


Comparative Efficacy of Regional Analgesic Interventions in Open versus Laparoscopic Hepatic Surgery: A Network Meta-Analysis

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Purpose: To compare the analgesic efficacy and safety of various regional analgesic techniques in patients undergoing hepatic surgery, with prespecified subgroup analyses for open and laparoscopic approaches.

Patients and Methods: This study adhered to PRISMA-NMA guidelines. Randomized controlled trials (RCTs) comparing regional analgesia techniques in adults undergoing hepatic surgery were identified from PubMed, Embase, Web of Science, and the Cochrane Library. Primary outcomes were postoperative 24-hour pain scores and opioid consumption; the secondary outcome was postoperative nausea and vomiting (PONV). Bayesian network meta-analysis was performed, and interventions were ranked using surface under the cumulative ranking curve (SUCRA) values.

Results: Twenty-three RCTs (1,382 patients) were included. In the main analysis, intrathecal morphine (ITM) was ranked highest for reducing 24-hour pain scores (SUCRA 91%), and erector spinae plane block (ESPB) and transversus abdominis plane block (TAPB) significantly reduced 24-hour opioid consumption compared with control. However, no statistically significant differences were found among the active interventions in network comparisons for pain scores or opioid consumption. No intervention significantly reduced the incidence of PONV. The certainty of evidence (GRADE) for all outcomes ranged from very low to moderate. Subgroup analysis suggested ESPB was most effective for opioid reduction in open surgery, while ITM was superior for both pain and opioid reduction in laparoscopic surgery.

Conclusion: Regional analgesic techniques provide opioid-sparing benefits after hepatic resection, but no technique demonstrated clear superiority over another in the main analysis. The choice of analgesic technique should be individualized. Subgroup analyses suggest ESPB may be preferred for open hepatectomy and ITM for laparoscopic procedures, although these findings are exploratory due to limited evidence certainty. Larger, high-quality RCTs are needed to strengthen the evidence for optimal analgesic strategies in hepatic surgery.

Keywords: nerve block, postoperative pain, analgesia, meta-analysis, liver resection

Introduction

Hepatic surgery, particularly partial hepatectomy, remains a critical intervention for treatment of liver malignancies and end-stage liver diseases.^{1,2} However, inadequate postoperative pain management continues to hinder optimal clinical outcomes. Globally, 35–52% patients undergoing hepatectomy experience moderate-to-severe pain, which is significantly correlated with a 1.87-fold increased risk of postoperative complications.^{3,4} Although surgical technique varies, the most frequent approaches for open liver resection include the use of a right subcostal incision or a reversed L-shaped incision. Therefore, liver resection, regardless of the surgical approach, can be associated with significant postoperative pain.⁵ Effective pain control can facilitate early mobilization and reduce the incidence of postoperative complications.⁶ Adequate pain management has been identified as a critical component for the success of an enhanced recovery after surgery (ERAS) program in patients undergoing liver resection.^{7–9}



Although traditional opioid-based regimens are effective for postoperative analgesia, they are associated with dose-dependent risks, including prolonged side effects such as postoperative nausea and vomiting (PONV), shivering, ileus, and urine retention.¹⁰ Consequently, ERAS protocols advocate multimodal analgesia, with regional anesthesia emerging as a cornerstone.¹¹ Techniques such as nerve blocks and neuraxial anesthesia are increasingly emphasized as central strategies, as they provide effective pain relief, reducing opioid requirements, and supporting faster recovery and mobilization. For example, the erector spinae plane block (ESPB) has been shown to reduce intra- and postoperative opioid consumption up to 72 hours, improve sleep quality, and enable 10-hour earlier ambulation versus controls.¹² Regional anesthetic techniques, such as the transversus abdominis plane block (TAPB) and ESPB, have demonstrated significant reductions in pain and opioid consumption in patients undergoing abdominal laparoscopic surgery.^{13,14} Furthermore, existing trials report heterogeneous outcomes, leading to uncertainty about the comparative efficacy and safety of regional techniques. Procedural heterogeneity, variable surgical contexts, and inconsistent reporting of secondary outcomes (eg., opioid consumption and PONV) further complicate the establishment of a consensus on the optimal approach.^{15,16}

Network meta-analysis (NMA) enables the simultaneous comparison of multiple interventions, even in the absence of direct head-to-head trials, and provides probabilistic rankings of techniques.¹⁷ RCTs and pairwise meta-analysis demonstrate benefits of regional blocks.^{18,19} However, hepatobiliary surgery lacks a stratified clinico-biological consensus regarding interventions. Furthermore, while existing guidelines such as those from PROSPECT provide recommendations for open hepatectomy, the comparative efficacy of regional techniques in the increasingly prevalent laparoscopic approach remains underexplored. This NMA synthesizes evidence from RCT comparing regional analgesia – including thoracic paravertebral block (TPVB), TAPB, ESPB, quadratus lumborum block (QLB), thoracic epidural analgesia (TEA) – as well as intrathecal morphine (ITM) in hepatic surgery. The primary endpoints include pain scores (NRS/VAS), cumulative opioid consumption and the incidence of PONV. Through Bayesian hierarchical modeling and prespecified subgroup analyses stratified by surgical approach (open vs. laparoscopic), we aim to establish probability-based intervention rankings and provide evidence to inform organ-specific ERAS protocols, thereby addressing a key gap in the comparative evidence for laparoscopic hepatic surgery.

Materials and Methods

Registry Information

This systematic review and meta-analysis adhered strictly to the extended guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses incorporating network meta-analyses (PRISMA-NMA).²⁰ The study was registered with PROSPERO (CRD 420251062957). Ethical approval and informed consent were not required due to the nature of the study, which involved the synthesis of published data.

Search Strategy

The systematic search was conducted across four major databases: PubMed, Embase, Web of Science, and the Cochrane Library, covering publications up to July 22, 2025. The search was restricted to articles published in English. The key search terms included “hepatectomy,” “liver surgery,” “erector spinae plane block,” “quadratus lumborum block,” “transversus abdominis plane block,” and thoracic paravertebral block. Detailed search strategy for each database is provided in [Supplementary Material 1](#). The search process was carried out as teamwork by two reviewers, SMY and JL, with discrepancies resolved by a third reviewer, HHY.

Inclusion and Exclusion Criteria

Studies were included if they met the following criteria: (a) adult patients (≥ 18 years) undergoing elective open or laparoscopic hepatic resection, such as lobectomy, partial hepatectomy, living donor hepatectomy, or liver resection for malignancies; (b) adoption of regional analgesic techniques, including TPVB, TAPB, ESPB, quadratus lumborum block (QLB), or epidural analgesia (TEA), combined with general anesthesia; (c) reporting of postoperative pain scores (VAS/NRS), opioid consumption, or PONV; (d) randomized controlled trials (RCTs) published in peer-reviewed journals with full-text availability and detailed reporting of methodology and outcome reporting.

Exclusion criteria included the following: (a) studies involving pediatric populations, emergency surgeries, non-hepatic abdominal surgeries, liver transplant recipients or combined multi-organ resections; (b) case reports, animal studies, or studies with incomplete outcome data; (c) studies conducted on animals or cadavers; (d) studies lacking a control group or employing non-comparable comparator regimens, such as non-equivalent opioid dosing; (e) studies not reporting quantitative data on pain, opioid consumption, or PONV; (f) non-randomized studies, observational cohorts, abstracts, conference proceedings, or publications in non-English without translation.

