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CLINICAL TRIAL REPORT

Effect of Intraoperative Intravenous Lidocaine on Postoperative Delirium in Elderly Patients Undergoing Posterior Lumbar Interbody Fusion

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Purpose: This study aimed to evaluate the effect of intraoperative intravenous (IV) lidocaine on the incidence of postoperative delirium (POD) in elderly patients undergoing major spinal surgery.

Patients and Methods: In this prospective, single-center randomized clinical trial, elderly patients scheduled for elective posterior lumbar interbody fusion (PLIF) with instrumentation spanning two or more vertebral segments were enrolled. A total of 270 patients were randomized to receive either intravenous lidocaine (Group L) or saline (Group C). Group L received lidocaine at a bolus dose of 1.5 mg/kg before induction, followed by continuous infusion at 1.5 mg/kg/h until the end of surgery, while Group C received an equivalent volume of saline. All patients underwent standardized general anesthesia. The primary outcome was the incidence of postoperative delirium (POD) within 5 days after surgery. Secondary outcomes included delirium severity, onset, duration, and subtype (hypoactive, hyperactive, or mixed), postoperative visual analog scale (VAS; 0–100 mm) pain scores, intraoperative anesthetic consumption, 24-hour sufentanil consumption and patient-controlled intravenous analgesia (PCIA) attempts, and perioperative adverse events.

Results: The lidocaine group had a lower incidence of postoperative delirium (8.9% vs 20.7%; RR, 0.43; 95% CI, 0.23–0.81; $P < 0.05$). Among patients who developed delirium, the duration was comparable between groups, while severity scores were higher and time to onset was shorter in the control group. Within the first 24 hours postoperatively, the lidocaine group had lower VAS scores, fewer PCIA attempts, and a reduced cumulative sufentanil dose. Opioid-related adverse events, including nausea and vomiting, were less frequent, with no cases of local anesthetic toxicity, and the overall hospital stay was comparable.

Conclusion: In elderly patients undergoing PLIF, intraoperative intravenous lidocaine (1.5 mg/kg administered before induction, followed by continuous infusion at 1.5 mg/kg/h until the end of surgery) lowered the occurrence of postoperative delirium (POD) within the first 5 days after surgery.

Keywords: lidocaine, postoperative delirium, posterior lumbar interbody fusion, elderly patients

Introduction

POD is an acute neuropsychiatric syndrome that adversely affects recovery, prolongs hospital stay, increases medical costs, and even elevates mortality risk.[1,2] The reported incidence of POD in elderly surgical patients ranges from 20% to 45%.[3] Although its exact pathogenesis remains unclear, neurotransmitter imbalance and neuroinflammation have been proposed as key mechanisms.[4]

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With the global aging population, the number of elderly patients undergoing spinal surgery is steadily increasing. POD in elderly patients was reported to have an incidence of up to 40.5% after spine surgery.[5] Spinal surgery is associated with higher rates of POD compared with other orthopedic procedures. This may be partly due to factors related to the prone position during surgery.[6] Postoperative pain is common after major spinal surgery, and opioids, though standard for analgesia, as well as pain itself, have both been associated with an increased risk of delirium.[5,7,8] Accordingly, perioperative pain management has been emphasized to reduce POD.[9]

Lidocaine is an inexpensive, widely available, and relatively safe compound. As a local anesthetic and class IB antiarrhythmic agent, it readily crosses the blood-brain barrier and exhibits analgesic and anti-inflammatory properties.[10] It has increasingly been incorporated into multimodal perioperative anesthesia regimens.[11,12] The neuroprotective potential of lidocaine was first demonstrated in a feline model of cerebral arterial gas embolism, and subsequent clinical studies have supported its perioperative neuroprotective effects.[13–15] Previous clinical studies have extensively examined the effects of intravenous lidocaine on postoperative analgesia, opioid consumption, intraoperative anesthetic requirements, gastrointestinal recovery, and length of hospital stay.[16,17] However, these analyses primarily involved patients undergoing major abdominal surgery, and for major spinal surgery, the conclusions are conflicting, and the quality of evidence remains limited. To date, no clinical study has examined the effect of lidocaine on POD in elderly patients undergoing major spinal surgery.

Therefore, investigating the impact of intravenous lidocaine on POD and pain after PLIF is clinically important. We hypothesize that intraoperative IV lidocaine would reduce the incidence of POD in elderly patients, possibly mediated by its effects on attenuating postoperative pain and reducing opioid consumption.

Materials and Methods

Ethics and Registration

This study was registered in the Chinese Clinical Trial Registry (www.chictr.org.cn, registration number: ChiCTR2500095927). The study was approved by the Ethics Committee of the Second Hospital of Shanxi Medical University (Approval No. [2024]YX462), and all enrolled patients provided written informed consent.

