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ORIGINAL RESEARCH

Lidocaine-Based vs Sufentanil-Based PCIA After Pulmonary Resection Surgery: A Randomized Controlled Trial

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Background: We investigated the efficacy and safety of lidocaine-based patient-controlled intravenous analgesia (PCIA), compared with sufentanil-based PCIA on postoperative pain and recovery quality in patients undergoing thoracoscopic lung surgery.

Methods: We recruited 160 patients undergoing thoracoscopic lung surgery who were randomized to receive lidocaine-based PCIA (1.5 mg/kg/h) or sufentanil-based PCIA (2 μg/mL) within 48 hours postoperatively. The primary endpoint was visual analogue scores (VAS) pain scores at 6, 12, 24, and 48 hours postoperatively. Postoperative quality of recovery-15 (QoR-15) scores and other prespecified endpoints were also recorded.

Results: VAS pain scores at rest and during coughing in the lidocaine group were significantly lower at 6, 12, and 24 hours postoperatively ($P<0.05$), with no difference at 48 hours ($P>0.05$). QoR-15 scores in the lidocaine group were higher on postoperative day (POD) 1 ($P<0.001$) and POD2 ($P<0.001$), with significant differences in the two dimensions of postoperative physical comfort and pain ($P<0.001$). The lidocaine group also experienced a shorter time to first flatus, defecation, and ambulation ($P<0.05$), with no difference in the length of postoperative hospitalization and thoracic drainage time ($P>0.05$). The serum IL-6, TNF-α, IL-8, cortisol, and epinephrine concentrations were lower in the lidocaine group on POD1 and POD2 ($P<0.05$). The incidence of postoperative nausea and vomiting in the lidocaine group was lower ($P<0.05$), with no differences in other adverse events ($P>0.05$).

Conclusion: Compared with sufentanil-based PCIA, lidocaine-based PCIA significantly relieved postoperative pain and improved recovery quality after thoracoscopic lung surgery with fewer postoperative adverse events, which is a considerable choice for postoperative analgesia.

Trial Registration: This study was retrospectively registered at the Chinese Clinical Trial Registry on March 1st, 2023 (number ChiCTR2300068840).

Keywords: thoracoscopic lung surgery, intravenous lidocaine, postoperative analgesia, quality of recovery

Background

Postoperative pain is the most common symptom following thoracic surgery,[1] with approximately 70% of patients experiencing moderate to severe pain.[2] Even after thoracoscopic lung surgery, the incidence of acute pain ranges from 30% to 60%.[3–5] Postoperative pain not only causes various adverse physiological and psychological consequences but also limits postoperative respiratory exercises. Inadequate coughing impairs mucociliary clearance, thereby increasing the risk of pulmonary complications such as pneumonia and atelectasis after surgery.[6] Additionally, poorly controlled pain and reduced patient mobility trigger a stress response that can cause postoperative hypercoagulability, increasing the

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risk of deep vein thrombosis and pulmonary embolism. Furthermore, acute postoperative pain can progress to chronic pain if not properly managed.[7,8] Therefore, effective postoperative analgesia is essential.

A variety of analgesic techniques are available after thoracoscopic lung surgery, including epidural analgesia (EA), thoracic paravertebral block (TPB), and the widely used patient-controlled intravenous analgesia (PCIA). Although certain regional analgesia techniques can provide effective pain relief, their use is often limited by technical challenges, contraindications, and potential complications such as dural puncture, hematoma, infection, hypotension, and urinary retention.[9–14] PCIA is widely accepted as a less invasive and effective method of analgesia.[15] Studies have shown that PCIA provides effective pain relief compared to EA and TPB.[16] Opioids remain the primary analgesics in PCIA; however, their side effects—including nausea, vomiting, constipation, urinary retention, somnolence, and respiratory depression—increase morbidity and delay recovery.[17] Consequently, identifying alternative analgesic regimens that can provide effective pain control while improving patient outcomes has become a key focus in perioperative pain management.

Lidocaine is a widely used amide-type local anesthetic that has attracted increasing attention for perioperative intravenous infusion. Recent studies indicate that intravenous lidocaine can reduce postoperative pain and opioid requirements,[18,19] modulate inflammatory and stress responses,[20–22] and accelerate recovery of gastrointestinal function, all of which contribute to improved postoperative outcomes.[23,24] However, lidocaine has rarely been used in patients undergoing thoracic surgery, and there is currently no research on its application in PCIA for this population. Therefore, the aim of our study was to explore the efficacy and safety of lidocaine-based PCIA compared to sufentanil-based PCIA on postoperative pain and recovery quality in patients undergoing thoracoscopic lung surgery.

Although intravenous lidocaine is generally considered safe, it is not routinely used in PCIA due to concerns regarding potential toxicity. Neurological symptoms may develop at plasma concentrations above 5–8 μg/mL, while severe cardiovascular events are usually associated with levels exceeding 10 μg/mL.[25] Therefore, close monitoring—such as cardiac monitoring and regular assessment of serum lidocaine concentration—is recommended. Previous studies suggested a loading dose of 1–2 mg/kg and a maintenance infusion of 1–3 mg/kg/h to keep plasma concentrations below 5 μg/mL for perioperative use.[26,27] Based on these findings and safety considerations, this study selected a postoperative lidocaine infusion dose of 1.5 mg/kg/h and excluded patients with hepatic or renal dysfunction to minimize the risks of accumulation and toxicity. In addition, blood concentrations of lidocaine were monitored throughout the study.