Study Selection

The selection of studies followed a rigorous, standardized process. Abstract and title screening was conducted collaboratively by SMY and JL, while full-text screening was performed independently by WJH. Duplicate studies were identified and removed using the clinical scientific research platform. References were managed using Clarivate EndNote 21. Discrepancies during the study selection process were resolved by the third reviewer, HHY. Study characteristics, including country, population, and language, were meticulously extracted to ensure a comprehensive analysis.

Data Extraction and Processing and Outcomes

Data extraction was conducted independently by two reviewers, SMY and JL, to ensure methodological rigor and minimize bias. The extracted information included surgery type, assessment timepoints, sample size, and patient age. Any discrepancies arising during data extraction were resolved by WJH, acting as the designated discrepancy resolution reviewer.

The outcomes were categorized into primary and secondary endpoints. The primary outcomes were the pain scores reported by VAS or NRS and opioid consumption at 24 h after surgery. This time point was selected as a standardized, early postoperative benchmark to assess the initial analgesic efficacy of interventions, while also acknowledging the distinct pain trajectories and mechanisms that may differ between open and laparoscopic procedures. The secondary outcome was PONV, analyzed as a dichotomous outcome within 24 h postoperatively. PONV was defined as any reported nausea, vomiting, or use of rescue antiemetics. All data on opioid consumption was standardized to morphine equivalents utilizing a standardized converter.²¹ These endpoints were selected based on their clinical significance and their ability to elucidate the efficacy and safety of the interventions under evaluation. The distinguishing between primary and secondary outcomes allowed for a structured analysis, emphasizing the main therapeutic effects while accounting for potential adverse events.

Study Risk of Bias Assessment

The methodological rigor of the included studies was evaluated with the Cochrane Risk of Bias Tool, version 2 (RoB 2). This tool examines potential biases in the following domains: randomization processes, compliance with intended interventions, management of missing outcome data, methods of outcome measurement, and selective reporting.²² Each study was rated as having low risk, some concerns, or high risk of bias for every domain. Two reviewers independently performed the bias assessments. Any disagreements were resolved through consultation with a third reviewer, leading to a consensus-based final judgment. Furthermore, confidence in the evidence derived from the included studies was evaluated using the Confidence in Network Meta-Analysis (CINeMA) framework. This approach systematically considers six key domains: within-study bias, reporting bias, indirectness, imprecision, heterogeneity, and incoherence.

Data Analysis

Statistical synthesis was performed using the clinical scientific research platform in R software (version 4.3.2), employing a random-effects model to account for variability across studies. Effect sizes for continuous variables were reported as mean \pm standard deviation (SD) or median (interquartile range [IQR]), with corresponding 95% confidence intervals (CrIs). Heterogeneity was evaluated using Cochran's Q test and Higgins I^2 statistic, with I^2 values of 25%, 50%, and 75% indicating mild, moderate, and high heterogeneity, respectively. A Cochran's Q test results with a p -value < 0.05 were

considered indicative of significant heterogeneity. Comparisons were made against a control group to ensure clarity in intervention efficacy.

Geometry of the Network

Network plots illustrating the relationships among interventions were generated using the `networkplot` function. The NMA was conducted within a Bayesian framework through Markov Chain Monte Carlo (MCMC) simulations, utilizing the “`gemtc`” package in R software.²³ Convergence was assessed using the Brooks-Gelman-Rubin plot method, ensuring that the Gelman-Rubin statistic was less than 1.1. This methodological rigor ensured reliable estimates and minimized biases inherent in the analysis process.

Assessment of Inconsistency

Global inconsistency was evaluated using UME models, which provide a refined framework for accommodating multi-arm trials and visualizing evidence in complex networks.²⁴ Local inconsistency was assessed using the node-splitting method, which separated direct evidence from indirect evidence for specific comparisons.²⁵ Inconsistencies were considered non-significant if the *p*-value exceeded 0.05, suggesting that no substantial inconsistency was detected within the network model.

Rank Probabilities of the Interventions

Ranking probabilities of interventions were calculated using cumulative probability plots and Surface Under the Cumulative Ranking (SUCRA) values.²⁶ SUCRA values ranged from 0% to 100%, with higher values indicating greater probabilities of effectiveness. This ranking system facilitated the comparison of interventions based on their overall efficacy, with SUCRA values providing both intuitive and statistically robust insights into the relative performance of treatments.

Subgroup Analysis

To further explore the potential impact of surgical approaches on analgesic efficacy, we performed prespecified subgroup analyses stratified by surgical type: open hepatectomy versus laparoscopic hepatectomy. For each subgroup, network meta-analyses were conducted separately for the three primary outcomes: postoperative pain scores, cumulative opioid consumption and postoperative nausea and vomiting (PONV). The analytic framework and statistical models were consistent with those of the main analyses. Direct and indirect comparisons were synthesized using Bayesian hierarchical models, with inconsistency assessed by node-splitting and deviance information criterion (DIC) statistics. Surface under the cumulative ranking (SUCRA) values were calculated to estimate the relative ranking probability of each intervention within each subgroup. This stratified approach allowed evaluation of whether the comparative effectiveness of regional or neuraxial techniques varied between open and laparoscopic procedures, given their inherent differences in incision size, tissue trauma, and postoperative recovery profiles.

Additional Analysis

Publication bias was assessed using funnel plots, complemented by Egger’s test to statistically identify asymmetry. While the methods employed were robust, future methodological improvements could incorporate advanced machine learning algorithms for bias detection and adaptive sensitivity analysis to enhance reliability.

Certainty/Quality of Evidence Assessment

The certainty of evidence was evaluated using the GRADE approach, which evaluates both downgraded and upgraded rating domains.²⁷ In this study, we use the GRADE-NMA framework to assess the certainty of the evidence on which each pair of comparisons within the network is based. Downgraded domains included risk of bias, inconsistency, indirectness, imprecision, and publication bias. For instance, heterogeneity across trials or wide confidence intervals led to downgrades by -1 or -2 , depending on the severity of concerns. Upgraded domains—such as large effect size, plausible residual confounding, and dose-response gradients—were reserved for observational studies with compelling evidence. Based on these domains, the quality of evidence was rated as high, moderate, low, or very low, providing a transparent evaluation of the strength of findings.

Results

Study Selection

A total of 835 records were identified through comprehensive database searches, including PubMed (n = 345 records), EMBASE (n = 224 records), Web of Science (n = 132 records), and Cochrane Library (n = 134 records). After the removal of duplicates, 604 unique records remained for screening. During the title and abstract screening process, 456 records were excluded based on predefined criteria, including conference abstracts (n = 49), letters (n = 30), comments (n = 27), reviews/meta-analysis (n = 104), trial protocols (n = 4), observational studies (n = 169), animal studies (n = 5), case reports (n = 48), and records available only as abstracts (n = 20). Subsequently, 148 full-text articles were assessed for eligibility, resulting in the exclusion of 125 articles for reasons such as wrong patient population (n = 33), studies from the same population (n = 4), wrong intervention (n = 64), lack of outcomes of interest (n = 2), and insufficient data for analysis (n = 22). Ultimately, 23 studies met the eligibility criteria and were included in the meta-analysis (Figure 1).

