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DATABASE ANALYSIS

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Opioid-Sparing Effects of Peripheral Nerve Blocks in Kidney Transplant Recipients: A Systematic Review and Meta-Analysis

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Background: Kidney transplantation (KT) is frequently associated with substantial postoperative pain, while opioid use in these patients increases the risk of adverse outcomes. Peripheral nerve blocks (PNBs) have been proposed as opioid-sparing strategies; however, evidence in kidney transplant recipients remains inconsistent, likely due to heterogeneity in block techniques, variability in perioperative analgesic regimens, and differences in study design and methodological rigor. This systematic review and meta-analysis aimed to evaluate the impact of PNBs on postoperative analgesia in kidney transplant recipients.

Material/Methods: A systematic search of PubMed, EMBASE, the Cochrane Library, and Web of Science was conducted through April 2025 following the Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies reporting 24-h postoperative opioid consumption in adult kidney transplant recipients were included. The primary outcome was cumulative opioid use within 24 hours after surgery, expressed as intravenous morphine or fentanyl.

Results: Twelve studies met the inclusion criteria, of which 10 contributed to the quantitative synthesis. Pooled analysis showed that PNBs significantly reduced 24-h morphine consumption compared with control analgesia (pooled mean difference=-16.20 mg of intravenous morphine equivalents, 95% confidence interval -24.66 to -7.74; P=0.0002). Heterogeneity was high (I^2=99%), but no study reported higher opioid use or increased adverse events in the PNB groups.

Conclusions: PNBs appear to be an effective opioid-sparing adjunct for postoperative analgesia in kidney transplant recipients. However, the available evidence remains limited, and further well-designed comparative trials are needed to define their role within multimodal analgesic strategies in this population.

Keywords: Analgesia • Analgesics, Opioid • Nerve Block • Pain Management • Postoperative Care • Transplantation

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Introduction

Kidney transplantation (KT) is a life-saving treatment for end-stage kidney disease but often involves significant postoperative pain due to the surgical procedure [1]. As adequate analgesia can support graft perfusion and promote early mobilization, effective pain control is essential [2]. Conversely, inadequate pain control can provoke physiological stress responses and contribute to adverse postoperative outcomes [3,4].

Opioids have traditionally served as the cornerstone of postoperative analgesia. However, their use in kidney transplant recipients is complicated by impaired renal clearance and multiple comorbidities, which heighten the risk of adverse effects such as respiratory depression, over-sedation, and neurotoxicity [5]. In addition, previous studies have shown that excessive systemic opioid exposure, particularly through intravenous or oral administration, is associated with higher mortality and an increased risk of graft failure after transplantation [6,7]. Given these risks, postoperative pain management remains a major challenge in this population, emphasizing the need for safer, opioid-sparing analgesic strategies specifically tailored to kidney transplant recipients [8].

Recently, multimodal analgesia has emerged as a central concept in perioperative pain management to reduce opioid use through complementary techniques [9]. Peripheral nerve blocks (PNBs) play an important role within this framework by providing site-specific somatic analgesia through temporary interruption of afferent sensory transmission [10]. Local anesthetics used in PNBs inhibit voltage-gated sodium channels in peripheral nerves, thereby blocking nociceptive signaling without producing generalized sedation, sympathetic blockade, or motor weakness [11]. Unlike neuraxial techniques, truncal blocks such as the transversus abdominis plane (TAP), quadratus lumborum (QL), or erector spinae plane (ESP) block selectively target sensory pathways while preserving respiratory function and hemodynamic stability, an important consideration in kidney transplant recipients who are particularly vulnerable to opioid-induced respiratory depression due to impaired drug clearance and altered pharmacokinetics [12,13]. Several clinical trials in KT have suggested that such blocks can reduce opioid requirements and improve pain control [3,14].

Nevertheless, the evidence remains inconsistent in kidney transplant recipients. Studies vary widely in block technique, timing, perioperative regimens, and methodological rigor, leaving the overall magnitude of benefit and consistency of findings uncertain. To address this knowledge gap, this systematic review and meta-analysis aimed to evaluate the impact of PNBs on postoperative analgesia in kidney transplant recipients, focusing on their potential to reduce opioid requirements and improve recovery outcomes. This review was designed to provide an integrated synthesis of current evidence and to inform safer and more effective postoperative pain management strategies in this high-risk population.

Material and Methods

Literature Search and Inclusion Criteria

This systematic review and meta-analysis were conducted in accordance with the Cochrane Collaboration's methodology and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study protocol was registered prospectively in the International Prospective Register of Systematic Reviews (PROSPERO; CRD420251174892). This systematic review and meta-analysis included randomized controlled trials (RCTs), retrospective comparative studies, and propensity score-matched (PSM) studies that investigated the use of PNBs for postoperative pain management in adult kidney transplant recipients. Eligible studies were published in English between January 2005 and April 2025. Studies were excluded if they involved pediatric populations, used spinal or epidural anesthesia, or lacked a comparative control group.

