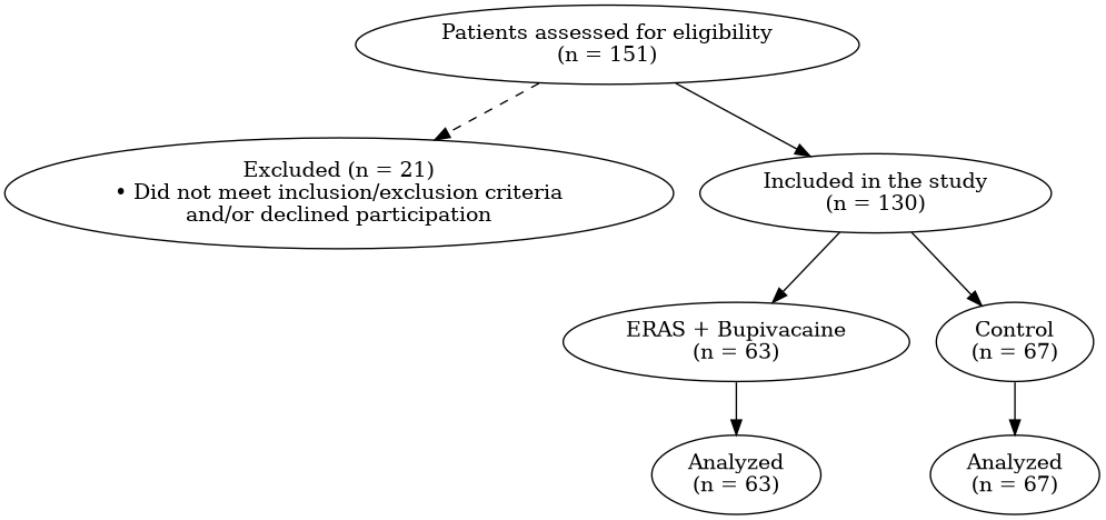

Figure 1.
Study Flow Diagram for the patients included in the study

Table I
Baseline demographic and perioperative characteristics

Parameter	ERAS + Bupivacaine (n = 63)	Control (n = 67)	p value
Age (years)	62.5 ± 10.2	65.6 ± 11.6	0.110
Female sex, n (%)	36 (57.1)	37 (55.2)	0.965
BMI (kg/m²)	27.5 ± 3.9	28.2 ± 4.2	0.305
ASA I (%) II (%) III (%)	 12 (19.0) 38 (60.3) 13 (20.6)	 14 (20.9) 40 (59.7) 13 (19.4)	0.960
Acute cholecystitis grade* I II	 38 (60.3) 25 (39.7)	 39 (58.2) 28 (41.8)	0.942
Operative time (min)	74.0 ± 17.1	77.4 ± 18.8	0.295
Estimated blood loss (mL)	41.7 ± 23.6	43.8 ± 23.9	0.617

Values are presented as mean ± standard deviation or number (%). Acute cholecystitis severity was classified according to the Tokyo Guidelines 2018

Statistically significant differences were maintained at 6 and 12 hours postoperatively, whereas pain scores at 24 hours were comparable between the two groups, indicating that the analgesic benefit of local bupivacaine was most evident during the immediate postoperative period (Figure 2, Table II).

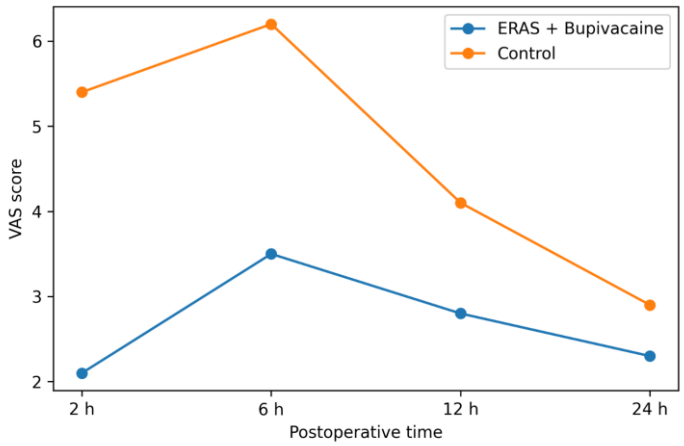

Figure 2.
Comparative evolution of VAS score in the 2 study groups

Table II

Postoperative pain intensity (VAS score)

Time point	ERAS + Bupivacaine (n = 63)	Control (n = 67)	p value
2 h (rest)	2.1 ± 0.6	5.4 ± 1.1	< 0.001*
6 h (coughing)	3.5 ± 0.8	6.2 ± 1.3	0.008*
12 h (rest)	2.8 ± 0.5	4.1 ± 0.9	0.003*
24 h (mobilization)	2.3 ± 0.4	2.9 ± 0.6	0.080

* statistically significant (< 0.05)

Postoperative analgesic requirements

Patients receiving perioperative bupivacaine required significantly less rescue analgesia during the first 24 postoperative hours than those in the control group. Mean intravenous tramadol consumption was reduced by approximately two-thirds in the intervention group, while metamizole requirements were also significantly lower.