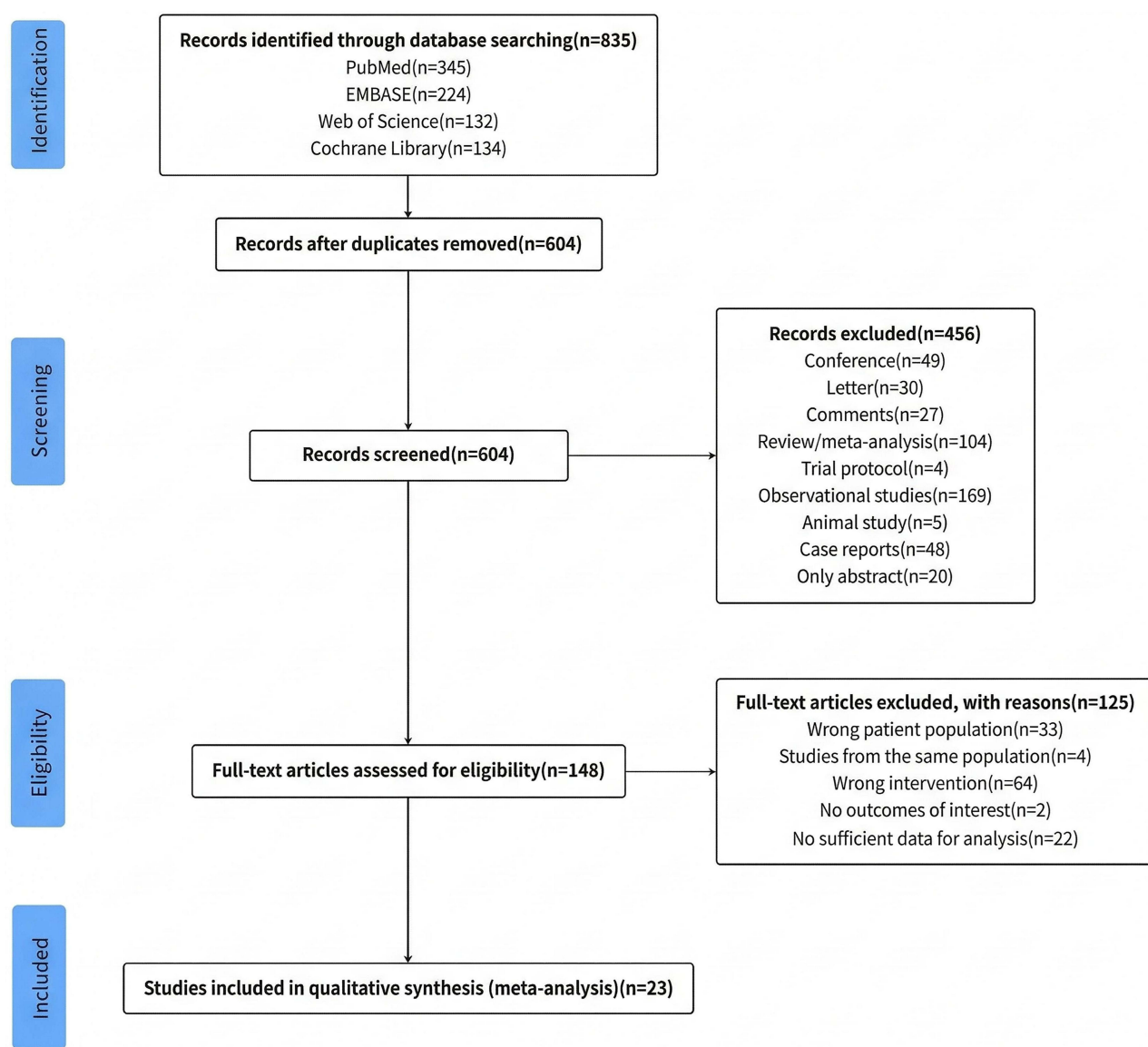


Figure 1 Flow chart of the process of study selection.

Study Characteristics

The meta-analysis incorporated data from a total of 1,382 participants, comprising 694 individuals (50.21%) in the experimental group and 688 individuals (49.73%) in the control group. The mean age of participants was 50.81 years (SD = 15.57) in the experimental group and 51.73 years (SD = 15.48) in the control group. The characteristics of these studies are summarized in [Table 1](#) and [Supplementary Material 2](#). The baseline surgical characteristics included a range of procedures, such as lobe donor hepatic resection, liver resection, hepatectomy, living donor laparoscopic hepatectomy, and hepatectomy for hepatocellular carcinoma (HCC). The diversity in surgical approaches underscores the applicability of findings across a broad spectrum of hepatic surgeries.

Table 1 Baseline Characteristics of Studies Included in the Network Meta-Analysis

Study	Country	Surgery Type	Sample Size (E/C)	Intervention	Outcomes	Outcome Measures
Moussa AA-2008 ²⁸	Saudi Arabia	Open donor hepatectomy	12/12	TPVB	Opioid consumption	Morphine PCA
Chen H-2014 ²⁹	China	Open tumor hepatectomy	22/22	TPVB	Pain score; opioid consumption; PONV	NRS; Sufentanil PCIA; nausea and vomiting
Schreiber KL-2016 ³⁰	United States	Open tumor hepatectomy	41/39	TEA/TPVB	Pain score; opioid consumption; PONV	VRS; Hydromorphone PCA; Incidence of pruritus, nausea
Erdogan MA-2017 ³¹	Turkey	Open donor hepatectomy	22/22	TAPB	Opioid consumption	Morphine
Kitlik A-2017 ³²	Turkey	Open donor hepatectomy	25/25	TAPB	Pain score; opioid consumption; PONV	VAS; Morphine PCA; Nausea and vomiting incidence
Kang R-2019 ³³	South Korea	Laparoscopic donor hepatectomy	27/27	ESPB/ITM	Pain score; opioid consumption; PONV	NRS; Sufentanil PCIA; nausea/vomiting
Qiao XF-2019 ³⁴	China	Open tumor hepatectomy	51/49	TAPB	Pain score	VAS
Zhu Q-2019 ³⁵	China	Open tumor hepatectomy	30/30	QLB	Pain score; PONV	NRS; Sufentanil PCIA; Nausea and vomiting
Fu J-2020 ³⁶	China	Open donor hepatectomy	30/30	ESPB	Pain score	VAS
Zhang J-2020 ³⁷	China	Laparoscopic hepatectomy	24/23	TAPB	Pain score; opioid consumption; PONV	VAS; Sufentanil PCIA; Nausea and vomiting
Kang R-2021 ³⁸	South Korea	Laparoscopic donor hepatectomy	30/29	ESPB/ITM	Pain score; opioid consumption	NRS; Fentanyl PCA
Kim D-2021 ³⁹	Korea	Laparoscopic hepatectomy	35/35	ESPB	Pain score; opioid consumption; PONV	NRS; Fentanyl PCA; incidence of nausea and vomiting
Pang M-2021 ⁴⁰	China	Laparoscopic hepatectomy	30/30	QLB	Opioid consumption	Oxycodone PCIA and sufentanil
Elshafie MA-2022 ⁴¹	Egypt	Open tumor hepatectomy	20/20	ESPB	Opioid consumption; PONV	Fentanyl consumption; Nausea and vomiting incidence
Hacıbeyoğlu G-2022 ⁴²	Turkey	Open hepatectomy	25/25	ESPB	Opioid consumption	Morphine PCA
Huang X-2022 ¹²	China	Open hepatectomy	25/25	ESPB	Pain score	VAS
Lee S-2022 ⁴³	Korea	Laparoscopic donor hepatectomy	27/27	QLB/ITM	Pain score; opioid consumption	NRS; Morphine
Zubair M-2022 ⁴⁴	Pakistan	Open donor hepatectomy	40/40	ESPB/TEA	Pain score; opioid consumption	VAS; Morphine equivalents

(Continued)

Table 1 (Continued).