Patient Inclusion and Exclusion Criteria

This study included 270 elderly patients who underwent posterior lumbar interbody fusion (PLIF) at the Second Hospital of Shanxi Medical University from January 2025 to July 2025. Inclusion criteria were (1) age 65–90 years, (2) ASA physical status I–III, (3) BMI 19–28 kg/m^2, and (4) elective posterior lumbar interbody fusion (PLIF) with instrumentation spanning two or more vertebral segments, to standardize surgical trauma and analgesic requirements. Exclusion criteria were (1) allergy to lidocaine or other amide local anesthetics, (2) preoperative mental or cognitive disorders or communication difficulties, (3) significant sinus bradycardia (<50 bpm) or severe cardiovascular disease, (4) symptomatic cerebrovascular disease, (5) liver or kidney dysfunction, and (6) long-term preoperative opioid use. Withdrawal criteria comprised patient refusal, intraoperative allergic reactions, or severe perioperative adverse events requiring discontinuation at the physician's discretion.

Randomization and Masking

This prospective, single-center, double-blind randomized controlled trial used computer-generated random numbers, with group allocations sealed in opaque envelopes and trial drugs prepared accordingly. A designated anesthesiologist administered the study drugs, managed anesthesia, and monitored intraoperative safety, while postoperative follow-up was performed by trained investigators blinded to allocation. To ensure blinding, both lidocaine and saline were colorless and odorless, and identical syringes were used for infusion.

Perioperative Management and Interventions

All patients fasted for at least 8 hours and abstained from clear fluids for 2 hours before surgery. Upon arrival in the operating room, standard monitoring was applied, including pulse oximetry, noninvasive blood pressure,

electrocardiography, and bispectral index (BIS). After patients had rested supine for 10 minutes, stable vital signs were recorded as baseline values.

Patients were randomized to the lidocaine group (Group L) or the control group (Group C) according to whether intravenous lidocaine infusion was administered. In Group L, lidocaine was administered as a bolus of 1.5 mg/kg over 15 minutes before induction, followed by continuous infusion at 1.5 mg/kg/h until the end of surgery. In Group C, an equal volume of normal saline was infused in the same manner.

Anesthesia was induced with sufentanil (0.3–0.4 μg/kg), cis-atracurium (0.2 mg/kg), and etomidate (0.2–0.6 mg/kg). Tracheal intubation was performed when the BIS value dropped below 60. Mechanical ventilation was applied with a target end-tidal carbon dioxide of 35–45 mmHg. Anesthesia was maintained with a continuous infusion of propofol (4–12 mg/kg/h), titrated to maintain a BIS value between 40 and 60, together with remifentanil (0.05–0.30 μg/kg/min). Propofol and remifentanil were discontinued at skin closure. Hemodynamic stability was maintained with ephedrine, atropine, or methoxamine as required. After extubation, patients were transferred to the post-anesthesia care unit (PACU).

Postoperative analgesia was provided using a patient-controlled intravenous analgesia (PCIA) regimen consisting of sufentanil 100 μg and ondansetron 16 mg diluted with normal saline to 100 mL. The background infusion rate was 2 mL/h, with a bolus dose of 1 mL, a lockout interval of 15 minutes, and a maximum limit of 10 mL/h. If pain control was inadequate (VAS ≥40 mm or upon patient request), an intravenous rescue dose of sufentanil (1–5 μg) was administered at the discretion of the attending anesthesiologist.

Adverse events, including hypotension, bradycardia, hypertension, tachycardia, and local anesthetic toxicity, were recorded. These were managed with intravenous ephedrine, atropine, urapidil, or esmolol as appropriate, and local anesthetic toxicity was treated according to established rescue protocols.

Outcome Measurement

Primary Outcome

The incidence of POD within the first 5 postoperative days was assessed, with delirium defined as acute to subacute onset over hours to days.[18] POD was evaluated using the Confusion Assessment Method (CAM), a tool applicable by clinicians without psychiatric training.[19] Diagnosis required patient interviews meeting four criteria: (1) acute onset or fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered consciousness, with criteria 1 and 2 plus either 3 or 4 indicating delirium. Assessments were performed twice daily (08:00 and 20:00), with additional episodes identified via interviews with companions, nurses, and medical records.

Secondary Outcomes

The secondary outcomes included:

1. Delirium severity, assessed using the Confusion Assessment Method-Severity (CAM-S).[20] The total CAM-S score ranges from 0 to 7. Each delirium symptom (except fluctuation) was rated as absent (0), mild (1), or marked (2). Acute onset or fluctuation was rated as absent (0) or present (1). The onset and duration of delirium were also recorded.
2. Postoperative pain intensity measured by the Visual Analogue Scale (VAS) at 2, 4, 8, 12, 24, and 48 hours after surgery.
3. Opioid consumption, including intraoperative remifentanil dose, cumulative sufentanil consumption from PCIA within 24 hours postoperatively, and the total number of patient-triggered PCIA attempts within 24 hours.
4. Perioperative adverse events were recorded, including opioid-related (respiratory depression, dizziness or somnolence, nausea or vomiting), lidocaine-related (local anesthetic toxicity symptoms such as hearing loss, metallic taste, slurred speech, perioral numbness, tinnitus, dizziness, or tremor), and other events such as hypertension defined as mean arterial pressure greater than 120% of baseline, hypotension defined as mean arterial pressure less than 70% of baseline or below 65 mmHg, tachycardia defined as heart rate greater than 120% of baseline, bradycardia defined as heart rate below 45 beats per minute, cardiac arrest, or surgical site infection requiring debridement.

