



Regional analgesia techniques for lumbar spine surgery: a frequentist network meta-analysis

Boohwi Hong, MD, PhD^{a,b,d}, Sujin Baek, MD^{a,b}, Hyemin Kang, MD^{a,b}, Chahyun Oh, MD, PhD^{a,b}, Yumin Jo, MD, PhD^{a,b}, Soomin Lee, MD, PhD^{a,b}, Seyeon Park, RN, PhD^{c,*}

Background: Various regional analgesia techniques are used to reduce postoperative pain in patients undergoing lumbar spine surgery. Traditionally, wound infiltration (WI) with local anesthetics has been widely used by surgeons. Recently, other regional analgesia techniques, such as the erector spinae plane block (ESPB) and thoracolumbar interfascial plane (TLIP) block, are being used for multimodal analgesia. The authors aimed to determine the relative efficacy of these using a network meta-analysis.

Materials and methods: The authors searched PubMed, EMBASE, the Cochrane Controlled Library, and Google Scholar databases to identify all randomized controlled trials that compared the analgesic efficacy of the following interventions: ESPB, TLIP block, WI technique, and controls. The primary endpoint was postoperative opioid consumption during the first 24 hours after surgery, while the pain score, estimated postoperatively at three different time periods, was the secondary objective.

Results: The authors included 34 randomized controlled trials with data from 2365 patients. TLIP showed the greatest reduction in opioid consumption compared to controls [mean difference (MD) = -15.0 mg; 95% CI: -18.8 to -11.2]. In pain scores, TLIP had the greatest effect during all time periods compared to controls (MD = -1.9 in early, -1.4 in middle, -0.9 in late). The injection level of ESPB was different in each study. When only surgical site injection of ESPB was included in the network meta-analysis, there was no difference compared with TLIP (MD = 1.0 mg; 95% CI: -3.6 to 5.6).

Conclusions: TLIP showed the greatest analgesic efficacy after lumbar spine surgery, in terms of postoperative opioid consumption and pain scores, while ESPB and WI are also alternative analgesic options for these surgeries. However, further studies are needed to determine the optimal method of providing regional analgesia after lumbar spine surgery.

Keywords: erector spinae plane block, lumbar spine surgery, nerve block, network meta-analysis, postoperative pain, thoracolumbar interfascial plane block

Introduction

Lumbar spine surgery is a commonly performed orthopedic or neurosurgical procedure associated with moderate-to-severe postoperative pain^[1]. Timely and adequate pain management

^aDepartment of Anesthesiology and Pain Medicine, Chungnam National University Hospital, ^bDepartments of Anesthesiology and Pain Medicine, College of Medicine, Chungnam National University, ^cDepartment of Nursing, College of Nursing, Chungnam National University and ^dBiomedical Research Institute, Chungnam National University Hospital, Daejeon, Korea

B.H. and S.B. contributed equally to this work as co-first author.

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*Corresponding author. Address: Department of Nursing, College of Nursing, Chungnam National University, Jung-gu, Munhwa-ro 266, Daejeon 35015, South Korea. Tel: +82 425 808 329; fax: +86 425 808 309. E-mail address: park_sy@cnu.ac.kr (S. Park).

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HIGHLIGHTS

- Various regional analgesia techniques are used to reduce postoperative pain in patients undergoing lumbar spine surgery.
- We employed a network meta-analysis to assess the postoperative analgesic efficacy of erector spinae plane block, thoracolumbar interfascial plane (TLIP) block, wound infiltration, and controls.
- TLIP block showed the greatest analgesic efficacy after lumbar spine surgery.
- The erector spinae plane block performed at the surgical level showed similar efficacy to the TLIP block.

after spinal surgery is important for early ambulation and improving functional outcomes. There are several types of surgery, such as laminectomy, decompression, fusion, and discectomy, depending on the type and invasiveness of the disease^[2]. The intensity of postoperative pain is dependent on various nociceptive and neuropathic pain mechanisms^[3], which come into play in response to mechanical irritation, compression, or postoperative inflammation in the related anatomical structures.

Traditionally, wound infiltration (WI) with local anesthetics has been widely used by surgeons to manage postoperative pain following lumbar spine surgery^[4]. The method is simple, safe, and may reduce the use of opioids, additional complications during perioperative periods, the duration of hospitalization, and

costs. However, the clinical significance of these advantages was small and limited to the immediate postoperative period^[4].

Recently, other regional analgesia techniques, such as the erector spinae plane block (ESPB)^[5–7] and thoracolumbar interfascial plane (TLIP) block^[8–10], are being used for multimodal analgesia for lumbar spine surgery. These techniques target the dorsal rami of the spinal nerves to anesthetize the posterior midline area.

Although many studies have reported the efficacy of these regional analgesia techniques and compared their effectiveness in spine surgery, the relative efficacy of these techniques has not been compared using network meta-analysis (NMA). NMA is a statistical technique for estimating the effect size of several studies with multiple interventions or treatments. The indirect comparisons of different groups that have never been directly compared are possible through a third or another comparator. If multiple treatment groups are to be compared at the same time, a mixed treatment comparison can be performed using both direct and indirect comparison studies. Thus, NMA identifies the most superior group and estimate a relative ranking^[11]. Therefore, we identified and reviewed all articles that have investigated the effects of various methods of postoperative analgesia in lumbar spine surgery and used NMA to rank these methods according to their effectiveness.

Our primary outcome was opioid consumption during the first 24 hours after surgery, and we evaluated pain severity at three different postoperative periods, namely early, middle, and late, as the secondary outcome.

Materials and methods

This study was conducted in accordance with the recommended guidelines of the Preferred Reporting Items for Systematic Review and Meta-Analysis^[12] and registered with the International Prospective Register of Systematic Reviews (PROSPERO, CRD42022309271).

Data source and search strategy

A literature search was conducted independently by two authors to identify eligible studies for this systematic review and meta-analysis. The databases searched were PubMed, EMBASE, and the Cochrane Library. Medical Subject Heading and text terms were combined and followed by Boolean logical operators. The language was limited to English, and an exhaustive search was conducted using the following Medical Subject Heading terms: [{"Lumbar spine" OR "Spinal stenosis OR Spondylolisthesis) AND (Decompression OR "Surgical Procedures, Operative")}] AND [{"Thoracolumbar interfascial plane block" OR TLIP OR "Erector spinae plane block" OR ESPB) AND ("Anesthesia, Local" OR "Local anesthetic infiltration")}]". The primary search was conducted in January 2022, and an additional search was conducted on 28 February 2022 during the revision to include more recent studies. The reference lists of selected articles were searched manually. Full search strategies for individual data are provided in Figure 1.

Inclusion and exclusion criteria

Studies were deemed eligible if they were randomized controlled trials (RCTs), published in English, and reported postoperative pain scores in both experimental and control groups, or outcomes

as pain scores and quantity of opioids consumed. Non-RCTs (quasiexperimental design), abstracts, conference proceedings, unpublished grey literature, and review studies were excluded. Among regional analgesia techniques, studies that used continuous block by catheterization and adjuvants were excluded.

Review procedure

Study selection involved six steps. First, two investigators imported the titles and abstracts of identified articles into a reference management software (EndNote 20; Clarivate) and performed a preliminary review. Second, duplicate articles were identified and eliminated using the reference management software. Third, they independently reviewed all imported studies and excluded those that did not conform to the inclusion criteria, such as study design, participants, type of intervention, or comparisons. Fourth, three investigators independently reviewed all the titles and abstracts for relevance. Fifth, we retrieved the full text of the papers that met all the inclusion criteria for data extraction and linked multiple reports of the same study. Lastly, the finalized studies were confirmed and coded for analysis by two investigators. The coding sheets were independently checked for accuracy by investigators not involved in the review process.