Study	Country	Surgery Type	Sample Size (E/C)	Intervention	Outcomes	Outcome Measures
Lee S-2024 ⁴⁵	Korea	Laparoscopic hepatectomy	46/46	QLB	Opioid consumption; PONV	Oxycodone PCA (morphine equivalents); Nausea and vomiting incidence
He X.-2018 ⁴⁶	China	Open hepatectomy	30/30	TAPB	Pain score	NRS
Kang RA-2021 ⁴⁷	Korea	Laparoscopic hepatectomy	42/43	ESPB/QLB	Opioid consumption; PONV	NRS; Fentanyl PCA (morphine equivalents); Incidence of nausea, vomiting and pruritus
Mao Y-2023 ⁴⁸	China	Open hepatectomy	30/29	TAPB/QLB	Opioid consumption; PONV	Morphine equivalents; Nausea and vomiting incidence
Mostafa M-2023 ⁴⁹	Egypt	Open hepatectomy	30/30	TAPB/ESPB	Pain score; opioid consumption	NRS; Morphine

Risk of Bias

The methodological quality assessment of the included RCTs showed that most studies had low risk of bias in randomization and completeness of follow-up using the Cochrane RoB-2 tool. The primary concerns regarding bias were related to outcome measurement (eg., subjective outcomes such as pain scores) and selective reporting (mainly due to the lack of published study protocols), resulting in “some concerns” in these domains. However, many trials incorporated objective secondary outcomes (eg., opioid consumption), maintained standardized postoperative protocols, and were prospectively registered. Overall, the risk of bias was predominantly rated as “some concerns,” with very few studies classified as high risk (Figure 2).

Geometry of the Network

The network consisted of six distinct interventions with pairs of direct comparisons across all reported outcomes, including postoperative pain scores, opioid consumption, and PONV. The network geometry revealed 9 comparisons for postoperative pain scores, 11 comparisons for opioid consumption, and 8 comparisons for PONV. This structure provided a well-connected network, enabling robust analysis of both direct and indirect evidence (Figure 3).

Results Under Different Outcomes

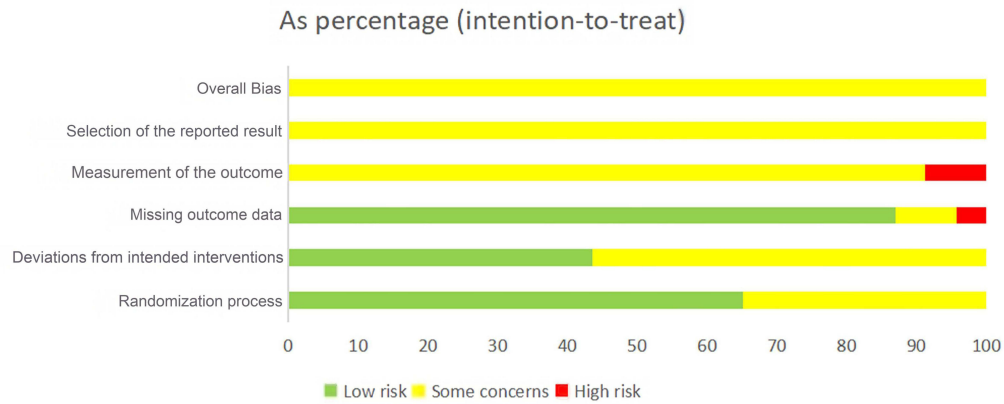
Postoperative Pain Scores

Fifteen studies encompassing a total of 888 participants were analyzed for postoperative pain scores. In the direct comparison, TAPB was also associated with a significant reduction compared with control -0.78 mg (95% credible interval [CrI]: $[-1.49, -0.06]$; $p < 0.05$). In the network comparison, ITM demonstrated a significant reduction in pain scores versus control -1.36 mg (95% credible interval [CrI]: $[-2.52, -0.21]$). All other network and direct comparisons yielded insignificant overall effect sizes (Table 2 and Supplementary Material 3.1). The heterogeneity analysis demonstrated low variability, with an I^2 statistic of 2.6%, indicating consistency across included studies. The GRADE certainty of evidence for this outcome ranged from very low to low (Supplementary Material 4.1). Regarding inconsistency, no evidence of global or local inconsistency was detected, with the difference in Deviance Information Criterion (DIC) value calculated as -0.618 and all local comparisons showing p -values > 0.05 . Based on SUCRA values, the ranking is as follows: ITM (91%), ESPB (59%), TAPB (57%), TEA (50%), QLB (43%), TPVB (38%) (Figure 4 and Supplementary Material 5.1). Despite the highest SUCRA rankings, network comparisons revealed no statistically significant differences between any interventions for postoperative pain scores.

Opioid Consumption

Eighteen studies involving 1,012 participants were included in the analysis of opioid consumption. Direct comparison indicated a significant reduction in opioid consumption favoring TAPB versus control (mean difference [MD]:

A



B

Study ID	D1	D2	D3	D4	D5	Overall
Chen H-2014 ⁴⁰	+	!	+	!	!	!
Elshafie MA-2022 ⁵⁰	!	+	+	!	!	!
Erdogan MA-2017 ⁴²	!	+	+	-	!	!
Fu J-2020 ⁴⁶	+	+	+	!	!	!
Hacibeyoğlu G-2022 ⁵¹	!	+	+	!	!	!
He X.-2018 ⁵⁵	+	+	+	!	!	!
Huang X-2022 ¹²	+	+	+	!	!	!
Kang R-2019 ³⁰	+	!	+	!	!	!
Kang R-2021 ³¹	+	!	+	-	!	!
Kang RA-2021 ⁵⁶	+	+	+	!	!	!
Kim D-2021 ⁴⁸	!	+	+	!	!	!
Kitlik A-2017 ⁴³	!	!	+	!	!	!
Lee S-2022 ⁵²	+	!	+	!	!	!
Lee S-2024 ⁵⁴	+	!	+	!	!	!
Mao Y-2023 ⁵⁷	+	+	+	!	!	!
Mostafa M-2023 ⁵⁸	+	!	-	!	!	!
Moussa AA-2008 ³⁹	+	+	+	!	!	!
Pang M-2021 ⁴⁹	+	!	!	!	!	!
Qiao XF-2019 ⁴⁴	!	!	!	!	!	!
Schreiber KL-2016 ⁴¹	+	!	+	!	!	!
Zhang J-2020 ⁴⁷	!	!	+	!	!	!
Zhu Q-2019 ⁴⁵	!	!	+	!	!	!
Zubair M-2022 ⁵³	!	!	+	!	!	!

+ Low risk
! Some concerns
- High risk

D1 Randomisation process
 D2 Deviations from the intended interventions
 D3 Missing outcome data
 D4 Measurement of the outcome
 D5 Selection of the reported result

Figure 2 Risk of bias assessment using the Cochrane RoB 2 tool. **(A)** Summary of risk of bias judgements across all included studies. **(B)** Risk of bias assessment for each individual study. Domains: D1, Randomization process; D2, Deviations from intended interventions; D3, Missing outcome data; D4, Measurement of the outcome; D5, Selection of the reported result. Judgements: +, Low risk; !, Some concerns; -, High risk.