Methods

Study Design and Patients

This single-center, double-blinded, randomized and controlled trial was approved by the Ethics Committee of Gansu Provincial Hospital on December 26th, 2022 (ID: No.2022–454) and registered at the Chinese Clinical Trial Registry on March 1st, 2023 (number ChiCTR2300068840). This trial was conducted in compliance with the Declaration of Helsinki. All patients participating in the trial signed written informed consent.

Patients aged 18–65 years with a body mass index (BMI) of 18–28 kg/m² and classified as American Society of Anesthesiologists (ASA) physical status I or II who were scheduled to undergo thoracoscopic pneumonectomy were eligible for inclusion in this study. Exclusion criteria included a history of mental illness, hepatic or renal dysfunction, allergy to lidocaine, history of seizures, severe cardiac disease (including heart failure, severe heart block, preexcitation syndrome, etc.), chronic pain or long-term opioid dependence, conversion from thoracoscopic surgery to thoracotomy, communication disorders or inability to understand the assessment scales, and discontinuation of the PCIA pump during the study period. All surgical procedures, including wedge resection, segmentectomy, and lobectomy, were performed by the same surgical team.

Patients were randomly assigned to either the sufentanil group or the lidocaine group in a 1:1 ratio using a random number table generated by SPSS 25.0. Allocation concealment was maintained with sequentially numbered, sealed, opaque envelopes, which were opened only after patient enrollment. Study medications were prepared by an independent nurse who was not involved in data collection or analysis. Throughout the trial, all patients, anesthesiologists, surgeons, nurses, and personnel responsible for data collection and analysis remained blinded to group assignments.

The PCIA pumps were prepared by a designated anesthesiology nurse according to group allocation and standardized protocols. For the sufentanil group, the PCIA solution contained sufentanil (2 μg/kg) and flurbiprofen axetil (200 mg), diluted to a total volume of 300 mL with 0.9% saline. For the lidocaine group, the PCIA solution contained lidocaine (administered at an infusion rate of 1.5 mg/kg/h, based on previous studies[26,27]) and flurbiprofen axetil (200 mg), also diluted to a total volume of 300 mL with 0.9% saline. All PCIA pumps were administered continuously for 48 hours postoperatively, with identical external appearance and programmed parameters: initial bolus dose of 2 mL, continuous background infusion at 6 mL/h, patient-controlled bolus dose of 2 mL, lockout interval of 20 minutes, and a maximum total dose of 12 mL per hour.

Anesthesia Protocol

After patients were admitted to the operating room, routine monitoring was initiated, including electrocardiogram (ECG), non-invasive blood pressure, heart rate, and oxygen saturation. Venous access was established in the upper limbs, and the Bispectral Index was also monitored. Anesthesia was induced with intravenous midazolam (0.05 mg/kg), sufentanil (0.4–0.6 μg/kg), etomidate (0.15–0.3 mg/kg), and cis-atracurium (0.2 mg/kg). A double-lumen bronchial tube of appropriate size was selected based on the patient's condition and positioned using a fiberoptic bronchoscope. Following tracheal intubation, mechanical ventilation commenced. Anesthesia was maintained with intravenous propofol (6–8 mg/kg/h), remifentanil (0.2–0.4 μg/kg/min) and dexmedetomidine (0.5–1.0 μg/kg/h). Cis-atracurium 0.1 mg/kg was intermittently administered intraoperatively. Vasoactive drugs were used as needed to keep the patient's hemodynamic level stable during operation. All anesthetic drugs were discontinued immediately after the operation. Sufentanil 0.1 μg/kg was added before skin incision and after skin suture in both groups.

All patients were transferred to the post-anesthesia care unit after surgery and connected to the PCIA pump by a nurse anesthetist who was not involved in the dispensing of the PCIA pump. Patients in both groups did not receive any additional analgesic treatments (eg, intercostal nerve block, epidural block, and local infiltration of the wound) postoperatively. All patients underwent continuous electrocardiographic monitoring during infusion of the study drug and training of follow-up personnel in monitoring early signs and symptoms of local anesthetic toxicity. Postoperatively, depending on the patient's pain need, one dose of tramadol hydrochloride injection (100 mg) was administered intravenously for remedial analgesia if the patient reported VAS pain score of ≥4 and did not receive pain relief after pressing the PCIA pump for an additional dose, or if the VAS resting score was ≥7. For the management of PONV, 4 mg of ondansetron was administered intravenously. Preoperatively, all patients were given a detailed explanation of how to use the PCIA pump, the VAS pain rating scale, and the 15-item Quality of Recovery questionnaire (QoR-15) scale. The QoR-15 scale consists of 15 questions, and the score of each question ranges from 0 to 10, with the lowest total score of 0 and the highest score of 150. The higher the total score and each score, the better the quality of patients' postoperative recovery.

Serum and Plasma Analysis

Serum concentrations of inflammatory factors (IL-6, TNF-α, IL-8) and stress hormones (cortisol, epinephrine) were measured using enzyme-linked immunosorbent assay (ELISA). Blood samples were collected preoperatively and on postoperative day (POD) 1 and POD2.

