Randomized Controlled Trial

Quadratus Lumborum Block Spares Postoperative Opioid Usage but Does Not appear to Prevent the Development of Chronic Pain After Gastrointestinal Surgery

Qing-Ren Liu, MD[1,2], Jue Xie, MD[2], Yu-Chen Dai, MD[2], Mu-Huo Ji, MD[3], Cheng-Mao Zhou, MD[4], Han-Wen Gu, MD[4], Hui-Jie Shang MD[4], Xing-Bing Sun, MD[1], and Jian-Jun Yang, MD, PhD[4]

From: [1]Department of Anesthesiology, Xishan People's Hospital of Wuxi City, Wuxi, China; [2]Department of Anesthesiology, Zhongda Hospital, Medical School, Southeast University, Nanjing, China; [3]Department of Anesthesiology, The Second Affiliated Hospital, Nanjing Medical University, Nanjing, China; [4]Department of Anesthesiology, Pain and Perioperative Medicine, The First Affiliated Hospital of Zhengzhou University, Zhengzhou, China

Address Correspondence:
Jian-Jun Yang MD, PhD
School of Medicine
Southeast University
87 Dingjiaqiao, Nanjing, 210009, China
E-mail: yjyangjj@126.com

Disclaimer: This work was supported by the Wuxi Municipal Health Commission (grant number T202035).

Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.

Manuscript received: 12-23-2020
Revised manuscript received: 04-06-2021
Accepted for publication: 04-19-2021

Free full manuscript: www.painphysicianjournal.com

Background: Regional anesthesia has been used to reduce acute postsurgical pain and to prevent chronic pain. The best technique, however, remains controversial.

Objectives: The aim of this study was to assess the short- and long-term postoperative analgesic efficacy of ultrasound-guided quadratus lumborum block (QLB) in open gastrointestinal surgery.

Study Design: A randomized, double-blinded, controlled trial.

Setting: Operating room; postoperative recovery room and ward.

Methods: One hundred eighteen patients underwent elective gastrointestinal surgery randomly assigned into 2 groups (QLB group or control group). Before anesthetic induction, QLB was performed bilaterally under ultrasound guidance using 20 mL of 0.375% ropivacaine or saline solution at each abdominal wall. The primary outcome was cumulative oxycodone consumption within 24 h after surgery. The secondary outcomes were acute pain intensity, incidence of chronic pain, and incidence of postoperative nausea or vomiting (PONV), dizziness, and pruritus.

Results: The cumulative oxycodone consumption was significantly lower in the QLB group during the first 6, 6-24, 24, and 48 h postoperatively when compared to the control group. At rest or during coughing, the numeric rating scale scores were significantly lower at 1, 3, 6, and 12 h postoperatively in the QLB group compared to the control group. There were no significant differences between the 2 groups regarding the incidence of chronic postoperative pain at 3 or 6 months after surgery. Significant differences were found in the incidence of PONV between the two groups, but other complications, such as dizziness and pruritus, did not differ significantly.

Limitations: We did not confirm the QLB effectiveness with sensory level testing after local anesthetic injection. Cumulative oxycodone consumption could have been affected by the patients' use of oxycodone for nonsurgical pain.

Conclusions: Ultrasound-guided QLB provided superior short-term analgesia and reduced oxycodone consumption and the incidence of PONV after gastrointestinal surgery. However, the incidence of chronic pain was not significantly affected by this anesthetic technique.

Key words: Quadratus lumborum block, acute pain, chronic pain, gastrointestinal surgery, ultrasound guidance

Pain Physician 2021: 24:E1191-E1198

Postoperative pain management, as an integral part of enhanced recovery after surgery (ERAS) protocols after gastrointestinal surgery, has always been a challenging issue. Multiple regional analgesic techniques have been used to manage pain in recent decades. However, the best technique remains controversial. As is well known, epidural anesthesia has provided effective postoperative analgesia, but it is not commonly used due to the complex operation and high incidence of hypotension. Transversus abdominis plane (TAP) block can reduce postoperative pain, but the analgesic effect is limited because of its narrow coverage and short duration. In addition, TAP block cannot relieve visceral pain effectively (1-3). Therefore, it is essential to develop a more effective regional analgesic technique for patients undergoing abdominal surgery.

Quadratus lumborum block (QLB), as a recently described truncal regional block technique, can anesthetize thoracolumbar nerves according to different anatomic sites of local anesthetic injection relative to the latissimus dorsi, quadratus lumborum muscle, psoas muscle, and erector spinae muscles. Recent clinical studies have shown that QLB provides effective analgesia for total hip replacement surgery (4,5) and inguinal hernia repair (6,7). In addition, QLB has been used for perioperative analgesia in patients undergoing upper and lower abdominal surgeries, such as cholecystectomy (8,9), cesarean delivery (3,10), gynecologic surgery (11), and colorectal surgery (12,13). Moreover, some scholars have suggested that QLB may alleviate visceral pain to a certain extent (10,14).

