Comparison of Ultrasound-guided Bilateral Anterior Quadratus Lumborum Block at the Lateral Supra-arcuate Ligament with Conventional Epidural Block in Patients Undergoing Laparoscopic Radical Gastrectomy: A Randomized Controlled Study

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Abstract

Background: To test the novel ultrasound (US)-guided bilateral anterior quadratus lumborum block (QLBA) at the lateral supra-arcuate ligament (supra-LAL) technique combined with postoperative intravenous analgesia was a viable alternative approach of conventional thoracic epidural analgesia (TEA) for laparoscopic radical gastrectomy (LRG). **Methods:** Three hundred and four patients scheduled for LRG were randomized 1:1 into QLBA group: receiving a novel pathway of US-guided bilateral QLBA at the supra-LAL before general anesthesia (GA) and patient-controlled intravenous analgesia (PCIA) after surgery, and TEA group: receiving TEA before GA and patient-controlled epidural analgesia following surgery. The difference in procedure time between the treatment groups was set as the primary endpoint. **Results:** Compared to TEA, procedure time was significantly shorter in the QLBA group (13.19 ± 0.78 vs. 15.65 ± 3.49, $P = 0.001$). At 5–10 min after block, QLBA group achieved more dermatomes coverage of cold sensory block with both $P < 0.001$ and less influence on mean artery pressure. Intraoperative consumption of propofol and remifentanil were comparable between the two groups (1116.21 ± 199.76 vs. 1166.45 ± 125.31 ug, $P = 0.245$ and remifentanil 1.83 ± 0.41 vs. 1.81 ± 0.37 ng, $P = 0.988$). However, the QLBA group was associated with less intraoperative consumption of norepinephrine and atropine, shorter time to urinary catheter removal, and out-of-bed activity. No significant difference in extubation time, pain scores at rest and exercising across all time points postoperation was observed between two groups. **Conclusion:** Compared with conventional TEA, the novel technique combined with PCIA was an equivalent effective multimodal analgesic protocol for LRG. There were some advantages of technical simplicity with shorter procedure time, wider anesthetized dermatomes, less influence on intraoperative hemodynamic variables, fewer postoperative adverse events, and improved several sensible parameters of postoperative recovery.

Trial Registration: The study was registered in the Chinese Clinical Trial Registry on November 02, 2022 (ChiCTR2200065325).

Keywords: Bilateral anterior quadratus lumborum block, epidural analgesia, lateral supra-arcuate ligament, patient-controlled epidural analgesia, patient-controlled intravenous analgesia, ultrasound guidance

Introduction

Gastric cancer (GC) remains one of the important cancers worldwide, which ranks fifth for incidence and fourth for mortality globally, responsible for over one million new cases and an estimated 769,000 deaths in 2020.[1] Laparoscopic radical gastrectomy (LRG) has been rapidly accepted and widely employed in the treatment of GC in various countries, especially in China, since the feasibility and safety of this minimally invasive approach were first reported by Kitano *et al*. in 1994.[2] Thoracic epidural analgesia (TEA) is widely considered the gold standard analgesia for pain management in open abdominal surgery since it

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provides a strong analgesic effect for pain control, improved respiratory function, and decreased chest-related morbidity.[3] Nevertheless, the use of TEA in laparoscopic surgery remains controversial. The study of Liu *et al*. showed that TEA exerted a little effect on early immunity, and contributed to postoperative analgesia and recovery when used as an anesthetic method for laparoscopic surgery. Its application value was higher than the transverse abdominis plane block.[4] Whereas some studies revealed that it may not be indispensable in the laparoscopic surgery population, its benefit of better postoperative pain alleviation is at the expense of increased risks of hypotension, motor weakness, and urinary retention as compared to the conventional opioid-based patient-controlled intravenous analgesia (PCIA).[5,6] Recently, multimodal analgesia (MMA) using combinations of analgesics with different mechanisms is recommended for perioperative analgesia regimen because it reduces opioid consumption, improves pain relief, minimizes adverse events, facilitates recovery after surgery, and decreases hospitalization stay.[7] As an emerging component of multimodal modalities, quadratus lumborum block (QLB) has been shown to provide effective somatic and visceral in abdominal surgery.[8] However, conventional QLB has disadvantages, including difficulty in identifying anterior thoracolumbar fascia, low success rate, and slow onset resulting in inaccurate effects. Currently, a novel pathway of anterior QLB (QLBA) at the lateral supra-arcuate ligament (supra-LAL) has been proposed by Wang Y *et al.* in 2020, which allows LA to be directly injected anterior to quadratus lumborum (QL) muscle at the level of supra-LAL to circumvent the obstacle of the lateral arcuate ligament (LAL); therefore, it provides a shorter way for LA to spread into the lower thoracic paravertebral space with the goal of blocking dermatomes at T6-L2 at 5 min after administration to overcome the shortcoming of the conventional QLB.[9,10] However, few researches have focused on the effects of this novel technique on perioperative analgesia in patients undergoing LRG for GC. We therefore designed this prospective randomized controlled trial to test the hypothesis that if using combinations of the novel technique of ultrasound (US)-guided bilateral QLBA at the supra-LAL with PCIA following surgery might be as effective as the conventional TEA for perioperative analgesia and a viable alternative due to the benefit of technical simplicity and enhanced postoperative recovery.