Moreover, a substantially greater proportion of patients in the ERAS plus bupivacaine group did not require postoperative opioid administration, confirming the opioid-sparing effect of local bupivacaine within the multimodal ERAS analgesic protocol (Table III).

Table III

Rescue analgesic requirements during the first 24 postoperative hours

Parameter	ERAS + Bupivacaine (n = 63)	Control (n = 67)	p value
Tramadol (mg, IV)	50.0 ± 25.0	150.0 ± 50.0	< 0.001*
Metamizole (g, IV)	2.0 ± 1.0	4.0 ± 1.0	< 0.001*
Patients without opioid requirement, n (%)	41 (65.1)	10 (14.9)	< 0.001*

* statistically significant (< 0.05)

Postoperative recovery outcomes

Postoperative recovery outcomes are summarized in Table IV and illustrated in Figure 4. Patients receiving perioperative bupivacaine demonstrated significantly faster functional recovery than those in the control group. Time to first mobilization, resumption of oral intake, and recovery of gastrointestinal function, assessed by time to first flatus, were all significantly shorter in the intervention group.

In addition, the incidence of postoperative nausea and vomiting (PONV) was significantly lower among patients receiving bupivacaine (7.9% *vs*. 26.9%, p = 0.006). This improvement was accompanied by a significant reduction in the length of hospital stay, with patients in the intervention group being discharged earlier than those managed with standard perioperative analgesia (Figure 3, Table IV).

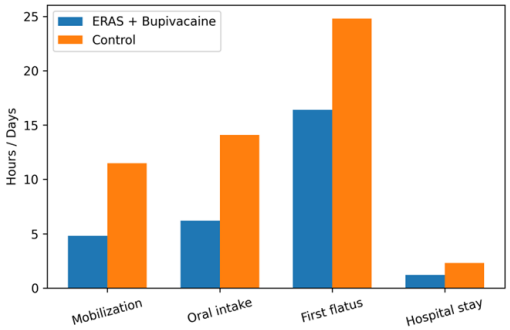

Figure 3.

Comparative postoperative outcomes in the two study groups

Table IV

Postoperative recovery outcomes

Parameter	ERAS + Bupivacaine (n = 63)	Control (n = 67)	p value
Time to first mobilization (h)	4.8 ± 1.2	11.5 ± 3.1	<0.001*
Time to oral intake (h)	6.2 ± 1.5	14.1 ± 2.8	<0.001*
Time to first flatus (h)	16.4 ± 3.2	24.8 ± 4.5	<0.001*
PONV, n (%)	5 (7.9)	18 (26.9)	0.006*
Length of hospital stay (days)	1.2 ± 0.4	2.3 ± 0.7	<0.001*

* statistically significant (< 0.05)

Safety outcomes

No cases of local anesthetic systemic toxicity (LAST), seizures, clinically significant cardiac arrhythmias, neurological complications, or major cardiovascular events related to bupivacaine administration were observed during the study period. Minor postoperative adverse events were uncommon and occurred at similar frequencies in both groups. Mild trocar-site pain, local ecchymosis, transient dizziness, and transient hypotension or bradycardia were infrequent, with no statistically significant between-group differences. Consistent with the recovery outcomes, postoperative nausea and vomiting occurred significantly less frequently in the ERAS plus bupivacaine group than in the control group ($p = 0.006$). No patient requires intensive care unit admission because of complications related to the local anesthetic technique (Table V).

Table V

Postoperative adverse events

Adverse event	ERAS + Bupivacaine (n = 63)	Control (n = 67)	p value
Mild trocar-site pain, n (%)	5 (7.9)	7 (10.4)	0.765
Local ecchymosis, n (%)	2 (3.2)	3 (4.5)	1
Transient dizziness, n (%)	2 (3.2)	3 (4.5)	1
PONV, n (%)	5 (7.9)	18 (26.9)	0.006
Transient hypotension/bradycardia, n (%)	0 (0.0)	2 (3.0)	0.497
Local anesthetic systemic toxicity (LAST)	0	0	NA
Neurological complications	0	0	NA
Major cardiovascular events	0	0	NA
ICU admission	0	0	NA

p values were calculated using Fisher's exact test due to small expected cell counts.