Steady-state plasma concentrations are typically reached after 24 hours of continuous intravenous infusion,[28] and lidocaine-based PCIA was maintained for up to 48 hours in this study. Therefore, in the lidocaine group, venous blood samples were collected at 24 and 48 hours postoperatively to analyze plasma lidocaine concentrations using high-performance liquid chromatography–tandem mass spectrometry. During the postoperative intravenous infusion, patients were monitored by ECG and closely followed up. The follow-up personnel had been trained to recognize the early signs and symptoms of lidocaine toxicity. If drowsiness, tinnitus, dizziness, numbness of the mouth and tongue, metallic taste, convulsions, or arrhythmias occurred, the PCIA pump infusion was stopped immediately, and oxygen was administered via mask to maintain airway patency. Midazolam or propofol was prepared in advance for anticonvulsant therapy, along with a 20% lipid emulsion to manage potential toxicity.

Endpoints

The primary endpoint was VAS pain scores (0–10 points) assessed at rest and during coughing at 6, 12, 24, and 48 hours postoperatively. Secondary endpoints included the incidence of remedial analgesia, the time of first press and the number of effective presses of PCIA; QoR-15 scores (preoperative, and at 24 and 48 hours postoperatively); the serum concentrations of IL-6, TNF-α, IL-8, cortisol, and epinephrine (preoperative, POD1 and POD2). We kept track of the first flatus, defecation, and walking after surgery, as well as the time of thoracic drainage and the length of hospital stay postoperatively. We also kept track of any adverse events that happened, such as postoperative nausea and vomiting (PONV), pulmonary complications, and lidocaine toxic reactions like numbness around the mouth, metallic taste, tinnitus, dizziness, hallucinations, and drowsiness.

Statistical Analysis

Sample size was calculated using repeated measures analysis with PASS version 2021 software. In a pilot study with 14 patients per group, the mean VAS scores for coughing at 6, 12, 24, and 48 hours postoperatively were 1.90, 2.27, 2.83, and 1.39 in the lidocaine group, and 2.31, 2.64, 2.23, and 1.62 in the sufentanil group. Assuming a two-sided alpha of 0.05, a power of 0.80, and a 20% dropout rate, the required sample size was calculated to be 56 patients per group.

Baseline characteristics of the two groups were assessed using the Shapiro–Wilk test to determine normality of distribution. Continuous variables that followed a normal distribution were expressed as means ± standard deviation (mean ± SD), while non-normally distributed continuous variables were presented as medians and interquartile ranges. Categorical variables were described using counts and percentages (n, %). For continuous variables, an independent samples *t*-test was employed to analyze mean differences when the data followed a normal distribution. In contrast, the Mann–Whitney *U*-test was used for non-normally distributed variables. Categorical data were analyzed using the Chi-square test; when the expected frequency was less than 5, Fisher's exact test was utilized.

For repeated measures, if the data followed a normal distribution, repeated measures ANOVA was employed, with post hoc pairwise comparisons conducted using the Bonferroni correction. If the data did not meet the normality assumption, generalized estimating equations (GEE) with an appropriate working correlation matrix were used to analyze the main effects and interaction effects of group and time. Simple effects were compared between groups using the Mann–Whitney *U*-test, supplemented with Friedman test and Wilcoxon signed-rank test for analysis. A p-value of <0.05 was considered statistically significant.

Results

Patients

From January 2023 to December 2023 160 patients were enrolled in this trial, of whom two did not meet the inclusion criteria and two refused to participate. A total of 156 enrolled patients were randomized in a 1:1 ratio into sufentanil and lidocaine groups with 78 patients in each group. During the course of the study, eight converted to open thoracic lung resection, and four who did not complete the full postoperative PCIA for analgesia were excluded, resulting in a total of 144 patients being included in the statistical analysis (Figure 1). There were no statistically significant differences in the general characteristics and intraoperative data of the included patients, including age, body mass index, gender, ASA classification, duration of surgery, and type of surgery (Table 1).

Efficacy

Compared with sufentanil, lidocaine significantly reduced VAS pain scores for resting and coughing at 6, 12, and 24 hours postoperatively (Rest: $P=0.005$, $P<0.001$, $P<0.001$; Coughing: $P=0.010$, $P=0.030$, $P=0.010$), while VAS pain scores at 48 hours were comparable (Rest: $P=0.071$; Coughing: $P=0.257$) (Figure 2A and B and supplementary Table 1). Besides, lidocaine significantly delayed the time to first press PCIA and reduced remedial analgesia ($P=0.014$, $P=0.014$). There was no difference between the two groups in the number of effective PCIA ($P>0.05$) (Table 2).

Compared with the baseline level, the total QoR-15 scores at 24 and 48 hours postoperatively decreased in both groups. However, lidocaine made the decline much smaller, and the total scores were higher than in the sufentanil group

