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IMPACT OF QUADRATUS LUMBORUM BLOCK AND EPIDURAL ANALGESIA ON FUNCTIONAL RECOVERY OF THE LIVER AFTER SURGICAL RESECTION FOR COLORECTAL LIVER METASTASES

The aim of the study was to evaluate the impact of quadratus lumborum block (QL block) compared to epidural analgesia (EA) on the postoperative liver functional recovery, coagulation profile, metabolic changes, and hemodynamic stability in patients undergoing liver resection for colorectal liver metastases. **Materials and Methods.** This prospective randomized study included 64 patients allocated in a 1:1 ratio to EA or QL block groups. 56 patients (28 per group) were included in the final analysis. The primary endpoints were the postoperative alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lactate levels. Secondary endpoints included protein-synthetic markers, coagulation parameters (fibrinogen, prothrombin index), and thromboelastography (TEG) variables. **Results.** Both analgesic techniques provided comparable postoperative hepatic and coagulation profiles. The QL block group demonstrated a significant but clinically minimal elevation in ALT/AST on postoperative day 1. The lactate dynamics was similar between the groups without significant differences. Protein-synthetic (albumin, total protein) and coagulation markers showed no significant intergroup differences. TEG revealed transient postoperative alterations characteristic of liver resection; LMM identified consistently higher G values and platelet counts in the QL block group, although these differences lacked clinical significance. No analgesia-related complications were observed. **Conclusions.** The QL block is a safe and effective alternative to epidural analgesia following liver resection, providing a comparable profile of hepatic function, coagulation status, and hemodynamic stability. Minor statistical differences in selected parameters did not translate into clinical relevance. The QL block may be a rational option for patients with contraindications to EA or increased risk of hemodynamic instability.

Keywords: quadratus lumborum block, epidural analgesia, liver resection, colorectal liver metastases, thromboelastography, liver function, lactate, postoperative analgesia, coagulation, ERAS.

Hepatic resection remains a high-risk surgical procedure despite substantial progress in operative techniques, preoperative optimization, and multidisciplinary perioperative care. Perioperative morbidity ranges from 20 to 45%, while mortality may reach up to 5%, depending on the extent of resection, baseline liver function, comorbidities, and institutional expertise [1–3]. The most common postoperative complications include liver failure (6–12%), infectious complications (up to

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25%), bleeding (up to 15%), and coagulopathies resulted from impaired synthetic activity of hepatocytes [4, 5].

Posthepatectomy liver failure (PHLF) remains the most serious postoperative complication, with mortality rates reaching 60% in severe cases [6–8]. Its development depends not only on the extent of resection but also on several contributing factors, including chemotherapy-associated hepatic injury (steatosis, sinusoidal obstruction syndrome), intraoperative hypotension, and disturbances in hepatic microcirculation.

The choice of anesthetic strategy plays a crucial role in mitigating perioperative risk. The use of inhalational anesthetics and high-dose opioids has been shown to associate with immunosuppression, hypotension, impaired hepatic perfusion, and delayed postoperative recovery [9, 10]. In this context, regional anesthesia techniques, such as epidural analgesia (EA) and the quadratus lumborum block (QL block), represent the key components of multimodal perioperative pain management.

The Enhanced Recovery After Surgery (ERAS) Society guidelines for liver resection (2022) do not recommend routine use of epidural analgesia because of the risk of prolonged hypotension and the challenges associated with correcting postoperative coagulopathy. Instead, peripheral fascial plane blocks such as QL, TAP, and ESP are suggested, as they provide effective analgesia without systemic hemodynamic effects [2, 3]. The PROSPECT methodology (2023) also supports the utility of fascial plane blocks for major laparotomies, including liver surgery, although it highlights the limited evidence available for this specific patient population [4]. A randomized study by Bielka et al. [11] demonstrated that the psoas compartment block in elderly patients with proximal femoral fractures provided effective analgesia, reduced opioid requirements, and did not induce significant blood pressure fluctuations. These findings support the safety of fascial plane blocks in patients at high risk of hemodynamic instability; they can be extrapolated to abdominal surgery, including liver resections, where maintaining adequate perfusion is critical.

The recent systematic reviews and randomized trials (2023–2024) show that the QL block effectively reduces postoperative pain, decreases opioid consumption by 25–40%, stabilizes hemody-

namics, and is associated with fewer adverse effects (particularly hypotension and nausea) compared with EA [6, 9, 12, 13]. However, most of these studies were conducted in patients undergoing other major abdominal procedures (nephrectomy, cystectomy, hysterectomy, etc.), making it difficult to directly extrapolate these findings to liver resections.

Cochrane systematic reviews (2020–2024) confirm that the QL block is an effective component of multimodal analgesia: it reduces opioid consumption by 25–40% and pain intensity during the first 48 postoperative hours. Moreover, the QL block carries a lower risk of hypotension compared with EA and does not require correction of coagulation disorders, which is critical in liver resection patients [5]. The mechanism of the action of the QL block involves the spread of the local anesthetic into the fascial planes of the posterior abdominal wall, allowing blockade of both somatic and visceral components of pain. Randomized trials demonstrate that QL block provides analgesia lasting up to 48 h and reduces visual analogue scale (VAS) scores by at least 2 points compared with TAP block [6, 7]. Nevertheless, the evidence specific to liver resection remains limited.

Regarding disease relevance, colorectal cancer (CRC) is the third most common malignancy worldwide and the second leading cause of cancer-related mortality. In 2024, approximately 1.9 million new CRC cases and over 930,000 deaths were reported globally [14]. The liver is the most frequent site of metastasis, with approximately 50% of patients developing hepatic metastases during their lifetime [15].

Resection of colorectal liver metastases remains the only potentially curative treatment modality for selected patients. After radical resection, the overall 5-year survival rates range from 35–58%, and may exceed 70% in carefully selected cohorts [16]. Therefore, the optimization of perioperative care, including advances in analgesic strategies, has a direct impact on outcomes in this large patient population.