To the best of our knowledge, there are few randomized controlled trials (RCTs) reporting the effectiveness of QLB for acute postsurgical pain (APSP) after gastrointestinal surgery and no such RCTs for chronic postsurgical pain (CPSP). Case reports have shown that posterior QLB can effectively control postoperative pain in patients undergoing total or subtotal gastrectomy (15,16). Meanwhile, Ökmen et al (8) have found that posterior QLB provides effective analgesia in patients undergoing laparoscopic cholecystectomy. Hence, in this prospective RCT, we also used posterior QLB approaches, in which local anesthetics are deposited deep into the posterior thoracolumbar fascia between the quadratus lumborum and erector spinae muscles.

We hypothesized that QLB could reduce analgesic consumption during the first 6, 24, and 48 h after gastrointestinal surgery. We also measured secondary outcomes, such as acute pain level, incidence of chronic pain, intraoperative remifentanil consumption, and postoperative adverse effects.

Methods

Design and Patients

This prospective, double-blinded, randomized controlled trial was approved by the Independent Ethics Committee (IEC) for Clinical Research of Zhongda Hospital, affiliated to Southeast University (No. 2019ZDSYLL084-P01). The protocol was registered at the Chinese Clinical Trial Registry (ChiCTR1900024855). Written informed consent was obtained as a condition to participate in the study, and CONSORT guidelines were followed.

Patients aged 18 to 80 years who had American Society of Anesthesiologists physical status (ASA) I-III and were scheduled for elective gastrointestinal surgery due to gastric or colorectal cancer were enrolled in the study between August 2019 and January 2020. Patients with coagulation dysfunction, body mass index (BMI) less than 15 kg/m^2 or greater than 30 kg/m^2, infection at the puncture site, severe heart and lung disease, hepatic and renal insufficiency, mental illness, and self-expression disorders were excluded. Patients were randomly assigned to the QLB combined with general anesthesia group (QLB group) or general anesthesia group (control group). Randomization was performed using a computer random number generator (http://www.randomization.com). The group allocation numbers were concealed in sequentially numbered envelopes. All participants and investigators were blinded to the group assignment.

Anesthetic Procedure

After the placement of standard monitoring devices, all patients received ultrasound-guided QLB using 20 mL of 0.375% ropivacaine or saline solution at the bilateral abdominal wall before anesthetic induction. A curvilinear probe (2-6 MHz) was placed in the posterior axillary line between the costal margin and iliac crest to identify the quadratus lumborum muscle, psoas muscle, erector spinae muscles, and transverse process. A 22-gauge, 100 mm needle was advanced with the in-plane technique from the posterolateral to medial direction until the needle tip got to the medial edge of the quadratus lumborum between the quadratus lumborum and erector spinae muscle and within the middle thoracolumbar fascia.

General anesthesia was induced with intravenous (IV) administration of 0.3 mcg/kg sufentanil, 2 to 2.5 mg/kg propofol, and 0.6 mg/kg rocuronium. Anesthesia was maintained by continuous sevoflurane inhalation (minimal alveolar concentration 0.7-1.0) and 0.05-0.2 mcg kg^{1} min^{1} remifentanil infusion with an intermittent infusion of cisatracurium. During skin closure, sufentanil (0.1 mcg/kg, IV) was given for analgesia, and ondansetron (0.1 mg/kg, IV) was given for antiemetic prophylaxis. All patients were transferred to the postanesthesia care unit (PACU) with antagonism of the neuromuscular blockade using neostigmine and atropine. Extubation was performed when the patients were completely awake, and their muscle tone was restored fully.

All gastrointestinal cancer operations were performed by the same group of surgeons, which included 4 surgeons. Surgical technique and extent of surgery followed with the standardization of surgery as described in previous consensus guidelines for the management of gastric and colorectal cancers. After surgery, patients received standardized postoperative pain management. In the PACU, patients received oxycodone (2 mg, IV) when the numeric rating scale (NRS) score at rest was > 3. On the ward, patients received celecoxib 200 mg orally every 12 h and self-administered pain medication through a patient-controlled intravenous analgesia (PCIA) device (0.5 mg/mL oxycodone, without background infusion, bolus 4 mL, lockout time 5 min) for 48 h.

Outcome Measurements

The primary outcome was cumulative oxycodone consumption within 24 h after surgery. The cumulative oxycodone consumption in the first 6, 6-24, 24, and 48 h postoperatively was collected. The secondary outcomes were acute pain level, incidence of chronic pain, intraoperative remifentanil consumption, and adverse effects. The pain intensity was assessed using an NRS (0 = no pain at all, 10 = strongest pain imaginable) (17) at rest and during coughing. The vital signs and pain scores were recorded at 1, 3, 6, 12, 24, and 48 h after surgery. Any adverse effects, such as nausea, vomiting, dizziness, and pruritus, were recorded. At 3 and 6 months after surgery, all patients were asked to assess the occurrence of chronic pain at the site of the operation using the NRS score by phone. We defined CPSP when the pain NRS score at rest was ≥ 1.

