Systematic Review

A Systematic Review and Meta-analysis of the Analgesic Effects of Lidocaine Administered Intravenously or Intraperitoneally Post-Abdominal Surgery

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Background: Reducing postoperative pain is still a tremendous challenge for perioperative clinicians. Lidocaine is a local anesthetic that belongs to the amide class and has anti-inflammatory, anti-hyperalgesic, and analgesic effects. Extensive research has been conducted to determine the optimal route for its administration.

Objective: To compare the efficacy of perioperative intravenous lidocaine with that of intraperitoneal lidocaine on postoperative analgesia in patients undergoing abdominal surgery.

Study Design: EMBASE, PubMed, and The Cochrane Library were searched for randomized controlled trials published through December 2022 that compared patients receiving perioperative intravenous lidocaine with those receiving intraperitoneal lidocaine. The primary outcome measures included the pain score, as evaluated by the Visual Analog Scale, and opioid analgesia requirements. The secondary outcome measures were hospitalization length, gastrointestinal function recovery, etc. The data were acquired and recorded in electronic spreadsheets that had been designed for this purpose.

Methods: This systematic review's design was based on the Cochrane Handbook for Systematic Reviews of Interventions and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) method was used to examine the certainty of the evidence. Furthermore, we examined the dependability of the calculated (favorable) treatment effects through considerations of information size and modified significance thresholds (trial sequential analysis).

Results: Seven trials including 478 patients were included. Our meta-analysis demonstrates that compared with intravenous lidocaine, patients who received intraperitoneal lidocaine had lower pain scores at 4 hours (mean difference [MD] 1.40; 95% CI, 0.22 to 2.59); 12 hours (MD 0.18; 95% CI, 0.06 to 0.30); and 24 hours (MD –0.12; 95% CI –0.40 to 0.17) postsurgery. However, no obvious difference in opioid consumption ($P > 0.05$) was found. In addition, the intraperitoneal lidocaine group had a longer postsurgery hospital stay than the intravenous lidocaine group (95%CI, –0.17 to –0.00; $I^2 = 0\%$). Intravenous lidocaine was more beneficial for achieving gastrointestinal return than intraperitoneal lidocaine (95% CI, –0.26 to –0.10; $I^2 = 2\%$).

Limitations: The sample size of enrolled RCTs was small, which could potentially result in an overestimation or underestimation of the treatment effect in the collected data. There was high heterogeneity among the studies.

Conclusion: This meta-analysis suggests that post-abdominal surgery intraperitoneal lidocaine administration has a better analgesic effect than intravenous lidocaine, with a lower pain score. However, intravenous lidocaine is more beneficial for gastrointestinal recovery after abdominal surgery.

Key words: Lidocaine, abdominal surgery, intravenous, intraperitoneal, postoperative pain, opioid consumption, meta-analysis, trial sequential analysis

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Every year, more than 300 million patients across the globe undergo a major surgical procedure (1). Acute postoperative pain (POP) is one of the most common complications after surgery. It can prolong a hospital stay and increase medical costs during the postoperative period (2). Furthermore, insufficient postoperative analgesia is associated with pulmonary embolism, deep vein thrombosis, myocardial infarction, coronary artery ischemia, delayed wound healing, pneumonia, chronic pain, and insomnia (3). Thus, adequate postoperative analgesia is of great importance to optimize perioperative care by minimizing the body's stress response to surgical procedures (4,5).

Opioids have traditionally been a fundamental component of POP management strategies. Opioid medications have impressive analgesic properties; however, they are associated with adverse events, including postoperative nausea and vomiting (PONV), postoperative ileus, opioid addiction, and delayed postoperative recovery (6-8). Thus, alternative therapeutic strategies for POP are urgently needed.

The modern multimodal, opioid-sparing approach is a major aspect in the optimization of postoperative analgesia (9). This has prompted investigation into the potential benefits of utilizing local anesthetics, ketamine, and gabapentin (10).

Lidocaine is a local anesthetic that belongs to the amide class and has anti-inflammatory, antihyperalgesic, and analgesic effects (11). In addition to its use in traditional nerve blocks, it can also exert its analgesic effects via anatomical block when administered intravenously or intraperitoneally. Since it was first reported in 1950 (12), intraperitoneal lidocaine has been widely used for the clinical treatment of POP, mainly in laparoscopic cholecystectomy, open surgery, gynecology, and other laparoscopic procedures. About 2 mg/kg-3.5 mg/kg lidocaine is sprayed around the surgical site at the initiation of pneumoperitoneum or parietal peritoneal closure (13-15).