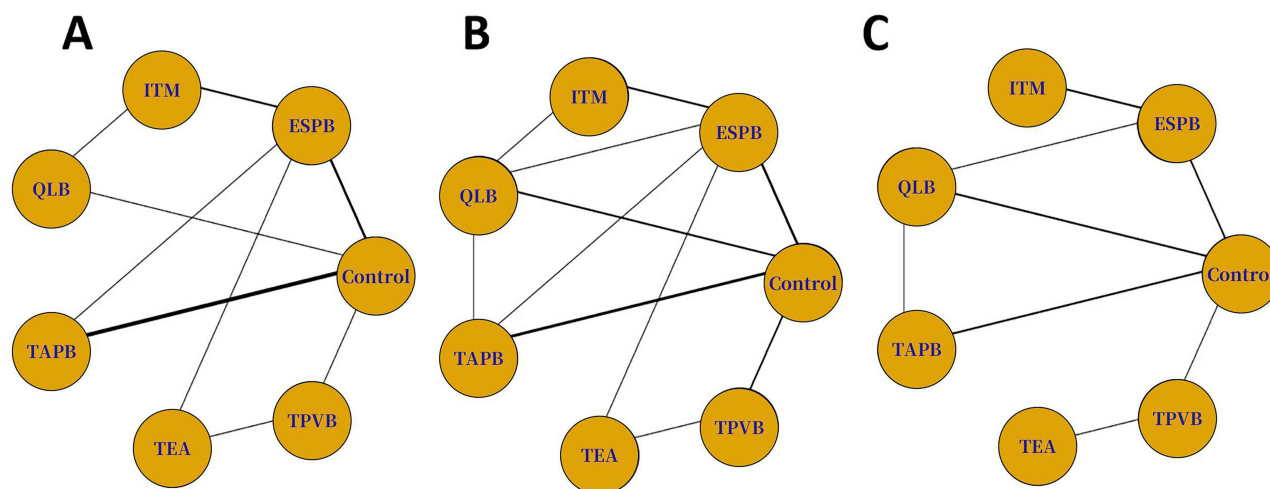


Figure 3 Network geometry plot. (A) Pain score; (B) Opioid consumption; (C) Incidence of PONV. Lines connect the interventions that have been studied in direct comparison in the eligible RCTs. The width of the lines represents the cumulative number of RCTs for each pairwise comparison and the size of every node is proportional to the number of randomized participants. ESPB, erector spinae plane block; TPVB, thoracic paravertebral block; TAPB, transversus abdominis plane block; QLB, quadratus lumborum block; TEA, thoracic epidural analgesia; ITM, intrathecal morphine; PONV, postoperative nausea and vomiting.

-22.40 mg; 95% credible interval [CrI]: [-27.78 to -17.02]; $p < 0.01$). Network comparisons revealed ESPB as significantly superior to control (mean difference [MD]: -36.77 mg; 95% credible interval [CrI]: [-57.95, -15.43]) (Table 3 and Supplementary Material 3.2). Heterogeneity was low, with an I^2 value of 3.9%, confirming consistency across the studies. The GRADE certainty was rated as very low to moderate (Supplementary Material 4.2). No evidence of global or local inconsistency was observed, with a DIC difference of -0.0234 and all local comparisons yielding p -values > 0.05 . Based on SUCRA values, the ranking is as follows: ITM (88%), ESPB (79%), TEA (57%), TAPB (44%), QLB (41%), TPVB (37%), Control (5%) (Figure 5 and Supplementary Material 5.2).

PONV

Twelve studies with 740 participants were analyzed for PONV. No intervention demonstrated statistically significant superiority in reducing PONV incidence. Moreover, network comparisons revealed insignificant effect sizes for all intervention groups (Table 4 and Supplementary Material 3.3). The heterogeneity for PONV was low, with an I^2 statistic of 9.3%. The GRADE certainty was rated as very low to low (Supplementary Material 4.3). While no local inconsistency was detected (all $p > 0.05$), as well as global inconsistency was not present, with a DIC difference of -0.90. Based on SUCRA values, the ranking is as follows: ESPB (72%), TPVB (60%), QLB (57%), TEA (53%), ITM (45%), TAPB (39%), Control (25%) (Figure 6, Supplementary Material 5.3 and summary rankings are presented in Table 5).

Table 2 The Network League Tables of Comparisons of Pain Scores Between Interventions

Control	ESPB	ITM	QLB	TAPB	TEA	TPVB
Control	-0.71 (-1.43, 0.02)	-1.36 (-2.52, -0.21)	-0.47 (-1.76, 0.85)	-0.69 (-1.42, 0.07)	-0.58 (-2.02, 0.81)	-0.37 (-1.67, 1.00)
0.71 (-0.02, 1.43)	ESPB	-0.65 (-1.67, 0.36)	0.24 (-1.11, 1.58)	0.03 (-0.89, 0.97)	0.14 (-1.20, 1.46)	0.34 (-1.02, 1.84)
1.36 (0.21, 2.52)	0.65 (-0.36, 1.67)	ITM	0.89 (-0.42, 2.21)	0.68 (-0.61, 2.00)	0.78 (-0.86, 2.40)	0.99 (-0.65, 2.75)
0.47 (-0.85, 1.76)	-0.24 (-1.58, 1.11)	-0.89 (-2.21, 0.42)	QLB	-0.22 (-1.68, 1.27)	-0.11 (-1.95, 1.73)	0.11 (-1.70, 1.99)
0.69 (-0.07, 1.42)	-0.03 (-0.97, 0.89)	-0.68 (-2.00, 0.61)	0.22 (-1.27, 1.68)	TAPB	0.11 (-1.45, 1.60)	0.32 (-1.16, 1.86)
0.58 (-0.81, 2.02)	-0.14 (-1.46, 1.20)	-0.78 (-2.40, 0.86)	0.11 (-1.73, 1.95)	-0.11 (-1.60, 1.45)	TEA	0.22 (-1.19, 1.76)
0.37 (-1.00, 1.67)	-0.34 (-1.84, 1.02)	-0.99 (-2.75, 0.65)	-0.11 (-1.99, 1.70)	-0.32 (-1.86, 1.16)	-0.22 (-1.76, 1.19)	TPVB

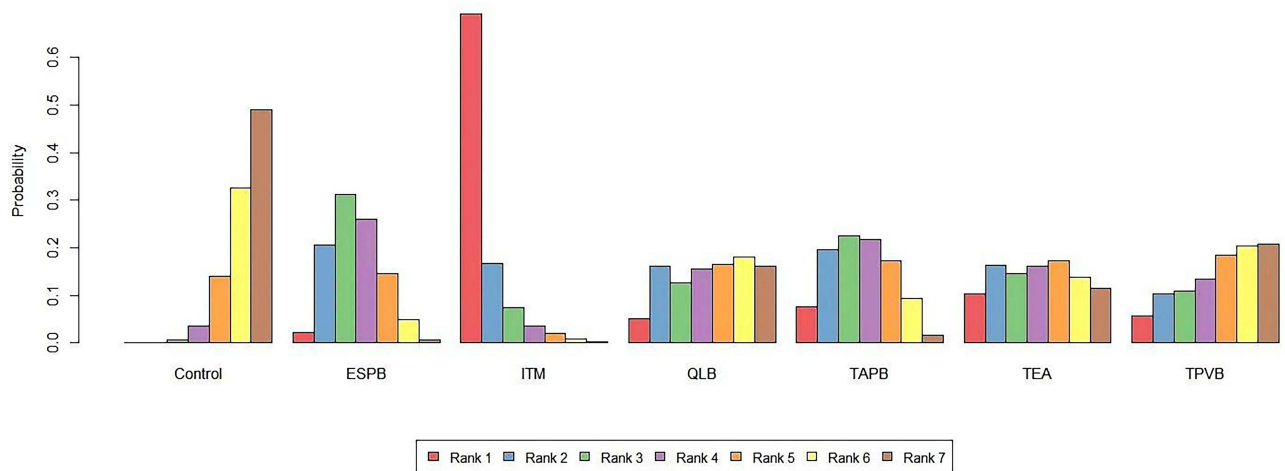


Figure 4 Ranking probabilities of interventions for postoperative pain scores based on SUCRA. A higher SUCRA value (closer to 100) indicates a higher probability of being the most effective intervention. The color gradient from red (Rank 1, best) to brown (Rank 7) represents the probability of each intervention achieving a given rank.