Despite encouraging results of QL block use in major abdominal surgery, the evidence regarding its application specifically during liver resection remains limited. Existing studies do not consistently account for the unique hemodynamic challenges and heightened risk of coagulopathy in this population. Data on the impact of the QL block on the

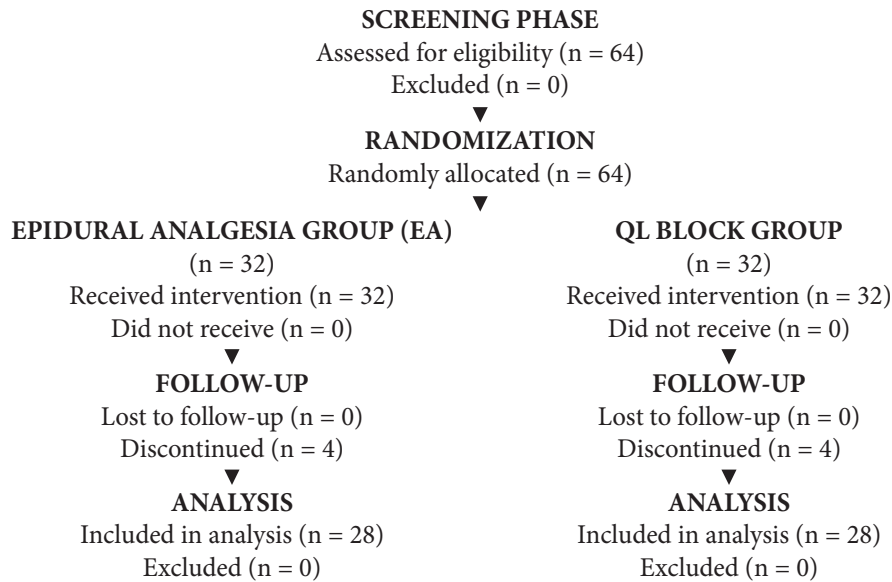


Fig. 1. Patient allocation flow chart

functional recovery (time to mobilization, return of bowel function) and length of hospital stay after liver resection are inconsistent. The effect of QL block on the incidence of PHLF and other complications also remains unclear. Therefore, further randomized controlled trials are required to evaluate the efficacy and safety of the QL block in patients undergoing liver resection.

Materials and Methods

This was a single-center, prospective, randomized, and parallel-group study conducted at the National Cancer Institute (Kyiv, Ukraine) between 2023 and 2025. The study protocol was approved by the Institutional Ethics Committee of the National Cancer Institute. The written informed consent was obtained from all participants before enrollment and the initiation of any study-related procedures.

The preoperative assessment included a comprehensive clinical evaluation (physical examination; verification of tumor type, stage, and extent; and assessment of hepatic metastatic burden); laboratory testing (complete blood count, comprehensive biochemical panel, standard coagulation profile, and urinalysis); and imaging and instrumental diagnostics (ultrasound, echocardiography, contrast-enhanced computed tomography of the chest, abdomen, and pelvis and, when indicated, contrast-enhanced magnetic resonance imaging). The three-dimensional reconstruction of the DICOM images with subsequent segmental volumetry and

metastatic lesion mapping was performed when required. The endoscopic evaluations (colonoscopy and esophagogastroduodenoscopy) were routinely completed. Additional biophysical studies (EPR spectroscopy, zymography) and morphological analyses using immunohistochemical techniques were carried out when indicated.

A total of 64 patients meeting the eligibility criteria were enrolled at the screening stage. After 1:1 randomization, patients were allocated into two equal groups of 32 participants: the EA group and the quadratus lumborum block group (QL2, posterior approach). During follow-up, 4 patients from each group withdrew consent and were excluded from further participation. The final statistical analysis included 56 patients: 28 in the EA group and 28 in the QL block group. The patient allocation flow diagram complied with the CONSORT guidelines (Fig. 1).

Patients were eligible for inclusion if they had one or multiple colorectal liver metastases confirmed by contrast-enhanced CT or MRI; if the metastases were considered potentially resectable with preservation of at least 30% functionally viable liver parenchyma; if they had an American Society of Anesthesiologists (ASA) Physical Status physical status of I–III; a body mass index (BMI) ≤ 35 kg/m²; no cirrhosis beyond Child-Pugh class A; and were aged 18 years or older.

Exclusion criteria included: refusal to participate at any stage of the study; local infection at the anticipated puncture site; coagulopathy or thrombocytopenia ($<100 \times 10^9/L$); international normalized

ratio (INR) >1.5 or activated partial thromboplastin time (aPTT) >40 seconds with normal fibrinogen level; presence of >3 pulmonary metastases or peritoneal carcinomatosis; acute infectious conditions; hepatic encephalopathy \geq grade II according to the West-Haven scale; decompensated cardiopulmonary disease; and any other contraindications to regional analgesia techniques or general anesthesia.

No premedication was administered. In the EA group, an epidural catheter was placed before induction of general anesthesia at the Th₇₋₈ or Th₈₋₉ level. After a negative aspiration test, 10–12 mL of 0.125% bupivacaine combined with 200 μ g fentanyl was administered. The sensory block level was documented preoperatively. Postoperative analgesia was maintained via continuous epidural infusion of 0.125% bupivacaine at 6–8 mL/h for 72 h.

In the QL block group, bilateral ultrasound-guided quadratus lumborum block type QL2 (posterior approach) was performed with 25 mL of 0.25% bupivacaine administered on each side. General anesthesia was standardized in both groups: induction with propofol, fentanyl, and atracurium, followed by maintenance with sevoflurane at MAC <0.9. Intraoperative opioid use was minimized. If heart rate or arterial pressure increased by >20% from baseline, fentanyl bolus (1 μ g/kg) was administered.