Data extraction

Information from the included articles was independently extracted by two reviewers, and each selection was reviewed twice by both reviewers together. To evaluate the outcomes in individual studies, pain scores and opioid consumption were determined for each group, and the mean and SD were obtained. Median and interquartile ranges, as approximations of mean and SD, were determined using an estimation method proposed by Wan *et al.*^[13]. When outcome data were available only as a graph, a virtual ruler was used to extract the value by matching the interval between the basic unit of the plot and the ruler. Effect sizes and standard errors were calculated. Additional data, including location, sample size, characteristics of individual study populations, and intervention designs, were extracted using a predesigned data extraction table.

Outcome definitions

The primary outcome was cumulative opioid consumption during the first 24 hours after surgery. All opioids were converted to equianalgesic intravenous (i.v.) morphine doses (i.v. morphine 1 mg = i.v. fentanyl 10 µg = i.v. sufentanil 2 µg = i.v. tramadol 10 mg = i.v. pethidine 7.5 mg)^[14,15]. The secondary outcome was a pain score assessed at three time periods during the first 24 hours after surgery, namely, early (up to 6 h), middle (6–18 h), and late (18–24 h). When multiple data points were available for each time period, pain scores closest to 1 h for early, 12 h for middle, and 24 h for late were used. Pain scores determined using visual analog scales (VASs) were converted to a 0–10 analog scale to permit statistical evaluation.

Data synthesis and statistical analysis

A random-effects NMA within a frequentist framework was performed using R software, version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria), and the 'netmeta' package for frequentist NMA^[16,17]. A network plot was constructed to evaluate both direct and indirect comparisons of

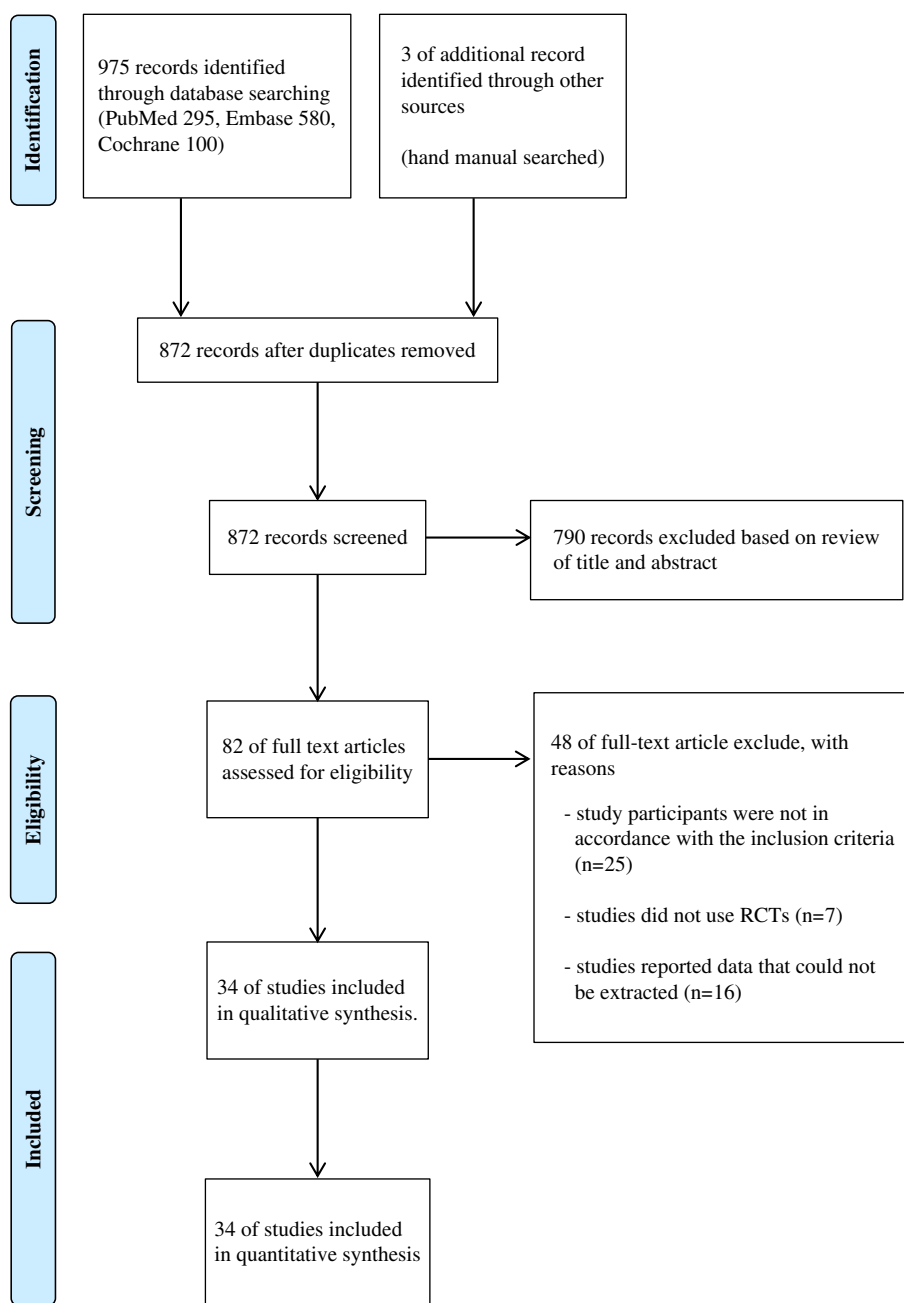


Figure 1. Study flow diagram. RCT, randomized controlled trial.

network structure using data from all included studies. Heterogeneity was evaluated using the I^2 statistic. The Q -statistic, based on the full design-by-treatment interaction random-effects model, was calculated to evaluate global inconsistencies^[18]. Local inconsistencies between direct and indirect effects were evaluated using the net splitting technique. If the P value of the net splitting was below 0.05, we presumed a significant disagreement (inconsistency) between the direct and indirect estimates. Net split results were visualized as forest plots, with a direct evidence plot showing the percentage of direct and indirect evidence used for each estimated comparison. A mean path length greater than 2 indicated that a comparison estimate

should be interpreted with caution. In addition, a net heat plot was constructed to ascertain the importance of each comparison and detect any inconsistencies in the design. A network league table and forest plot were obtained to evaluate the results of the comparisons between interventions. Outcomes are presented as mean differences (MDs) with a 95% CI. To rank the analgesic interventions according to their efficacy, we used the P scores, which are based solely on the point estimates and SEs of the network estimates^[19]. In addition, the resampling method with 100,000 simulations is used to calculate the surface under the cumulative ranking curves (SUCRA) for frequentist NMA. The P score and SUCRA ranged from 0 to 1, where, statistically, 1

indicated the best and 0 the worst. Any potential publication bias was assessed using comparison-adjusted funnel plots and Egger's test. To enhance the applicability of the study findings, we used Grading of Recommendations Assessment, Development, and Evaluation (GRADE) (Table 4) to evaluate the evidence level of the included outcomes. We rated the quality of the evidence as very low, low, moderate, and high. The ratings depended on the presence of risk in five areas: methodological quality, directness of evidence, heterogeneity, precision of effect estimates, and publication bias. The GRADE approach appraises the quality of a body of evidence for each outcome based on five domains: (1) risk of bias of the included studies (methodological quality), (2) inconsistency (i.e. heterogeneity), (3) indirectness (relevance to the review question), (4) imprecision (i.e. confidence intervals), and (5) risk of publication bias^[20].

Results

Baseline characteristics of the included studies

The literature screening process and results are shown in Figure 1. The screening sequence of the Preferred Reporting Items for Systematic Review and Meta-Analysis 2009 flow diagram, which compared the analgesic efficacy of TLIP block, ESPB WI, and controls (no block), identified 34 studies^[21–54], corresponding to a total of 2365 patients.

In total 978 records were obtained from the initial literature search. Based on full-text examination, 48 records were excluded for various reasons: 25 studies were not in accordance with the inclusion criteria, 7 studies were not RCTs, and 16 studies reported data that could not be extracted (Fig. 1). Table 1 lists the characteristics of the included studies, while Table 2 provides data on the number of included studies and enrolled patients sorted by outcome. The raw data of this NMA is provided as Supplementary Materials 1, Supplemental Digital Content 1, <http://links.lww.com/JS9/A98>.