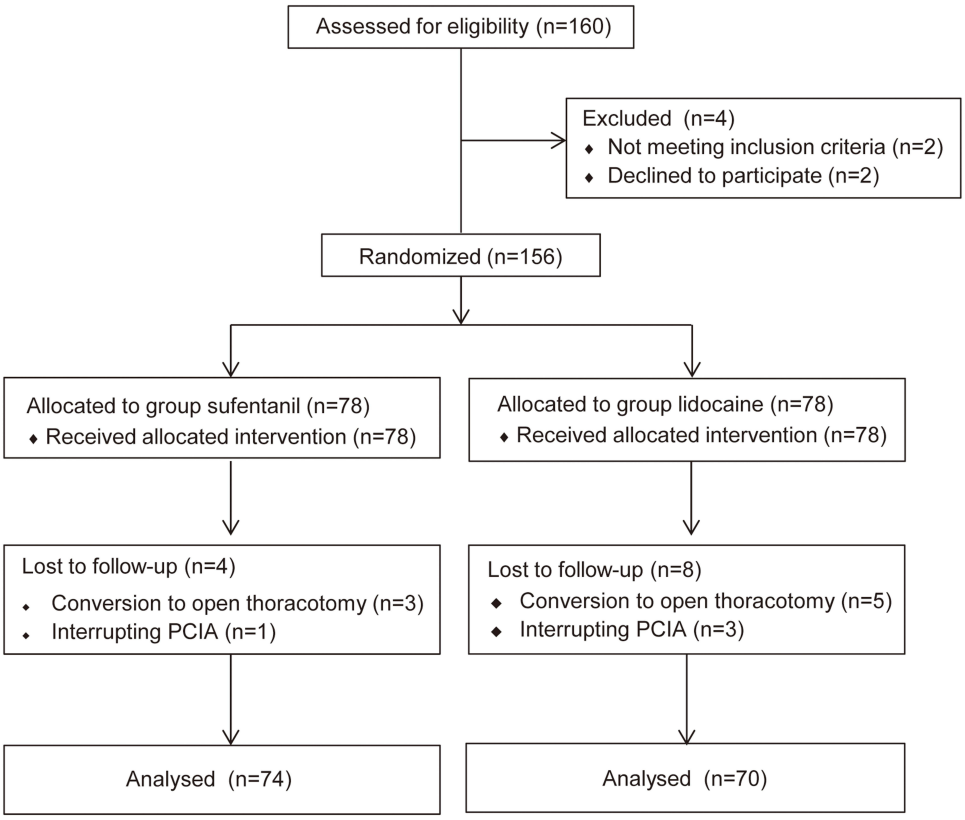

Figure 1 Study flow diagram.

(24 hours: 114.76±6.67 vs 109.05±7.50; difference, −5.70; 95% CI, −8.05 to −3.36; $P<0.001$; 48 hours: 126.34±5.87 vs 121.58±6.94; difference, −4.76; 95% CI, −6.89 to −2.64; $P<0.001$) (Figure 3 and supplementary Table 2). Furthermore, there was a significant improvement in two dimensions of physical comfort and pain with lidocaine ($P<0.001$, $P<0.001$) (Table 3). Patients with lidocaine experienced a significantly faster onset of first postoperative flatus, defecation, and ambulation than those in the sufentanil group ($P<0.001$, $P<0.001$, $P=0.036$). There was no statistical difference in length of hospital stay after surgery and chest drainage ($P=0.978$, $P=0.333$) (Table 4).

Table 1 Patient Demographic and Clinical Parameters

Variables	Sufentanil (n=74)	Lidocaine (n=70)	*P*
Age (years)	49.56 ± 6.19	51.08 ± 6.69	0.246
Height (cm)	165.50 ± 2.73	167.17 ± 5.80	0.027
Weight (kg)	60.45 ± 4.12	61.09 ± 4.46	0.373
BMI (kg/m^2)	21.57 ± 1.28	21.90 ± 1.04	0.095
Gender (M/F)	36/38	31/39	0.275
ASA physical status (I/II)	39/35	32/38	0.703
Operation time (minutes)	192 ± 40	204 ± 41	0.056
Intraoperative bleeding (mL)	24.78 ±5.27	24.44 ± 4.90	0.689
Type of surgery, n (%)			0.736
Lobectomy	45 (60.81%)	40 (57.14%)	
Segmentectomy	18 (24.32%)	21 (30%)	
Wedge resection	11 (14.86%)	9 (12.86%)	
Preoperative global QoR-15 score	138.66 ± 4.94	140.15 ± 2.88	0.061

Notes: Data are presented as mean ± SD or number (percentage).
Abbreviations: ASA, American Society of Anesthesiologists; QoR-15, the 15-item Quality of Recovery questionnaire; BMI, body mass index; SD, standard deviation.

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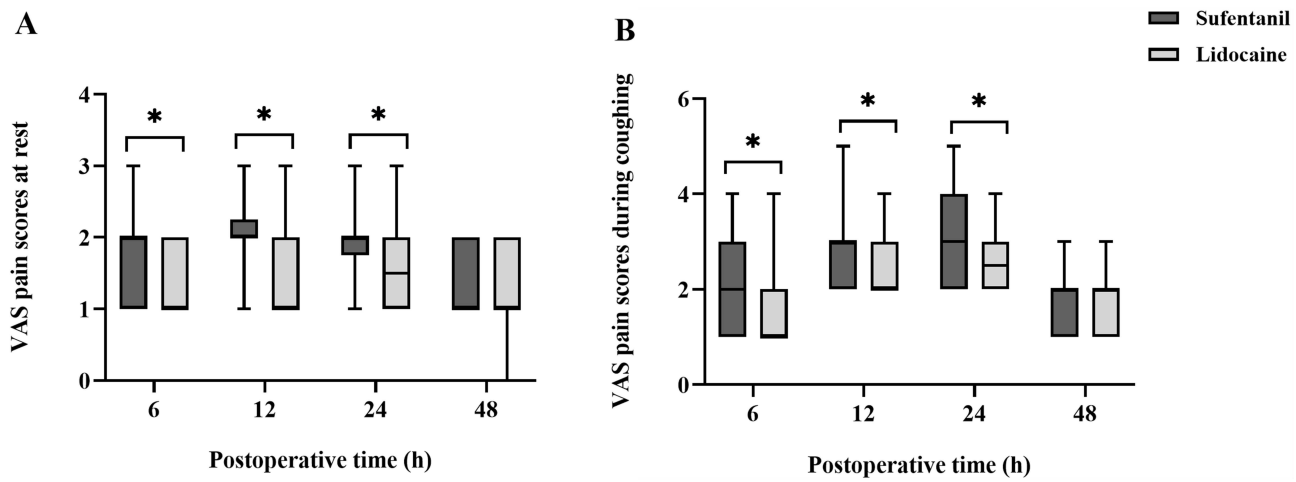