Demographic characteristics such as gender, age, height, weight, and underlying medical diseases such as hypertension and diabetes were collected on the day before surgery. Moreover, patients were asked to rate their average expected pain intensity for the first day postoperatively (on a scale from 0 = no pain at all to 10 = strongest pain imaginable) (18). The Hospital Anxiety and Depression Scale (HADS) (19) was used to assess the preoperative state of anxiety and depression. Data related to remifentanil consumption during the operation, blood loss, perioperative inflammatory response (the serum levels of IL-6 and TNF-α), duration of anesthesia, duration of surgery, length of hospital stay, tube retention time, and time to leave bed (time to the first getting out of bed after surgery) were collected. Perioperative hemodynamic parameters such as the heart rate (HR) and mean arterial pressure (MAP) were recorded at different time points, including preinduction (T0), before skin incision (T1), 1 min after skin incision (T2), just before the end of surgery (T3), before extubation (T4), 5 min after extubation (T5), and just before PACU discharge (T6).

Statistical Analysis

The sample size was calculated on the basis of analgesic consumption within 24 h after surgery. A previous study revealed that the mean morphine consumption is 37.5 mg with a standard deviation (SD) of 28.4 mg for colorectal surgery using ultrasound-guided QLB 24 h postoperatively and that QLB can reduce morphine consumption by 30% (12). Using a 2-sample t test, 50 patients per group would be required in accordance with a significance level of 0.05 and power of 0.8. In consideration of the possible dropout rate of up to 15%, we enrolled 59 patients per group.

IBM SPSS software Version 23.0 (SPSS Inc., Chicago, IL) was used to analyze the data. Continuous variables are presented as the mean ± SD or as the median (interquartile range), and categorical variables are presented as numbers (percentages). Assumptions of normality for continuous variables were assessed using normal probability plots. Between-group differences were evaluated using the independent sample t test or Mann-Whitney U test for continuous variables except for the pain NRS score, HR, or MAP. Categorical variables were compared between groups using the chi-square test or Fisher's exact-test. Repeated measures analysis of variance was used for time series data such as the pain NRS score, HR, and MAP. A *P* value of < 0.05 was considered statistically significant.

Results

Fig. 1 presents the Consolidated Standards of Reporting Trials flowchart for this study. A total of 118 patients were approached for participation between August 2019 and January 2020. Of these, 106 met the inclusion criteria and were randomized. All randomized patients were followed up according to the protocol. The basic characteristics of the patients included in this trial are shown in Table 1. The 2 groups were not significantly different in terms of demographics, psychological state, or clinical data. The length of hospital stay and intraoperative remifentanil consumption did not differ between groups, but the time to leave bed in the QLB group was shorter when compared to the control group (Table 2).

Oxycodone consumption after 24 h was significantly lower in the QLB group than in the control group (17.2 ± 6.4 mg vs 27.2 ± 8.7 mg, $P < 0.001$). Moreover, the cumulative oxycodone consumption was significantly lower in the QLB group than in the control group during the first 6, 6-24, and 48 h postoperatively. However, no significant difference was noted 24-48 h postoperatively (Fig. 2).

At rest or during coughing, the NRS scores were significantly lower at 1, 3, 6, and 12 h postoperatively in the QLB group than in the control group. Up to 24 and 48 h postoperatively, no significant differences were observed between groups regarding pain scores (Fig. 3).

The perioperative hemodynamic parameters, including HR and MAP, are shown in Supplement Fig. 1. There were no significant differences at any single time point. The serum levels of IL-6 and TNF-α were significantly lower on day 1 postoperatively in the QLB group than in the control group (Table 2).

Nausea occurred in 12 (24%) patients in the QLB group and 23 (46%) patients in the control group, while vomiting occurred in 2 (6%) patients in the QLB group and 8 (16%) patients in the control group. Significant differences were found between the 2 groups ($P = 0.021$ and $P = 0.046$, respectively). However, other complications, such as dizziness and pruritus, did not differ significantly (Table 2).

At 3 months postoperatively, 2 patients were lost to follow-up in the QLB group. The incidences of CPSP in the QLB and control groups were 39.6% and 40%, respectively ($P = 0.996$). Then, one patient in the control group was lost to follow-up at 6 months. Although the incidence of CPSP was lower in the QLB group than in the control group (14.6% vs 22.4%, $P = 0.319$), no significant difference between groups was detected (Table 2).