Statistical Analysis

Sample Size

No previous study has investigated the effect of intraoperative lidocaine infusion on the incidence of POD following major spine surgery. Previous studies have indicated that a reduction in delirium incidence by at least one-third from baseline is considered clinically meaningful.[21] In our prior clinical cohort study at this hospital, the incidence of POD was 21% in elderly patients undergoing posterior thoracolumbar fusion surgery. The sample size for the present study was calculated using a two-sided test with a significance level of 0.05 and a power of 0.80. Assuming a delirium incidence of 21% in the control group, 121 patients per group would be required to detect a 60% reduction in POD in the lidocaine group. Considering the 10% dropout rate, 135 patients will be enrolled per group, for a total of 270 participants.

Date Analysis

All statistical analyses were performed using SPSS 27.0 (IBM, Armonk, NY, USA) and R 4.1.3 (R Core Team, Vienna, Austria). Continuous variables with a normal distribution are presented as mean ± standard deviation (SD) and compared between groups using the independent-samples *t*-test. Non-normally distributed continuous variables are presented as median (interquartile range, IQR) and compared using the Mann–Whitney *U*-test, with Hodges–Lehmann estimates and 95% confidence intervals (CI) reported. Categorical variables were compared using the chi-square test or Fisher's exact test, and relative risks (RR) with 95% CI were calculated.

The primary outcome, the incidence of postoperative delirium, was analyzed in the intention-to-treat (ITT) population, which included all randomized patients. To assess the robustness of the findings, sensitivity analyses were conducted, including a per-protocol (PP) analysis that excluded patients without postoperative POD assessment, and an analysis addressing missing data. As the proportion of missing data was <5%, extreme-case imputation was applied, considering missing values in the control group as POD-negative and in the lidocaine group as POD-positive. Kaplan–Meier analysis was used to evaluate time to delirium onset. For repeated-measures outcomes, including postoperative VAS scores at 2, 4, 8, 12, 24, and 48 hours, linear mixed models (LMM) were used, adjusting for preoperative VAS scores.

Results

A total of 294 patients were initially assessed for eligibility, of whom 24 were excluded (10 did not meet the inclusion criteria and 14 declined to participate). The remaining 270 patients were randomized equally into two groups (n = 135 each). During follow-up, two patients in the lidocaine group and one in the control group declined postoperative assessments (Figure 1), resulting in an overall attrition rate of 1.1%.

Baseline Characteristics

Baseline characteristics, including preoperative cognitive function assessed by the Mini-Mental State Examination, were comparable between the two groups (Table 1).[22] Intra-operative profiles are summarized in Table 2. Intraoperative remifentanil consumption was significantly lower in the lidocaine group than in the control group (2.3 ± 0.7 μg vs 2.5 ± 0.6 μg, $P < 0.001$), while other intraoperative parameters did not differ significantly.

Primary Outcome

According to the ITT analysis (n = 270), the incidence of delirium was significantly lower in the lidocaine group compared with the control group, occurring in 8.9% (12/135) versus 20.7% (28/135) (RR, 0.43; 95% CI, 0.23–0.81; $P = 0.010$) (Table 3).

Sensitivity Analysis

In sensitivity analyses, consistent results were observed. In the PP population (n = 267), the incidence was 9.0% (12/133) in the lidocaine group versus 20.9% (28/134) in the control group (RR, 0.43; 95% CI, 0.23–0.81; $P = 0.011$). An analysis using extreme-case imputation, in which missing values in the control group were considered POD-negative and those in the lidocaine group POD-positive, also showed a lower incidence in the lidocaine group (10.4%, 14/135 vs 20.7%, 28/135; RR, 0.50; 95% CI, 0.28–0.91; $P = 0.029$), confirming the robustness of the findings (Table 3).