Search Strategy and Data Extraction

Two authors independently conducted data extraction. A search of PubMed, EMBASE, the Cochrane Library, and Web of Science was conducted through April 2025. The search combined population terms ("kidney transplantation", "renal transplantation"), intervention terms ("peripheral nerve block", "transversus abdominis plane (TAP) block", "quadratus lumborum (QL) block", "erector spinae plane (ESP) block", "anterior quadratus lumborum (AQL) block", "ilioinguinal–iliohypogastric (II-IH) block", "regional anesthesia", "neuraxial block", "multimodal analgesia"), and outcome terms ("opioid consumption", "morphine", "analgesia", "pain control", "postoperative pain"). RCTs and observational studies, including retrospective cohort and PSM studies, were eligible if they reported postoperative opioid consumption within 24 hours in either mean±standard deviation (SD) or median and interquartile range (IQR). From each included study, 2 reviewers independently extracted data using a standardized form. Extracted information included study characteristics, interventions, and outcomes (means, SDs, standard errors [SEs], 95% confidence intervals [CIs], number of events, and sample size). For trials that did not report means and SDs directly, authors were contacted up to 2 times to obtain missing data; if unavailable, median and IQR values were converted [15]. Discrepancies between reviewers were resolved by discussion and consensus. Descriptive data about each study (study design, goals, patient age, sample size, local anesthetic volume and concentration, and postoperative analgesia) were extracted into a data table (**Table 1**).

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Table 1. Summary of included studies evaluating peripheral nerve blocks for postoperative analgesia in adult kidney transplant recipients.

Study	n	Patients	Groups (n)	Primary outcome	Study design	Local anesthetics, volume and concentration, adjuvants	Postoperative analgesia
Shoeibi et al [16]	42	All	IG-IH + intercostal (21) vs Control (21)	24 hr morphine consumption	RCT (single-blind)	Bupivacaine 0.5% (4 mL ×3 sites + epi 5 µg per syringe)	↓ VAS (all time points 1-24 h median 1 vs 4-6 controls); ↓ 24 h morphine (12.7±10.5 vs 34.9±5.9 mg); no block complication
Mukhtar et al [17]	20	All	TAP (10) vs Control (10)	24 hr morphine consumption)	Pilot study	Bupivacaine 0.5% 20 mL (single injection post-induction)	TAP group; ↓ morphine use (10.4±4.5 vs 28.9±7.1 mg); VAS ↓ at 3,6,12 h; less nausea & sedation at 3, 6 hr
Freir et al [18]	65	DDKT	TAP (32) vs Control (33)	Opioid consumption /pain	RCT (double-blind)	Levobupivacaine 0.375% 20 mL (landmark technique)	No difference in 24 h morphine (31.6 vs 32.6 mg); VAS no difference; nausea ↑ in TAP group (53% vs 24%)
Mohammadi et al [19]	44	All	TAP (22) vs Control (22)	24 hr morphine consumption (and NRS)	RCT (double-blind)	Bupivacaine 0.25% 15 mL + epi 5 µg/mL (US-guided single-shot)	↓ morphine (10.8±9.5 vs 41.2±3.8 mg); NRS ↓ at 1-24 h (all $P<0.001$); no block complication
Khaled MA et al [20]	60	All	TAP (30) vs Control (30)	24 hr morphine consumption and VAS	RCT (open label)	Bupivacaine 0.5% 20 mL (pre-incisional, US-guided)	↓ intra-op fentanyl (367.5 vs 426.3 µg); ↓ PACU morphine (3.7 vs 6.6 mg); ↓ 24 h dose (27.8 vs 42.6 mg); VAS ↓ at 6, 24 h
Gopwani SR et al [21]	50	All	TAP (13) vs Control (37)	24 hr morphine consumption	Retrospective chart review	Bupivacaine 0.25% 20 mL (US-guided, TAP plane injection)	Median morphine ↓ at 6 h (2.46 vs 7.27 mg), 12 h (3.88 vs 10.2 mg), 24 h (6.96 vs 14.75 mg) $P<0.01$
Hanson et al [22]	120	All	TAP (59) vs IV Lidocaine (61)	24 hr morphine consumption	RCT (open label)	Bupivacaine 0.25% 30 mL + epi (US-guided unilateral TAP)	24 h cumulative morphine use: TAP (14.6±3.2 mg) vs Lido group (15.9±2.4 mg); $P<0.001$; 24-hour cumulative consumption for the TAP 18 mg (IQR: 7-30.5) and for the Lido group was 15 mg (IQR: 8.5-28) pain scores no diff; non-inferior
Sharipova et al [14]	28	LDKT	ESP (14) vs Control (14)	Morphine reduction	Retrospective case-control	ESP block (T10-T11, bupivacaine 0.25% 20 mL initial +0.125% 20 mL q6h ×24 h)	↓ NRS (2.1±1.1 vs 3.3±1.2 rest); ↓ morphine (4.7±6.2 vs 15.9±7.1 mg); ↓ PONV
Theeraratvarasin et al [23]	46	All	QL (23) vs LWI (23)	NRS + morphine consumption	RCT (double-blind)	Bupivacaine 0.25% 20 mL (US-guided inside-out QL3 vs LWI)	↓ NRS at 2 h (5 [IQR 4-7] vs 7 [IQR 7-8]) and 4 h (3 vs 6); ↓ cumulative morphine (5 [IQR 3-8] vs 8 [IQR 5-13])

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Table 1 continued. Summary of included studies evaluating peripheral nerve blocks for postoperative analgesia in adult kidney transplant recipients.