Figure 2 Postoperative VAS pain scores at rest (**A**) and during coughing (**B**) at various time points in patients receiving lidocaine-based or sufentanil-based PCIA within 48 hours postoperatively. Data are median with error bars showing interquartile range. *P<0.05, the sufentanil group versus the lidocaine group.
Abbreviation: PCIA, patient-controlled intravenous analgesia.

Lidocaine Blood Concentration

The blood concentration of lidocaine at 24 hours postoperatively was measured at 2.97±0.50 μg/mL, while the concentration at 48 hours increased to 3.84±0.41 μg/mL. At 48 hours after the operation, the blood concentration of lidocaine in one patient reached 5.12 μg/mL, but no toxic symptoms appeared (Table 5).

Postoperative Inflammatory Response and Stress Reaction

There was no difference in the basal level of IL-6, IL-8, and TNF-α between the two groups (P>0.05). At 24 hours postoperatively, IL-6, IL-8, and TNF-α concentrations increased but were significantly suppressed in the lidocaine group, with concentrations lower than those with sufentanil (P=0.033, P=0.008, P=0.015). At 48 hours postoperatively, IL-6, IL-8, and TNF-α concentrations showed a decreasing trend in both groups, with a greater decrease in the lidocaine group, resulting in significantly lower levels than those with sufentanil (P=0.021, P<0.001, P=0.001) (Figure 4 and supplementary Table 3).

Preoperative serum cortisol and epinephrine concentrations were comparable among the two groups (all P>0.05). Both cortisol and epinephrine levels showed a tendency to increase and then decrease postoperatively. The cortisol and epinephrine concentrations in the lidocaine group were lower than those in the sufentanil group on POD1 and POD2, and the difference was statistically significant (POD1: P=0.03, P=0.038; POD2: P<0.001, P=0.005) (Figure 5 and supplementary Table 4).

Postoperative Adverse Events

The incidence of PONV was significantly lower with lidocaine compared with sufentanil (20% vs 47.3%, P=0.001). Additionally, postoperative dizziness occurred significantly more frequently in the sufentanil group than in the lidocaine group (29.73% vs 11.43%, P=0.007). There were no postoperative pulmonary complications (pneumonia, pulmonary

Table 2 Postoperative Analgesia Between the Two Groups

Variables	Sufentanil (n=74)	Lidocaine (n=70)	*P*
Patients with remedial analgesia (%)	26 (35.13%)	12 (17.14%)*	0.014
Time to first press of PCIA (hours)	9 (5.00–12.25)	10.00 (7.75–14.00)*	0.014
Number of PCIA effective pressing	6 (3–9)	5 (2–9)	0.112

Notes: Data are presented as number (percentage) or median (Interquartile range). *P<0.05, the sufentanil group versus the lidocaine group.
Abbreviation: PCIA, patient-controlled intravenous analgesia.

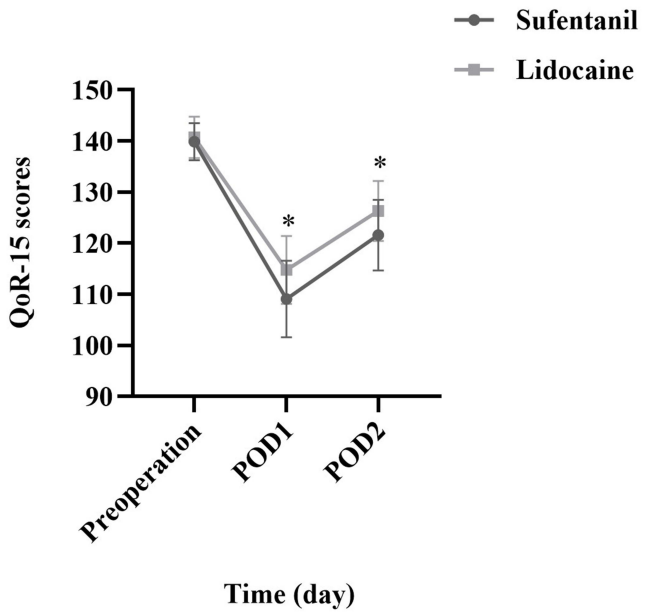

Figure 3 Comparison of total QoR-15 scores between the two groups. Data are presented as mean ± SD. *P<0.05, the sufentanil group versus the lidocaine group.
Abbreviations: QoR-15, the 15-item Quality of Recovery questionnaire; SD, standard deviation; POD, postoperative day.

atelectasis, hypoxemia, etc.) in either patient. There were no lidocaine toxic reactions such as tinnitus, phantom vision, numbness of the mouth and tongue, metallic taste, and cardiac arrhythmias (Table 6).