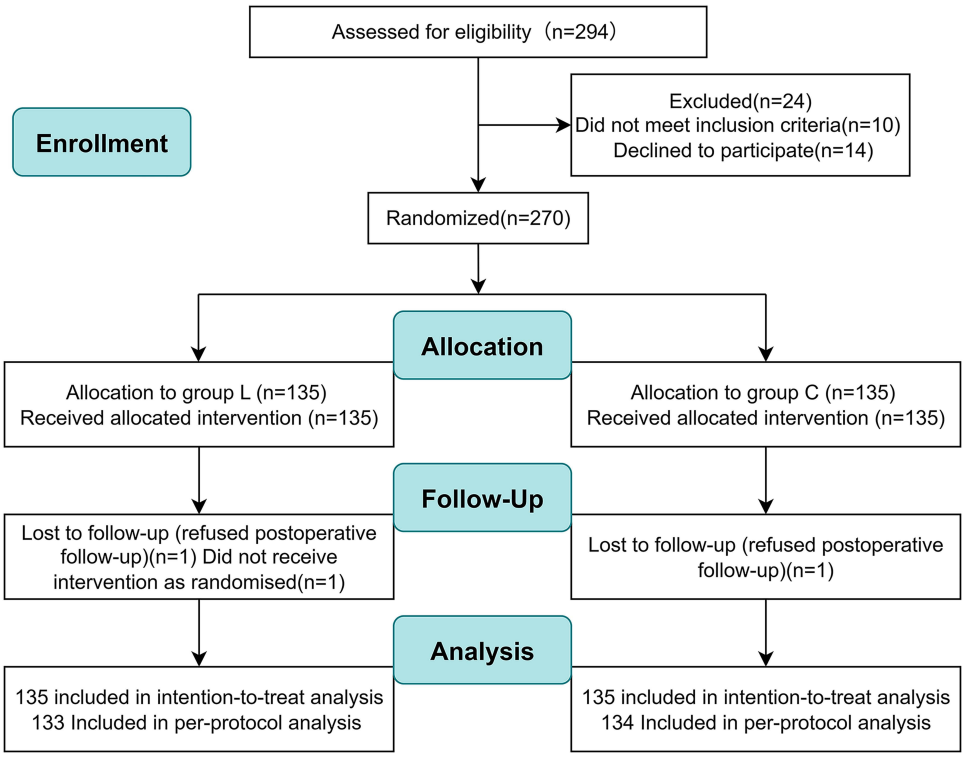

Figure 1 The study's flowchart.

Secondary Outcome

Postoperative Delirium Related Outcomes

Among patients who developed delirium, the duration was comparable between the two groups (median [IQR], 1 [1–3.25] days in the control group vs 1 [1–3] days in the lidocaine group; $P = 0.767$). Delirium severity scores were significantly higher

Table 1 Patient Characteristics

	Group C (n=135)	Group L (n=135)	P
Age (years)	76.0±6.0	74.8±5.3	0.087
Height (cm)	162.8±7.5	163.1±8.2	0.739
Weight (kg)	65.2±12.0	63.5±10.3	0.204
Sex (Male/Female)	69/66	71/64	0.903
BMI (kg/m^2)	24.6±4.5	24.0±3.7	0.133
Smoking (Yes/No)	45/90	51/84	0.525
Education (years)	4.9±2.7	4.7±2.0	0.433
ASA (II/III)	95/40	99/36	0.685*
MMSE	27 (26–28)	27 (26–28)	0.405
CCI	4.7±2.3	4.4±2.1	0.265
Preoperative VAS	4.5±1.2	4.5±1.7	0.738
Preoperative analgesic use (Yes/No)	80/55	74/61	0.539

Notes: Data were presented as mean ± standard deviation, median (IQR) or (number/number) as appropriate. *P < 0.05 versus Group C.

Abbreviations: BMI, Body Mass Index; ASA, American Society of Anesthesiologists; MMSE, Mini-Mental State Examination; CCI, Charlson Comorbidity Index; VAS, Visual Analogue Scale.

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Table 2 Comparison of Intraoperative and Postoperative Profiles Between the Lidocaine and Control Groups

	Group C (n=135)	Group L (n=135)	P
Number of levels	3 (3–3)	3 (3–3)	0.784
Operation time (min)	223.2±22.8	223.5±20.7	0.904
Infusion duration of study drug (min)	213.2±22.8	213.5±20.7	0.904
Infusion volume of study drug (mL)	28.7±4.8	28.6±5.1	0.820
Extubation time (min)	13 (10–14)	13 (10.5–14)	0.906
Length of PACU stay (min)	35.5±4.1	35.9±4.4	0.496
Total propofol dose (mg)	740.3±107.2	753.9±112.3	0.308
Intraoperative remifentanil (mg)	2.5±0.6	2.3±0.7*	<0.001
Blood loss (mL)	340 (300–420)	350 (300–415)	0.184
Urine volume (mL)	280 (240–340)	280 (250–340)	0.698
Total fluid infusion (mL)	1800 (1600–1800)	1800 (1700–1900)	0.679
Time-weighted mean arterial pressure (mmHg)	83±8	83±9	0.834
Time-weighted heart rate (beats/min)	74±8	73±6	0.058

Notes: Data were presented as mean ± standard deviation, or median (IQR) as appropriate. *$P < 0.05$ versus Group C.
Abbreviation: PACU, Post-Anesthesia Care Unit.