Study	n	Patients	Groups (n)	Primary outcome	Study design	Local anesthetics, volume and concentration, adjuvants	Postoperative analgesia
Sindwani et al [24]	60	All	QLB (30) vs Placebo (30)	Opioid consumption	RCT (double-blind)	0.25% bupivacaine 20 mL (single injection QLB type 1)	NRS significantly lower at 1, 4, 8, 12, 24 h (P<0.001); ↓ fentanyl use (242±95 µg vs 769±90 µg); no PONV or motor weakness reported
Ojha et al [25]	62	LDKT	Continuous TAP (31) vs Epidural (31)	Opioid consumption	RCT (open label)	TAP: posterior approach US-guided 20 mL 0.25% ropivacaine + continuous infusion (24 h); Epidural: 0.25% ropivacaine 4-10 mL/h	NRS at rest and on coughing similar between groups (all P>0.05); 24 h fentanyl uses 685±77 µg (TAP) vs 695±78 µg (Epidural); non-inferior analgesia; no complications
Chae et al [3]	524	LDKT	TAP(262) vs LWI (262)	Opioid consumption and pain scores	Retrospective PS-matched analysis	0.375% ropivacaine 20 mL (US-guided single-shot TAP vs LWI by surgeon)	VAS ↓ at 1 h (3.5±1.1 vs 4.7±1.4), 4 h (3.6±1.0 vs 4.7±1.4), 8 h (3.0±0.9 vs 3.8±1.5), P<0.001; ↓ opioid use (fentanyl 68±31 µg vs 119±72 µg; IV-PCA 55.9±10.2 vs 69.7±18.2 mL); no toxicity or PONV difference

This table presents the key characteristics and outcomes of studies included in the meta-analysis, detailing study design, patient population, type of nerve block, anesthetic regimen, timing of intervention, and postoperative analgesic outcomes. Reported variables include opioid consumption, pain scores, complications, and other clinically relevant endpoints. "↓"denotes a decrease, "↑" denotes an increase. DDKT – deceased-donor kidney transplantation; LDKT – living-donor kidney transplantation; RCT – randomized controlled trial; PSM – propensity score-matched; TAP – transversus abdominis plane; QL – quadratus lumborum; ESP – erector spinae plane; II-IH – ilioinguinal–iliohypogastric; LA – local anesthetic; PCA – patient-controlled analgesia; VAS – visual analog scale; NRS – numeric rating scale; POD – postoperative day; NS – not significant; NA – not available; US – ultrasound; PACU – post-anesthesia care unit; LWI – local wound infiltration; Lido – lidocaine; epi – epinephrine; IQR – interquartile range; q6h – every 6 hours; mg – milligram; µg – microgram; mL – milliliter.

Population

The meta-analysis included studies involving adult patients (aged ≥18 years) who underwent kidney transplantation, including both living-donor kidney transplantation (LDKT) and deceased-donor kidney transplantation (DDKT). Studies involving pediatric populations, donor-only surgery, or nonsurgical interventions were excluded.

Intervention and Comparator

Eligible studies evaluated perioperative pain control interventions involving PNBs (eg, TAP block, QL block, ESP block). These interventions were compared with either placebo (sham block, saline injection), standard intravenous patient-controlled analgesia (IV-PCA), or alternative regional techniques. Studies comparing one block technique versus another (eg, TAP vs QL) were also included.

Outcomes

The primary outcome was cumulative opioid consumption within 24 hours after surgery, expressed as intravenous morphine milligram equivalents (MME). When postoperative fentanyl consumption was reported, doses were converted to intravenous morphine equivalents using standard equianalgesic ratios when feasible. If reliable conversion was not possible because of heterogeneous dosing protocols or reporting formats, these outcomes were summarized descriptively rather than included in quantitative pooling.

Secondary outcomes included postoperative pain scores and predefined safety outcomes, including postoperative nausea and vomiting (PONV), opioid-related adverse events (eg, respiratory depression or over-sedation), and block-related complications (eg, local anesthetic systemic toxicity, infection, or