Discussion

This study demonstrated that lidocaine-based PCIA, compared to sufentanil-based PCIA, resulted in a statistically significant reduction in postoperative pain during the first 24 hours following thoracoscopic lung surgery, as evidenced

Table 3 Comparison of the 15-Item Quality of Recovery Questionnaire (QoR-15) Scores Between the Two Groups

Variables	Sufentanil (n=74)	Lidocaine (n=70)	*P*
Preoperation			
Total QoR-15 score	139.88 ± 3.64	140.71 ± 4.07	0.196
POD1			
Total QoR-15 score	109.05 ± 7.50	114.76 ± 6.67*	<0.001
Physical comfort	31.14 ± 3.76	40.83 ± 3.35*	<0.001
Physical independence	3.18 ± 2.35	3.00 ± 2.20	0.645
Psychological support	18.88 ± 1.40	18.61 ± 1.62	0.297
Pain	16.04 ± 2.94	18.50 ± 1.81*	<0.001
Emotional state	33.46 ± 2.17	34.03 ± 2.44	0.141
POD2			
Total QoR-15 score	121.58 ± 6.94	126.34 ± 5.87*	<0.001
Physical comfort	42.88 ± 2.89	45.21 ± 2.66*	<0.001
Physical independence	4.04 ± 2.00	4.50 ± 1.76	0.147
Psychological support	19.62 ± 0.72	19.50 ± 1.02	0.406
Pain	17.91 ± 2.25	19.83 ± 0.48*	<0.001
Emotional state	36.84 ± 2.16	37.04 ± 2.56	0.603

Notes: Data are presented as mean ± SD. **P*<0.05, the sufentanil group versus the lidocaine group.
Abbreviations: QoR-15, the 15-item Quality of Recovery questionnaire; SD, standard deviation; POD, postoperative day.

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Table 4 Postoperative Recovery Variables Between the Two Groups

Variables	Sufentanil (n=74)	Lidocaine (n=70)	*P*
Time to first flatus (hours)	39.05 ± 16.87	28.96 ± 10.32*	<0.001
Time to first defecation (hours)	66.18 ± 14.53	55.09 ± 20.16*	<0.001
Time to first ambulation (hours)	20.00 (17.00–24.25)	18.50 (16.00–22.00)*	0.036
Length of hospital stay (days)	6.89 ± 1.54	6.90 ± 1.90	0.978
Drainage duration (days)	5 (4–6)	5 (4–7)	0.333

Notes: Data are presented as mean ± SD or median (Interquartile range). *P<0.05, the sufentanil group versus the lidocaine group.

Table 5 Plasma Lidocaine Concentration

Postoperative Time	Plasma Lidocaine Concentration (μg/mL)	Maximum Concentration (μg/mL)
24 hours	2.97 ± 0.50	4.11
48 hours	3.84 ± 0.41	5.12

Notes: Data are presented as mean ± SD or concentration values.

by VAS scores at rest and during coughing at 6, 12, and 24 hours. Although a universally accepted minimal clinically important difference (MCID) threshold for VAS pain scores has not been established, multiple studies suggest that a reduction of approximately 1 point on a 10-point scale may be considered clinically meaningful.[29–31] In this study, the VAS reductions observed during the early postoperative period (6–12 hours) approached this threshold, supporting the potential clinical relevance of lidocaine's analgesic effect. This was a single-center study with a relatively short follow-up period. Future multi-center studies with longer-term follow-up are needed to validate these findings.

Lidocaine-based PCIA significantly reduced pain levels during the first 24 hours postoperatively, consistent with findings from other studies using intravenous lidocaine in spinal surgery, which also showed reduced pain scores within the first 24 hours after surgery.[32] In this trial, the time to the first press of PCIA and the incidence of remedial analgesia were both significantly delayed in the lidocaine group, indicating an advantage of lidocaine for early postoperative pain management. Although there was no significant difference in pain scores at 48 hours postoperatively, this may be due to effective pain control achieved in the early postoperative period. The primary sources of pain after thoracoscopic lung surgery include surgical incisions, intercostal nerve and lung parenchyma injuries, chest drain irritation, and systemic inflammation.[33,34] Lidocaine acts as a sodium channel blocker, inhibiting pain signaling by blocking sodium channels, and also interacts with potassium and calcium channels, NMDA receptors, and other systems that contribute to its analgesic effects.[35–37] Furthermore, intravenous lidocaine's anti-inflammatory properties help reduce neurogenic