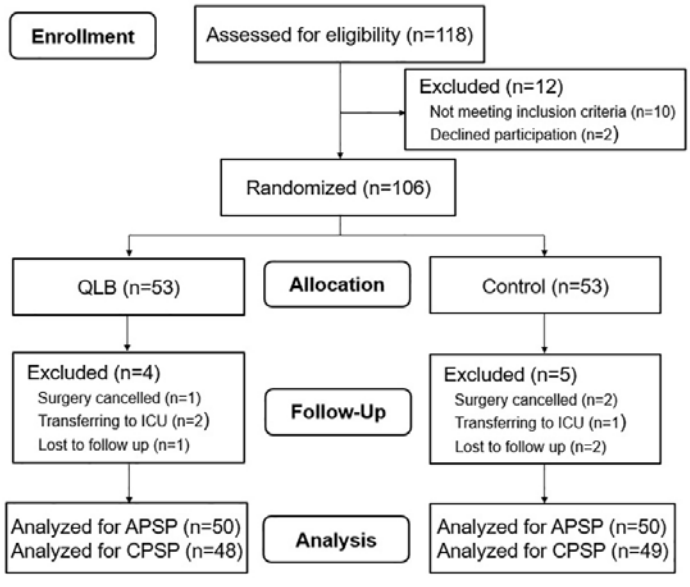


Fig. 1. *Flowchart of the study.*
Abbreviations: QLB: quadratus lumborum block, APSP: acute postsurgical pain, CPSP: chronic postsurgical pain.

Discussion

The current study was performed to assess the short- and long-term analgesic efficacy of QLB in patients undergoing open gastrointestinal surgery. Our results showed that preoperative ultrasound-guided bilateral QLB provided superior pain relief in the early postoperative period, reduced the cumulative analgesic consumption, and resulted in an earlier time to leave bed and a lower incidence of PONV. On the other hand, the incidence of CPSP in the QLB group was lower but not significantly affected by the performance of the block. These findings have important clinical implications for the choice of anesthetic plan.

Ultrasound-guided QLB is a relatively new fascial plane block. Local anesthetic can be injected adjacent to the quadratus lumborum in order to

Table 1. *Demographic, psychological and clinical characteristics of patients.*

Variables	QLB group n = 50	Control group n = 50	*P* value
Age (year)	64.6 ± 9.4	62.2 ± 11.9	0.261
Male	30 (60%)	29 (58%)	0.839
BMI (kg/m²)	23.5 ± 3.1	22.9 ± 3.9	0.406
Hypertension	25 (50%)	27 (54%)	0.689
Diabetes	4 (8.0%)	7 (14.0%)	0.338
Preoperative chronic pain	12 (24%)	13 (26%)	0.817
ASA physical status			0.219
ASA I	4 (8%)	7 (14%)	
ASA II	43 (86%)	36 (72%)	
ASA III	3 (6%)	7 (14%)	
Site of surgery			0.253
Stomach	21 (42%)	29 (58%)	
Colon	21 (42%)	14 (28%)	
Rectum	8 (16%)	7 (14%)	
Duration of surgery (min)	172.3 ± 45.3	183.1 ± 54.0	0.281
Duration of anesthesia (min)	206.3 ± 46.2	202.9 ± 58.9	0.749
Blood loss, mL	200 (100-212.5)	200 (100-212.5)	0.688
Tube retention time (days)	7.7 ± 2.5	8.9 ± 3.4	0.064
HADS: anxiety	2.0 (0.0-5.0)	3.5 (1.0-8.0)	0.080
HADS: depression	2.0 (1.0-6.0)	2.5 (1.0-7.0)	0.304
Expected postsurgical pain	5.0 (3.0-6.0)	5.0 (4.0-7.0)	0.079

Notes: Data are presented as mean ± standard deviation, median (interquartile range), or number (percentage).
Abbreviations: QLB: quadratus lumborum block, BMI: body mass index, ASA: American Society of Anesthesiologists, HADS: Hospital Anxiety and Depression Scale.

Table 2. *Outcome measurement of patients.*

Variables	QLB group n = 50	Control group n = 50	*P* value
Remifentanil consumption (mcg)	852.0 ± 365.3	984.3 ± 356.5	0.161
Time to leave bed (h)	42 ± 12.5	57.0 ± 17.1	<0.001
Length of hospital stay (days)	18.2 ± 5.4	18.6 ± 5.5	0.770
Inflammatory response			
IL-6 (baseline) (pg/mL)	6.08 (5.3-9.9)	5.55 (3.5-8.54)	0.16
IL-6 (POD1) (pg/mL)	18.1 (13.0-28.1)	34.2 (22.8-54.3)	< 0.001
TNF-α (baseline) (pg/mL)	29.3 (26.2-46.9)	37.2 (29.3-42.4)	0.225
TNF-α (POD1) (pg/mL)	55.5 (40.7-68.3)	81.7 (63.2-89.8)	< 0.001
Adverse effects			
Nausea	12 (24%)	23 (46%)	0.021
Vomiting	2 (6%)	8 (16%)	0.046
Dizziness	11 (22%)	16 (32%)	0.260
Pruritus	2 (4%)	4 (8%)	0.678
Incidence of CPSP			
3-month	19 (39.6%) (n = 48)	20 (40%) (n = 50)	0.966
6-month	7 (14.6%) (n = 48)	11 (22.4%) (n = 49)	0.319

Notes: Data are presented as mean ± standard deviation, median (interquartile range), or number (percentage).
Abbreviations: QLB: quadratus lumborum block, POD1: postoperative day 1.

attain different levels of nerve block. Ökmen et al (8) found that posterior QLB provided effective analgesia in patients undergoing laparoscopic cholecystectomy because it covered the T7-L10 dermatomes. Moreover, an anatomic study showed that posteromedial QLB could provide better cranial spread than posterolateral QLB, and the total extent of the injectate distribution in posteromedial QLB was similar to that in low thoracic erector spinae plane block (20). Therefore, in this study, we utilized posteromedial QLB approaches, where local anesthetics are deposited deep to the posterior thoracolumbar fascia between the quadratus lumborum and erector spinae muscles.