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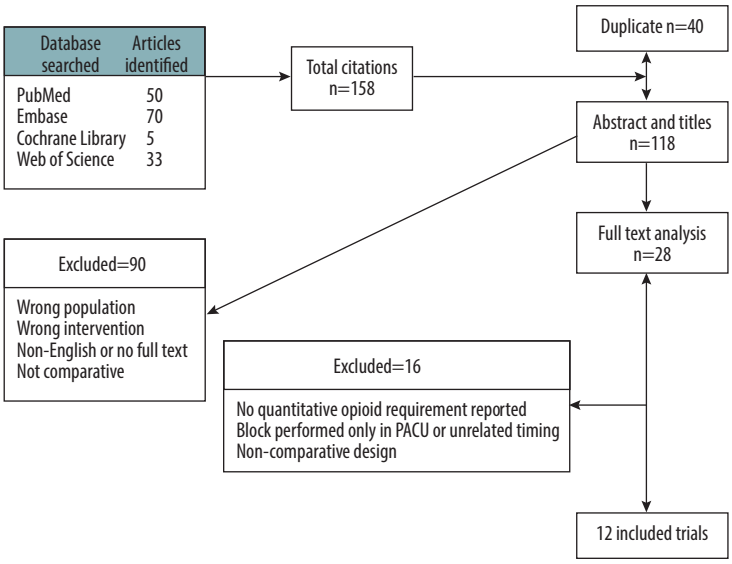

Figure 1. Flow diagram of study selection according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) guidelines. Flowchart showing the identification, screening, eligibility, and inclusion of studies according to the PRISMA 2020 guidelines. PACU – post-anesthesia care unit.

transient neurologic symptoms). Safety outcome data were extracted independently by 2 reviewers using a standardized data extraction form. Because definitions, reporting formats, and assessment time points for these outcomes varied substantially across the included studies, quantitative pooling was not appropriate. Therefore, safety outcomes were summarized descriptively.

Risk of Bias Assessment

The risk of bias of the included RCTs was independently assessed by 2 reviewers using the Cochrane Risk of Bias tool.

Statistical Analysis

All statistical analyses were performed using Review Manager (RevMan version 5.3.5, Copenhagen, the Nordic Cochrane Centre, the Cochrane Collaboration) and R software (Rex 3.7.1.0) with the meta and metasens packages. For continuous outcomes, weighted mean differences (MDs) with 95% CIs were calculated. When 2 or more studies reported comparable outcomes, a meta-analysis was conducted. Given the substantial heterogeneity across studies, random-effects models using the DerSimonian-Laird method were applied. Heterogeneity was quantified using the I^2 statistic, with thresholds of 25% to 49%, 50% to 74%, and ≥75% representing low, moderate, and high heterogeneity, respectively. Publication bias was assessed through funnel plot visualization and formally tested using Egger's test. The Copas selection model was applied, confirming that the direction of the pooled effect remained consistent despite potential bias. $P<0.05$ was considered statistically significant.

Results

Article Search Results

A total of 283 records were identified across 4 databases: PubMed (n=74), Embase (n=105), Cochrane Library (n=6), and Web of Science (n=98). After removing 82 duplicates, 201 records remained for title and abstract screening. Of these, 168 studies were excluded for reasons such as inappropriate population, irrelevant intervention, non-English language, inaccessible full text, or non-comparative study design. A total of 33 full-text articles were reviewed for eligibility, and 21 were excluded for the following reasons: absence of full text, insufficient outcome data, non-comparable postoperative pain management methods, or use of epidural/spinal anesthesia, which was an exclusion criterion. Finally, 12 studies met the inclusion criteria and were included in the systematic review. The overall study selection process is illustrated in **Figure 1** as PRISMA flow chart. **Table 1** presents the trial characteristics. The risk of bias was assessed exclusively for RCTs using the Cochrane Collaboration tool (**Table 2**), and most of these studies demonstrated a low overall risk of bias.

Postoperative 24-Hour Morphine Consumption

Ten studies contributed to the 24-hour opioid consumption meta-analysis. Nine studies reported postoperative intravenous morphine consumption during the first 24 hours [14,16-23]. In an additional study (Sindwani et al [24]), postoperative intravenous fentanyl consumption was reported as cumulative IV-PCA bolus dosing without background infusion and was therefore converted to intravenous MME using standard equianalgesic

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Table 2. Cochrane Collaboration risk-of-bias summary: evaluation of bias domains for randomized controlled trials included in this review.

Study	Randomization process	Allocation concealment	Blinding (participants/ personnel)	Blinding of outcome assessment	Incomplete data	Selective reporting	Overall risk
Shoeibi et al [16]	Low	Unclear	Unclear	Low	Low	Low	Some concerns
Mukhtar et al [17]	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Some concerns
Freir et al [18]	Low	Low	Low	Low	Low	Low	Low
Mohammadi et al [19]	Low	Unclear	Low	Low	Low	Low	Some concerns
Khaled MA et al [20]	Low	Low	Low	Low	Low	Low	Low
Hanson et al [22]	Low	Low	Low	Low	Low	Low	Low
Theeraratvarasin et al [23]	Low	Low	Low	Low	Low	Low	Low
Sindwani et al [24]	Low	Low	Low	Low	Low	Low	Low
Ojha et al [25]	Low	Low	Unclear (open label)	Low	Low	Low	Some concerns