Table 3 Comparison of Primary Outcomes Between the Lidocaine and Control Groups

	Incidence of Delirium No./Total (%)		RR (95% CI)	P
	Group C	Group L		
Intention to treat[a]	28/135 (20.7%)	12/135 (8.9%)*	0.429 (0.228–0.807)	0.010
Per protocol[b]	28/134 (20.9%)	12/133 (9.0%)*	0.432 (0.229–0.813)	0.011
Extreme-case imputation[c]	28/135 (20.7%)	14/135 (10.4%)*	0.500 (0.275–0.907)	0.029

Notes: Data are presented as number of patients (%). [a]Intention-to-treat analysis included all randomized participants not excluded, analyzed according to original treatment assignment. [b]Per-protocol analysis excluded participants lost to follow-up (L group, n=2; C group, n=1). [c]For missing data, delirium status was imputed as positive in group L and negative in group C.*$P < 0.05$ versus Group C.
Abbreviations: CI, confidence interval; RR, relative risk.

in the control group compared with the lidocaine group (median [IQR], 4.5 [4–6] vs 3 [3–5]; $P = 0.045$). The distribution of delirium subtypes (hypoactive, hyperactive, and mixed) did not differ significantly between groups ($P = 0.897$) (Table 4). The time to delirium in all participants also differed (Log rank test, P=0.0055) (Figure 2).

Table 4 Comparison of Postoperative Delirium–Related Outcomes Between the Lidocaine and Control Groups

	Group C (n=28)	Group L (n=12)	P
Duration of delirium, d, median (IQR)	1 (1–3.25)	1 (1–3)	0.767
Delirium severity scores, d, median (IQR)	4.5 (4–6)	3 (3–5)*	0.045
Type of delirium, no (%)			0.897
Hypoactive	17 (12.7)	7 (5.3)	
Hyperactive	5 (3.7)	3 (2.3)	
Mixed	6 (4.5)	2 (1.5)	

Notes: Data were presented as number (percentage) or median (IQR) as appropriate. *$P < 0.05$ versus Group C.

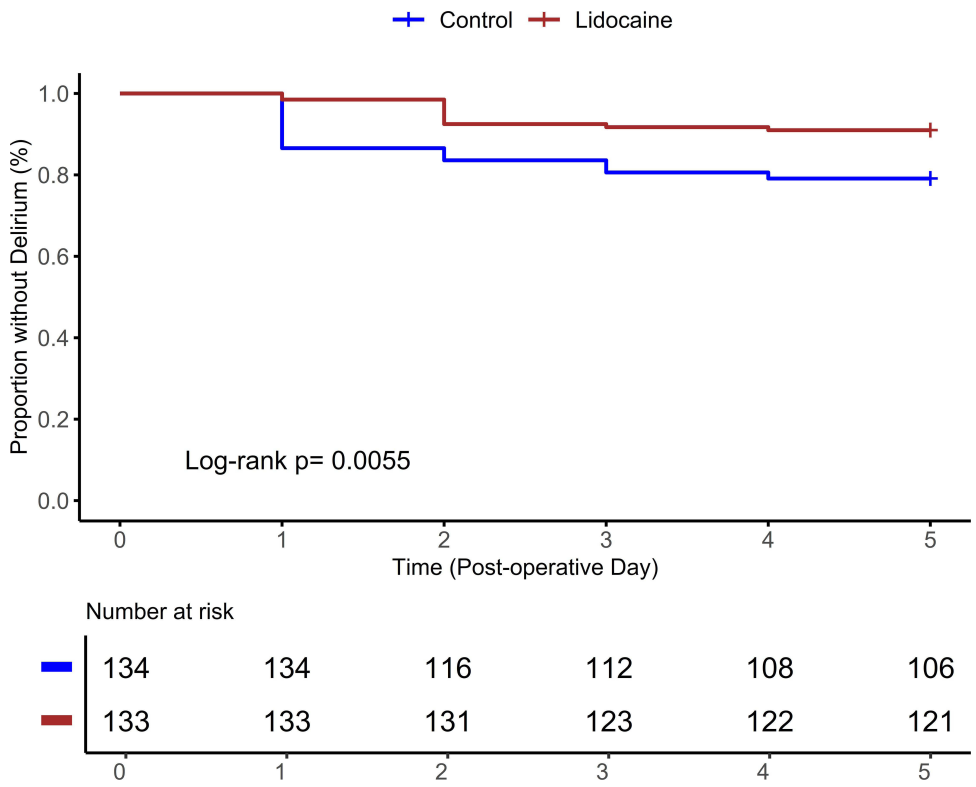

Figure 2 Kaplan–Meier curves showing time to postoperative delirium in the lidocaine and control groups. There was a significant difference between the two groups (Log rank test, $P = 0.0055$).