Subgroup Analysis

In subgroup analysis stratified by surgical type, no intervention demonstrated a significant reduction in pain scores compared with control in open hepatectomy, although SUCRA rankings favored ESPB (83%), followed by TAPB (63%) and TEA (63%). In laparoscopic hepatectomy, intrathecal morphine (ITM) significantly reduced pain scores versus control (MD -1.22 mg; 95% CrI: -2.46 to -0.003), ranking highest (92%), with ESPB (57%) and QLB (47%) following (Figure 7, Table 6 and Supplementary Material 6.1). For opioid consumption, ESPB was superior to control in the open subgroup (MD -54.70 mg; 95% CrI: -90.04 to -20.03), ranking highest (85%) alongside QLB (70%) and TEA (58%), whereas ITM significantly reduced opioid use in the laparoscopic subgroup (MD -18.6 mg; 95% CrI: -34.81 to -1.95), ranking first (88%), followed by TAPB (77%) and ESPB (51%) (Figure 7, Table 6 and Supplementary Material 6.2). Regarding PONV, no intervention achieved significant reductions compared to control in either subgroup, although SUCRA rankings indicated ESPB (99%) as the most favorable in open procedures, while ITM (88%) and TAPB (77%) were most likely to be effective in laparoscopic procedures (Figure 7, Table 6 and Supplementary Material 6.3).

Publication Bias

Publication bias was assessed across the outcomes using Egger’s Test. No evidence of publication bias was detected for PONV ($p = 0.67$). However, a potential risk of publication bias was observed for postoperative pain scores ($p = 0.036$) and opioid consumption ($p = 0.041$) (Figure 8).

Table 3 The Network League Tables of Comparisons of Opioid Consumption Between Interventions

Control	ESPB	ITM	QLB	TAPB	TEA	TPVB
Control	-36.77 (-57.95, -15.43)	-43.82 (-77.49, -10.92)	-18.73 (-43.15, 5.27)	-19.76 (-42.69, 2.66)	-26.39 (-64.68, 11.93)	-16.18 (-46.00, 13.94)
36.77 (15.43, 57.95)	ESPB	-7.16 (-35.67, 21.23)	17.90 (-7.67, 43.46)	16.83 (-9.83, 43.54)	10.38 (-27.00, 47.29)	20.43 (-12.88, 54.93)
43.82 (10.92, 77.49)	7.16 (-21.23, 35.67)	ITM	25.24 (-6.88, 57.17)	24.15 (-11.90, 60.64)	17.49 (-27.75, 64.09)	27.62 (-13.81, 71.22)
18.73 (-5.27, 43.15)	-17.90 (-43.46, 7.67)	-25.24 (-57.17, 6.88)	QLB	-1.05 (-29.11, 27.24)	-7.53 (-50.15, 35.10)	2.60 (-34.21, 40.54)
19.76 (-2.66, 42.69)	-16.83 (-43.54, 9.83)	-24.15 (-60.64, 11.90)	1.05 (-27.24, 29.11)	TAPB	-6.54 (-49.15, 36.30)	3.58 (-32.78, 40.57)
26.39 (-11.93, 64.68)	-10.38 (-47.29, 27.00)	-17.49 (-64.09, 27.75)	7.53 (-35.10, 50.15)	6.54 (-36.30, 49.15)	TEA	10.15 (-26.97, 48.06)
16.18 (-13.94, 46.00)	-20.43 (-54.93, 12.88)	-27.62 (-71.22, 13.81)	-2.60 (-40.54, 34.21)	-3.58 (-40.57, 32.78)	-10.15 (-48.06, 26.97)	TPVB



Figure 5 Ranking probabilities of interventions for opioid consumption based on SUCRA. A higher SUCRA value (closer to 100) indicates a higher probability of being the most effective intervention. The color gradient from red (Rank 1, best) to brown (Rank 7) represents the probability of each intervention achieving a given rank.

Discussion

Key Findings and Comparative Efficacy

Effective postoperative pain management after hepatic resection remains a central clinical challenge. This Bayesian NMA, the first to compare multiple regional and neuraxial techniques across both open and laparoscopic approaches, synthesizes data from 23 RCTs (1,382 patients). The most salient finding is that no regional analgesic technique demonstrated statistically significant superiority over another in the primary network comparisons for 24-hour pain scores or opioid consumption. The certainty of evidence (GRADE) for these comparisons ranged from low to very low. This fundamental context is crucial for interpreting the subsequent, more nuanced findings.

Within this framework of statistical equipoise, interventions showed varied efficacy compared to the control. For pain scores, ITM and TAPB demonstrated significant reductions versus control. For opioid consumption, ESPB and TAPB were superior to control. Probability-based rankings (SUCRA) suggested ITM and ESPB had the highest likelihood of being optimal for pain relief and opioid-sparing, respectively. However, these rankings should be viewed as exploratory and hypothesis-generating rather than definitive proof of clinical superiority, given the lack of statistical significance between active comparators and the limited evidence quality. No intervention significantly reduced the incidence of PONV compared to control or other active techniques. Low statistical heterogeneity and no inconsistency were observed across outcomes, supporting the robustness of the network model.

Table 4 The Network League Tables of Comparisons of PONV Between Interventions

Control	ESPB	ITM	QLB	TAPB	TEA	TPVB
Control	0.32 (0.03, 1.65)	0.61 (0.02, 7.68)	0.47 (0.07, 2.39)	0.74 (0.11, 4.86)	0.47 (0.01, 35.27)	0.40 (0.02, 8.73)
3.15 (0.61, 34.95)	ESPB	1.94 (0.24, 15.08)	1.49 (0.21, 16.72)	2.33 (0.25, 49.00)	1.48 (0.02, 266.97)	1.23 (0.04, 76.42)
1.63 (0.13, 45.41)	0.52 (0.07, 4.18)	ITM	0.77 (0.05, 20.87)	1.20 (0.06, 50.33)	0.76 (0.01, 212.44)	0.63 (0.01, 67.60)
2.12 (0.42, 14.66)	0.67 (0.06, 4.70)	1.30 (0.05, 20.61)	QLB	1.57 (0.20, 16.71)	0.99 (0.01, 122.43)	0.83 (0.02, 34.42)
1.35 (0.21, 8.90)	0.43 (0.02, 3.99)	0.84 (0.02, 15.63)	0.64 (0.06, 5.04)	TAPB	0.62 (0.01, 74.12)	0.53 (0.01, 20.38)
2.13 (0.03, 161.36)	0.68 (0.00, 56.84)	1.32 (0.00, 165.84)	1.01 (0.01, 94.17)	1.61 (0.01, 177.39)	TEA	0.82 (0.04, 17.19)
2.52 (0.11, 60.31)	0.81 (0.01, 23.17)	1.59 (0.01, 74.64)	1.20 (0.03, 40.57)	1.89 (0.05, 76.60)	1.22 (0.06, 23.87)	TPVB