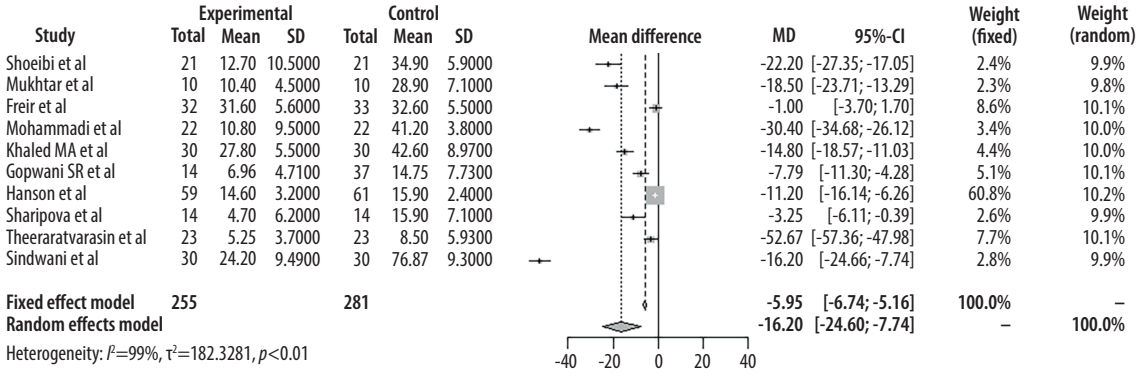

Figure 2. Forest plot showing the pooled mean difference (MD) in 24-hour intravenous morphine consumption between peripheral nerve block (PNB) and control groups. Each horizontal line represents an individual study with its 95% confidence interval (CI); square size reflects study weight in the random-effects model. The diamond represents the overall pooled estimate, indicating significantly lower morphine requirements in the PNB group (MD=-16.20 mg; 95% CI, -24.66 to -7.74; P=0.0002). MD – mean difference; SD – standard deviation; CI – confidence interval.

ratios for inclusion in the quantitative synthesis. Two other fentanyl-based studies (Ojha et al [25] and Chae et al [3]) were not eligible for quantitative pooling because postoperative fentanyl exposure was reported as heterogeneous composite measures (eg, mixed bolus and weight-based continuous infusion protocols or IV-PCA reservoir volume with basal infusion), precluding reliable and standardized conversion to morphine equivalents without introducing substantial methodological assumptions.

Postoperative opioid consumption within the first 24 hours, expressed as intravenous morphine equivalents (MME), was reported in 10 studies and analyzed using a random-effects model based on the DerSimonian-Laird method. The pooled MD favored the PNB group, showing significantly lower morphine requirements compared with control analgesia (MD=-16.20 mg; 95% CI, -24.66 to -7.74; P=0.0002). Between-study heterogeneity was considerable (I^2=99%, τ^2=182.33), and the Q statistic confirmed significant variability among included studies

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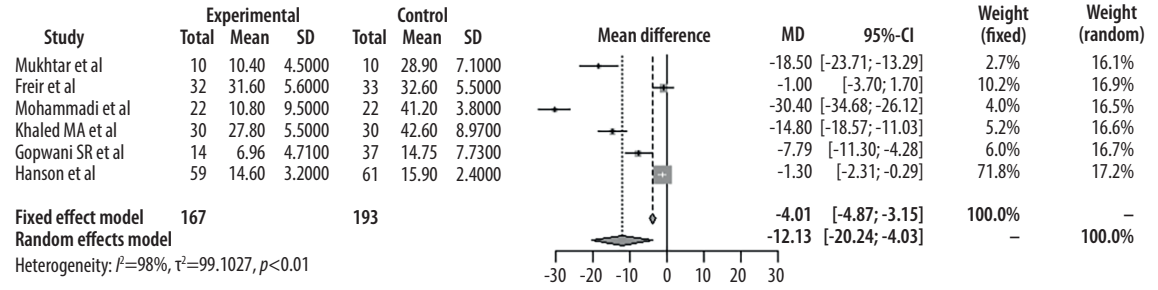

Figure 3. Forest plot showing the pooled mean difference (MD) in 24-hour intravenous morphine consumption between the transversus abdominis plane (TAP) block and control group. Each horizontal line depicts an individual study with its 95% confidence interval (CI); square size indicates study weight in the random-effects model. The diamond denotes the pooled estimate (MD=-12.13 mg; 95% CI -20.24 to -4.03; *P*=0.0033), favoring the TAP block for reducing postoperative opioid consumption. MD – mean difference; SD – standard deviation; CI – confidence interval.