Previous systematic reviews have shown that the application of intraperitoneal lidocaine significantly reduces opioid consumption and POP, as well as improving early recovery after major abdominal surgery (16,17). Subsequently, another systematic review reported that intravenous lidocaine markedly attenuates opioid consumption, early POP, and hospitalization length, as well as promoting gastrointestinal recovery, but the initially trialed doses had a high potential to cause adverse effects in the patients (18,19). However, little is known about the difference in the efficacy of postoperative analgesia between intraperitoneal lidocaine and intravenous lidocaine in abdominal surgery.

In this review, we systematically evaluated the difference between intraperitoneal lidocaine and intravenous lidocaine for postoperative analgesia in abdominal surgery. Furthermore, we examined the dependability of the calculated (favorable) treatment effects through considerations of information size and modified significance thresholds (trial sequential analysis).

Methods

This systematic review was designed based on the Cochrane Handbook for Systematic Reviews of Interventions (20) and was reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement (21). The protocol was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database (https://www.crd.york.ac.uk/PROSPERO; registration number: CRD42023388438).

Search Strategy

The Embase, Cochrane Library, and PubMed databases were searched for articles published before January 2023 without language and location limitation. The search terms were: "IV or intravenous or systemic", "intraperitoneal or intra-peritoneal or peritoneum", "laparotomy or abdominal surgery or laparoscopic or abdomen or surgery", and "local anesthetic or local anesthetic or lignocaine or lidocaine".

Selection Criteria

We only included randomized controlled trials that compared the effects of intraperitoneal lidocaine with of the effects of intravenous lidocaine on POP in adult patients undergoing any form of abdominal surgery under general anesthesia. We excluded studies with a lack of primary outcomes; studies with unavailable full texts; articles on other subjects; and case reports, review articles, and commentary studies.

Study Selection and Data Extraction

Once duplicates had been eliminated, 2 authors (YB and MD) individually assessed the titles and abstracts of the remaining articles for suitability. After excluding studies that failed to meet the inclusion criteria, the aforementioned reviewers analyzed the complete texts of the articles and extracted the relevant informa-

tion. In cases of disagreement between the reviewers, a third investigator (HL) resolved the issue.

We extracted the data, including the number of patients assigned to each group (intravenous lidocaine vs intraperitoneal lidocaine), demographic features of the studied population, type of surgery, details of lidocaine administration, duration of randomized controlled trial follow-up, and concomitant medications.

The primary outcomes were the resting Visual Analog Scale score for pain (a mark was made along the 10-cm line, where the marks at 0 and 10 cm represent no pain and the worst pain, respectively) at postoperative hours 4, 12, and 24, as well as opioid consumption at postoperative hours 4 and 24. The secondary outcome measures were hospitalization length, gastrointestinal function recovery, surgical complications (postoperative infection, thromboembolism, wound breakdown, etc.), adverse events (lidocaine toxicity), PONV, and inflammatory markers.

All the extracted data regarding opioid consumption were converted to morphine equivalent doses. Nonsteroidal anti-inflammatory drugs were not included in the meta-analysis. In the case of missing data, including standard deviations, we reached out to the authors of the pertinent studies to request the needed information.

Risk-of-bias Assessment

The methodological quality of the individual studies was evaluated independently by 2 authors (YB and MD) using the criteria of the Cochrane Collaboration (17). The standard risk-of-bias domains, which included allocation concealment, random-sequence generation, personnel and outcome assessors, patient blinding, selective reporting, and incomplete outcome data, were assessed. Each domain was classified at the study level as having a high, low, or unclear risk of bias.

Missing Data Estimate

In cases where continuous data were presented as median and range, we utilized a standardized validated tool to estimate the mean and standard deviation. If the standard error of the mean was provided, we converted it to standard deviation. Plot Digitizer v2.6.8 (plotdigitizer.com) was employed to extract graphical data.

Evidence Certainty Assessment

The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) method was applied to examine the certainty of the evidence (22,23). To accomplish this, the data collected in RevMan v5.4 (The Nordic Cochrane Centre for The Cochrane Collaboration) were imported into the guideline development tool (www.gradepro.org). The evidence was then classified into one of 4 categories: very low quality, low, moderate, or high. These classifications were based on specific assessment criteria (e.g., imprecision, inconsistency, indirect evidence, and risk of bias), as well as other factors (e.g., potential confounding variables and publication bias). The level of certainty of the evidence was also classified as very low, low, moderate, or high (24).