The present prospective comparative study evaluated the clinical effectiveness of conventional bupivacaine hydrochloride administered as part of a standardized Enhanced Recovery After Surgery (ERAS) protocol in patients undergoing emergency laparoscopic cholecystectomy for acute calculous cholecystitis. The results demonstrate that perioperative local administration of bupivacaine significantly reduced postoperative pain intensity during the first 12 hours after surgery, decreased rescue analgesic and opioid requirements, accelerated functional recovery, and shortened hospital stay without increasing the incidence of adverse events. These findings support the role of conventional bupivacaine as an effective component of multimodal analgesia in emergency minimally invasive biliary surgery.

The analgesic benefit demonstrated in the present study is consistent with the established pharmacological profile of bupivacaine. As a long-acting amide local anesthetic, bupivacaine produces reversible inhibition of voltage-gated sodium channels, preventing the generation and propagation of nerve impulses within peripheral sensory fibers (7, 11). The significant reduction in postoperative pain observed during the first postoperative hours corresponds to the expected pharmacokinetic and pharmacodynamic characteristics of conventional bupivacaine. Conversely, the lack of significant differences after 24 hours is likely explained by the progressive decline in local anesthetic activity following tissue redistribution and systemic metabolism (7, 11, 12).

An important feature of the analgesic protocol used in this study was the combination of pre-incisional port-site infiltration and intraperitoneal instillation of bupivacaine. These techniques provide complementary mechanisms of analgesia by targeting both somatic and visceral sources of pain associated with laparoscopic cholecystectomy (9, 13, 14). Mishra *et al*. (13) demonstrated that patients receiving pre-incisional local anesthetic infiltration experienced lower postoperative pain scores and reduced analgesic requirements compared with those treated with intraperitoneal instillation alone. While port-site infiltration primarily limits nociceptive transmission arising from surgical injury to the skin, subcutaneous tissue, muscle, and fascia, intraperitoneal administration predominantly attenuates visceral pain generated by peritoneal irritation and diaphragmatic stimulation, which are recognized contributors to postoperative abdominal discomfort and referred shoulder pain (9, 13, 14). The simultaneous modulation of these distinct pain pathways probably accounts for the superior analgesia observed during the immediate postoperative period.

A clinically important finding of the present study was the significant reduction in postoperative opioid consumption among patients receiving perioperative bupivacaine. Rescue tramadol requirements were substantially lower in the intervention group, and nearly two-thirds of these patients remained opioid-free during the first 24 postoperative hours. This opioid-sparing effect represents a fundamental principle of Enhanced Recovery After Surgery (ERAS) pathways, which emphasize effective multimodal analgesia while minimizing opioid exposure (6,15-17). Reducing opioid requirements has important clinical implications because it decreases the incidence of

opioid-related adverse effects, including postoperative nausea and vomiting, excessive sedation, respiratory depression, urinary retention, and delayed gastrointestinal recovery. Consequently, patients are more likely to achieve earlier mobilization, faster restoration of physiological function, and a shorter duration of hospitalization, all of which contribute to improved postoperative recovery (6, 15, 17).

The enhanced postoperative recovery observed in the intervention group may be explained by the combination of superior analgesia and reduced opioid requirements. Early mobilization, timely reintroduction of oral nutrition, restoration of gastrointestinal function, and decreased length of hospital stay are recognized as core outcomes of Enhanced Recovery After Surgery (ERAS) pathways (18, 19). Recovery following surgery is inherently multifactorial; however, adequate local pain control is considered a key component because it limits the physiological stress response to surgery while facilitating the preservation of normal function. In addition, the lower incidence of postoperative nausea and vomiting in the bupivacaine group is consistent with the established benefits of opioid-sparing multimodal analgesic strategies and further supports their role in optimizing postoperative recovery (18, 19).

Our findings are consistent with previous randomized clinical trials and systematic reviews evaluating local anesthetic techniques in laparoscopic cholecystectomy. Port-site infiltration with bupivacaine has consistently been associated with lower early postoperative pain scores and reduced opioid requirements, whereas intraperitoneal instillation has demonstrated additional benefits in controlling visceral pain and postoperative shoulder pain (20-24). Furthermore, a recent meta-analysis by Qin *et al*. (6) demonstrated that combining these techniques provides superior postoperative analgesia compared with either approach alone. The present study extends these findings to emergency laparoscopic cholecystectomy performed for acute calculous cholecystitis, a clinical setting characterized by active inflammation and greater physiological stress than elective surgery. The technique of anesthesia was analyzed by several studies and meta-analysis (25-28), comparing transverse abdominis plane (TAP) block with portsite infiltration, but with inconsistent results. Gül and Akbudak (23) demonstrated that surgeon-delivered bupivacaine infiltration achieved postoperative analgesia comparable to ultrasound-guided TAP and ESP blocks during laparoscopic cholecystectomy. Their findings suggest that simple local anesthetic techniques can provide effective pain control while avoiding the additional time, equipment, and expertise required for regional anesthesia. While Gül and Akbudak (23) evaluated patients undergoing elective laparoscopic cholecystectomy, our study extends these observations to emergency laparoscopic cholecystectomy for acute calculous cholecystitis. Despite the greater inflammatory burden associated with acute disease, combined port-site infiltration and intraperitoneal bupivacaine remained effective in reducing postoperative pain and analgesic requirements.