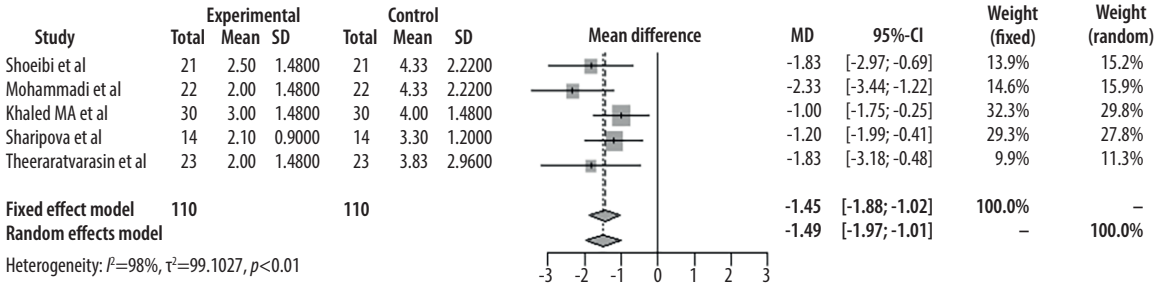

Figure 4. Forest plot showing the pooled mean difference (MD) in 24-hour rest visual analog scale (VAS) scores between PNB and control groups. Each horizontal line represents an individual study with its 95% confidence interval (CI); square size indicates study weight in the random-effects model. The diamond reflects the pooled estimate (MD=-1.49; 95% CI -1.97 to -1.01; *P*<0.001), showing lower postoperative pain scores in the PNB group. MD – mean difference; SD – standard deviation; CI – confidence interval; VAS – visual analog scale.

(Q=691.40, df=9, *P*<0.001). Despite this heterogeneity, all studies demonstrated a consistent direction of effect toward reduced opioid consumption with PNBs, with no study showing higher morphine use in the intervention group. Egger's regression test revealed significant funnel plot asymmetry (t=-3.12, df=8, *P*=0.0143), indicating the presence of small-study effects suggestive of potential publication bias. However, adjustment for potential publication bias using the Copas selection model yielded a nearly identical estimate MD=-16.22 (95% CI -25.59 to -6.85; *P*=0.0007). These results are illustrated in the forest plot presented in **Figure 2**.

A total of 6 studies implementing the TAP block were included in this subgroup analysis [17-22]. Postoperative 24-hour morphine consumption was analyzed using a random-effects model. The pooled MD was -12.13 mg (95% CI -20.24 to -4.03; *P*=0.0033). Between-study heterogeneity was substantial (Q=244.26, df=5, *P*<0.001; I^2=98%). Egger's test showed significant funnel plot asymmetry (t=-2.79, df=4, *P*=0.049), indicating the presence of small-study effects suggestive of potential publication bias. After adjustment using the Copas selection model, the pooled estimate remained stable (MD=-12.14 mg; 95% CI -20.42 to -3.86; *P*=0.004), suggesting minimal impact of publication bias (**Figure 3**).

Postoperative 24-Hour Fentanyl Consumption

Three studies (Sindwani et al [24], Ojha et al [25], and Chae et al [3]) reportedpostoperative 24-hour intravenous fentanyl consumption. Reported mean fentanyl use in the PNB groups ranged from 67.7±30.6 µg to 695.2±78.6 µg, compared with 119.1±71.8 µg to 768.7±90.3 µg in control or epidural groups. No study reported higher fentanyl requirements in the nerve block group. When reliable conversion to intravenous MME was not feasible because of heterogeneous dosing protocols or reporting formats, fentanyl-based outcomes were prespecified to be summarized descriptively rather than included in quantitative pooling. Owing to the limited number of eligible

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Table 3. Summary of meta-analysis results for outcomes.

Outcome	n	Pooled MD (95% CI)	*P* value	Heterogeneity	Copas selection model (95% CI)
24-hour morphine consumption (overall)	10	-16.20 mg (-24.66 to -7.74)	0.0002*	Q=691.40 df=9, *P*<0.001; I^2=99%, τ^2=182.33	MD=-16.22 mg (95% CI -25.59 to -6.85; P=0.0007)
24-hour morphine consumption (TAP subgroup)	6	-12.13 mg (-20.24 to -4.03)	0.0033*	Q=244.26, df=5, *P*<0.001; I^2=98%, τ^2=99.10	MD=-12.14 mg (95% CI -20.42 to -3.86; P=0.004)
24-hour resting VAS score	5	-1.49 (-1.97 to -1.01)	<0.001*	Q=4.90, df=4, *P*=0.30; I^2=18%, τ^2=0.056	MD=-1.45 mg (95% CI -1.88 to -1.02; *P*<0.001)

This table summarizes the pooled quantitative results of the included studies evaluating the effect of peripheral nerve blocks (PNBs) on postoperative analgesia in kidney transplantation. The random-effects model (DerSimonian-Laird method) was used to calculate pooled mean differences (MDs) and 95% confidence intervals (CIs). Heterogeneity was assessed using the Q statistic, I^2, and τ^2. For publication bias, adjusted estimates using the Copas selection model are presented when available. * *P*<0.05. MD – mean difference; CI – confidence interval; VAS – visual analog scale; TAP – transversus abdominis plane.

trials and substantial variability in reporting units and dosing methodologies, a pooled quantitative meta-analysis could not be conducted for the 2 fentanyl-based studies (Ojha et al [25] and Chae et al [3]).

Rest Pain Scores

The 24-hour resting visual analog scale (VAS) scores for individual and pooled studies are shown in **Figure 4**. A total of 5 studies reporting 24-hour resting VAS scores were included in the quantitative synthesis [14,16,19,20,23]. Thepooled MD in 24-hour resting VAS scores between the peripheral nerve block and control groups was -1.49 (95% CI -1.97 to -1.01; *P*<0.001) under a random-effects model. Heterogeneity was low (Q=4.90, df=4, *P*=0.30; I^2=18%). Egger's regression test did not show statistically significant funnel plot asymmetry (t=-2.85, df=3, *P*=0.065), although a borderline trend toward small-study effects was observed. Adjustment with the Copas selection model yielded a comparable estimate (MD=-1.45; 95% CI -1.88 to -1.02; *P*<0.001), indicating that the results were stable and minimally affected by potential publication bias.