Postoperative Pain Outcomes

Preoperative resting VAS pain scores did not differ significantly between groups (Table 1). In the LMM analysis, preoperative VAS was included as a covariate, and data were fitted using maximum likelihood estimation. Compared with the control group, the lidocaine group showed significantly lower adjusted mean resting VAS scores at 2, 4, 8, 12, and 24 hours postoperatively, but not at 48 hours, when both groups exhibited a slight increase. Overall, the adjusted mean resting VAS score was significantly lower in the lidocaine group than in the control group (3.17 [95% CI, 3.07–3.27] vs 3.47 [95% CI, 3.38–3.56]; $P < 0.001$, Bonferroni-corrected). Resting VAS scores declined significantly over time ($P < 0.001$), with no significant group-by-time interaction (Wald test, $P = 0.218$) (Figure 3). The lidocaine group had significantly fewer PCIA attempts within the first 24 hours after surgery compared with the control group (median [IQR], 6.0 [3.0–11.0] vs 22.0 [13.0–35.0]; $P < 0.001$). The Hodges–Lehmann estimate of the median difference was 15.0 (95% CI, 12.0–19.0). In addition, the cumulative sufentanil dose administered via PCIA during the first 24 postoperative hours was significantly lower in the lidocaine group (median [IQR], 54.0 [50.5–59.0] vs 72.0 [62.0–84.0]; $P < 0.001$). The Hodges–Lehmann estimate of the median difference was 17.0 (95% CI, 14.0–20.0) (Figure 4).

Adverse Events and Recovery Outcomes

Postoperatively, the lidocaine group had a significantly lower incidence of opioid-related adverse events, including nausea ($P = 0.038$) and vomiting ($P = 0.014$). No cases of local anesthetic toxicity occurred in either group. Other adverse events did not differ significantly between groups. Length of hospital stay was comparable between groups ($P = 0.319$) (Table 5).

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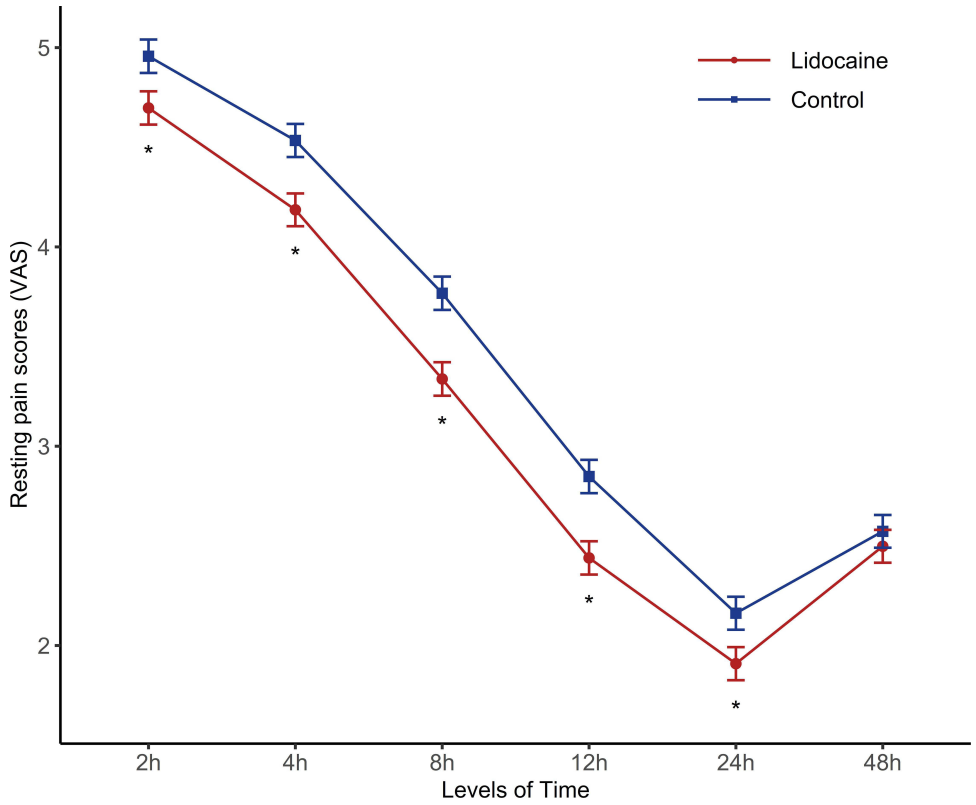

Figure 3 Estimated marginal means of postoperative resting VAS pain scores over time in the Lidocaine and Placebo groups. Data were derived from linear mixed-effects models adjusted for baseline VAS. Error bars represent standard errors of the mean. *Indicates significant between-group differences at each time point (Bonferroni-adjusted $P < 0.05$).