Monitoring included electrocardiography, invasive arterial pressure measurement, pulse pressure variation, non-invasive cardiac output monitoring using estimated continuous cardiac output (esCCO) technology, capnography, and standard vital parameters. Fluid therapy followed a restrictive regimen (crystalloids 2–3 mL/kg/h). The target mean arterial pressure (MAP) was maintained at \geq 65 mmHg; norepinephrine infusion (0.2–0.4 μ g/kg/min) was used when required.

All patients received 1 g of intravenous paracetamol and 50 mg of dexketoprofen preoperatively. Postoperatively, patients received paracetamol 1 g three times daily and dexketoprofen 50 mg three times daily. Morphine 10 mg subcutaneously was used as rescue analgesia.

Primary endpoints included lactate concentration at the end of surgery and at 24 hours postoperatively, as well as alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels on postoperative days 1 and 3.

Secondary endpoints included total bilirubin levels on postoperative days 1 and 3; coagulation parameters (fibrinogen, prothrombin index (PTI)); thromboelastography (TEG) parameters (R, K, α , MA, G, LY) measured preoperatively and on postoperative days 1 and 3; hepatic encephalopathy grade according to the West-Haven scale (preoperatively and on day 3); and hemodynamic parameters (arterial pressure and heart rate) at key surgical time points. Hepatic encephalopathy scores were assessed, but no clinically significant abnormalities were detected in either group, consistent with the reported outcomes.

Methods of statistical analysis. The minimum required sample size was determined based on the primary endpoint — changes in the postoperative transaminase levels. According to the pilot data and published literature, the expected between-group difference was approximately 1.1 mmol/L with a standard deviation of 1.4. With $\alpha = 0.05$, power = 80% ($\beta = 0.2$), and a 1:1 allocation ratio, the minimum sample size required was 28 patients per group. The actual number of participants included in the analysis ($n = 56$) provided sufficient statistical power for evaluating the primary outcomes.

The continuous variables were presented as mean \pm standard deviation (M \pm SD) or median [25th–75th percentile], depending on distribution normality assessed using the Shapiro–Wilk test and Q–Q plots. Categorical variables were reported as absolute numbers and percentages. Student's *t*-test was used for normally distributed variables, and the Mann-Whitney U test was used when distribution criteria were not met. The categorical variables were compared using Pearson's χ^2 test or Fisher's exact test. Within-group changes over time (preoperative baseline, postoperative day 1 and day 3) were assessed using the Wilcoxon signed-rank test.

To evaluate the effects of analgesic technique and time on laboratory parameters, linear mixed-effects models (LMM) with repeated measures were constructed. Fixed effects included Group (EA/QL), Time (baseline, day 1, day 3), and the Group \times Time interaction. Patient ID was modeled as a random intercept. Sensitivity analyses adjusted for age, BMI, sex, and blood loss demonstrated no meaningful impact on the primary conclusions. Log-transformation was applied when normality assumptions were violated. Reported outputs included *p*-values for the effects of time, group, and their interaction.

The proportion of missing data did not exceed 5%. Mixed-effects models allowed retention of all available observations without excluding patients. Multiple imputation (MICE) was used for systematic missingness. The main analysis followed a per-protocol approach, with the robustness of findings confirmed through intention-to-treat analysis.

Graphical representations included boxplots, line plots with standard errors, histograms, Q-Q plots, and correlation matrices. Visualizations were generated using GraphPad Prism v.10 and Python libraries (Matplotlib, Seaborn).

In addition to statistical significance, clinical relevance was assessed, particularly regarding the impact of analgesic technique on postoperative liver function, hemodynamic stability, and coagulation status.

Results

A total of 56 patients who underwent liver resection for metastatic CRC were included in the study. The patients were assigned to two groups: (EA, (n = 28)) and (QL block, (n = 28)). The groups did not differ in age, sex, anthropometric characteristics, or intraoperative blood loss ($p > 0.05$), indicating baseline comparability (Table 1). The predominant diagnoses were metastatic adenocarcinoma of the rectum and sigmoid colon. Most patients had metastatic CRC ($\approx 65\%$), with the majority demonstrating involvement of liver segments S5—S8. Laparoscopic resections were more common in the QL block group (40% vs. 25% in the EA group).

A review of the overall dataset revealed isolated missing laboratory values (up to 5%), primarily on postoperative day 3. The use of mixed-effects models allowed incomplete observation sequences to be included without excluding any patients. The re-

sults of the intention-to-treat (ITT) analysis were consistent with the per-protocol analysis, confirming the robustness of the findings. Although the actual sample size (n = 56) was slightly smaller than the calculated sample size (n = 64), sensitivity analyses showed no change in the direction or magnitude of the main associations.

Intraoperative blood loss was comparable between groups (Table 1), indicating that differences in blood loss were not attributable to variations in surgical technique or the extent of operative trauma. The groups were homogeneous by BMI; therefore, obesity has been ruled out as a cofounder affecting coagulation responses.

Both groups demonstrated a marked postoperative elevation of ALT and AST, peaking on postoperative day 1 with subsequent decline by day 3 ($p < 0.001$ for within-group changes), consistent with the expected pattern of ischemia-reperfusion injury. On postoperative days 1 and 3, ALT and AST values were significantly higher in the QL block group than in the EA group ($p < 0.05$). Baseline enzyme levels were significantly lower in the QL group, likely due to distribution asymmetry and higher standard deviations in the EA group. The overall downward trajectory of transaminase levels by postoperative day 3 was similar between the groups (Table 2).

In the postoperative period, both study groups demonstrated similar patterns of changes in key biochemical and coagulation parameters, reflecting the systemic response to surgical trauma and the transition into the catabolic phase (Table 3).