A summary of all pooled quantitative results – including overall morphine consumption, TAP subgroup analysis, and 24-hour resting VAS scores – is provided in **Table 3**.

Safety Outcomes

Secondary outcomes were variably reported across the included studies, with substantial heterogeneity in assessment methods and time points, precluding quantitative synthesis. PONV was reported in 6 studies, with the incidence ranging from 8% to 53% in PNB groups and 6% to 40% in control or standard analgesia groups. Across studies, the direction of effect was inconsistent, and no statistically significant pattern was observed. No study reported severe opioid-related adverse effects such as respiratory depression or over-sedation. Block-related complications were rare; isolated cases included transient mild lower abdominal numbness or hip flexor weakness, which resolved spontaneously. No local anesthetic systemic toxicity, infection, or hematoma was reported in any of the included trials.

Discussion

This meta-analysis identified a significant reduction in 24-hour intravenous morphine administration among kidney transplant recipients receiving PNBs (pooled MD -16.20 mg; 95% CI -24.66 to -7.74). Substantial heterogeneity was present across studies (I^2=99%), yet none of the trials demonstrated higher opioid requirements in the intervention arm, and 3 additional studies evaluating fentanyl-based regimens showed the same directional effect. Considered collectively, the findings reveal a consistent and reproducible opioid-sparing association across varied analgesic strategies.

The observed heterogeneity likely reflects meaningful clinical and technical variability among included trials. As summarized in **Table 1**, local anesthetic volumes varied substantially (15 to 30 mL), and block techniques differed between landmark-based and ultrasound-guided approaches; such differences can alter injectate spread and the consistency of fascial plane identification, thereby influencing analgesic efficacy. In addition, trials differed in anesthetic concentration and the use of adjuvants, block timing relative to incision (pre- versus postoperative),

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and whether the intervention was delivered as a single-shot versus catheter-based technique, all of which can affect duration and magnitude of opioid sparing. Variability in co-interventions – such as the components of multimodal analgesia, intraoperative anesthetic technique, and institutional opioid titration protocols – as well as differences in outcome ascertainment (eg, conversion to morphine equivalents and inclusion of rescue dosing) likely further contributed to between-study variation.

The clinical importance of this opioid reduction becomes clearer when framed within the transplant-specific physiologic context. These recipients frequently present with impaired renal clearance and altered protein binding, while simultaneously receiving immunosuppressive and cardiovascular medications that increase susceptibility to drug accumulation, excessive sedation, and ventilatory compromise [26,27]. Beyond these well-recognized systemic risks, experimental evidence suggests that opioid exposure can also influence renal cellular integrity. In particular, κopioid receptor activation has been shown to trigger TRPC6-dependent calcium influx, disrupt the actin cytoskeleton, and produce foot-process effacement, whereas morphine-related signaling reduces slit-diaphragm proteins such as nephrin and podocin – changes that collectively heighten susceptibility to albumin leakage and structural injury [28,29]. These injury pathways can be further intensified under hypertensive or stress conditions, a pattern that parallels the hemodynamic fluctuations commonly encountered during the early post-transplant period. Importantly, these mechanistic observations derive primarily from experimental and non-perioperative models and should therefore be regarded as hypothesis-generating rather than directly translatable clinical evidence in the perioperative transplant setting. Accordingly, the present findings do not demonstrate that perioperative opioid reduction prevents podocyte injury; rather, they are directionally consistent with a biologically plausible framework suggesting potential renal vulnerability under excessive opioid exposure [30]. Although causal relationships cannot be established from the available clinical data, the opioid-sparing effect observed in this meta-analysis is directionally consistent with experimental findings that suggest a biologically plausible rationale for supporting glomerular stability soon after transplantation.

Pain-related outcomes strengthened this interpretation. A pooled reduction in 24-hour resting VAS scores (MD -1.49) approaches commonly accepted minimal clinically important difference (MCID) thresholds for acute postoperative pain. In acute pain settings, a change of approximately 1.3 to 1.8 points on a 10-point scale has been suggested to represent a clinically meaningful difference [31,32], and the magnitude observed in our analysis falls within this range. Although modest in absolute magnitude, this reduction is therefore likely to be clinically meaningful. The decrease in pain scores paralleled the reduction in opioid requirements, providing consistent evidence of improved analgesic efficacy. Because postoperative opioids are titrated to patient-reported pain, the simultaneous reduction in pain intensity and opioid consumption supports a genuine analgesic benefit rather than reflecting prescribing variability. Improved early pain control can also contribute to short-term physiologic stability in the immediate postoperative period. However, as functional recovery endpoints – such as time to ambulation, bowel recovery, or length of hospital stay – were not evaluated in the included studies, these findings should be interpreted as demonstrating enhanced analgesic efficacy rather than confirmed improvements in broader postoperative recovery outcomes.