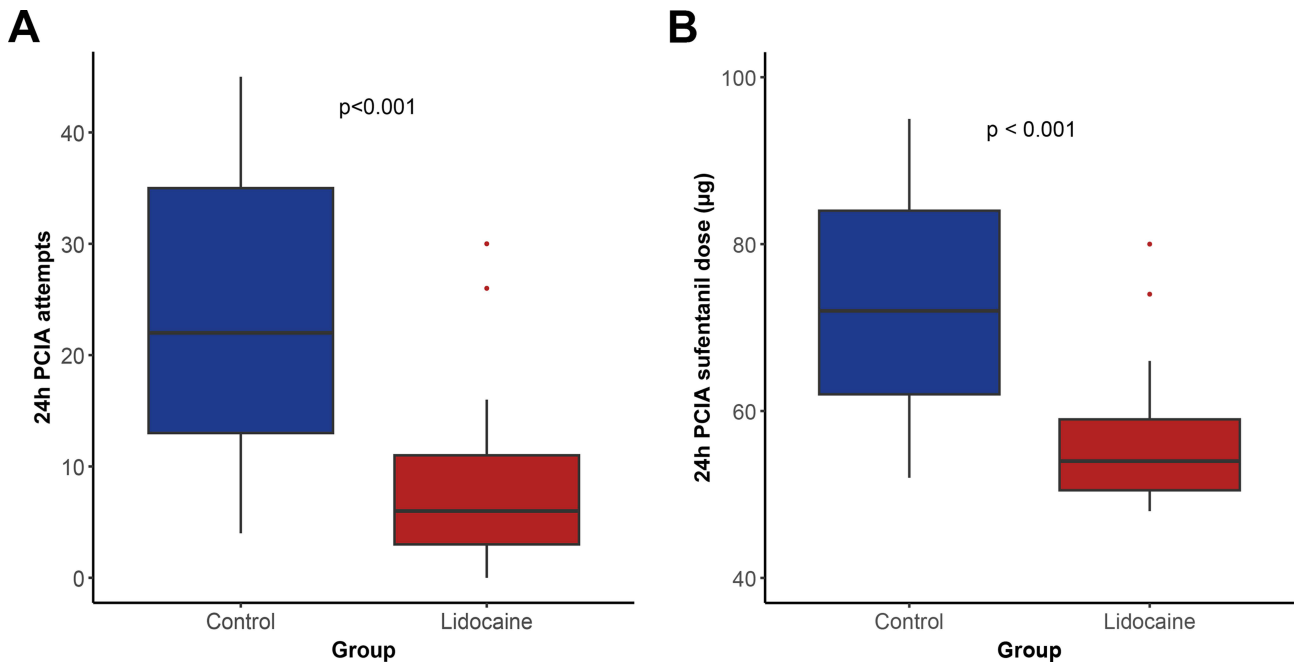

Figure 4 Comparison of postoperative pain management outcomes between lidocaine and control groups. (**A**) Number of PCIA attempts within 24 hours post-surgery. The lidocaine group showed significantly fewer attempts compared to controls ($P < 0.001$). (**B**) Total sufentanil dose (μg) administered via PCIA during the first 24 postoperative hours. The lidocaine group required substantially lower opioid doses than controls ($P < 0.001$).

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Table 5 Comparison of Other Postoperative Parameters Between the Lidocaine and Control Groups

	Group C (n=135)	Group L (n=135)	P
Perioperative Adverse Events (Yes/No)			
Respiratory depression	0/135	0/135	1.000
Dizziness or Drowsiness	21/114	10/125	0.056
Nausea	26/109	13/122*	0.038
Vomiting	17/118	5/130*	0.014
Local anesthetic toxicity	0/135	0/135	1.000
Hypertension	18/117	13/122	0.445
Hypotension	8/127	10/125	0.807
Tachycardia	7/128	5/130	0.768
Bradycardia	14/121	18/117	0.572
Cardiac arrest present	0/135	0/135	1.000
Wound infection requiring debridement	2/133	0/135	0.498
Length of Hospital Stay (d)	5.6±0.9	5.5±0.6	0.319

Notes: Data were presented as (number/number) or mean ± standard deviation as appropriate.
*$P < 0.05$ versus Group C.

Discussion

In this study, we investigated the impact of IV lidocaine on the incidence of POD in older patients undergoing major spinal surgery and found that it was associated with a lower incidence of POD within 5 days after surgery compared with the control group. Moreover, our findings support that IV lidocaine was associated with a clinically significant reduction in intraoperative and postoperative opioid requirements, which in turn may mitigate the risk of postoperative delirium.

The mechanisms underlying POD are multifactorial and not yet fully elucidated, with proposed contributors including neuroinflammation, oxidative stress, neurotransmitter imbalance, and disturbances in metabolic homeostasis.[23–25] Intravenous lidocaine, beyond its role as a local anesthetic, exerts analgesic and anti-inflammatory effects by inhibiting sodium channels, reducing cytokine release, suppressing nociceptive transmission, and blocking NMDA receptors.[26,27] These mechanisms may collectively attenuate neuroinflammation and oxidative stress, thereby providing potential benefits not only for pain control but also for reducing the risk of delirium. Our findings were consistent with a previous study in elderly patients undergoing thoracoscopic surgery, although statistical significance was not achieved in that study.[28] This may be attributed to the relatively small sample size (n = 30 per group), the evaluation of delirium as a secondary outcome, and the limited assessment period, which was restricted to postoperative days 2 and 7. In contrast, our finding was supported by another randomized study conducted in elderly patients (aged >65 years, ASA physical status I–II) undergoing spine surgery, which demonstrated that intravenous lidocaine was associated with significantly higher MMSE scores at 3 days postoperatively compared with the control group, suggesting a potential neuroprotective effect of lidocaine in this surgical population.[14] However, this study was limited by a relatively small sample size and focused on early postoperative cognitive outcomes. Taken together, these two referenced clinical studies indicate that IV lidocaine exerts its effects by modulating traditional inflammatory and oxidative stress pathways, as evidenced by changes in plasma levels of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), oxidative stress markers such as superoxide dismutase (SOD) and cortisol, and neuronal injury biomarkers including neuron-specific enolase (NSE). These actions may partially explain the potential mechanism by which IVL reduces the incidence of POD. Additionally, in our study, lidocaine appeared to reduce the severity of delirium and delay its onset, although the overall duration and subtype distribution were similar between groups.