Methods

Study design and patients

In accordance with the Declaration of Helsinki, this prospective randomized controlled study was approved by the Scientific Research Ethics Committee of Putian First Hospital, affiliated with Fujian Medical University (PTFH2020-53X) and registered at the Chinese Clinical Trial Registry (ChiCTR2200065325). Written informed consent was obtained from each participant. A total of 304 patients scheduled for LRG for GC in our anesthesia center were recruited for the study from November 11, 2022, to April 30, 2023 [Figure 1]. Patients aged between 18 and 80 years with the American Society of Anesthesiologists (ASA) physical status classification score of II-III were included in the study. Exclusion criteria were as follows: (1) refusal to participate; (2) thoracic spinal deformities; (3) contraindications for regional anesthesia; (4) allergy to LA or opioids; (5) chronic use of narcotic analgesics; (6) severe cardio-cerebrovascular dysfunction or severe respiratory or hepatorenal disease; (7) psychiatric disease; and (8) body mass index (BMI) 35 ≥g/m^2.

Randomization and masking

Randomization was performed using a web-based system (www.randomization.com) with permuted blocks of six, and the allocation sequence was maintained on a secure website by a nurse anesthetist who was not involved in the study until it was delivered to faculty anesthesiologists performing the block procedures on patient's arrival at the operating room. Patients were randomly assigned into two groups in a 1:1 ratio to receive either US-guided bilateral QLBA at the supra-LAL combined with PCIA for postoperative pain management (QLBA group) or TEA in combination with patient-controlled epidural analgesia (PCEA) for pain control following surgery (TEA group). Blinding to group allocation applied for the investigators who were responsible for outcome assessment and data analysis.

Procedure of QLBA at the lateral supra-arcuate ligament

All blocks were performed by the same four skilled anesthesiologists with at least 4 years' expertise in regional anesthesia techniques. Patients were positioned in the prone position with routine monitors. US scans were conducted using a convex probe (2–5 Hz, Labat, Shenzhen Huasheng Medical Technology Co., LTD), which was placed 3.5–4 cm lateral to the fifth lumbar spinous processes with its orientation marker directedly to the iliac crest. The transverse process (TP) of the 1st lumbar vertebral (L_1) and the 12th rib was subsequently identified using this sagittal method. The LAL was visualized by slightly shifting the probe toward the outside to position over the tip of L_1 TP. A triangular compartment was consequently identified between the diaphragm fascia and the QL muscle at the supra-LAL level. Beyond that, the kidney lying below the LAL and diaphragm descending with respiration were also recognized between the 12th rib and the 2nd lumbar TP. After local anesthesia with 1 mL of 0.5% lidocaine, the 22-gauge puncture needle was advanced from the caudal side toward the cephalic position using in-plane technique [Figure 2]. After negative aspiration and certification of the precise position of the needle tip in the above-mentioned triangular compartment, 20 mL of 0.25% ropivacaine was slowly injected on each side following repeated aspiration to avoid advertent intravascular injection. The same procedure was conducted on the contralateral side. Patients were subsequently placed in a supine position. A cold test using 70% ethanol was performed to evaluate the dermatomes of cold sensory loss at 5 min–10 min after block by a second consultant anesthesiologist who was blind to patients' allocation.