Among truncal PNB techniques, the TAP block was most frequently evaluated and exhibited a reproducible subgroup effect (mean 24-hour morphine reduction -12.13 mg). Its broad lower abdominal somatic coverage, clear sono-anatomic landmarks, and ease of implementation likely supported early clinical adoption. Several limitations, however, remain noteworthy. Single-shot TAP blocks provide analgesia for approximately 6 to 12 hours, and studies examining catheter-based extensions or adjunct-enhanced regimens have produced mixed results [33]. Technical variation – ranging from anesthetic concentration and volume to needle trajectory, depth of injection, ultrasound-guidance quality, and the structure of multimodal perioperative regimens – likely accounts for much of the observed interstudy heterogeneity [34]. A randomized trial relying on landmark-based placement without sensory confirmation reported no analgesic benefit, underscoring how inadequate injectate spread or imprecise fascial plane identification can diminish block efficacy [18]. Additional differences in block timing, operator expertise, continuous versus single-shot approaches, and institutional opioid titration norms further contributed to variability. Nevertheless, none of the included trials reported increased opioid needs or block-related complications. Even small decreases in opioid exposure can have tangible implications for kidney transplant recipients, a population prone to over-sedation, delayed extubation, impaired ventilatory mechanics, and prolonged recovery.

Beyond technique-specific considerations, the opioid-sparing effect demonstrated in this meta-analysis provides a useful framework for interpreting the broader perioperative implications of PNBs in KT within an enhanced recovery after surgery (ERAS) context. Regional analgesia remains an attractive option for transplant recipients in whom neuraxial techniques are often avoided due to anticoagulation, uremic platelet dysfunction, or hemodynamic vulnerability [35]. ERAS pathways emphasize opioid minimization and physiologic stability – priorities that are particularly relevant in this population given their altered drug metabolism and increased susceptibility to respiratory and gastrointestinal adverse effects [36,37]. In this

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regard, the consistent reduction in opioid requirements observed across studies suggests that PNBs can facilitate ERAS-aligned analgesic strategies by limiting systemic opioid exposure while maintaining adequate pain control, without inducing sympathetic blockade or additional sedation. Notably, however, ERAS-specific recovery endpoints – such as time to ambulation, bowel function, length of stay, or attainment of functional milestones – were not directly evaluated in the included trials. Therefore, the present findings should not be interpreted as demonstrating improved ERAS-defined recovery outcomes. Rather, they indicate that PNBs can be a supportive component within multimodal analgesic pathways that align with ERAS principles. Because structured, transplant-specific ERAS protocols remain heterogeneous and recovery targets are not yet uniformly standardized in KT, the integration of PNBs into such pathways should be viewed as hypothesis-generating rather than outcome-proven. Future prospective studies incorporating validated functional recovery metrics will be necessary to determine whether opioid-sparing regional techniques translate into measurable ERAS-related clinical benefits in KT [38,39].

This meta-analysis has several limitations that should be acknowledged. First, the primary outcome was restricted to 24-hour opioid consumption. Although this endpoint is objective and facilitates quantitative comparison, it provides only a limited view of analgesic efficacy and does not capture longer-term trajectories of pain or recovery; therefore, the observed opioid-sparing effect may not directly translate into broader clinical outcomes [40]. Moreover, no graft-specific clinical endpoints – such as early graft function, rejection rates, or long-term graft survival – were assessed in the included studies; therefore, any implications regarding graft health should be interpreted as speculative and hypothesis-generating rather than directly evidence-based. Second, substantial clinical heterogeneity was present beyond what statistical models could adjust for, as the included trials differed in block technique, timing, anesthetic regimen, and use of adjuvants [41]. Third, the conversion of medians and IQR to means and standard deviations, albeit methodologically necessary, assumes normal distribution and may have introduced bias, particularly in small samples [42]. Fourth, the degree of opioid-sparing observed across studies may not necessarily equate to superior analgesic quality, as multimodal regimens and institutional opioid titration protocols were inconsistently reported [41]. Finally, direct comparative evidence between truncal blocks was lacking, and the predominance of TAP block studies reflects data availability rather than proven superiority, leaving the relative efficacy of alternative techniques unresolved [43]. Future multicenter comparative trials should confirm these findings and incorporate standardized pain and functional recovery endpoints to ensure comparability across block methods.

Conclusions

PNBs are an effective opioid-sparing adjunct for postoperative analgesia in kidney transplant recipients. Pooled evidence demonstrates a significant reduction in 24-hour intravenous morphine consumption along with consistent improvements in pain scores. However, data for fentanyl-based regimens and for truncal block techniques other than TAP remain limited, highlighting important gaps in the current evidence base. To address these limitations, future studies should standardize opioid reporting using intravenous morphine milligram equivalents to enhance cross-study comparability and strengthen quantitative synthesis. In addition, high-quality randomized trials directly comparing different truncal block techniques – such as TAP versus QL or ESP blocks – are needed to determine the most effective regional analgesic strategy for this vulnerable population.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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