The total bilirubin level tended to increase on postoperative day 1 and declined by postoperative day 3. These findings indicate a transient hyperbilirubinemia associated with brief hepatocellular dysfunction and cholestatic changes following parenchymal liver resection.

Table 1. Baseline demographic and perioperative characteristics of the patients

Parameter	EA (n = 28)	QL block (n = 28)	<i>p</i>
Age, years	62.7 ± 8.2 (44—74)	58.3 ± 9.5 (42—75)	0.11
Weight, kg	77.2 ± 13.8 (54—107)	76.6 ± 14.1 (56—100)	0.87
Height, cm	169.2 ± 8.6 (152—180)	169.3 ± 8.5 (155—180)	0.97
BMI, kg/m ²	26.9 ± 3.2	26.8 ± 3.1	0.91
Sex (M/F)	15/13 (55%)	13/15 (46%)	0.99
Blood loss, mL	223 ± 88	216 ± 101	0.78

Postoperatively, a marked reduction in total protein was observed on day 1. By day 3, partial recovery was noted. These changes are consistent with postoperative hypoproteinemia due to surgical stress, blood loss, hemodilution, and activation of catabolic processes. The differences between the groups were insignificant ($p > 0.05$), indicating similar protein metabolism dynamics irrespective of analgesic technique (Table 3).

Albumin levels also decreased on postoperative day 1, reflecting the acute-phase response, fluid redistribution, and reduced hepatic albumin synthesis. A trend toward recovery was seen by day 3, although values remained below baseline. Intergroup differences were insignificant.

Coagulation potential (prothrombin index) decreased on day 1 in both groups, consistent with transient hypocoagulation due to the factor consumption, hemodilution, and functional adapta-

Table 2. Changes in ALT and AST levels in the groups across time points

Parameter	EA group (M ± SD)	QL block group (M ± SD)	<i>p</i>
ALT, I	39.5 ± 73.2	21.7 ± 8.1	0.031
ALT, II	269.7 ± 112.3	400.6 ± 180.5	0.015
$p^{(I-II)}$	0.001	0.001	
ALT, III	168.2 ± 81.6	272.8 ± 145.3	0.018
$p^{(I-III)}$	0.001	0.001	
AST, I	44.9 ± 55.3	30.7 ± 14.8	0.047
AST, II	274.6 ± 109.2	401.9 ± 141.6	0.009
$p^{(I-II)}$	0.001	0.001	
AST, III	170.7 ± 88.4	253.4 ± 117.9	0.024
$p^{(I-III)}$	0.001	0.001	

Notes: I — baseline; II — postoperative day 1; III — postoperative day 3; significance of differences was assessed by the Mann—Whitney U test.

Table 3. Changes in biochemical and hemostatic parameters in the groups across time points

Parameter	Time Point	EA group (n = 28)	QL block group (n = 28)	<i>p</i> -value
Bilirubin, $\mu\text{mol/L}$	I	14.8 ± 7.2	15.9 ± 8.4	0.64
	II	27.6 ± 11.3	26.9 ± 10.5	0.78
	III	20.3 ± 8.9	21.1 ± 9.6	0.81
Total protein, g/L	I	72.1 ± 5.6	71.3 ± 6.2	0.58
	II	56.3 ± 6.8	57.4 ± 7.1	0.62
	III	62.0 ± 6.9	61.1 ± 6.5	0.67
Albumin, g/L	I	46.0 ± 4.2	45.4 ± 4.0	0.71
	II	36.5 ± 4.6	37.0 ± 4.4	0.63
	III	37.6 ± 4.7	38.3 ± 4.5	0.58
PTI, %	I	108 ± 14	106 ± 12	0.52
	II	86 ± 9	89 ± 10	0.43
	III	101 ± 13	96 ± 11	0.39
Fibrinogen, g/L	I	3.5 ± 0.6	3.7 ± 0.7	0.48
	II	4.3 ± 1.0	3.8 ± 0.9	0.33
	III	4.7 ± 1.1	4.3 ± 0.8	0.41
Platelets, $\times 10^9/\text{L}$	I	186.9 ± 39.8	234.0 ± 53.6	0.018
	II	162.9 ± 44.1	211.0 ± 47.9	0.021
	III	145.2 ± 38.7	198.8 ± 46.2	0.014
Lactate, mmol/L	I	1.36 ± 0.42	1.34 ± 0.38	0.84
	II	1.65 ± 0.47	1.53 ± 0.41	0.46
	III	2.23 ± 0.56	2.02 ± 0.48	0.28

Notes: I — baseline; II — postoperative day 1; III — postoperative day 3; significance of differences was assessed by the Mann—Whitney U test.

tion of hepatocytes. By day 3, PTI values improved in both groups.

Fibrinogen levels demonstrated an opposite trend, gradually increasing by day 3 in both groups, reflecting an acute-phase protein synthesis and a compensatory hemostatic response.

In both study groups, platelet counts decreased postoperatively, which is typical for patients undergoing major hepatic resections. This pattern is associated with intraoperative blood loss, fluid-related hemodilution, activation of the coagulation cascade, and suppression of transient bone marrow megakaryocytes due to systemic inflammation. In the EA group, postoperative thrombocytopenia was a more pronounced, and in the QL block group, the mean platelet levels remained significantly higher at all time points compared to the EA group ($p < 0.05$, Mann — Whitney U test). Both groups demonstrated a moderate increase in lactate levels at the end of surgery, followed by a postoperative peak on day 1 (Table 3). These changes reflect activation of anaerobic metabolism due to transient microcirculatory disturbances and rela-

tive parenchymal hypoxia during the parenchymal transection phase.

Although the absolute lactate levels were consistently lower in the QL group at all time points, intergroup differences were insignificant ($p > 0.05$). This indicates a generally comparable ability of both analgesic strategies to support adequate tissue perfusion and oxygenation during the postoperative period.