Data Synthesis and Analysis

The data were analyzed with RevMan v5.4. The random-effects model with inverse-variance method was used to compare the continuous variables, and the outcomes were measured as the differences in the mean values. The study heterogeneity was assessed using the I^2 statistic. To verify the reliability of the trial sequential analysis results based on clinically significant estimates, we conducted the trial sequential analysis with empirical pooled estimates and model variance-based heterogeneity correction.

Results

In total, 615 publications were retrieved based on our search strategy. After duplicate removal, we retrieved 493 articles and chose 12 full-text articles for eligibility testing. Finally, 7 studies involving 478 patients who underwent abdominal surgery were included in the quantitative analysis, which included 241 patients who received intravenous local anesthetic and 237 patients who received intraperitoneal local anesthetic for postoperative analgesia (Fig. 1).

Table 1 summarizes the main characteristics of these 7 studies, including the type of procedure, research population, treatment modalities, and postoperative analgesia. These studies included 3 on laparoscopic cholecystectomy (13,25,26), one on abdominal hysterectomy (14), one on cesarean delivery (15), one on laparoscopic colon resection (27), and one on laparoscopic appendectomy (28).

Postoperative Pain

Pain at rest 4 hours postsurgery. Four studies involving 266 patients reported Visual Analog Scale (VAS) pain scores 4 hours postsurgery (14,15,28). The results show that intraperitoneal lidocaine significantly

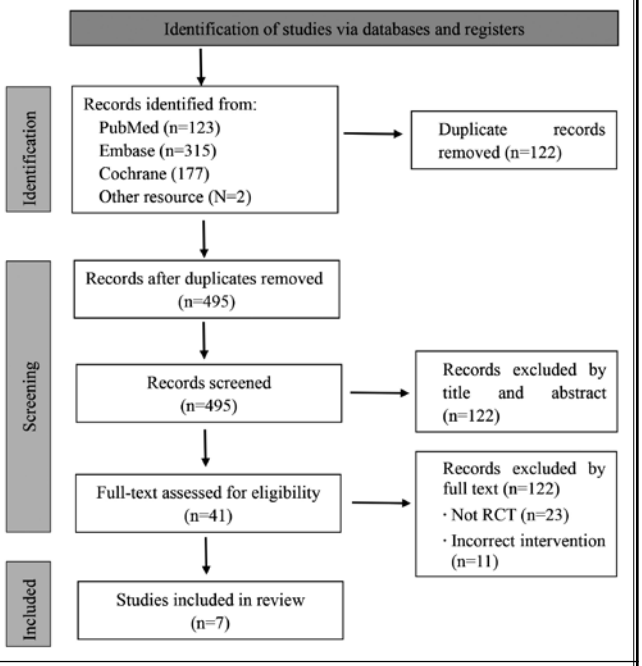

Fig. 1. *Flowchart of the search strategy. RCT, randomized controlled trial.*

reduced the pain score compared with intravenous lidocaine at 4 hours postsurgery (95% CI, 0.18 to 0.49; I^2 = 97%) (Fig. 2A).

To enhance the precision of our meta-analysis and establish the reliability of positive findings, we computed the necessary information size and respective monitoring thresholds. The trial sequential analysis for pain at 4 hours postsurgery (assumptions: α = 5%, β = 20%, mean difference [MD] and variance estimated on low-bias studies, heterogeneity correction: D2 = model variance-based) revealed a required information size of 52 patients (Fig. 2B). Therefore, the trial sequential analysis of the pooled meta-analysis (266 patients) showed firm evidence of pain relief with intraperitoneal lidocaine.

Pain at rest 12 hours postsurgery. Five studies involving 374 patients reported the pain score at 12 hours postsurgery (13-15,26,28). The results show that intraperitoneal lidocaine significantly reduced the pain score compared with intravenous lidocaine at 12 hours postsurgery (95% CI, 0.06 to 0.30; I^2 = 53%) (Fig. 2C).

Pain at rest 24 hours postsurgery. Six studies involving 428 patients reported the pain score at 24 hours postsurgery (13-15,26-28). The results show that intraperitoneal lidocaine significantly reduced the pain score compared with intravenous lidocaine at 24 hours postsurgery (95% CI, 0.03 to 0.19; I^2 = 14%) (Fig. 2E).

The trial sequential analysis for pain at 24 hours postsurgery revealed a required information size of 489 patients; the Z-curve crossed the traditional threshold and the trial sequential analysis threshold (Fig. 2F). Therefore, the trial sequential analysis of the pooled meta-analysis (428 patients) showed firm evidence of pain relief with intraperitoneal lidocaine.