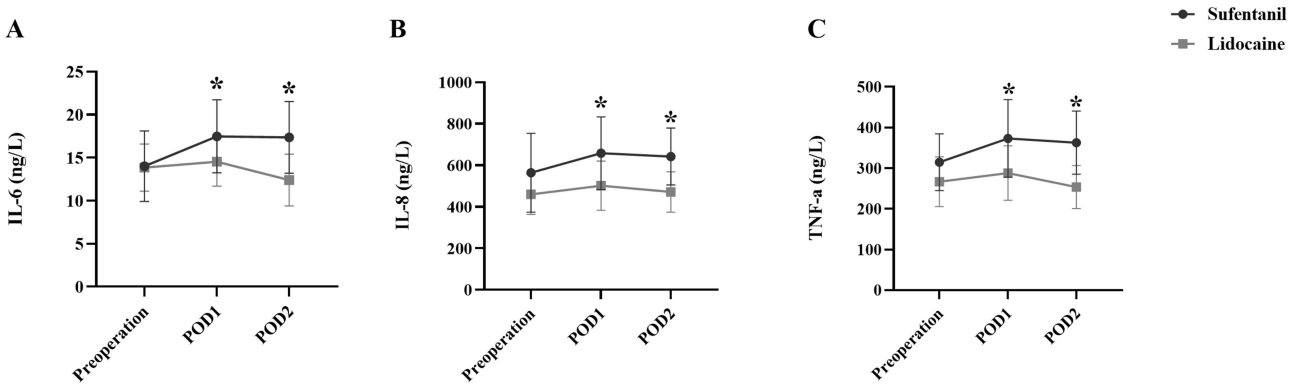

Figure 4 Serial changes in plasma concentrations of IL-6 (**A**), IL-8 (**B**) and TNF-α (**C**) between the two groups. Data are presented as mean ± SD. *P<0.05, the sufentanil group versus the lidocaine group.
Abbreviation: SD, standard deviation; POD, postoperative day.

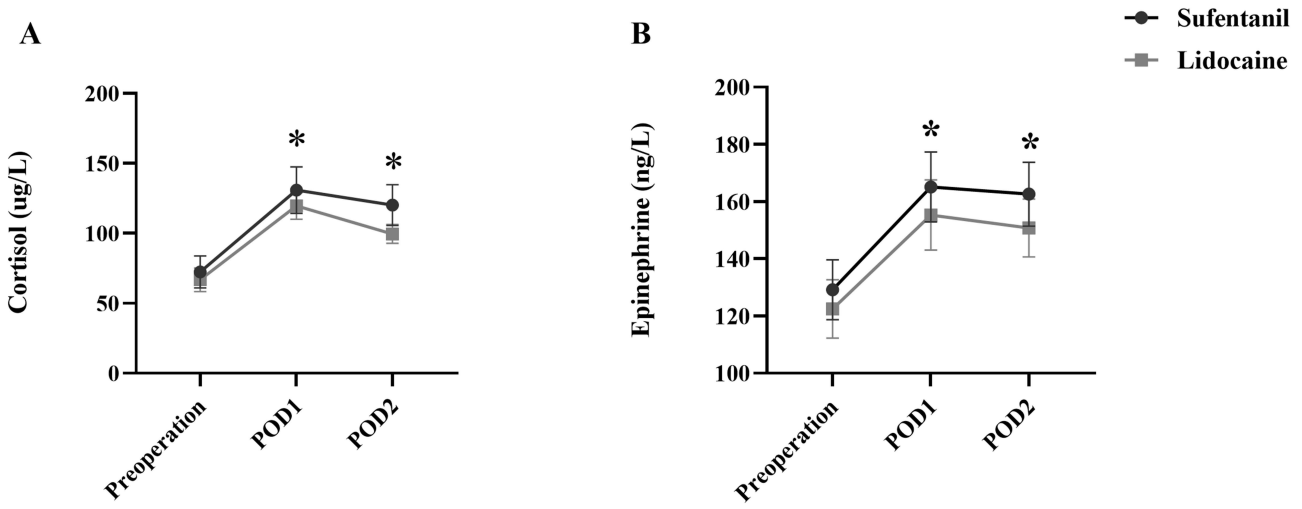

Figure 5 Serial changes in plasma concentrations of cortisol (**A**) and epinephrine (**B**) between the two groups. Data are presented as mean ± SD. *P<0.05, the sufentanil group versus the lidocaine group.
Abbreviation: SD, standard deviation; POD, postoperative day.

inflammation and the release of pro-inflammatory cytokines, which may further reduce postoperative pain.[21,38–41] This study confirmed that lidocaine-based PCIA significantly reduced serum IL-6, IL-8, and TNF-α concentrations, which likely contributed to the observed pain reduction.

The QoR-15 scale evaluates postoperative recovery across five dimensions: pain, mood, physical comfort, physical independence, and psychosocial support.[42] In this study, although the between-group differences in total QoR-15 scores were statistically significant, they did not reach the recently updated MCID of 6.0 points, as proposed by Myles and Myles.[43] Nonetheless, the results indicate a favorable trend toward improved recovery in the lidocaine group. Notably, the most pronounced benefits were observed in the physical comfort and pain domains. These findings are consistent with previous research, such as a study involving supratentorial tumor resection, in which intravenous lidocaine improved recovery quality scores.[44] The domain-specific improvements observed in this study suggest that lidocaine-based PCIA may offer added value, particularly for patients experiencing more pronounced postoperative pain or discomfort. These findings support the consideration of individualized assessment when determining the routine use of lidocaine in clinical practice.