Methodological quality and risk of bias

Individual studies were assessed using the Cochrane Collaboration's Risk of Bias (ROB) tool^[20] and ranked according to a low/high/unclear grading scale (Fig. 2). The ROB assessment was performed in Reviewer Manager (5.4 version). The overall quality of the 34 studies included was moderate. Included articles with clear explanations of random sequence generation and allocation concealment had a low risk of bias, whereas those without explanations had a high risk or were unclear. Some studies showed possible bias in patient selection and methodology, with 75% showing an unclear or high risk of bias in performance concealment and 80% in blinding of outcome assessment. Importantly, no significant publication bias (Egger's regression test, $P > 0.05$) was evident in any of the included studies (page 16 of Supplementary Materials 2–5, Supplemental Digital Content 2, <http://links.lww.com/JS9/A99>; Supplemental Digital Content 3, <http://links.lww.com/JS9/A100>; Supplemental Digital Content 4, <http://links.lww.com/JS9/A101>; Supplemental Digital Content 5, <http://links.lww.com/JS9/A102>). A comparison-adjusted funnel plot yielded a visually symmetric plot for both opioid consumption and pain scores at all three time periods studied (page 16 of Supplementary Materials 2–5, Supplemental Digital Content 2,

<http://links.lww.com/JS9/A99>; Supplemental Digital Content 3, <http://links.lww.com/JS9/A100>; Supplemental Digital Content 4, <http://links.lww.com/JS9/A101>; Supplemental Digital Content 5, <http://links.lww.com/JS9/A102>). The quality of evidence was rated as very low to low, as per the GRADE system (Table 2).

Heterogeneity and consistency test

The results of the I^2 and Q statistics (based on the full design-by-treatment interaction random-effects model) indicated that a random-effects model may be suitable for revealing any inconsistency or heterogeneity in our network model (Table 2). Furthermore, the colored background of the net heat plot implied that a random-effects model may be appropriate for our data (pages 12 and 13 of Supplementary Materials 2–5, Supplemental Digital Content 2, <http://links.lww.com/JS9/A99>; Supplemental Digital Content 3, <http://links.lww.com/JS9/A100>; Supplemental Digital Content 4, <http://links.lww.com/JS9/A101>; Supplemental Digital Content 5, <http://links.lww.com/JS9/A102>). The direct evidence plot (pages 6 of Supplementary Materials 2–5, Supplemental Digital Content 2, <http://links.lww.com/JS9/A99>; Supplemental Digital Content 3, <http://links.lww.com/JS9/A100>; Supplemental Digital Content 4, <http://links.lww.com/JS9/A101>; Supplemental Digital Content 5, <http://links.lww.com/JS9/A102>) and the forest plot of the net splitting results (pages 14 and 15 of Supplementary Materials 2–5, Supplemental Digital Content 2, <http://links.lww.com/JS9/A99>; Supplemental Digital Content 3, <http://links.lww.com/JS9/A100>; Supplemental Digital Content 4, <http://links.lww.com/JS9/A101>; Supplemental Digital Content 5, <http://links.lww.com/JS9/A102>) were used to evaluate local inconsistency.

Efficacy outcomes (NMA)

Of the included studies, 32 RCTs^[21,22,24–46,48–54] had reported on opioid consumption, while 30^[21,23–26,28–40,42–50,52–54], 30^[21,23–26,28–40,42–50,52–54], and 31^[21,24–26,28–54] RCTs had provided data on pain scores for the early, middle, and late periods, respectively.

The network between the ESPB and controls was greater than that between other techniques, followed by that between the WI and TLIP blocks. Compared to the controls, as shown in Figure 3A, TLIP blocks showed the greatest analgesic effect as opioid consumption was the least (MD = -15.0 mg; 95% CI: -18.8 to -11.2), followed by ESPB (MD = -9.7 mg; 95% CI: -12.1 to -7.4), WI (MD = -8.3 mg; 95% CI: -11.6 to -5.0). Even compared with ESPB (MD = 5.3 mg; 95% CI: 1.0–9.6) and WI (MD = 6.7 mg; 95% CI: 2.0–11.4), TLIP blocks showed significant reduction in opioid consumption (Fig. 3B).

Next, compared to controls, pain scores were lowest after TLIP during the early period (MD = -1.9, 95% CI: -2.7 to -1.1), followed by ESPB and WI (Fig. 4A). In the middle and late period, TLIP blocks and ESPB showed superior analgesic effects over controls in reducing the pain score, whereas WI did not have a significant effect (Fig. 4B, C). Local inconsistency between the WI and controls was significant in opioid consumption (Table 2). Table 3 shows the network league table, which provides both direct comparison and full model results.

Table 1**Characteristics of included studies.**

| References | Year | Country | Surgery | Group (n) | Block level | Local anesthetics | Block timing | Opioid data | Nonopioid multimodal analgesia protocol | Pain score data form (early, middle, late period) (h) |
|--|------|----------|--|---------------------------|---|--|----------------------|------------------------------|---|---|
| Milligan <i>et al.</i> ^[21] | 1993 | Ireland | Elective lumbar discectomy | Control (30) WI (30) | 10 ml into the wound, 5 ml laterally into the erector spini muscle, 5 ml subcutaneously along both margins of the wound | 20 ml of 0.5% bupivacaine | Before wound closure | Morphine | NA | Table (1,8,24) |
| Mack <i>et al.</i> ^[22] | 2001 | USA | Single level, unilateral microscopic lumbar discectomy | Control (10) WI (10) | Into the wound | 15 ml of 0.25% bupivacaine | Before wound closure | Morphine | NA | NA |
| Mirzai <i>et al.</i> ^[23] | 2002 | Turkey | Lumbar disc surgery for single-level unilateral herniated nucleus pulposus | Control (22) WI (22) | Paravertebral muscles and subcutaneous tissue | 20 ml of 0.25% bupivacaine | During wound closure | Meperidine, NA for 24 h data | NA | Plot (1,12,NA) |
| Yörükoglu <i>et al.</i> ^[24] | 2005 | Turkey | Elective surgery for lumbar disc disease within 3 hours | Control (20) WI (20) | Paraspinal muscle and skin | 30 ml of 0.25% bupivacaine | Before wound closure | Meperidine | Naproxen sodium tablets (75 mg) as required | Plot (0.5,12,24) |
| Ersayli <i>et al.</i> ^[25] | 2006 | Turkey | Scheduled first unilateral lumbar discectomy | Control (15) WI (15) | Musculus multifidi near the operated level | 30 ml of 0.25% bupivacaine | Before wound closure | Morphine | NA | Table (1,8,24) |
| Esmail <i>et al.</i> ^[26] | 2008 | Iran | Surgery for one level lumbar intervertebral disc herniation | Control (83) WI (83) | Subcutaneous tissue | 20 ml of 2% lidocaine with 1/500 000 epinephrine | Before incision | Morphine (intramuscular) | NA | Table (6,12,24) |
| Gurbet <i>et al.</i> ^[27] | 2008 | Turkey | Surgery for unilateral lumbar disc herniation | Control (19) WI (19) | Musculus multifidi near the operated level | 30 ml of 0.25% levobupivacaine | Before wound closure | Morphine | Diclofenac (75 mg) as rescue analgesic | NA |
| Ozyilmaz <i>et al.</i> ^[28] | 2012 | Turkey | Elective single space lumbar discectomy | Control (20) WI (20) | Over the incision line on the paravertebral muscles and cutaneous and subcutaneous tissue | 20 ml of 0.75% levobupivacaine | Before wound closure | Pethidine | Diclofenac (75 mg) as rescue analgesic | Plot (1,12,24) |
| Mohta <i>et al.</i> ^[33] | 2019 | India | Tubercular spine surgery | Control (16) WI (16) | Wound | 0.375% ropivacaine 3 mg/kg with adrenaline 5 µg/ml and dexmedetomidine 1 µg/kg in a total volume of 0.8 ml/kg | Before wound closure | Morphine | Diclofenac (1 mg/kg) or tramadol (1 mg/kg) at the time of wound closure | Plot (0.5,8,24) |
| Kraiwananapong <i>et al.</i> ^[39] | 2020 | Thailand | One or two levels of lumbar spinous process splitting laminectomy due to degenerative lumbar spinal stenosis | Control (26) WI (23) | Wound (30 ml) and 20 ml for paraspinal muscle bilaterally | Total volume 50 ml of levobupivacaine 100 mg, morphine 5 mg, ketorolac tromethamine 30 mg, epinephrine 0.25 mg and normal saline | Unknown | Morphine | Pregabalin (75 mg) at bedtime postoperatively | Plot (0,12,24) |
| Ahiskalioglu <i>et al.</i> ^[29] | 2018 | Turkey | Scheduled for 2 or 3 level posterior lumbar instrumentation surgery | Control (20) TLIP (20) | L3, modified plane | 20 ml of 0.25% bupivacaine | Unknown | Fentanyl | Non specified supplementary analgesia | Plot (1,12,24) |
| Ammar <i>et al.</i> ^[30] | 2018 | Egypt | Single or multiple level lumbar discectomy | Control (35) TLIP (35) | L3, original plane | 20 ml of 0.25% bupivacaine, 20 ml of 1% lidocaine | After induction | Morphine | Intravenous paracetamol (1 g) every 6 h | Plot (2,12,24) |
| Chen <i>et al.</i> ^[31] | 2019 | China | Lumbosacral spine fusion surgery | Control (30) TLIP (30) | L3, original plane | 30 ml of 0.375% ropivacaine | After induction | Sufentanil | Intravenous flurbiprofen (50 mg) at end of surgery | Plot (1,12,24) |