From a pharmaceutical perspective, conventional bupivacaine hydrochloride remains an attractive local anesthetic despite the availability of newer formulations and alternative agents. Although liposomal bupivacaine provides prolonged drug release and extended analgesia, its substantially higher cost limits its routine use in many healthcare systems (8). Similarly, levobupivacaine and ropivacaine offer improved cardiovascular safety profiles because of their stereoselective pharmacological properties (25); however, conventional racemic bupivacaine remains widely available, inexpensive, and highly effective when administered within recommended dosage limits. Consequently, conventional bupivacaine provides an appropriate balance of efficacy, safety, accessibility, and cost-effectiveness, making it a practical choice for routine clinical practice, particularly in emergency surgical settings.

Safety remains a critical consideration whenever long-acting local anesthetics are administered. Because bupivacaine exhibits relatively high affinity for myocardial sodium channels, inadvertent intravascular injection or excessive systemic absorption may result in local anesthetic systemic toxicity (LAST) (29-31). In the present study, no episodes of LAST, neurological complications, clinically significant cardiac arrhythmias, or major cardiovascular events were observed. Strict adherence to recommended maximum doses, incremental administration, careful aspiration before injection, and immediate availability of lipid emulsion therapy probably contributed to the favorable safety profile observed. These findings confirm that conventional bupivacaine can be administered safely when evidence-based recommendations for local anesthetic administration are respected.

Several limitations should be acknowledged. First, this was a single-center prospective comparative study with a relatively limited sample size, which may restrict the generalizability of the findings. Second, postoperative outcomes were evaluated only during the early recovery period, precluding assessment of longer-term pain control and patient-reported quality-of-life measures. Third, although baseline demographic and operative characteristics were comparable between groups, the non-randomized design cannot completely eliminate the possibility of residual confounding. Finally, the present investigation evaluated conventional bupivacaine hydrochloride only; therefore, no direct comparisons can be made with levobupivacaine, ropivacaine, or liposomal bupivacaine formulations.

Despite these limitations, the present study demonstrates that perioperative administration of conventional bupivacaine hydrochloride represents a safe and effective pharmacological strategy for optimizing multimodal analgesia within ERAS pathways for emergency laparoscopic cholecystectomy. By combining prolonged peripheral sodium channel blockade with opioid-sparing analgesia, conventional bupivacaine contributes to improved postoperative recovery while maintaining an excellent safety profile (23, 32). Future multicenter randomized studies comparing conventional bupivacaine with newer local anesthetic formulations and alternative regional analgesic techniques are warranted to further optimize perioperative pain management in emergency biliary surgery.

Conclusions

Conventional bupivacaine hydrochloride administered as part of a standardized ERAS protocol provides effective multimodal analgesia for patients undergoing emergency laparoscopic cholecystectomy for acute calculous cholecystitis. Perioperative port-site infiltration combined with intraperitoneal instillation was associated with reduced early postoperative pain, lower opioid requirements, earlier mobilization, faster recovery of gastrointestinal function, and shorter hospital stay, while maintaining a favorable safety profile with no cases of local anesthetic systemic toxicity. The clinical benefits observed in this study are consistent with the pharmacodynamic properties of bupivacaine, including prolonged sodium channel blockade and sustained peripheral sensory analgesia during the period of greatest postoperative pain. These findings support the incorporation of conventional bupivacaine into ERAS-based multimodal analgesic protocols as a safe, effective, and cost-efficient strategy for optimizing perioperative recovery in emergency biliary surgery. Further multicenter randomized controlled studies with larger patient populations and longer follow-up are warranted to validate these findings and to compare conventional bupivacaine with newer local anesthetic formulations and alternative regional analgesic techniques.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article. The other data generated in the present study may be requested from the corresponding author.

Ethics approval and consent to participate

All experimental procedures were approved by the Ethics Committee of the Emergency University Hospital Bucharest (Approval no. 63461/20.10.2023). Informed consent was obtained from all patients included in the study.

AI use disclosure

Not applicable.

Conflict of interest

The authors declare no conflict of interest.

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