Opioid Consumption

Seven studies involving 478 patients reported opioid consumption at 24 hours postsurgery (13-15, 25-28). The results show no significant difference in opioid consumption between the 2 groups at 24 hours postsurgery (95% CI, –3.74 to 0.97; I^2 = 98%) (Fig. 3A).

The trial sequential analysis for opioid consumption at 24 hours postsurgery indicated a required information size of 3,234 patients (Fig. 3B). Therefore, the trial sequential analysis of the pooled meta-analysis (478 patients) showed insufficient evidence for the estimated treatment outcomes; therefore, more research is needed.

Secondary Outcomes

Four studies involving 249 patients reported the length of hospital stay (15,26-28). The results show that the intraperitoneal lidocaine group had a longer postsurgery hospital stay than the intravenous lidocaine group (95% CI, –0.17 to –0.00; I^2 = 0%) (Fig. 4A).

Five studies involving 299 patients reported the time to return of gastrointestinal function (15,25,26,27,28)., The results show that intravenous lidocaine was more beneficial for achieving gastrointestinal return than intraperitoneal lidocaine (95% CI, –0.26 to –0.10; I^2 = 2%) (Fig. 4B).

Five studies reported the incidence of PONV (14,24,26,27,28). The incidence of PONV was consistent between the 2 groups (odds ratio [OR] 0.92; 95% CI, 0.49 to 1.70; I^2 = 0%) (Fig. 4C).

Four studies showed the incidence of postoperative complications (13,24,27,28), showing no difference between the 2 groups (OR 0.91; 95% CI, 0.48 to 1.73; I^2 = 0%) (Fig. 4D).

Toxicity

The procedure's duration determined the shortest infusions (13,15,25,28), while the longest were for 72 hours postoperatively (27). One study reported that 2 patients in the intravenous lidocaine group and one

Table 1. *Characteristics of the studies included*

Study	Patients groups (n)	Age (mean ± SD)	Type of surgery	Interventions	Postoperative analgesia
Kim 2011 [28]	IVLA (22) IPLA (25)	41.23 ± 15.23 37.32 ± 20.65	Laparoscopic appendectomy	IVLA: 1.5 mg/kg bolus before incision+2 mg/kg/h infusion during the operation IPLA: 3.5 mg/kg lidocaine intraperitoneal instillation at the initiation of the pneumoperitoneum	PCIA (fentanyl bolus 0.1 ug/kg, a lock-out interval of 15 min and a continuous infusion of 0.1 ug/ kg per h); If the VAS score was >3 cm despite the bolus, an additional 50 ug of fentanyl was administered IV until the pain was below a VAS score of 3 cm.
Yang 2013 [23]	IVLA (26) IPLA (22)	45.61 ± 12.17 47.39 ± 13.99	Laparoscopic cholecystectomy	IVLA: 1.5mg/kg bolus before incision +2 mg/kg/h infusion during the operation IPLA: 3.5mg/kg, 1/4 sprayed on upper surface of the liver under the right subdiaphragmatic space, 1/4 on under the left subdiaphragmatic space, 1/2 around the cholecystectomy site.	PCIA (fentanyl bolus 0.1 ug/kg, a lock-out interval of 15 min and a continuous infusion of 0.1 ug/ kg per h); If the VAS score was >3 cm despite the bolus, an additional 50 ug of fentanyl was administered IV until the pain was below a VAS score of 3 cm.
Ram 2014 [22]	IVLA (25) IPLA (25)	42.56 ± 11.13 42.4 ± 9.88	Laparoscopic cholecystectomy	IVLA: 1.5mg/kg bolus before incision + 2 mg/kg/h infusion during the operation IPLA: 100 mL 0.2% lidocaine was deposited in the right diaphragmatic surface	IV morphine 1mg every 10 minutes until VAS < 3 cm, then followed by PCIA (morphine: 1 mg bolus doses on patient's demand. The lockout period was set at 15 min)
Samimi 2015 [25]	IVLA (36) IPLA (35)	46.2 ± 12.9 49.3 ± 10.6	Laparoscopic hysterectomy	IVLA: 1.5 mg/kg bolus before incision + 2 mg/kg/h infusion to 1 h after surgery IPLA: 3.0 mg/kg lidocaine diluted to 50 mL, before closure of wound t	IV morphine when patients asked analgesic or her VAS was ≥ 4 cm.
Murad 2016 [26]	IVLA (50) IPLA (50)	27.62 ± 3.85 27.88 ± 4.53	Cesarean section	IVLA: 1.5 mg/kg bolus before incision + 2 mg/kg/h infusion to during the operation IPLA: 3.5 mg/kg lidocaine diluted to 50 mL, with parietal peritoneal closure	Declofenac sodium 75 mL intramuscular every 12 h for the first 24 h, with additional rescue analgesia in the form of pethidine 50 mg intramuscular given upon patient request.
MacFater 2022 [27]	IVLA (28) IPLA (26)	65.67 ± 10.82 73.50 ± 9.05	Laparoscopic colectomy	IVLA: 2 mg/kg (maximum 100 mg) bolus before incision + 1.5 mg/kg/h infusion for 72 h IPLA: 2 mg/kg (maximum 100 mg) bolus before incision + 1.5 mg/kg/h infusion for 72 h	PCIA (morphine 1 mg every 5 minutes up to 12 mg per hour),
Lapisatepun 2022 [24]	IVLA (54) IPLA (54)	54.93 ± 10.53 52.61 ± 12.37	Laparoscopic cholecystectomy	IVLA: 1.5 mg/kg bolus before incision +1.5 mg/kg/h infusion during the operation IPLA: 2 mg/kg administered at the gallbladder bed and under the diaphragm after the cholecystectomy was done	IV morphine 3-4mg for VAS ≥ 7 cm every 20 minutes at the PACU, IV morphine 3-4mg for VAS ≥ 7 cm every 2 hours at the ward,