| | | | | | | | | | | |
|---|------|---------|--|---------------------------|--|---|------------------|---------------------------|--|-------------------|
| Ozmen <i>et al.</i> ^[34] | 2019 | Turkey | Elective single-level herniated lumbar disc surgery | Control (40) TLIP (40) | L3, modified plane | 40 ml of 0.25% bupivacaine | Before induction | Fentanyl | Dexketoprofen (50 mg) at near end of surgery and postoperative 12 h | Plot (1,12,24) |
| Eltaher <i>et al.</i> ^[42] | 2021 | Egypt | Elective spine surgery (discectomy, laminectomy, and spinal fixation) | Control (30) TLIP (30) | L3, original plane | 40 ml of 0.25% bupivacaine | Unknown | Morphine | Intravenous paracetamol (1 g) every 8 h | Table (2,12,24) |
| El Ghamry <i>et al.</i> ^[32] | 2019 | Egypt | Elective posterior lumbar interbody fusion due to double level lumbar spondylolisthesis (L3–L5) | Control (30) ESPB (30) | L3 | 40 ml of 0.25% bupivacaine | Before induction | Morphine | Intravenous paracetamol (1 g) every 6 h, Ketorolac loading (30 mg) and every 8 h (15 mg) | Plot (2,12,24) |
| Yayik <i>et al.</i> ^[35] | 2019 | Turkey | One or two-level open lumbar decompression surgery | Control (30) ESPB (30) | L3 | 40 ml of 0.25% bupivacaine | Before induction | Tramadol | Ibuprofen (400 mg) every 12 h | Table (2,12,24) |
| Eskin <i>et al.</i> ^[38] | 2020 | Turkey | Elective lumbar decompression surgery for one or two vertebral levels | Control (40) ESPB (40) | The vertebra in the middle of the incision line | 40 ml of 0.25% bupivacaine | After surgery | Tramadol | Intravenous paracetamol 10 mg/kg, tenoxicam 10 mg After induction, Intravenous paracetamol (1 g) every 8 h, Dexketoprofen (50 mg) every 24 h | Table (2,12,24) |
| Singh <i>et al.</i> ^[40] | 2020 | India | Elective lumbar spine surgery (prolapsed lumbar intervertebral disk, lumbar stenosis, or laminectomy) | Control (20) ESPB (20) | T10 | 40 ml of 0.5% bupivacaine | Before induction | Morphine | Intravenous diclofenac (1.5 mg/kg) every 8 h | Table (0,12,24) |
| Zhang <i>et al.</i> ^[41] | 2020 | China | Open posterior lumbar decompression surgery (prolapsed lumbar intervertebral disk, lumbar stenosis) | Control (30) ESPB (30) | T12 | 50 ml of 0.3% ropivacaine | Before induction | Morphine | NA | Table (NA, NA,24) |
| Finnerty <i>et al.</i> ^[43] | 2021 | Ireland | Open thoracolumbar vertebral decompression for degenerative stenosis or trauma at two or more levels, with or without fusion | Control (30) ESPB (30) | Mid-point of the planned incision | 40 ml of 0.25% levobupivacaine | After induction | Oxycodone | Intravenous paracetamol (1 g) every 6 h, Oral ibuprofen (400 mg) every 8 h | Plot (0,12,24) |
| Goel <i>et al.</i> ^[44] | 2021 | India | Elective single-level transforaminal lumbar interbody fusion surgery | Control (50) ESPB (51) | Surgical level | 40 ml of 0.25% bupivacaine | After induction | Fentanyl Oral morphine | Intravenous paracetamol (1 g) and dexketoprofen (50 mg) after induction, Intravenous paracetamol (1 g) every 6 h, Ketorolac (30 mg) after induction, Intravenous paracetamol (1 g) every 6 h, ketorolac (30 mg) every 8 h, and pregabalin (75 mg) once a day | Table (2,12,24) |
| Jin <i>et al.</i> ^[45] | 2021 | China | Elective two-level or three-level lumbar laminoplasty for lumbar spinal stenosis | Control(32) ESPB(30) | Vertebral levels of the surgery | 40 ml of 0.375% ropivacaine | After induction | milligram equivalent | Intravenous parecoxib (40 mg and intramuscular pethidine (50 mg) as rescue analgesic | Plot (1,12,24) |
| Wahdan <i>et al.</i> ^[46] | 2021 | Egypt | Lumbar spine procedures on any two levels between L1 and L5 (discectomy, laminectomy, and fixation) | Control (70) ESPB (70) | Operating level | 40 ml of 0.25% levobupivacaine | After induction | Morphine | Intravenous ketorolac (30 mg) every 8 h | Plot (0,12,24) |
| Yeşiltaş <i>et al.</i> ^[48] | 2021 | Turkey | Posterior spinal instrumentation and fusion for spondylolisthesis | Control (28) ESPB (28) | Freehand ESPB technique directly by the surgical team under vision | 20 ml (1:1) mixture solution of 0.25% bupivacaine and 1.0% lidocaine 0.25% bupivacaine and 1.0% lidocaine | End of surgery | Morphine | Paracetamol every 8 h | Table (1,12,24) |
| Yörükoğlu <i>et al.</i> ^[49] | 2021 | Turkey | Elective single-level lumbar microdiscectomy | Control (26) ESPB (28) | Surgical level | 40 ml of 0.25% bupivacaine | Before surgery | Morphine | Tramadol (100 mg) and paracetamol (1 g) at end of surgery, Intravenous tenoxicam (20 mg) as recue analgesic | Table (1,12,24) |
| Yu <i>et al.</i> ^[50] | 2021 | China | Posterior internal fixation for single-level lumbar fracture | Control (40) ESPB (40) | Fractured lumbar vertebra | 60 ml of 0.25% bupivacaine | After induction | Sufentanil | Flurbiprofen included in patient controlled analgesia | Table (6,12,24) |
| Zhang <i>et al.</i> ^[51] | 2021 | China | Lumbar spine surgery | Control (29) ESPB (30) | T10 | 50 ml of 0.3% ropivacaine | Before induction | Morphine | Flurbiprofen (50 mg), dezocine (0.1–0.2 mg/kg) and dexmedetomidine (0.3 µg/kg) | Table (NA, NA,24) |
| Zhang <i>et al.</i> ^[52] | 2021 | China | | | L3 | 40 ml of 0.4% ropivacaine | | Sufentanil | | Plot (4,12,24) |