QLB has been proposed to reduce opioid consumption and relieve pain. However, the benefit of QLB in pain management remains controversial. One possible reason is that the effectiveness of QLB is associated with the QLB approaches, types of surgery, and multimodal analgesic strategies. In most surgeries, such as cesarean section (3), gynecologic surgery (11), percutaneous nephrolithotomy (21), nephrectomy (22), and total hip arthroplasty (4), QLB has been proven to reduce postoperative pain and opioid consumption. These results are similar to those of our study, where cumulative oxycodone consumption during the first 6, 24, and 48 h postoperatively and pain NRS scores at rest or during coughing in the first 12 h were significantly different between groups. This can be explained because pre-

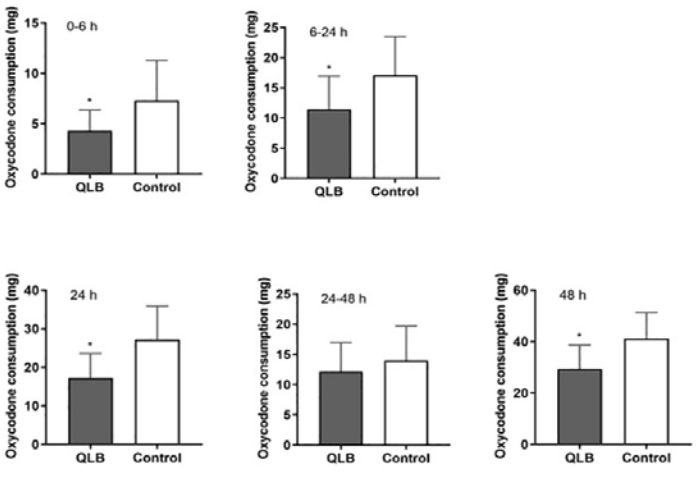


Fig. 2. *The cumulative oxycodone consumption 48 h postoperatively. Data are presented as the mean ± SD. The cumulative oxycodone consumption was significantly lower in the QLB group than in the control group for the first 6, 6-24, 24, 24-48, and 48 h postoperatively. *P < 0.001.*
Abbreviation: QLB: quadratus lumborum block.

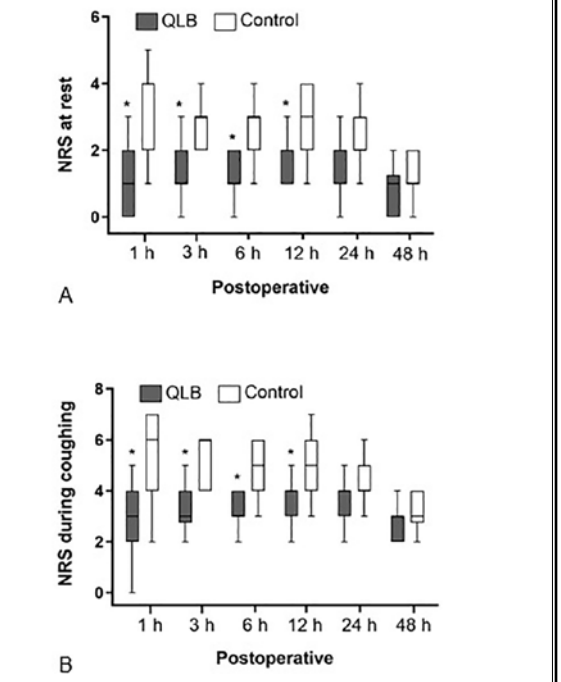


Fig. 3. *Pain at rest and during coughing in the postoperative 48 h period. A, NRS at rest. B, NRS during coughing. Data are presented as the median, range and interquartile range. At rest or during coughing, the NRS scores were significantly lower at 1, 3, 6, and 12 h postoperatively in the QLB group than in the control group (*P < .001).*
Abbreviation: QLB: quadratus lumborum block. .

emptive analgesia using regional blocks can prevent hyperpathia by inhibiting peripheral and central sensitization.

However, a randomized controlled trial showed that QL2 block could not spare opioid usage and decrease pain 24 h after colorectal resection (23). The findings contrast with our study because the standard multimodal analgesia included local wound infiltration with 10 mL of xylocaine 2%, which can also relieve postoperative pain. Thus, the analgesic effect of QLB was possibly concealed by local wound infiltration.