In both groups, postoperative lactate elevation was significant, reflecting metabolic stress and increased oxygen demand during surgery. In the EA group, lactate increased significantly by the end of surgery ($p = 0.031$), with a peak on day 1 ($p = 0.004$). In the QL group, only a trend toward elevation was observed at the end of surgery ($p = 0.052$), with a significant increase occurring on day 1 ($p = 0.009$).

This difference in timing suggests a trend toward a more delayed and less pronounced lactate rise in patients receiving the QL block. However, since intergroup differences did not reach statistical significance, these findings should be interpreted as physiologically plausible clinical observations ra-

Table 4. Thromboelastography parameters in the groups across time points

Parameter	Time point	EA group (M ± SD)	QL block group (M ± SD)	p-value
R, min	I	12.03 ± 5.03	13.07 ± 3.67	0.5582
	II	10.23 ± 5.39	9.57 ± 4.36	0.9245
	III	9.62 ± 3.59	7.90 ± 2.27	0.2743
K, min	I	3.40 ± 1.39	3.30 ± 1.33	0.8756
	II	3.73 ± 2.60	2.21 ± 0.94	0.1032
	III	3.22 ± 2.66	2.40 ± 0.73	0.3927
α, angle °	I	54.20 ± 9.72	52.05 ± 8.65	0.6241
	II	54.58 ± 14.52	58.94 ± 11.13	0.4467
	III	56.14 ± 17.36	57.28 ± 7.31	0.8928
MA, mm	I	68.45 ± 4.21	68.28 ± 4.25	0.8943
	II	61.36 ± 9.64	65.48 ± 3.55	0.1971
	III	65.69 ± 8.54	65.86 ± 8.61	0.9627
G, dyn · s/cm ² × 10 ³	I	9.27 ± 2.49	11.18 ± 2.06	0.0542
	II	9.50 ± 2.83	9.79 ± 1.57	0.6612
G	III	9.89 ± 2.79	9.06 ± 3.00	0.4718
LY, %	I	0.19 ± 0.60	0 ± 0	0.3125
	II	0.75 ± 1.07	0.52 ± 0.86	0.4773
	III	0.81 ± 0.83	0.73 ± 0.94	0.7334

Notes: I — baseline; II — postoperative day 1; III — postoperative day 3; significance of differences was assessed by the Mann — Whitney U test.

ther than confirmed effects. The delayed lactate rise in the QL group may indirectly indicate more stable hepatic perfusion, although overall metabolic stress remained comparable between the groups.

Thromboelastography (TEG) analysis showed that the R parameter (time to the initial fibrin formation) remained within reference limits at all time points and exhibited similar trends in both groups. A moderate increase in R was observed on postoperative day 1, indicating a transient reduction in plasma coagulation factor activity, followed by partial normalization by day 3. No significant intergroup differences were found ($p > 0.05$), suggesting comparable effects of EA and QL block on the initiation phase of coagulation (Table 4).

The dynamics of K parameter, which reflects the rate of fibrin polymerization and formation of a stable fibrin scaffold, the α -angle, representing the rate and efficiency of fibrin clot formation, and the MA parameter, which reflects the maximal strength of the platelet–fibrin clot, showed similar patterns in both groups, but intergroup differences were insignificant.

The G parameter (clot elasticity), which integrates the contributions of platelets and fibrinogen to overall clot firmness, remained within normal limits preoperatively ($8\text{--}12 \times 10^3 \text{ dyn} \cdot \text{s}/\text{cm}^2$). A moderate postoperative decrease was observed on day 1 in both groups, followed by partial recovery by day 3. The QL block group demonstrated a consistent tendency toward higher G values at all time points

($p \approx 0.05$), suggesting a slightly better clot mechanical stability and less pronounced transient suppression of the platelet–fibrin component of hemostasis compared to the EA group.

The LY parameter (degree of clot lysis) remained within physiological limits ($<2\%$) in most patients. A small increase in LY on postoperative day 1 in the EA group may indicate a transient fibrinolytic activation; however, its value was minimal and clinically insignificant. By postoperative day 3, LY values stabilized in both groups ($p > 0.05$), indicating restoration of the balance between coagulation and fibrinolysis.

In mixed-effects models adjusted for age, sex, BMI, and blood loss, a significant *time effect* was observed for all analyzed parameters, reflecting typical postoperative coagulation dynamics after liver resection. A significant *group effect* was identified only for platelet count and the G parameter, whereas no independent effect of the analgesic technique was confirmed for other variables. Multiple imputation of missing values using the MICE method did not alter the primary findings, confirming their robustness with respect to data preprocessing methods. Additionally, an intention-to-treat analysis was performed, demonstrating identical effect directions and values compared to the per-protocol analysis, supporting the stability of results regardless of analytical strategy.

At the same time, the type of analgesia (EA or QL block) did not exert an independent effect on

Table 5. Summary of LMM effects for key laboratory and TEG parameters

Parameter	Time effect	Group effect	Group \times Time interaction	Trend in QL block vs EA
ALT, AST	$p < 0.001$	$p = 0.72$	$p = 0.68$	Similar decreasing trend by day 3
Bilirubin	$p = 0.03$	$p = 0.61$	$p = 0.77$	Mild rise on day 1, no intergroup differences
Total protein, Albumin	$p < 0.001$	$p = 0.49$	$p = 0.55$	Decrease on day 1 with partial recovery
PTI	$p = 0.02$	$p = 0.40$	$p = 0.69$	Transient reduction, similar in both groups
Fibrinogen	$p = 0.004$	$p = 0.53$	$p = 0.81$	Increase by day 3 (acute-phase response)
Platelets	$p = 0.001$	$p = 0.04^*$	$p = 0.15$	Higher values in QL group at all time points
Lactate	$p < 0.001$	$p = 0.62$	$p = 0.71$	Transient postoperative elevation, no differences
R (TEG)	$p = 0.03$	$p = 0.48$	$p = 0.42$	Prolonged on day 1, no differences
K (TEG)	$p = 0.08$	$p = 0.11$	$p = 0.21$	Slightly shorter in the QL group, not significantly
α -angle	$p = 0.04$	$p = 0.57$	$p = 0.60$	Recovery toward day 3
MA	$p = 0.02$	$p = 0.09$	$p = 0.17$	Slightly more stable in the QL group
G	$p = 0.01$	$p = 0.04^*$	$p = 0.12$	Higher in the QL group at all time points
LY	$p = 0.49$	$p = 0.68$	$p = 0.81$	No differences; fibrinolysis absent