Table 1

(Continued)

| References | Year | Country | Surgery | Group (n) | Block level | Local anesthetics | Block timing | Opioid data | Nonopioid multimodal analgesia protocol | Pain score data form (early, middle, late period) (h) |
|--------------------------------------|------|---------|--|----------------------------|---|---|-----------------|--------------------------------|---|---|
| Zhu <i>et al.</i> ^[53] | 2021 | China | Primary open posterior lumbar spinal fusion surgery | Control (30) ESPB (30) | L2 | 40 ml of 0.375% ropivacaine | Before surgery | | Flurbiprofen (1.5 mg/kg) loading at end of surgery and continuous infusion (6 mg/h) | Table (0.5,12,24) |
| | | | Posterior lumbar fusion surgery | Control (20) ESPB (20) | | Total 40 ml volume consisting of 20 ml of 0.5% bupivacaine, 10 ml of 2% lidocaine, and 10 ml of 0.9% NaCl | Before surgery | Oxycodone | Flurbiprofen (50 mg) before the end of surgery | |
| Asar <i>et al.</i> ^[54] | 2022 | Turkey | Elective spinal surgery with instrumentation involving single or multilevels in the lumbar or thoracic regions | Control (35) ESPB (35) | T10 | 20 ml of 0.5% bupivacaine (WI) | End of surgery | Total morphine equivalent dose | Intravenous paracetamol (1 g) and tramadol (1 mg/kg) before the end of surgery | Plot (1,12,24) |
| Ekinci <i>et al.</i> ^[37] | 2020 | Turkey | Single-level lumbar disc surgery | WI (30) TLIP (30) | Surgery site (WI) L3 (TLIP), modified plane | 40 ml of 0.25% bupivacaine (TLIP) | After induction | Fentanyl | Intravenous paracetamol (1 g) every 8 h | Table (2,8,24) |
| | | | Single-level lumbar discectomy and hemilaminectomy surgery | Control (30) TLIP (30) | | | After induction | Fentanyl | Intravenous paracetamol (1 g) every 6 h | Table (2,8,24) |
| Ciftci <i>et al.</i> ^[36] | 2020 | Turkey | Single-level lumbar discectomy and hemilaminectomy surgery | ESPB (30) Control (100) | L3, modified plane | 40 ml of 0.25% bupivacaine | After induction | Fentanyl | Intravenous paracetamol (1 g) every 6 h | Table (2,8,24) |
| Wang <i>et al.</i> ^[47] | 2021 | China | Lumbar spine fusion surgery | TLIP (102) ESPB (102) | L3 (TLIP), original plane T12 (ESPB) | 30 ml of 0.375% ropivacaine | After induction | Sufentanil, NA for 24 h data | Flurbiprofen included in patient controlled analgesia | Plot (1,12,24) |

ESPB, erector spinae plane block; NA, not applicable; TLIP, thoracolumbar interfascial plane; WI, wound infiltration.

Table 2 Model, heterogeneity, consistency test, and GRADE quality of evidence assessment for primary and secondary outcomes.

| Outcomes | Number of studies | Number of patients | Number of pairwise comparison | Number of designs | I ² (%) | Global P value | Consistency test | | Quality of the evidence (GRADE) | Comments |
|---|-------------------|--------------------|-------------------------------|-------------------|--------------------|----------------|---|--------------------------|---------------------------------|--|
| | | | | | | | Local P value | Local I ² (%) | | |
| Opioid consumption | 32 | 2017 | 34 | 5 | 96.8 | 0.095 | WI vs. control (0.020) and TLIP vs. WI (0.020) significant, other comparisons are insignificant | 0.00 | ⊕⊕⊕⊕Moderate quality | Pooled meta-analysis of included studies suggests that compared to control probably reduces opioid consumption |
| Early postoperative period (up to 6 h) pain score | 30 | 2188 | 34 | 5 | 97.3 | 0.472 | All comparisons are insignificant | 0.00 | ⊕⊕⊕⊕Low quality | Downgraded for concerns related to inconsistency and indirectness bias |
| Middle postoperative period (6–18 h) pain score | 30 | 2188 | 34 | 5 | 95.4 | 0.888 | All comparisons are insignificant | 0.00 | ⊕⊕⊕⊕Low quality | Downgraded for concerns related to inconsistency and publication bias |
| Late postoperative period (18–24 h) pain score | 31 | 2263 | 34 | 5 | 91.7 | 0.342 | ESPB vs. control (0.046) significant, other comparisons are insignificant | 0.00 | ⊕⊕⊕⊕Low quality | Downgraded for concerns related to imprecision, inconsistency, and publication bias |

GRADE Working Group grades of evidence.
 High quality: further research is very unlikely to change our confidence in the estimate of effect.
 Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
 Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
 Very low quality: we are very uncertain about the estimate.
 Global inconsistency based on the full design-by-treatment interaction random-effects model⁽¹⁸⁾; local inconsistency based on difference between direct and indirect estimates by net splitting technique.
 ESPB, erector spinae plane block; GRADE, Grading of Recommendations Assessment, Development, and Evaluation; I², Higgins' I²; TLIP, thoracolumbar inters fascial plane; WI, wound infiltration.

Ranking hierarchy

Table 4 shows the P scores for analgesic efficacy and ranking of the five groups. The TLIP block was ranked first for 24-h opioid consumption (0.997) and pain scores of all periods (0.933, 0.992, and 0.936). ESPB emerged second in all outcomes except for the late period pain score. WI ranked second in the pain score of the late period. The results of SUCRAs were similar to the P scores (pages 10 of Supplementary Materials 2–5, Supplemental Digital Content 2, <http://links.lww.com/JS9/A99>; Supplemental Digital Content 3, <http://links.lww.com/JS9/A100>; Supplemental Digital Content 4, <http://links.lww.com/JS9/A101>; Supplemental Digital Content 5, <http://links.lww.com/JS9/A102>). Figure 5 shows the cumulative probability curves for each outcome.

Exploratory subgroup analysis (opioid consumption)

The injection level of ESPB differed in each study. Additional analysis was performed by dividing the patients into fixed thoracic and lumbar levels, and surgical site levels. All three approach levels had significantly lower opioid consumption compared to the controls, but the effect size was the largest when injected according to the surgical level (MD = -12.2 mg; 95% CI: -15.4 to -9.0). There was no statistical difference between the surgical site level and lumbar level injection (MD = -5.0 mg; 95% CI: -10.7 to 0.6), but a significant difference was detected between the surgical site level and thoracic level injection (MD = -6.0 mg; 95% CI: -11.5 to -0.5) (Fig. 3C, page 17 of Supplementary Material 2, Supplemental Digital Content 2, <http://links.lww.com/JS9/A99>).

The TLIP block was divided into medial planes, as in the original method, between the multifidus and longissimus, and lateral planes, as in the modified method, between the longissimus and the iliocostalis, according to the injection plane. Both planes showed a significant difference compared to the controls, and there was no difference according to the method employed (lateral plane: MD = -16.5 mg; 95% CI: -22.2 to -10.9; medial plane: MD = -10.9 mg; 95% CI: -15.0 to -6.8) (page 21 of Supplementary Materials 2, Supplemental Digital Content 2, <http://links.lww.com/JS9/A99>).

Finally, when only surgical site injection of ESPB was included in NMA, there was no difference compared with TLIP block (MD = 1.0 mg; 95% CI: -3.6 to 5.6) (Fig. 3D, page 24 of Supplementary Materials 2, Supplemental Digital Content 2, <http://links.lww.com/JS9/A99>).