In this study, we used a new posteromedial approach for QLB, which provided a more extensive injectate distribution than posterolateral QLB. Huan et al (13) also demonstrated that compared to TAP block, posteromedial QLB can provide superior opioid-sparing and analgesia efficacy after laparoscopic colorectal surgery. Thus, the advantage of posteromedial QLB was further proven. On the one hand, we also found that QLB reduced opioid-related side effects such as PONV and advanced the first time to leave bed due to postoperative pain relief. In a randomized controlled study, QLB was correlated with a significantly lower NRS score of nausea at 24 h after laparoscopic gynecologic surgery, which could be explained by continuously greater pain and more analgesia consumption in the control group (11). On the other hand, we observed whether QLB could attenuate the perioperative inflammatory response. Cytokines such as IL-6 and TNF-α play an important role in perioperative pain, in which systemic inflammation may be an underlying mechanism (24). Our results showed that QLB was significantly associated with lower serum levels of IL-6 and TNF-α on postoperative day one. As discussed by Rahendra (25), QLB and epidural anesthesia showed comparable perioperative anti-inflammatory effects among living kidney donors undergoing laparoscopic nephrectomy. However, a previous study showed a different result: QLB could not dampen the perioperative inflammatory response in patients undergoing laparoscopic colorectal surgery (12). In their study, all participants received dexamethasone and ketorolac, both of which have potent anti-inflammatory properties (26-28). Thus, the authors suggest that QLB was unable to further attenuate the inflammatory response due to the presence of these 2 anti-inflammatory drugs. In our

study, celecoxib at a one-day dose was unable to cover the anti-inflammatory effect of QLB.

Regional anesthesia provides superior pain control immediately after surgery, but it has not been completely proven to prevent CPSP. Several systematic reviews (29,30) have found that epidural anesthesia and paravertebral block might prevent the development of CPSP in patients undergoing breast cancer surgery and thoracotomy, respectively. However, there is no convincing evidence for other surgeries, such as limb amputation, hernia repair, or cardiac or abdominal surgery. Our results did not show the benefit of QLB for preventing chronic pain despite the lower incidence of CPSP in the QLB group than in the control group. Similarly, a retrospective cohort study showed that TAP did not reduce the incidence of CPSP at 3 months and 6 months after selective colorectal surgery (31). In another randomized double-blinded trial, the combined administration of continuous systemic ketamine and epidural analgesia effectively prevented the development of chronic pain after major digestive surgery (32). Therefore, a multimodal analgesia strategy may provide a better effect on preventing CPSP.

Some predictors, such as preoperative chronic pain (33), anxiety (34), depression (35), and expected postsurgical pain (18), have been shown to be independently associated with acute pain and chronic pain after surgery. In this study, we collected data on preoperative chronic pain, anxiety, depression, and expected postsurgical pain, and the analysis showed no difference between the 2 groups. Thus, we further minimized the risk of bias by controlling for confounding factors. This is also an innovation in our study.

Our study had several limitations. First, we did not confirm the QLB effectiveness with sensory level testing after local anesthetic injection, as we felt this might affect group allocation blinding. We instead observed the spread patterns of the local anesthetic on ultrasound. Second, cumulative oxycodone consumption measured at various intervals could have been affected by the patients' use of oxycodone for nonsurgical pain, such as headache and back pain. Third, our study was built to detect a 30% difference in opioid consumption 24 h postoperatively, but the evaluation of chronic pain was not powered. Fourth, the different pathologies and operative techniques could cause heterogeneity, even if there was no significant difference in site of surgery between the 2 groups. Finally, we chose to use one specific type of QLB that has been described in the literature (13,20). We thus cannot apply our results to all types of QLB.

Conclusions

In conclusion, ultrasound-guided posteromedial QLB provided superior short-term analgesia and reduced oxycodone consumption and the incidence of PONV after gastrointestinal surgery. However, the incidence of chronic pain was not significantly affected by this anesthetic technique. Further studies are needed to support the role of QLB in acute pain control, particularly in the context of chronic pain management.

Acknowledgments

The authors would like to thank the Biobank, Zhongda Hospital, Southeast University for specimen preservation and thank the Wuxi Municipal Health Commission for financial supports.

Author Contributions

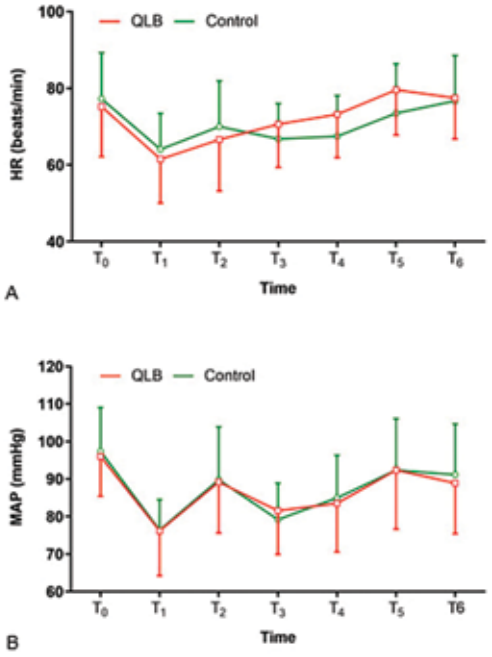
Qing-Ren Liu: Conceptualization, Methodology, Software, Validation, Formal analysis, Data curation, Writing - original draft, Writing - review & editing. Jue Xie: Methodology, Software, Validation. Yu-Chen Dai: Data curation, Writing -original draft. Mu-Huo Ji: Conceptualization, Investigation, Resources. Cheng-Mao Zhou: Data curation, Software, Formal analysis. Han-Wen Gu and Hui-Jie Shang: Resources, Validation. Xing-Bing Sun: Conceptualization, Visualization, Supervision. Jian-Jun Yang: Conceptualization, Writing - review & editing, Supervision, Funding acquisition.