most coagulation parameters according to the mixed-effects models. Only the platelet count ($p = 0.04$) and the G parameter ($p = 0.04$) remained consistently higher in the QL block group across all observation points, which may suggest less pronounced platelet consumption and slightly better clot mechanical stability in these patients. No signs of hypocoagulation or pathological fibrinolytic activation were detected in either group. Overall, the QL block demonstrates a safety profile comparable to epidural analgesia with respect to coagulation and hepatic function in the postoperative period following liver resection.

Discussion

Postoperative rehabilitation after liver resection requires a well-balanced analgesic strategy that not only provides adequate pain control but also maintains systemic hemodynamic stability, coagulation balance, and microcirculatory function. According to the ERAS Society recommendations, techniques associated with hypotension or delayed recovery should be avoided in favor of the fascial plane blocks or multimodal approaches with a minimal systemic impact [2]. However, the role of central neuraxial techniques in hepatobiliary surgery remains a subject of ongoing debate. Meta-analyses demonstrate their analgesic efficacy but also highlight increased risks of coagulopathy, hypotension, and delayed mobilization [17]. In this context, our study aimed to compare the safety profiles of EA and the QL block in patients undergoing anatomical and non-anatomical liver resections, with a focus on functional, metabolic, and hemostatic parameters.

The dynamics of laboratory markers in our cohort generally corresponded to the expected postoperative pattern after hepatectomy: a transient increase in transaminases on postoperative day 1, a decrease in the total protein and albumin concentrations, a short-term elevation in INR followed by normalization, and an increase in fibrinogen as part of the acute-phase response [18, 19]. In the QL block group, the ALT and AST levels were slightly higher during the early postoperative period; however, these elevations were not accompanied by reductions in the synthetic liver function or impairments in coagulation parameters. This indicates that the analgesic technique did not exert clinically

meaningful effects on the hepatocellular function. Similar findings have been reported in studies evaluating fascial plane blocks, specifically QL and ESP blocks, which did not worsen liver functional parameters in patients after hepatectomy or other major abdominal procedures [20–22].

In our cohort, the QL block was associated with more stable platelet-related hemostatic activity, as evidenced by higher MA and G values on TEG. These parameters reflect the mechanical stability of the clot, and their reduction on postoperative day 1 in both groups indicates a transient platelet dysfunction that recovered by day 3. The consistently higher G values in the QL block group throughout the observation period may reflect a better preservation of coagulation potential in the setting of a more stable microcirculation and the absence of systemic sympathetic blockade. Similar temporal TEG changes after liver resection — prolonged R/K times and reduced MA/G with subsequent normalization — have been described in clinical studies using a viscoelastic testing (VET), where these alterations were transient and not associated with clinically significant hypocoagulation [23–25].

Assessment of liver enzyme activity remains an important marker of hepatocellular function after surgery. In our study, we observed a transient elevation of ALT and AST on postoperative day 1, followed by a decline by day 3, consistent with the typical course of ischemia–reperfusion injury without evidence of significant hepatocellular dysfunction. This pattern aligns with previous reports showing that short periods of ischemia during parenchymal transection and subsequent reperfusion trigger oxidative stress and pro-inflammatory cytokine release, resulting in transient transaminase elevations [26–28]. Similar ischemia–reperfusion patterns were demonstrated in our earlier work, where sevoflurane preconditioning during liver resection reduced lactate levels and stabilized transaminase activity postoperatively, underscoring the role of anesthetic strategy in mitigating reperfusion injury [29]. These findings are consistent with those reported by Semenko et al. [30], who demonstrated that sevoflurane exhibits a pronounced cardioprotective effect and reduces the risk of bupivacaine-induced myocardial toxicity during combined general and regional anesthesia, prolonging the time to the onset of arrhythmias and asystole.

In our cohort, the ALT and AST levels were moderately higher in the QL block group on postoperative day 1 compared with the EA group. Although this difference was significant, its magnitude was small and not accompanied by any impairment in synthetic or coagulation function, indicating limited clinical relevance. Given the stable INR, albumin, and fibrinogen values across the groups, a more plausible explanation is a slightly larger or longer parenchymal transection in certain QL block patients rather than an effect of the analgesic technique.

A similar pattern of cytolytic enzyme dynamics with fascial plane blocks has been described in the randomized study by Zhu et al. [31], in which QL block after open liver resection did not impair hepatic function or increase complication rates. Likewise, Malik et al. [32] confirmed the absence of adverse effects of fascial blocks on hepatic functional parameters in donors undergoing right hepatectomy. In addition, the QL block has been associated with a faster functional recovery and shorter hospital stays.

The gradual decline in transaminases by postoperative day 3 corresponds to improvement of regional perfusion and activation of reparative mechanisms in hepatic tissue. Christ et al. [33] demonstrated that normalization of ALT/AST reflects the completion of the compensatory adaptation phase and correlates with the regenerative capacity of the liver remnant. The morphofunctional studies, including those by Shen et al. [34], confirm that key microcirculatory alterations resolve approximately 72 h after surgery, matching the clinical trajectory observed in our patients.