Table 6 Adverse Events Between the Two Groups Within 48 Hours Postoperatively

Adverse Events	Sufentanil (n=74)	Lidocaine (n=70)	*P*
PONV	35 (47.30%)	14 (20%)*	0.001
Dizziness	22 (29.73%)	8 (11.43%)*	0.007
Drowsiness	0	0	>0.999Δ
Visual hallucination	0	0	>0.999Δ
Numbness of the mouth and tongue	0	0	>0.999Δ
Metallic flavor	0	0	>0.999Δ
Tinnitus	0	0	>0.999Δ
Severe arrhythmia	0	0	>0.999Δ
Allergic reaction	0	0	>0.999Δ
Convulsions	0	0	>0.999Δ
Pulmonary complications	0	0	>0.999Δ

Notes: Data are presented as number (percentage). *P<0.05, the sufentanil group versus the lidocaine group.
Δ means Fisher's exact test.
Abbreviation: PONV, postoperative nausea and vomiting.

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Moreover, lidocaine accelerated gastrointestinal recovery, as evidenced by a shorter time to first flatus and defecation, similar to findings in a meta-analysis of colorectal surgery.[45] This effect may be attributed to lidocaine's ability to block inhibitory spinal and prevertebral reflexes, resist inflammation, and reduce perioperative opioid use.[23,46,47] Additionally, lidocaine reduced serum cortisol and epinephrine levels, indicating a lower stress response, which has been shown to improve postoperative outcomes.[48] Although lidocaine did not significantly affect the length of hospital stay or chest drainage duration, it did shorten the time to first ambulation, which is beneficial for early recovery.

PONV is a common complication after surgery, leading to patient dissatisfaction and increased healthcare costs. A recent meta-analysis found that intravenous lidocaine reduced the incidence of PONV,[23] and this study showed that lidocaine-based PCIA significantly reduced PONV incidence (20%) compared to sufentanil (47.30%). This reduction may be due to lidocaine's positive effects on gastrointestinal function, early ambulation, and opioid-sparing analgesia. Additionally, dizziness was less common in the lidocaine group, with a short duration and no occurrence while lying down, which may be related to fasting time before the operation and posture change of bedridden patients postoperatively. No postoperative pulmonary complications were observed in either group.

Although intravenous lidocaine is generally considered safe when administered within recommended dosing limits, careful monitoring remains essential—especially during prolonged infusions. In this study, a postoperative infusion rate of 1.5 mg/kg/h resulted in plasma concentrations well below the commonly cited toxicity threshold of 5 μg/mL in nearly all patients.[26] One patient reached a peak level of 5.12 μg/mL at 48 hours without any observable adverse effects. Similarly, a previous study in patients undergoing hepatectomy reported no signs of toxicity at levels slightly above this threshold (5.48 μg/mL measured immediately after anesthesia induction).[49] To ensure safety, this study excluded patients with hepatic or renal impairment. However, this highlights the need to consider potential risks in vulnerable populations, such as elderly patients or those with impaired lidocaine metabolism. Incorporating therapeutic drug monitoring in future large-scale trials may help ensure the safe use of lidocaine across broader clinical populations.

There are several limitations to this study. First, this was a single-center trial, which may limit the generalizability of these findings. Second, the study primarily focused on acute postoperative pain within a short-term follow-up period; therefore, the long-term effects of intravenous lidocaine, especially regarding the development of chronic postoperative pain, remain unknown. Third, we did not perform pharmacokinetic modeling or monitor plasma lidocaine concentrations to evaluate the risk of drug accumulation and related adverse events. Fourth, potential unmeasured confounders, such as individual genetic variability in lidocaine metabolism, were not assessed and may have influenced the outcomes. Fifth, we did not perform subgroup analyses based on baseline characteristics, which may have provided additional insights into the efficacy and safety of intravenous lidocaine in different patient populations. Further large-scale, multi-center studies with extended follow-up and comprehensive monitoring are warranted to address these limitations.

Conclusion

In conclusion, this single-center study suggests that lidocaine-based PCIA may be an effective and safe adjunct to multimodal analgesia for managing early postoperative pain in selected patients undergoing thoracoscopic lung surgery. In particular, it may serve as an opioid-sparing strategy for ASA I–II patients without major comorbidities, in institutions equipped for lidocaine monitoring. However, given the retrospective trial registration, the short 48-hour follow-up window, and the homogenous low-risk population, the generalizability of these findings is limited. Further multicenter, prospective studies with longer follow-up—including assessments of chronic pain at 3–6 months—are warranted to validate its long-term clinical utility. Additionally, standardized protocols and appropriate safety measures (eg, cardiac monitoring in high-risk patients) should be established before broader adoption.

Abbreviations

ASA, American Society of Anesthesiologists; BMI, Body Mass Index; EA, Epidural Analgesia; ECG, Electrocardiogram; ELISA, Enzyme-Linked Immunosorbent Assay; IL-6, Interleukin-6; IL-8, Interleukin-8; LC-MS /MS, Liquid Chromatography–Tandem Mass Spectrometry; PCIA, Patient-Controlled Intravenous Analgesia; POD,

Postoperative Day; PONV, Postoperative Nausea and Vomiting; QoR-15, 15-item Quality of Recovery Questionnaire; SD, Standard Deviation; TNF-α, Tumor Necrosis Factor-alpha; TPB, Thoracic Paravertebral Block; VAS, Visual Analogue Scale.

Data Sharing Statement

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This trial was approved by the Ethics Committee of Gansu Provincial Hospital on December 26th, 2022 (ID: No. 2022-454). All patients participating in the trial signed written informed consent.

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Author Contributions

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

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Disclosure

The authors declare that they have no competing interests.

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