References

1. El Sherif FA, Mohamed SA-B, Kamal SM. The effect of morphine added to bupivacaine in ultrasound guided transversus abdominis plane (TAP) block for postoperative analgesia following lower abdominal cancer surgery, a randomized controlled study. *J Clin Anesth* 2017; 39:4-9.
2. Oh TK, Yim J, Kim J, et al. Effects of preoperative ultrasound-guided transversus abdominis plane block on pain after laparoscopic surgery for colorectal cancer: A double-blind randomized controlled trial. *Surg Endosc* 2017; 31:127-134.
3. Blanco R, Ansari T, Riad W, Shetty N. Quadratus lumborum block versus transversus abdominis plane block for postoperative pain after cesarean delivery: A randomized controlled trial. *Reg Anesth Pain Med* 2016; 41:757-762.
4. Elsharkawy H, El-Boghdadly K, Barnes TJ, et al. The supra-iliac anterior quadratus lumborum block: a cadaveric study and case series. *Can J Anaesth* 2019; 66:894-906.
5. Kukreja P, MacBeth L, Sturdivant A, et

al. Anterior quadratus lumborum block analgesia for total hip arthroplasty: A randomized, controlled study. *Reg Anesth Pain Med* 2019; rapm-2019-100804.

6. Aksu C, Gürkan Y. Ultrasound guided quadratus lumborum block for postoperative analgesia in pediatric ambulatory inguinal hernia repair. *J Clin Anesth* 2018; 46:77-78.
7. Öksüz G, Arslan M, Urfalıoğlu A, et al. Comparison of quadratus lumborum block and caudal block for postoperative analgesia in pediatric patients undergoing inguinal hernia repair and orchiopexy surgeries: A randomized controlled trial. *Reg Anesth Pain Med* 2020; 45:187-191.
8. Ökmen K, Metin Ökmen B, Topal S. Ultrasound-guided posterior quadratus lumborum block for postoperative pain after laparoscopic cholecystectomy: A randomized controlled double blind study. *J Clin Anesth* 2018; 49:112-117.
9. Baytar Ç, Yılmaz C, Karasu D, et al. Comparison of ultrasound-guided subcostal transversus abdominis plane block and quadratus lumborum block in laparoscopic cholecystectomy: A prospective, randomized, controlled clinical study. *Pain Res Manag* 2019; 2019:2815301.
10. Krohg A, Ullensvang K, Rosseland LA, Langesæter E, Sauter AR. The analgesic effect of ultrasound-guided quadratus lumborum block after cesarean delivery: A randomized clinical trial. *Anesth Analg* 2018; 126:559-565.
11. Ishio J, Komasawa N, Kido H, Minami T. Evaluation of ultrasound-guided posterior quadratus lumborum block for postoperative analgesia after laparoscopic gynecologic surgery. *J Clin Anesth* 2017; 41:1-4.
12. Dewinter G, Coppens S, Van de Velde M, et al. Quadratus lumborum block versus perioperative intravenous lidocaine for postoperative pain control in patients undergoing laparoscopic colorectal surgery: A prospective, randomized, double-blind controlled clinical trial. *Ann Surg* 2018; 268:769-775.
13. Huang D, Song L, Li Y, Xu Z, Li X, Li C. Posteromedial quadratus lumborum block versus transversus abdominal plane block for postoperative analgesia following laparoscopic colorectal surgery: A randomized controlled trial. *J Clin Anesth* 2020; 62:109716.
14. Yuan Q, Cui X, Fei Y, Xu Z, Huang Y. Transmuscular quadratus lumborum block versus thoracic paravertebral block for acute pain and quality of recovery after laparoscopic renal surgery: study protocol for a randomized controlled trial. *Trials* 2019; 20:276.
15. Cardoso JM, Sá M, Reis H, et al. [Type II Quadratus lumborum block for a subtotal gastrectomy in a septic patient]. *Braz J Anestesiol* 2018; 68:186-189.
16. Sá M, Cardoso JM, Reis H, et al. [Quadratus lumborum block: Are we aware of its side effects? A report of 2 cases]. *Braz J Anestesiol* 2018; 68:396-399.
17. Rothaug J, Weiss T, Meissner W. How simple can it get? Measuring pain with NRS items or binary items. *Clin J Pain* 2013; 29:224-232.
18. Pan PH, Tonidandel AM, Aschenbrenner CA, Houle TT, Harris LC, Eisenach JC. Predicting acute pain after cesarean delivery using three simple questions. *Anesthesiology* 2013; 118:1170-1179.
19. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67:361-370.