Thus, our findings confirm that the QL block, when applied within a multimodal analgesic strategy, does not impair the hepatocellular function, and the observed biochemical changes are physiologic and transient. This supports the safety of the method even in patients at increased risk of hepatic dysfunction or in cases where EA is contraindicated.

Postoperative elevation of lactate was observed in both groups with gradual normalization by postoperative days 2–3. This pattern corresponds to expected metabolic changes associated with reperfusion and transient hepatic hypoperfusion after parenchymal transection [26, 28]. In our study, lactate levels increased at the end of surgery, peaked on postoperative day 1, and then declined to base-

line by day 3. Similar transient hyperlactatemia after liver resection has been reported and is attributed to temporary reductions in hepatic blood flow and transient limitations in hepatocyte lactate clearance [38]. With restored perfusion and stable hemodynamics, the lactate levels typically normalize within 48–72 h. In the absence of sustained hypotension or hypoxia, these changes lack adverse prognostic significance [35].

No patient demonstrated clinical or laboratory signs of persistent hypoxia, severe hypotension, or metabolic acidosis that would suggest inadequate microcirculation or critical ischemia. This pattern is consistent with the findings from multidisciplinary observations, in which transient postoperative lactate elevation after hepatectomy was not associated with the increased complication rates in the absence of other contributing clinical factors [27, 28].

Comparison of the groups revealed similar lactate trajectories, with no significant differences in peak values or normalization rates, reflecting comparable tissue oxygenation. At the same time, the QL block group exhibited less variability in lactate levels during the early postoperative period. However, this tendency did not reach statistical significance and should therefore be considered a physiologic observation that warrants further confirmation. A plausible explanation is a greater hemodynamic stability in QL block patients, as this technique does not induce systemic sympathetic blockade or significant reductions in mean arterial pressure [36].

In contrast, EA may lead to vasodilation and reduced systemic vascular resistance, which in some cases is accompanied by hypotension, particularly in patients with a reduced myocardial contractility or hypovolemia [37]. Such effects may influence hepatic perfusion, whereas the QL block provides a more uniform blood flow and more favorable microcirculatory conditions. Similar stability of systemic and regional perfusion with QL and ESP blocks has been reported by Mostafa et al. [22] and Akerman et al. [21], where these analgesic techniques were used within the ERAS protocols for abdominal surgery, including liver resections.

Thus, the postoperative increase in lactate after hepatectomy is transient and does not represent critical hypoperfusion. The QL block provides adequate tissue oxygenation, comparable to epidural analgesia in terms of analgesic efficacy and homeostatic stability, while being associated with less pro-

nounced hemodynamic fluctuations. This makes it a reasonable alternative to EA, particularly in patients at risk of hypotension or coagulopathy [17, 21, 22, 25].

Changes in protein-synthetic markers reflect the adaptive hepatic response to surgical stress and reperfusion injury. In our study, a moderate decrease in the total protein and albumin was observed on postoperative day 1, with partial recovery by day 3. Concurrently, the fibrinogen levels increased, and PTI decreased slightly, forming a typical laboratory pattern of the acute-phase response following major hepatic surgery.

The reduction in albumin concentration is multifactorial. The primary driver is the metabolic shift toward catabolism in the setting of systemic inflammation, mediated by interleukin-6, TNF- α , and other cytokines that suppress albumin gene transcription while stimulating the acute-phase protein synthesis [38]. Additional contributors include hemodilution from intraoperative fluid administration and redistribution of intravascular fluid into the interstitial space, characteristic of the early postoperative period [39].

The rise in fibrinogen observed in most patients by day 3 reflects the activation of acute-phase protein synthesis in the liver. This adaptive process represents the gradual restoration of hepatocellular functional capacity. The parallel increase in fibrinogen and normalization of PTI demonstrate recovery of hepatic synthetic ability and a balanced hemostatic response [40, 41].

Neither epidural analgesia nor the QL block adversely affected hepatic synthetic function. Despite differences in pharmacodynamic and hemodynamic characteristics, both techniques maintained a stable metabolic profile without evidence of impaired protein synthesis. Albumin, fibrinogen, and PTI did not differ significantly between the groups, confirming that the type of analgesia did not influence hepatic synthetic activity. Similar findings have been reported in studies describing the typical “postoperative triad” — acute-phase elevation of fibrinogen accompanied by transient reductions in albumin and dilutional changes of coagulation factors — after major abdominal surgery, including hepatectomy [42].

These results align with the current understanding of the phased recovery of liver function. During the first postoperative day, catabolic processes and

reduced synthesis of structural proteins predominate, whereas subsequent days mark a shift toward reparative activity and restoration of the synthetic function. This timeline highlights the high adaptive capacity of the liver and confirms the metabolic safety of both analgesic approaches.

The hemostatic status after liver resection is a crucial indicator of analgesic safety and postoperative microcirculatory stability. In our study, a transient decrease in platelet count was observed in both groups, being more pronounced in the EA group. This phenomenon is multifactorial: intraoperative blood loss, dilution from fluid therapy, platelet consumption at surgical sites, and transient suppression of megakaryocyte activity due to systemic inflammation.

In the QL block group, platelet reduction was less pronounced and normalized more rapidly. This difference likely reflects the hemodynamic stability associated with peripheral fascial plane blocks, which do not induce systemic sympathetic blockade. Preservation of splanchnic vascular tone promotes physiological blood distribution and prevents excessive platelet sequestration in the liver and spleen.