Discussion

Multiple regional analgesia techniques are used in clinical settings to improve postoperative pain management in lumbar spinal surgery, and our NMA not only demonstrated the potential benefits of these but also ranked them according to their efficacy^[55]. When compared to systemic analgesia, all three regional analgesia techniques significantly reduced cumulative opioid consumption during the first 24 h after surgery, and the TLIP block showed remarkable effectiveness in reducing opioid consumption.

The TLIP block used to block the dorsal rami of the thoracolumbar nerves was first described by Hand *et al.*^[9] in 2015. The plane in the original technique is close to the surgical incision

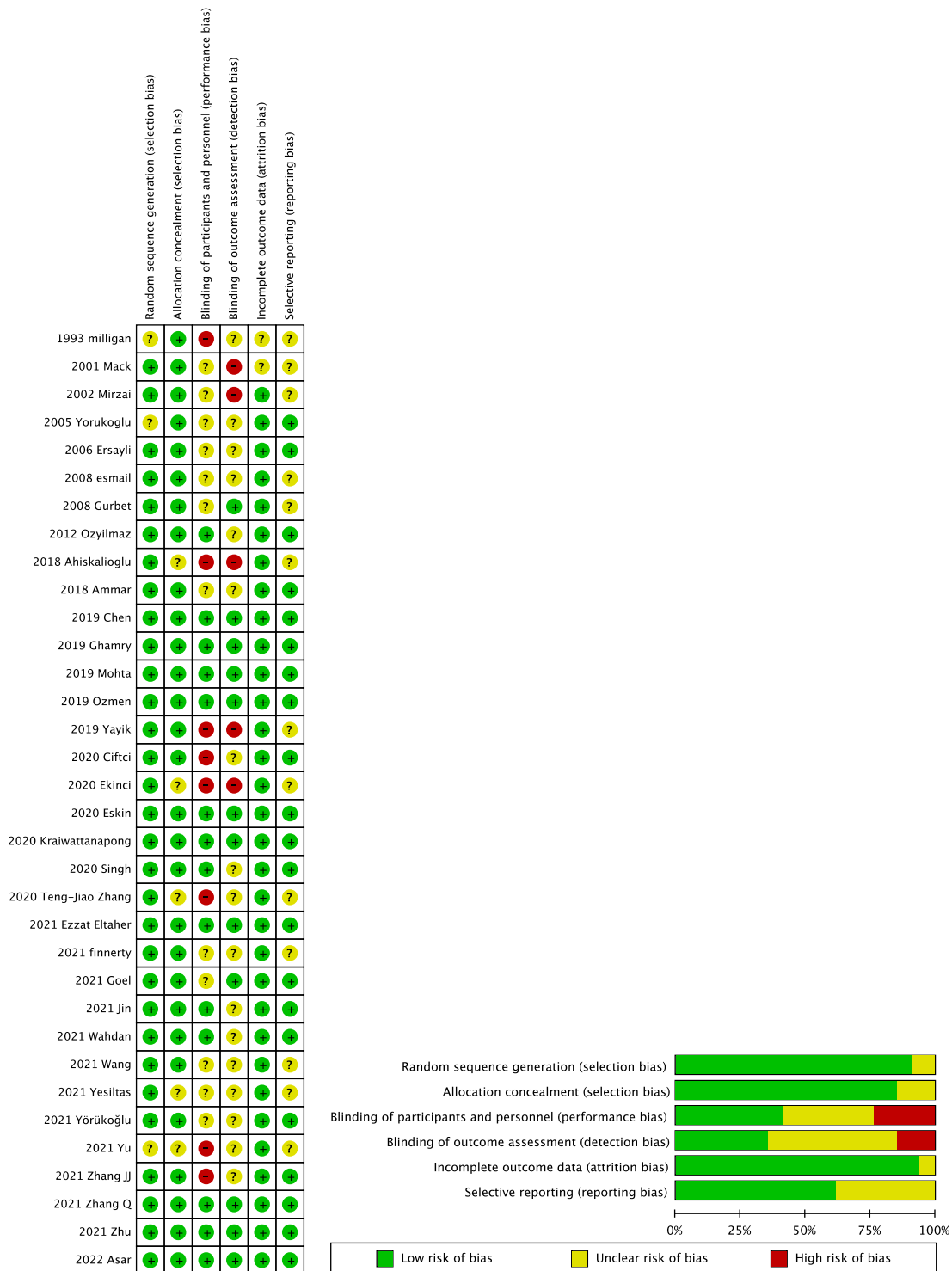


Figure 2. Assessment of risk of bias for included studies. The overall quality of the included. studies were deemed satisfactory.

site, between the multifidus and longissimus; therefore, the process is modified by injecting between the longissimus and iliocostalis into the lateral plane^[10]. Several studies report injecting into the original medial plane^[30,31,42,47], while modified planes have also been used in some studies^[29,34,36,37]. In one study that directly compared two planes, a modified TLIP block had a shorter

performance time, a higher success rate for a one-time block, and a similar analgesic effect compared with the classic TLIP block^[56]. In our exploratory analysis, there was no difference in opioid consumption between the two planes when comparing indirect effects. More well-planned RCTs are required to clarify this issue further.

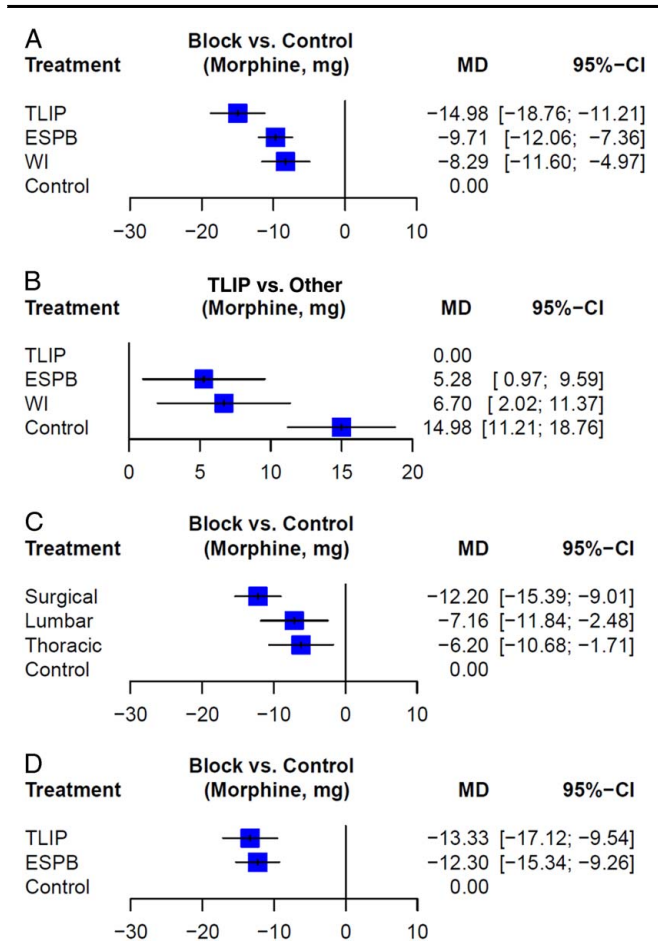


Figure 3. Forest plots for network meta-analysis. (A) Opioid consumption in the first 24 h compared with control. (B) Compared with thoracolumbar interfascial plane (TLIP). (C) Erector spinae plane block (ESPB) by injection level. (D) Only surgical site injection of ESPB included. Mean difference and 95% CI are shown.

Although both techniques target the dorsal rami, and TLIP block is a slightly more superficial block than ESPB, TLIP block showed a statistically superior effect compared to ESPB in our analysis. Three reasons can be inferred from these results. First, the level of the injection is more important in the ESPB than in the TLIP block. Second, when ESPB is performed at the lumbar level, the injection point may vary according to the relatively large transverse processes. Third, the TLIP block is more suitable for multilevel analgesia because it is relatively easy to hydrodissect compared to the ESPB.