patient in the intraperitoneal lidocaine group experienced symptoms of local anesthetic toxicity. The other 6 studies did not report any incidence of lidocaine toxicity.

Risk of Bias

Our meta-analysis found a low risk of bias regarding detection bias (blinding of outcome assessment), performance bias (blinding of patients and personnel), and selection bias (random-sequence generation). For allocation concealment and selective reporting, 6 out of the 7 studies were evaluated as having a low risk of bias based on quality assessment (Fig. 5).

Evidence Certainty Assessment

Table 2 presents the GRADE results. Nonserious risk of bias was identified for all criteria. The certainty of the evidence for the primary outcome was graded as moderate.

Discussion

In our meta-analysis, intraperitoneal lidocaine was more effective at reducing POP scores in abdominal surgery, although no obvious difference was found in postsurgery opioid consumption. However, our study also showed that intravenous lidocaine is more beneficial for gastrointestinal recovery post-abdominal surgery. Intravenous lidocaine also reduced the length of hospitalization fpost-abdominal surgery.

Utilizing multimodal analgesia techniques for the

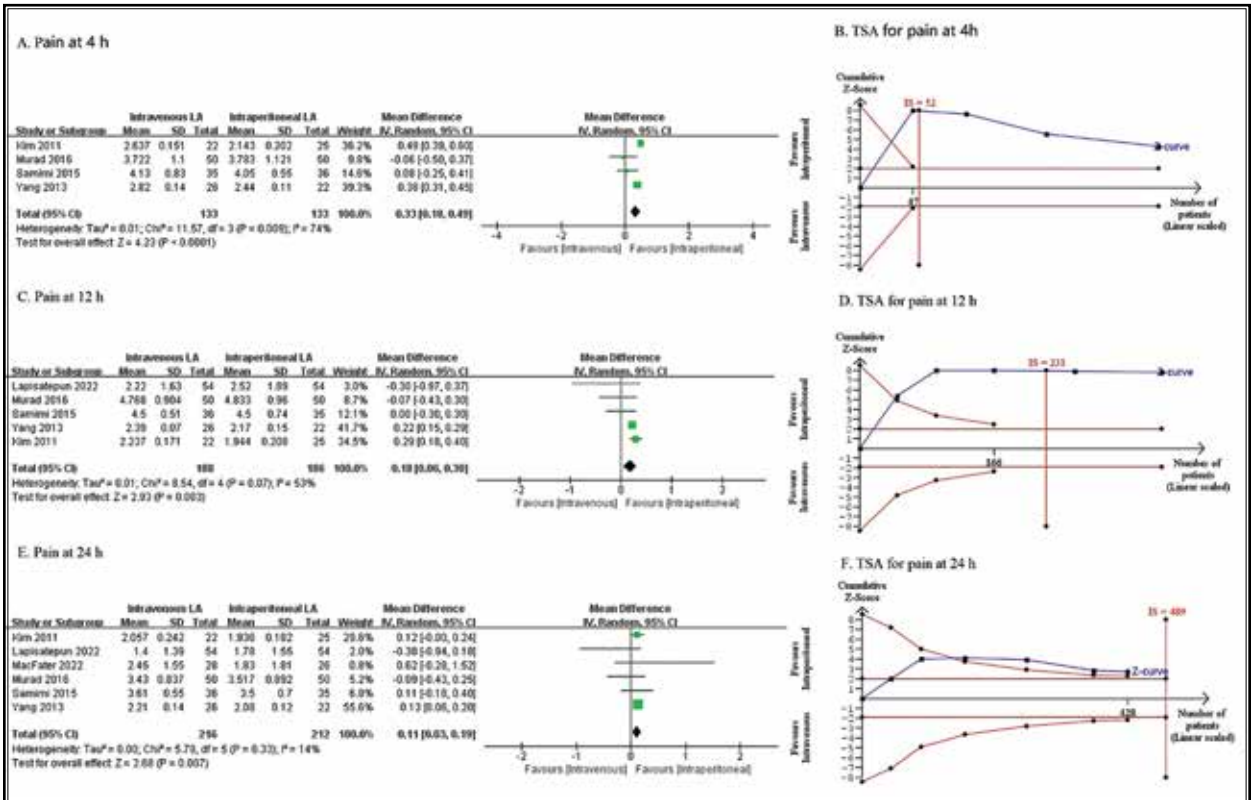

Fig. 2. *Postoperative pain assessed using the VAS score (0–10 cm). A, B. Forest plot and trial sequential analysis of the postoperative pain score at 4 hours postsurgery. C, D. Forest plot and trial sequential analysis of the postoperative pain score at 12 postsurgery. E, F. Forest plot and trial sequential analysis of the postoperative pain score at 24 hours postsurgery. VAS, Visual Analog Scale.*

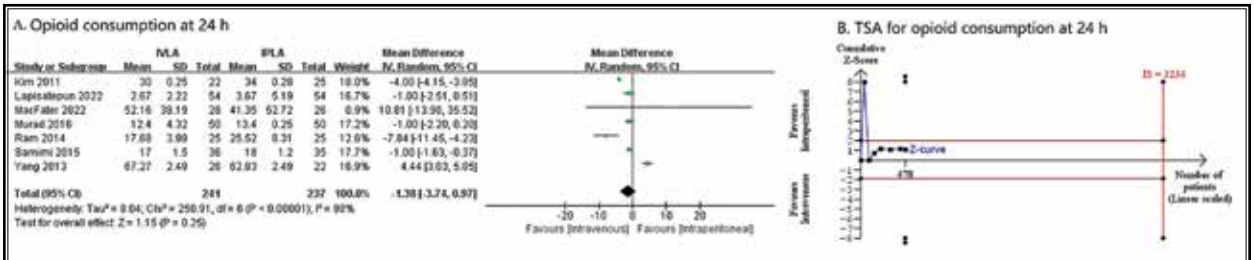

Fig. 3. *Postoperative opioid consumption at 24 hours postsurgery. A. Forest plot of opioid consumption at 24 hours postsurgery. B. Trial sequential analysis of opioid consumption at 24 hours postsurgery.*