TEG provided more detailed insight into the coagulation function. The dynamics of the R and K parameters in both groups (Tables 4 and 5) indicates restoration of the balance between coagulation and fibrinolysis [43]. MA (maximum amplitude) and G (clot strength) decreased on postoperative day 1 in both groups and recovered on day 3, indicating compensatory restoration of platelet and fibrinogen function. G values remained higher at all time points in the QL block group, suggesting greater clot stability. This likely reflects more physiological microcirculatory conditions and the absence of systemic sympathetic-mediated vasodilation [24]. The LY parameter indicated preserved fibrinolytic potential. Overall, the TEG profile after hepatectomy was characterized by a transient shift toward mild hypocoagulation, followed by a return to physiological equilibrium without signs of persistent hemostatic impairment [25].

The obtained results demonstrate that the QL block is not associated with hypocoagulatory effects and may contribute to maintaining a more stable TEG profile during the early postoperative period. In contrast to EA, whose sympatholytic effect may influence microcirculation and platelet function, the QL block provides effective analgesia

without systemic hemodynamic consequences. This makes it a safe analgesic strategy for patients at risk of coagulopathy after liver resection, where hemostatic stability is critical to preventing hemorrhagic and thrombotic complications.

Despite the robust findings, several limitations of this study must be acknowledged. First, follow-up was limited to the early postoperative period (up to three days), allowing evaluation of immediate metabolic and hemostatic responses to different analgesic techniques. The lack of long-term monitoring precludes conclusions regarding functional recovery, survival, or recurrence after liver resection. The literature suggests that anesthetic techniques may influence immunomodulatory processes and potentially affect oncologic outcomes.

Second, the sample size was relatively small. Although adequate for the primary endpoints, statistical power to detect subtle inter-group differences remains limited. Larger multicenter trials are needed to confirm these findings and determine their generalizability.

Third, the study had a single-center design. While this ensured methodological consistency, it limits external validity, as perioperative management strategies, surgical techniques, and anesthetic protocols may vary across institutions. Additionally, the analysis focused on objective laboratory

parameters without incorporating subjective pain assessments (VAS or NRS). The absence of these data limits the ability to fully assess postoperative comfort, a key element of multimodal analgesia.

Another limitation is the lack of an analysis linking biochemical changes to clinical complications such as bile leakage, bleeding, or posthepatectomy liver failure. Such data would provide more detailed insight into how analgesic techniques may influence postoperative trajectories.

Finally, although modern statistical methods (mixed-effects models, EM/MICE imputation) were applied to handling missing data, the possibility of systematic bias in longitudinal analyses cannot be fully excluded. Future prospective studies with larger cohorts and extended follow-up are needed to better characterize the interplay between analgesic techniques, hepatic function, and clinical outcomes.

In conclusion, the QL block is a safe and effective alternative to EA following liver resection, providing a comparable profile of hepatic function, coagulation status, and hemodynamic stability. Minor statistical differences in selected parameters did not translate into clinical relevance. The QL block may be a rational option for patients with contraindications to EA or increased risk of hemodynamic instability.

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ВПЛИВ QL-БЛОКУ ТА ЕПІДУРАЛЬНОЇ АНАЛГЕЗІЇ НА ФУНКЦІОНАЛЬНЕ ВІДНОВЛЕННЯ ПЕЧІНКИ ПІСЛЯ ХІРУРГІЧНОЇ РЕЗЕКЦІЇ ПРИ КОЛОРЕКТАЛЬНИХ МЕТАСТАЗАХ У ПЕЧІНКУ

Мета. Оцінити вплив блоку квадратного м'яза попереку (QL-блок) порівняно з епідуральною аналгезією (ЕА) на післяопераційне відновлення функції печінки, коагуляційний профіль, метаболічні зміни та гемодинамічну стабільність у пацієнтів, яким виконували резекцію печінки з приводу колоректальних метастазів. **Матеріали та методи.** У це проспективне рандомізоване дослідження було включено 64 пацієнти, розподілені у співвідношенні 1:1 на групи ЕА та QL-блоку. Під час спостереження по чотири пацієнти в кожній групі відкликали інформовану згоду; таким чином, до фінального аналізу включено 56 пацієнтів (28 у кожній групі). Первинними кінцевими точками були рівні аланінамінотрансферази (АлТ), аспартатамінотрансферази (АсТ) та лактату в післяопераційному періоді. Вторинні кінцеві точки включали показники білково-синтетичної функції печінки, коагуляційні параметри (фібриноген, протромбіновий індекс) та показники тромбоеластографії (ТЕГ). Статистичний аналіз проводили із застосуванням U-критерію Манна — Вітні, критерію Вілкоксона та лінійних моделей змішаних ефектів (ЛММ), із лог-трансформацією та множинною підстановкою пропущених значень (MICE) за потреби. **Результати.** Обидві методики аналгезії забезпечили порівнювані післяопераційні показники функції печінки та коагуляції. У групі QL-блоку відзначено статистично значуще, але клінічно мінімальне підвищення АлТ/АсТ на першу добу. Динаміка лактату була подібною між групами без достовірних відмінностей. Показники білково-синтетичної функції (альбумін, загальний білок) та коагуляційні параметри істотно не відрізнялися між групами. За даними ТЕГ спостерігали транзиторні зміни, характерні для резекції печінки; ЛММ виявив стабільно вищі значення G та кількості тромбоцитів у групі QL-блоку, проте ці відмінності не мали клінічної значущості. Ускладнень, пов'язаних із методами аналгезії, не зафіксовано. **Висновки.** QL-блок є безпечною та ефективною альтернативою ЕА після резекції печінки, забезпечуючи порівнюваний профіль функції печінки, коагуляційного статусу та гемодинамічної стабільності. Незначні статистичні відмінності окремих параметрів не мали клінічного значення. QL-блок може бути доцільним варіантом для пацієнтів із протипоказаннями до ЕА або підвищеним ризиком гемодинамічної нестабільності.

Ключові слова: блок квадратного м'яза попереку, епідуральна аналгезія, резекція печінки, колоректальні метастази печінки, тромбоеластографія, функція печінки, лактат, післяопераційна аналгезія, коагуляція, ERAS.