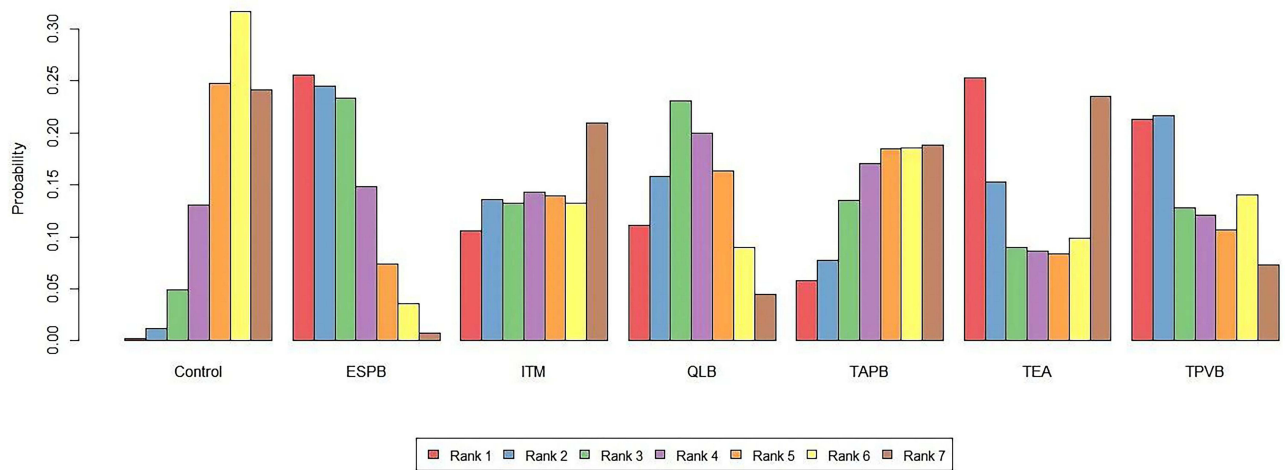


Figure 6 Ranking probabilities of interventions for PONV based on SUCRA. A higher SUCRA value (closer to 100) indicates a higher probability of being the most effective intervention. The color gradient from red (Rank 1, best) to brown (Rank 7) represents the probability of each intervention achieving a given rank.

Comparison with Existing Literature

Our findings regarding ESPB’s opioid-sparing effect contrast with recent meta-analyses by Qian J et al and Bhushan S et al which reported no significant opioid reduction with ESPB.^{50,51} The apparent discrepancies between our findings—such as the high ranking of fascial plane blocks (eg., ESPB) and the limited advantage of TEA in open surgery—and some existing recommendations (eg., PROSPECT guidelines which may prioritize neuraxial techniques) warrant consideration. These differences may be attributed to variations in the case mix (eg., proportion of donor vs. oncologic resections), defined endpoints (eg., 24-hour opioid consumption vs. pain scores at rest/activity), and the sample size and power of the included RCTs, which collectively influence the pooled effect estimates and rankings. Our analysis, by incorporating indirect evidence and a broader intervention spectrum, provides an updated, probability-based perspective that complements guideline narratives.

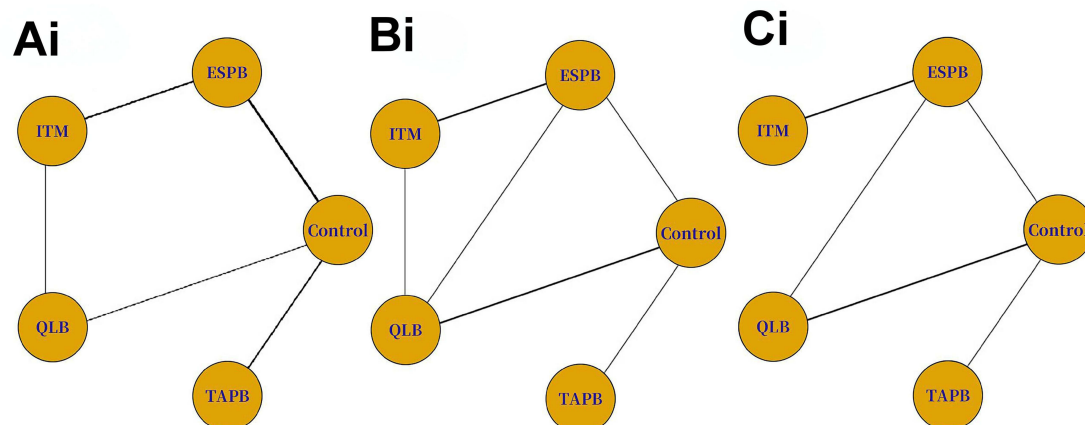
Clinical Implications and Mechanistic Insights

In summary, while specific techniques (ITM, TAPB, ESPB) showed advantages over conventional systemic analgesia, the lack of statistically significant differences between the active regional interventions themselves suggests comparable analgesic efficacy among the compared neuraxial and fascial plane techniques for hepatic surgery, based on the current evidence. Therefore, clinical decision-making should not rely solely on SUCRA rankings but should prioritize the surgical approach (open vs. laparoscopic), patient-specific factors, and institutional resources and expertise. The potential mechanistic

Table 5 Summary of SUCRA Rankings for Six Interventions

Intervention	Pain Scores		Opioid Consumption		PONV	
	SUCRA (%)	Rank	SUCRA (%)	Rank	SUCRA (%)	Rank
ITM	90.58	1	87.85	1	44.85	5
ESPB	58.78	2	79.07	2	72.07	1
TAPB	57.24	3	43.74	4	39.08	6
TEA	49.81	4	56.71	3	52.83	4
QLB	43.17	5	40.8	5	56.7	3
TPVB	37.91	6	36.64	6	59.93	2
Control	12.5	7	5.2	7	24.55	7

Laparoscopic hepatectomy



Open hepatectomy

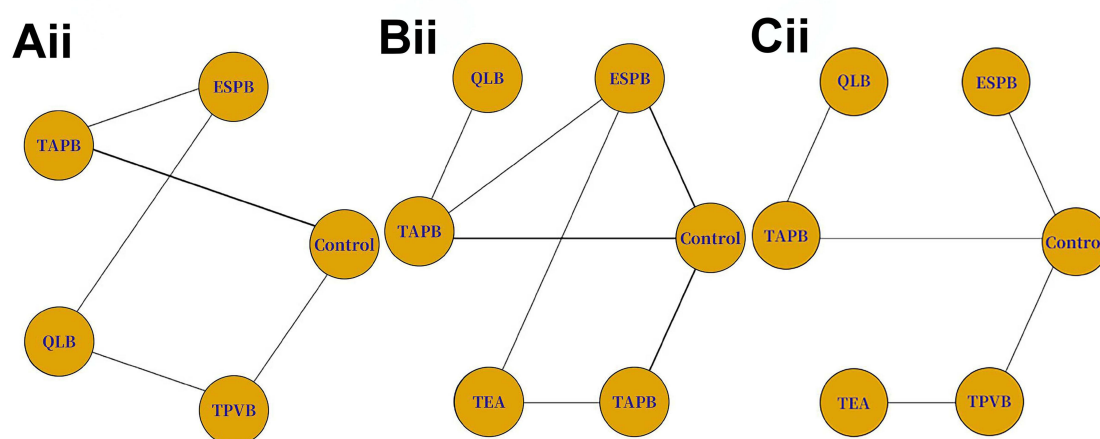


Figure 7 Network geometry plot of subgroup for laparoscopic vs. open hepatectomy. Upper panels (Ai, Bi, Ci) represent outcomes in patients undergoing laparoscopic hepatectomy; Lower panels (Aii, Bii, Cii) represent outcomes in patients undergoing open hepatectomy. **(A)** Pain score; **(B)** Opioid consumption; **(C)** Incidence of PONV. Lines connect the interventions that have been studied in direct comparison in the eligible RCTs. The width of the lines represents the cumulative number of RCTs for each pairwise comparison and the size of every node is proportional to the number of randomized participants.

superiority of one technique over another (eg., visceral coverage) cannot be confirmed by this aggregate data and requires dedicated physiological study. Mechanistic interpretations (eg., ITM's potential "ceiling effect" attributed to spinal opioid receptor binding, typically using morphine doses of about 400 μg and often without adjunct local anesthetic in the included studies) should be viewed cautiously as they were not directly assessed in this analysis.^{33,38} Adverse events like respiratory depression, pruritus, and urinary retention associated with ITM were reported in some included studies but were not systematically measured or meta-analyzed across all studies, limiting definitive safety comparisons.⁵²

The broader literature indicates that patients receiving ESPB are likely to experience reduced PONV compared to those managed with conventional opioid-based analgesia.^{51,53,54} This finding contrasts with conventional assumptions that linking opioid-sparing effects to reduced PONV, suggesting that PONV pathophysiology in hepatic surgery may involve additional factors beyond opioid exposure (eg., surgical stress, bile duct manipulation).^{55–57} Furthermore, the true effect of ESPB and other regional blocks on PONV remains obscured by the underreporting of null findings, as suggested by the evidence of publication bias.⁵⁸ Consequently, multimodal antiemetic prophylaxis tailored to individual patient risk remains essential, irrespective of the analgesic modality chosen.