We performed a subgroup analysis of ESPB to determine the reason for the superiority of the TLIP block. ESPB may have different effects, depending on the injection level. Several studies injected at a fixed thoracic level^[40,41,47,51,54], or fixed lumbar level^[32,35,52,53]. However, most surgeries perform the injection at the surgical level corresponding to the largest effect size^[38,43-46,48-50]. In addition, injection at the surgical site level reduced opioid consumption compared to that at the fixed thoracic level, and this was statistically significant. It is thought that the results showed a smaller effect size for ESPB than for TLIP block due to injection level differences between the studies

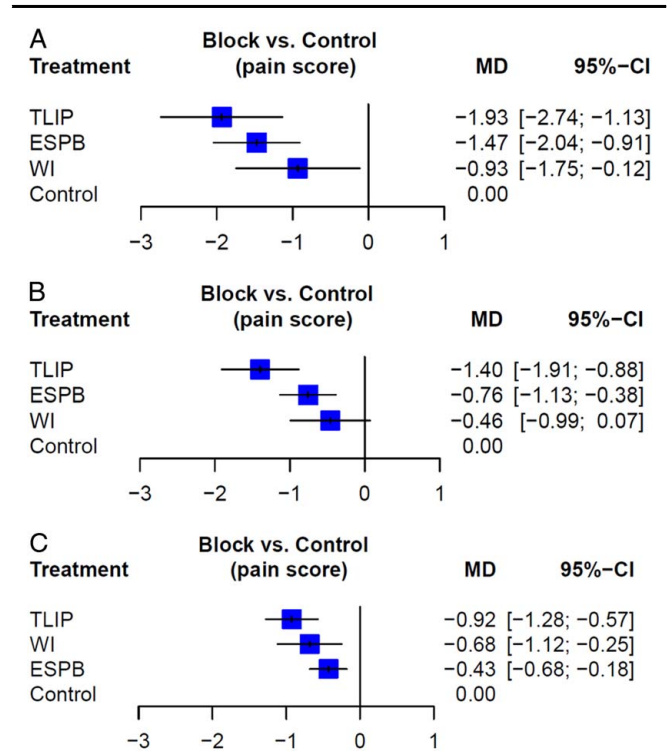


Figure 4. Forest plots for pain score (A) early postoperative period (up to 6 h). (B) Middle postoperative period (6–18 h). (C) Late postoperative period (18–24 h). Mean difference (MD) and 95% CI are shown. ESPB, erector spinae plane block; TLIP, thoracolumbar interfascial plane; WI, wound infiltration.

of ESPB. In this context, when only the surgical site injection of ESPB was included in the NMA, there was no difference compared with the TLIP block. In the studies on the TLIP blocks, injection was performed at the level of L-3, the location at which it was performed in all studies and as performed in the original paper. A direct comparison of ESPB and TLIP block was conducted by Wang *et al.*^[47]. It was not included in our analysis because the amount of opioid consumption 24 h postoperatively was unknown, but it can be seen that there is no difference between the two groups in terms of the number of PCA injections. Additionally, according to Ciftci *et al.*^[36], TLIP block and ESPB showed similar opioid consumption. Since the results of our analysis depend on indirect comparisons, more studies with direct comparisons are needed.

In a cadaveric study about ESPB, a fourth lumbar ESP injection had limited craniocaudal spread compared to injection in the thoracic region.^[57,58] In other words, the lumbar ESPB is localized at the injection level, and therefore it may be important to perform the injection according to the surgical level. The distance between the spinal process line and the neurovascular bundles is determined by the vertebral level, from 29 mm at L1 to 75 mm at L3^[59]. Therefore, the location of the injection on the large and long lumbar transverse process, determines whether the dorsal ramus is blocked or not.

The interfascial plane blocks are highly dependent on sufficient volumes of local anesthetics to spread between the muscle layers and fascial planes. The TLIP block is a plane block that separates two muscles, and such planes are easier to hydrodissect than

Table 3
Network league table for all the interventions for opioid consumption, pain score at early (up to 6 h), middle (6–18 h), and late (18–24 h) during the first 24 h postoperative period.

| | | | |
|--|---------------------|-----------------------|------------------------|
| Opioid consumption | | | |
| Control | 9.50 (7.13, 11.87) | 13.52 (9.32, 17.72) | 9.62 (6.12, 13.12) |
| 9.71 (7.36, 12.06) | ESPB | 0.00 (−0.21, 0.21) | — |
| 14.98 (11.21, 18.76) | 5.28 (0.97, 9.59) | TLIP | −16.53 (−26.02 – 7.04) |
| 8.29 (4.97, 11.60) | −1.42 (−5.46, 2.63) | −6.70 (−11.37, −2.02) | WI |
| Pain score: early postoperative period (up to 6 h) | | | |
| Control | 1.48 (0.90, 2.05) | 1.63 (0.76, 2.51) | 1.14 (0.27, 2.00) |
| 1.47 (0.91, 2.04) | ESPB | 0.75 (−0.96, 2.47) | — |
| 1.93 (1.13, 2.74) | 0.46 (−0.47, 1.40) | TLIP | −2.40 (−4.65; −0.15) |
| 0.93 (0.12, 1.75) | −0.54 (−1.53, 0.45) | −1.00 (−2.07, 0.07) | WI |
| Pain score: middle postoperative period (6–18 h) | | | |
| Control | 0.73 (0.35, 1.11) | 1.37 (0.80, 1.94) | 0.50 (−0.07, 1.07) |
| 0.76 (0.38, 1.13) | ESPB | 0.36 (−0.73, 1.45) | — |
| 1.40 (0.88, 1.91) | 0.64 (0.04, 1.24) | TLIP | −1.20 (−2.66, 0.26) |
| 0.46 (−0.07, 0.99) | −0.30 (−0.94, 0.35) | −0.93 (−1.63, −0.24) | WI |
| Pain score: late postoperative period (18–24 h) | | | |
| Control | 0.39 (0.13, 0.64) | 0.95 (0.56, 1.34) | 0.70 (0.22, 1.17) |
| 0.43 (0.18, 0.68) | ESPB | 0.05 (−0.65, 0.76) | — |
| 0.92 (0.57, 1.28) | 0.50 (0.09, 0.90) | TLIP | −0.30 (−1.30, 0.70) |
| 0.68 (0.25, 1.12) | 0.25 (−0.24, 0.75) | −0.24 (−0.76, 0.28) | WI |

Estimates are presented as mean differences (95% CI). Mean differences below 0 favor the column intervention and mean differences above 0 favor the row intervention. The upper triangle displays only the pooled effect size for the direct comparisons available in our network. No direct comparison is expressed in an empty field. The lower triangle contains the estimated effect sizes for each comparison, even if only indirect evidence was available. ESPB, erector spinae plane block; TLIP, thoracolumbar interfascial plane; WI, wound infiltration.

planes between bone and muscle. Therefore, the TLIP block may be better in terms of multilevel hydrodissection.

All three techniques compared in our study showed superior results compared to the controls. However, statistically significant differences are not always clinically significant. A difference of 10 mg or more in parenteral morphine^[60] and a change of 10 mm on a 100 mm VAS are commonly accepted as clinically significant^[61]. In both these respects, only TLIP block is suitable for lumbar spine surgery. However, even a small difference can have a different clinical meaning depending on the grade of the pain score at which it is effective. In our opinion, a change of ~1–2 points in pain scores in patients who had initially experienced moderate-to-severe pain should be considered a clinically significant difference; hence, a change in pain score from initial values of 4–5 points to less than 3 was defined as a clinically significant difference. Furthermore, a score of less than 33 points on the 100-point VAS scale is accepted as a state of well-controlled pain in clinical settings^[61].