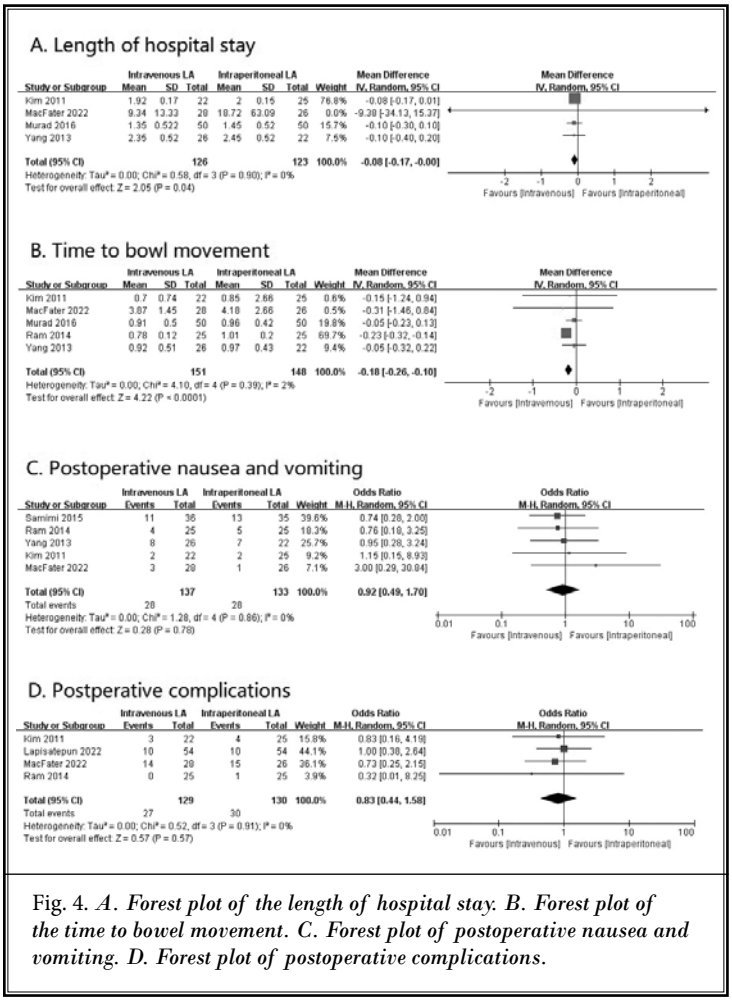

Fig. 4. *A. Forest plot of the length of hospital stay. B. Forest plot of the time to bowel movement. C. Forest plot of postoperative nausea and vomiting. D. Forest plot of postoperative complications.*

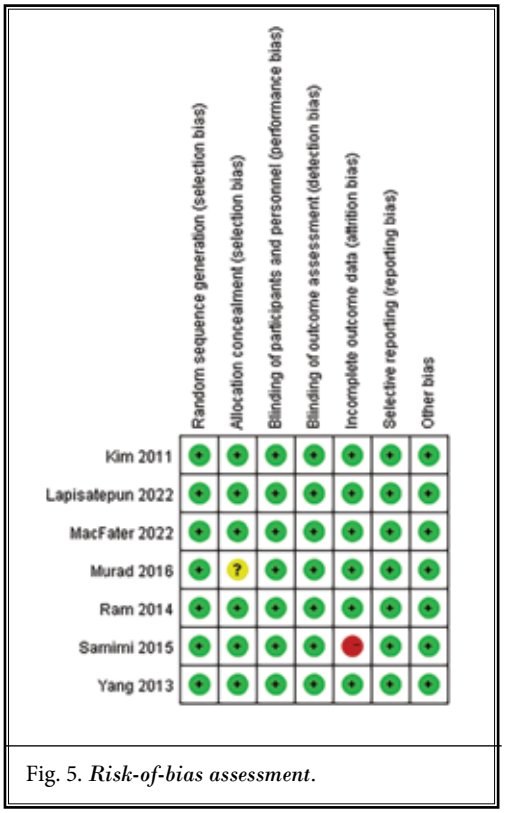

Fig. 5. *Risk-of-bias assessment.*

management of acute POP yields superior pain relief, leads to shorter hospital stays, and promotes faster recovery. Lidocaine is a local anesthetic that belongs to the amide class and has anti-inflammatory, antihyperalgesic, and analgesic effects. Systemic lidocaine has a biphasic analgesic effect, exhibiting both peripheral suppression of acute chemically induced pain (29,30) and central antihyperalgesic activity (31,32). The analgesic mechanisms of intravenous lidocaine vary, and include N-methyl-D-aspartate receptor blockade, muscarinic receptor blockade, sodium channel blockade, and suppression of poly-morphonuclear leukocyte activation and priming (33-36).

Intraperitoneal lidocaine exerts its analgesic effect through both local and systemic mechanisms. On the one hand, intraperitoneal lidocaine creates a temporary chemical barrier that effectively blocks the transmission of pain and other noxious stimuli through the gut-brain axis. This, in turn, can reduce the neuroendocrine response to surgical damage by preventing the activation of vagal afferents at the site of dissection (37). Several animal experiments have demonstrated that vagotomy can attenuate this response (38,39). On the other hand, lidocaine is rapidly absorbed into the circulation after intraperitoneal infusion, and systematic concentrations of lidocaine can be detected as early as 5 minutes after an intraperitoneal bolus infusion, with a max ranging from 15 to 40 minutes (40).

Our meta-analysis shows that although opioid consumption is similar in patients who receive intraperitoneal lidocaine vs those who receive intravenous lidocaine, POP scores are significantly lower in patients who receive intraperitoneal lidocaine. Furthermore, the trial sequential analysis results confirm the positive effects of intraperitoneal lidocaine on POP in patients who underwent abdominal surgery.