According to the guidelines, when opioids are used, routine monitoring for delirium is recommended in view of the increased risk of its occurrence.[29] Opioid analgesics may contribute to delirium by altering neurotransmission, disrupting sleep architecture, potentiating neuroinflammation, inducing hyperalgesia, or inducing neuronal and glial cell dysfunction and/or death.[30] These mechanisms provide a biological rationale for the association between opioid exposure and

postoperative delirium observed in clinical practice. In our study, intraoperative IV lidocaine significantly reduced intraoperative remifentanil consumption and decreased the cumulative sufentanil dose administered via PCIA during the first 24 postoperative hours by about 24%, consistent with previous reports.[27,31] This opioid-sparing effect was accompanied by a lower incidence of postoperative delirium, supporting opioid exposure as a modifiable risk factor in this population. Opioid use beyond 48 hours was not analyzed because PCA solutions were nearly exhausted by the second day. Regarding pain outcomes, although postoperative VAS scores within the first 24 hours were statistically lower in the lidocaine group, the between-group differences were less than 1 cm, consistent with an early study, and did not reach the minimal clinically important difference (MCID).[31] In our study, the reduction in early postoperative pain scores disappeared by 48 hours, and the decrease in delirium incidence was also confined to the first postoperative day, suggesting that lidocaine's effect may be limited to the intraoperative and immediate postoperative phases. In contrast, two other studies reported clinically meaningful reductions in early postoperative pain scores with IV lidocaine, which may be related to higher intraoperative infusion rates (2 mg/kg/h and 3 mg/kg/h, respectively) compared with our study. Furthermore, pain may fluctuate rapidly within a day and is not fully captured by single-timepoint VAS measurements. Notably, a recent study demonstrated that opioid use increases the risk of POD in a dose-dependent manner, independent of pain intensity.[32] These findings support our conclusion that intraoperative lidocaine provides a clinically meaningful opioid-sparing effect, which may help reduce delirium risk.

IV lidocaine showed no apparent safety issues in the observed outcomes. Postoperatively, the lidocaine group experienced fewer opioid-related adverse events, including nausea and vomiting, reflecting the significant opioid-sparing effect of IV lidocaine. No cases of local anesthetic toxicity occurred, and other adverse events, as well as the length of hospital stay were comparable between groups.

This study is the first randomized controlled trial to systematically evaluate the effect of intraoperative IV lidocaine on POD in elderly patients undergoing major spinal surgery, thereby addressing an important evidence gap. By restricting enrollment to patients receiving PLIF involving two or more vertebral segments, we standardized surgical trauma and postoperative analgesic requirements, ensuring a relatively homogeneous population and enhancing the validity of pain and delirium assessments.

Our study also has several limitations. First, we primarily assessed early postoperative outcomes and did not conduct long-term follow-up, which precludes evaluation of the potential long-term effects of lidocaine on cognitive function. Second, this was a single-center trial, which may limit the generalizability of our findings. Finally, we did not measure perioperative inflammatory or oxidative stress biomarkers, both of which have been implicated in the pathogenesis of delirium.

Current evidence regarding the long-term effects of intravenous lidocaine on postoperative cognitive function is limited and of variable quality, precluding definitive conclusions.[33,34] Future studies are warranted to further explore these outcomes and to determine whether they are influenced by infusion dose, duration, and timing. Moreover, large multicenter trials are needed to validate our findings and to formally quantify the extent to which opioid use mediates the relationship between lidocaine and postoperative delirium.

Conclusion

In conclusion, in elderly patients undergoing PLIF, perioperative intravenous lidocaine infusion effectively reduces the incidence of postoperative delirium within the first five days. These findings will hold significant value for the refinement of the Enhanced Recovery After Surgery (ERAS) concept.

Copyright Statement

Data Sharing Statement

Deidentified individual participant data underlying the results reported in this article will be made available upon request to qualified researchers, along with the study protocol. Data will be accessible beginning 6 months after publication and will remain available for 5 years. Requests should be directed to the corresponding author at xuesensu_sxpph@yeah.net.

Ethics Statement

The study was approved by the Ethics Committee of the Second Hospital of Shanxi Medical University (Approval No. [2024]YX462), and all enrolled patients provided written informed consent. The study complied with the Declaration of Helsinki.

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Disclosure

The authors declare that they have no conflicts of interest related to this work.

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