Recently, two procedure-specific postoperative pain management (PROSPECT) guidelines for spine surgery have been published. TLIP block and ESPB have not yet been mentioned in laminectomy^[62] and are not recommended in complex spine surgery due to limited procedure-specific evidence^[63]. They

searched for studies published until 31 March 2020, for laminectomy, and April 2020, for complex spine surgery. Since many of the studies included in our NMA were published later, it seems that they were not properly reflected. Additionally, in a recently published NMA by Bae *et al.*^[64] including studies published until January 2021, fascial plane block (no distinction between TLIP and ESPB) showed no effect in reducing opioid usage at postoperative 24 h. However, only five studies were included in their analysis, and in addition, one of them focused on cervical surgery. In our study, the NMA included many studies published after 2021. Further, the distinction between TLIP block and ESPB is a differentiating point of our study.

This study has several potential limitations. First, the included studies were highly heterogeneous. Despite including only RCTs with patients who underwent lumbar spinal surgery, the concentration of local anesthetics, technical details, and nonopioid multimodal analgesia were not consistent. In addition, there are so many different types of lumbar spinal surgery. Multilevel open surgery and single-level scope surgery will understandably have different pain pathophysiology. Although most of the studies were performed in elective surgery, the information on revision surgery was not known. Therefore, further analysis is required to validate our findings with more elaborate evidence. Second, the

Table 4
P-scores and ranking of the included techniques.

| | 1 | 2 | 3 | 4 |
|---|--------------|--------------|--------------|-----------------|
| Opioid consumption | TLIP: 0.9965 | ESPB: 0.5875 | WI: 0.4161 | Control: 0.0000 |
| Early postoperative period (up to 6 h) pain score | TLIP: 0.9333 | ESPB: 0.6753 | WI: 0.3871 | Control: 0.0042 |
| Middle postoperative period (6–18 h) pain score | TLIP: 0.9923 | ESPB: 0.6114 | WI: 0.3813 | Control: 0.0150 |
| Late postoperative period (18–24 h) pain score | TLIP: 0.9369 | WI: 0.6737 | ESPB: 0.3889 | Control: 0.0005 |

ESPB, erector spinae plane block; TLIP, thoracolumbar interfascial plane; WI, wound infiltration.

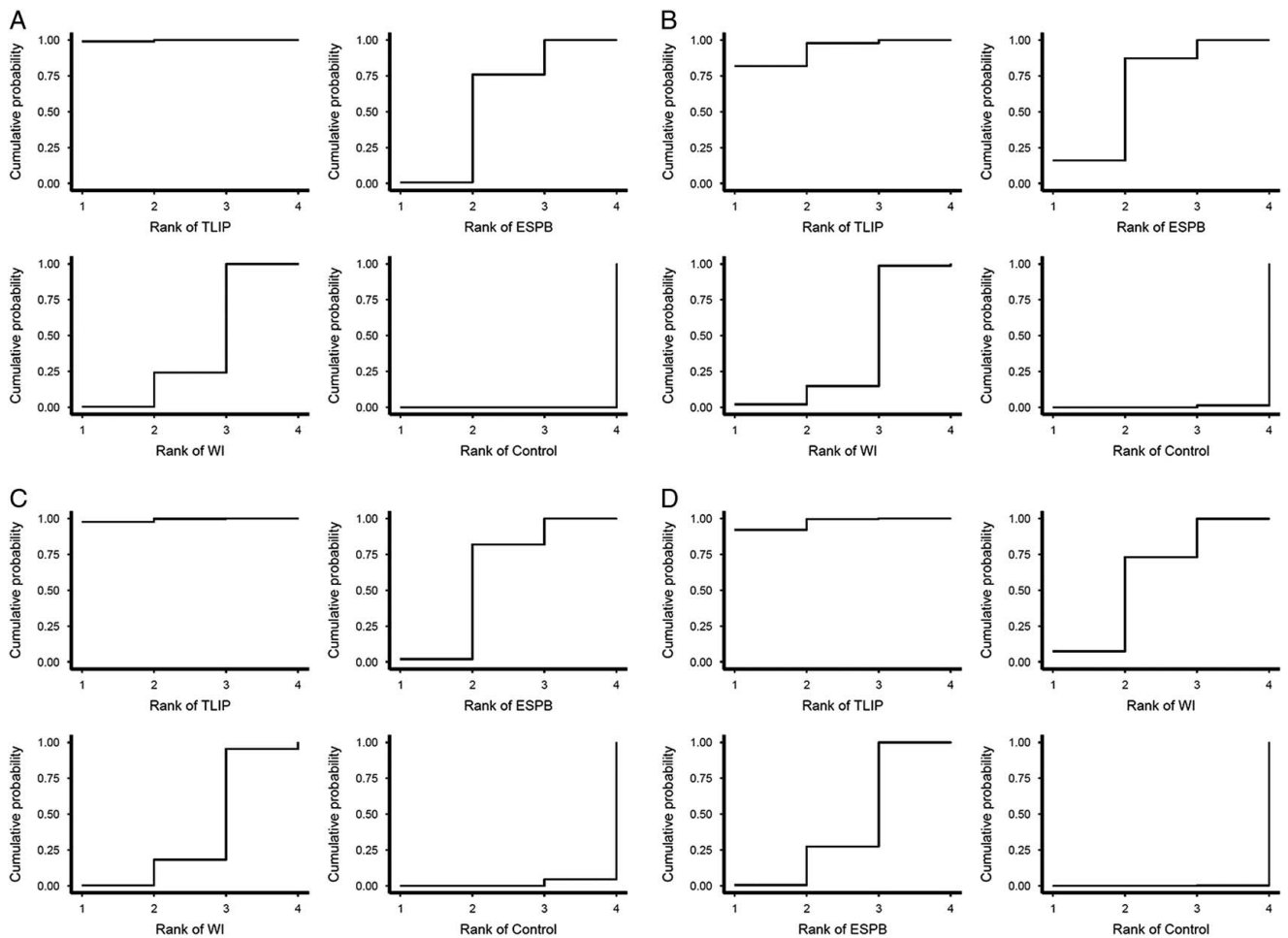


Figure 5. Cumulative probability curves of (A) opioid consumption (B) early postoperative period (up to 6 h), (C) middle postoperative period (6–18 h), and (D) late postoperative period (18–24 h). ESPB, erector spinae plane block; TLIP, thoracolumbar interfascial plane; WI, wound infiltration.

time points at which pain scores were measured were not consistent among the RCTs and were not presented as accurate values. To reduce any bias, we divided the time period into three intervals and used the values corresponding to each interval as representative values. Lastly, ESPB and TLIP are currently developing techniques that may lead to possible publication bias. Moreover, it may be too early to draw conclusions from this analysis alone.

Conclusions

The results of the NMA reported here are significant because a comparison of regional analgesic techniques based on their efficacy can help improve postoperative pain management in lumbar spinal surgery. The TLIP block showed outstanding analgesic effects and a significant reduction in opioid consumption even when compared with ESPB and WI. However, given that a significant reduction in opioid consumption was seen with the three regional analgesic techniques evaluated, using any of these regional blocks after lumbar spinal surgery seems reasonable. Thus, more refined studies are needed to determine the optimal regional analgesia technique that can improve postoperative pain management after lumbar spinal surgery.

Ethical approval

Not required.

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Author contribution

B.H. and S.P.: conception and design. B.H. and S.P.: acquisition and data. B.H. and S.P.: analysis and interpretation of data. B.H. and S.B.: drafting of manuscript. S.B., H.K., C.O., Y.J., S.L., and S.P.: critical revision of the manuscript for important intellectual content. B.H., S.B., and S.P.: statistical analysis. B.H. and S.P.: obtaining funding. S.P.: administrative, technical, or material support. B.H. and S.P.: supervision.

Conflicts of interest disclosure

The authors declare no conflicts of interest.

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Guarantor

Seyeon Park, RN, PhD, Department of Nursing, College of Nursing, Chungnam National University, Jung-gu, Munhwa-ro 266, Daejeon 35015, South Korea. Tel: +82 425 808 329, Fax: +86 425 808 309. E-mail: park_sy@cnu.ac.kr

Data availability statement

The original data reported in this article are accessible in the manuscript/supplementary materials; further queries may be sent to the corresponding author.

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