The positive effects of intraperitoneal lidocaine may be related to the fact that all the included studies examined patients who underwent abdominal surgery. Following major abdominal surgery, patients will typically have 2 distinct wounds: one on the outside of the body where the incision was made, and one on the

Table 2. *Assessment of the quality of evidence for each outcome of the systematic review - GRADE System.*

Assurence Assessment							Number Of Patients		Absolute Effect	Assurance	Importance
Number of studies	Study design	Risk of bias	Inconsistency	Indirect evidence	Inaccuracy	Other considerations	IVLA	IPLA			
Pain at 4 hours after surgery											
4	RCT	Not serious	Serious	Not serious	Not serious	No	133	133	SMD: 0.33 (0.18-0.49)	⊖⊖⊖ Moderate	Important
Pain at 12 hours after surgery											
5	RCT	Not serious	Serious	Not serious	Not serious	No	188	186	SMD: 0.18 (0.06-0.30)	⊖⊖⊖ Moderate	Important
Pain at 24 hours after surgery											
6	RCT	Not serious	Serious	Not serious	Not serious	No	216	212	SMD: 0.11 (0.03-0.19)	⊖⊖⊖ Moderate	Important
Opioids consumptions at 24 hours after surgery											
7	RCT	Not serious	Serious	Not serious	Not serious	No	241	237	SMD: 1.38 (-3.74-0.97)	⊖⊖⊖ Moderate	Important

RCT: randomized controlled trials, IVLA: intravenous local anesthetic, IPLA: intraperitoneal local anesthetic, SMD: standard mean difference.

inside where the surgical dissection occurred (16). The analgesic effects of intraperitoneal lidocaine include both systemic analgesic effects (40) and local block of the gut–brain axis, which transmits both nociceptive and painful stimuli (37). We conjecture these are the reasons that, compared with intravenous lidocaine, intraperitoneal lidocaine significantly decreased POP in patients who underwent abdominal surgery in the studies included in our meta-analysis.

Our meta-analysis shows that patients receiving intravenous lidocaine experience faster recovery of gastrointestinal functions. Several factors can affect gastrointestinal motility following abdominal surgery, including sympathetic hyperactivity, spinal reflex arc, vagus nerve sensitivity, inflammation, anesthetics, and opioids (41). Lidocaine has been demonstrated to enhance postoperative intestinal motility by inhibiting the afferent or efferent signals of the sympathetic inhibitory spinal and prevertebral reflexes, thereby minimizing their inhibitory effects on gastrointestinal motility (42). Furthermore, lidocaine has been shown to have anti-inflammatory properties, which can support gastrointestinal motility by decreasing inflammation. It can also help to minimize the need for opioids, which may cause gastrointestinal side effects (43). Slower gastrointestinal recovery may be associated with transient vagus nerve block (37). Vagus nerve stimulation has been shown to prevent postoperative ileus in preclinical models (41,44).

In our meta-analysis, only randomized double-blinded controlled trials were included, with an emphasis on patient dropout, allocation concealment, and proper randomization. Due to the small number of eligible articles, we carried out a trial sequential analysis to reduce random errors and improve the reliability of our positive meta-analysis findings (45).

The results confirm that patients receiving intraperitoneal lidocaine experience decreased POP. Although the GRADE quality of evidence for intraperitoneal lidocaine was downgraded because of significant heterogeneity among the included studies, the trials included in our meta-analysis were of moderate quality.

Our review has several limitations that should be noted. First, although 6 of the studies were considered to have a low risk of bias, the overall sample size of 478 patients may pose a risk of either overestimating or underestimating the treatment effect. Therefore, a trial sequential analysis was used to minimize random errors and calculate the information size.

Second, the patients did not receive a postopera-

tive infusion of lidocaine; only one study used lidocaine infusion for 3 days postsurgery. The limited infusion may have affected the outcomes because the half-life of lidocaine is 20–40 minutes.

Third, a significant heterogeneity was observed among the studies, which could be partly attributed to the lack of standardization of pain management protocols. The clinical differences among the studies could also contribute to this heterogeneity, such as the use of different surgical procedures in the 7 studies included in our meta-analysis. These differences may affect the outcomes and the response to pain management interventions, leading to variable results across studies.

In conclusion, when used in combination with other analgesic modalities, local anesthetics can provide significant pain relief benefits through a multimodal analgesic regimen. Our meta-analysis of 7 studies show that intraperitoneal lidocaine has an analgesic benefit over intravenous lidocaine in terms of a decrease in POP in patients who underwent abdominal surgery. However, this meta-analysis also shows that intravenous lidocaine is more beneficial for gastrointestinal recovery after abdominal surgery. Additional studies comparing the efficacy of more prolonged infusions of medications in a wider range of surgical procedures would be valuable in further understanding optimal pain management strategies.

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