Table 6 Summary of SUCRA Rankings for Subgroup Interventions

Intervention	Pain Scores		Opioid Consumption		PONV	
	SUCRA (%)	Rank	SUCRA (%)	Rank	SUCRA (%)	Rank
Laparoscopic hepatectomy						
ITM	92.19	1	87.77	1	16.68	5
ESPB	57.14	2	51.46	3	57.6	3
QLB	47.21	3	21.57	4	61.19	2
TAPB	34.33	4	76.6	2	72.22	1
Control	19.12	5	12.6	5	42.3	4
Open hepatectomy						
ESPB	82.87	1	84.61	1	99.29	1
TAPB	62.74	2	49.86	4	33.32	5
TEA	62.57	3	57.86	3	42.97	4
TPVB	34	4	31.66	5	48.76	2
Control	7.82	5	5.62	6	26.94	6
QLB	N/A	N/A	70.39	2	48.73	3

Abbreviations: VAS, Visual Analog Scale; ERAS, Enhanced recovery after surgery; PONV, Postoperative nausea and vomiting; ESPB, Erector spinae plane block; TAPB, Transversus abdominis plane block; NMA, Network meta-analysis; RCTs, Randomized controlled trials; TPVB, Thoracic paravertebral block; QLB, Quadratus lumborum block; TEA, Thoracic epidural analgesia; ITM, Intrathecal morphine; NRS, Numeric Rating Scale; PRISMA-NMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; MD, Mean difference; SD, Standard deviation; IQR, Interquartile range; CIs, Confidence intervals; CrIs, Credible Intervals; I², Higgins I²; MCMC, Markov Chain Monte Carlo; UME models, Unrelated Mean Effects models; SUCRA, Surface Under the Cumulative Ranking; GRADE, Grading of Recommendations Assessment, Development and Evaluation; HCC, Hepatocellular carcinoma; LAST, Local anesthetic systemic toxicity; RR, Relative risk; DIC, Deviance Information Criterion.

Limitations

Several limitations merit consideration. First, while SUCRA rankings provide a valuable hierarchy of interventions, they do not equate to clinical superiority without statistical significance, they should be interpreted with extreme caution when based on non-significant differences and low-certainty evidence. Second, a significant limitation is the underreporting and inability to perform a quantitative synthesis of safety data, particularly for intrathecal morphine (ITM)-related adverse events (eg., respiratory depression, pruritus). This precludes a comprehensive risk-benefit assessment across the compared techniques. Third, our analyses for certain outcomes, notably postoperative nausea and vomiting (PONV), were

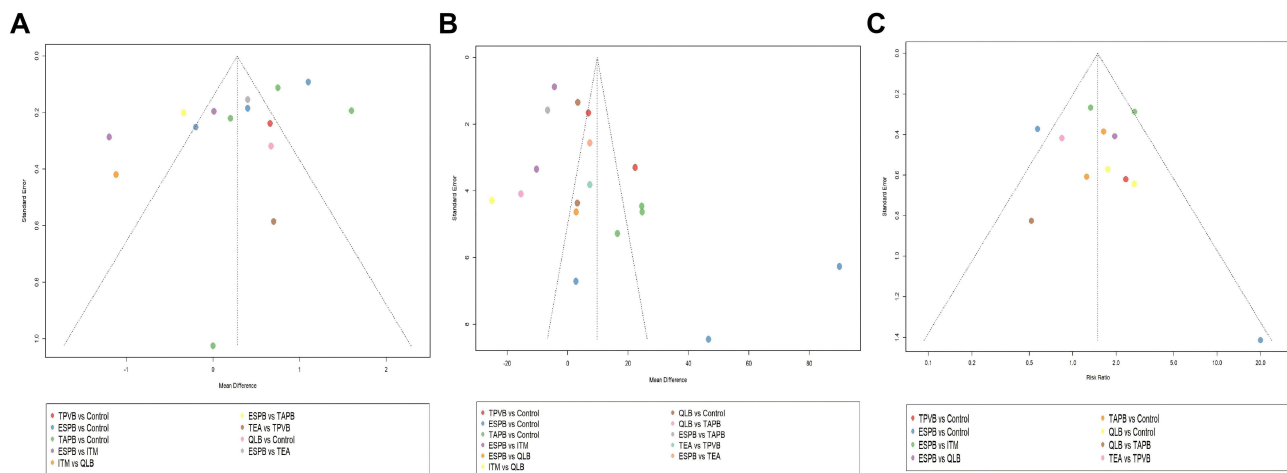


Figure 8 Comparison-adjusted funnel plot for presence of publication bias. (A) Pain score; (B) Opioid consumption; (C) Incidence of PONV. Symmetry suggests low publication bias risk, while asymmetry indicates potential bias. Data points: Represent comparison-specific effect estimates.

likely underpowered due to limited event data and variable reporting in primary studies. Furthermore, the comparative evidence for chronic post-surgical pain is absent, as available data are heavily skewed towards short-term perioperative outcomes. Finally, the potential impact of publication bias and small-study effects on the summary estimates, particularly for opioid consumption, cannot be ruled out and may inflate the perceived benefits of regional techniques. The evidence base also remains constrained by the predominance of small-scale studies, which limited more granular subgroup analyses. Future trials should routinely report more metrics to enable risk-adjusted analyses, which may have important clinical implications for facilitating larger sample sizes and high quality RCTs.

Conclusion

In summary, this NMA synthesizes evidence suggesting that regional analgesic techniques are associated with opioid-sparing benefits compared to conventional analgesia after hepatic resection. Subgroup analyses indicated a potential preference for ESPB in open surgery and for ITM in laparoscopic procedures, while ITM and TAPB showed advantages for pain reduction versus control. However, no statistically significant differences in analgesic efficacy or PONV reduction were demonstrated among the active regional interventions themselves. These probability-based rankings, derived from low to very low certainty evidence, should be considered exploratory. Clinical decision-making should therefore prioritize the surgical approach, patient-specific factors, and institutional resources over SUCRA rankings. A key contribution of this work is the novel comparative synthesis of evidence for laparoscopic hepatectomy, an area previously lacking comprehensive analysis. Substantial gaps remain regarding long-term outcomes and comparative safety profiles, underscoring the need for large, pragmatic trials with standardized outcome assessments.

Data Sharing Statement

All data generated during this study are included in this published article. Available upon request from the corresponding author at 136681973@qq.com.

Ethics Approval and Consent to Participate

The study was registered with the UK National Institute for Health Research's PROSPERO platform on 5 Jun 2025 (CRD 420251062957).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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