20. Elsharkawy H, Bajracharya GR, El-Boghdadly K, Drake RL, Mariano ER. Comparing two posterior quadratus lumborum block approaches with low thoracic erector spinae plane block: An anatomic study. *Reg Anesth Pain Med* 2019; rapm-2018-100147.
21. Dam M, Hansen CK, Poulsen TD, et al. Transmuscular quadratus lumborum block for percutaneous nephrolithotomy reduces opioid consumption and speeds ambulation and discharge from hospital: A single centre randomised controlled trial. *Br J Anaesth* 2019; 123:e350-e358.
22. Kwak K-H, Baek SI, Kim JK, Kim TH, Yeo J. Analgesic effect of ultrasound-guided preoperative unilateral lateral quadratus lumborum block for laparoscopic nephrectomy: A randomized, double-blinded, controlled trial. *J Pain Res* 2020; 13:1647-1654.
23. Boulianne M, Paquet P, Veilleux R, et al. Effects of quadratus lumborum block regional anesthesia on postoperative pain after colorectal resection: A randomized controlled trial. *Surg Endosc* 2020; 34:4157-4165.
24. Sommer C, Kress M. Recent findings on how proinflammatory cytokines cause pain: Peripheral mechanisms in inflammatory and neuropathic hyperalgesia. *Neurosci Lett* 2004; 361:184-187.
25. Rahendra R, Pryambodho P, Aditianingsih D, Sukmono RB, Tantri A, Melati AC. Comparison of IL-6 and CRP Concentration between quadratus lumborum and epidural blockade among living kidney donors: A randomized controlled trial. *Anesth Pain Med* 2019; 9:e91527.
26. Kim MH, Hahm TS. Plasma levels of interleukin-6 and interleukin-10 are affected by ketorolac as an adjunct to patient-controlled morphine after abdominal hysterectomy. *Clin J Pain* 2001; 17:72-77.
27. Carvalho B, Lemmens HJ, Ting V, Angst MS. Postoperative subcutaneous instillation of low-dose ketorolac but not hydromorphone reduces wound exudate concentrations of interleukin-6 and interleukin-10 and improves analgesia following cesarean delivery. *J Pain* 2013; 14:48-56.
28. El Azab SR, Rosseel PMJ, de Lange JJ, et al. Dexamethasone decreases the pro- to anti-inflammatory cytokine ratio during cardiac surgery. *Br J Anaesth* 2002; 88:496-501.
29. Weinstein EJ, Levene JL, Cohen MS, et al. Local anaesthetics and regional anaesthesia versus conventional analgesia for preventing persistent postoperative pain in adults and children. *Cochrane Database Syst Rev* 2018; 6:CD007105.
30. Levene JL, Weinstein EJ, Cohen MS, et al. Local anesthetics and regional anesthesia versus conventional analgesia for preventing persistent postoperative pain in adults and children: A Cochrane systematic review and meta-analysis update. *J Clin Anesth* 2019; 55:116-127.
31. Pan Z-Y, Hu Z-H, Zhang F, Xie WX, Tang YZ, Liao Q. The effect of transversus abdominis plane block on the chronic pain after colorectal surgery: A retrospective cohort study. *BMC Anesthesiol* 2020; 20:116.
32. Lavand'homme P, De Kock M, Waterloos H. Intraoperative epidural analgesia combined with ketamine provides effective preventive analgesia in patients undergoing major digestive surgery. *Anesthesiology* 2005; 103:813-820.
33. Edgley C, Hogg M, De Silva A, Braat S, Bucknill A, Leslie K. Severe acute pain and persistent post-surgical pain in orthopaedic trauma patients: A cohort study. *Br J Anaesth* 2019; 123:350-359.
34. McCowat M, Fleming L, Vibholm J, Dixon D. The Psychological predictors of acute and chronic pain in women following breast cancer surgery: A systematic review. *Clin J Pain* 2019; 35:261-271.
35. Dereu D, Savoldelli GL, Combescure C, Mathivon S, Rehberg B. Development of a simple preoperative risk score for persistent pain after breast cancer surgery: A prospective observational cohort study. *Clin J Pain* 2018; 34:559-565.



Supplement Fig. 1. ***The perioperative hemodynamic parameters. A, HR. B, MAP. Data are presented as the mean ± SD. There were no significant differences in HR and MAP at any single time point.***
Abbreviations: QLB: quadratus lumborum block, HR: heart rate, MAP: mean blood pressure, T0: preinduction, T1: before skin incision, T2: 1 min after skin incision, T3: just before the end of surgery, T4: before extubation, T5: 5 min after extubation, T6: just before PACU discharge.