Procedure of thoracic epidural analgesia

In all patients assigned to the TEA group, blocks were carried

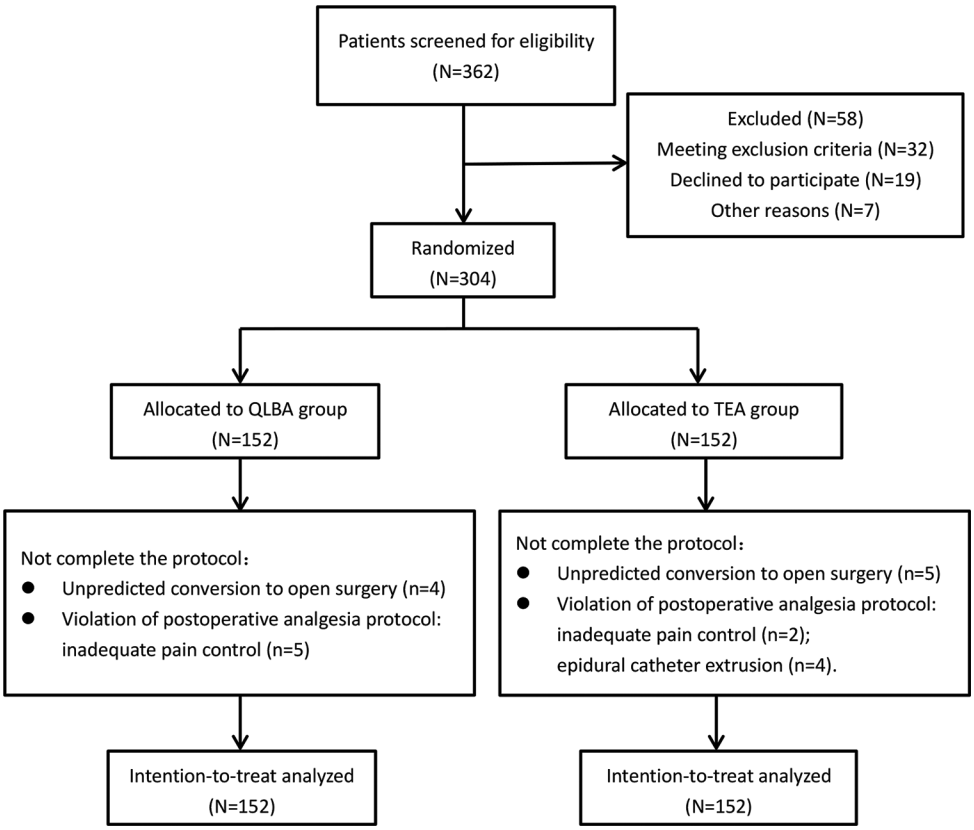

Figure 1: The consolidated standards of reporting trial diagram of patient recruitment. QLBA: Anterior quadratus lumborum block TEA: Thoracic epidural analgesia

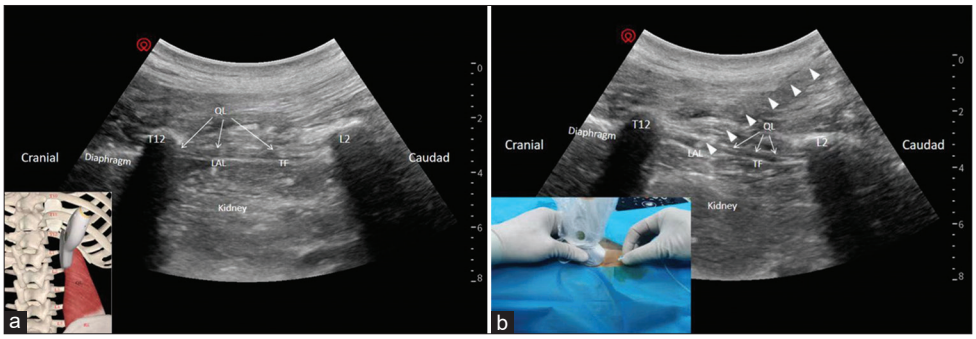

Figure 2: Anterior quadratus lumborum (QL) block at the lateral supra-arcuate ligament was performed under ultrasound guidance. (a) The lateral arcuate ligament was visualized by slightly shifting the probe toward outside to position over the tip of L1 transverse process using parasagittal approach. (b) Local anesthetic was directly injected anterior to QL muscle at the lateral supra-arcuate ligament using in-plane technique under the real-time guidance of ultrasound. QL: Quadratus lumborum, LAL: Lateral arcuate ligament

out by the same four anesthesiologists without US guidance. With the patient in the left lateral position, an 18G Tuohy needle was medially penetrated to the thoracic epidural space at the T9-10 level. Moreover, a catheter was subsequently advanced 3–5 cm into the thoracic epidural space after confirmation of successful epidural puncture using loss of resistance. After no aspiration of blood or cerebrospinal fluid, a 3 mL bolus of 1% lidocaine in combination with epinephrine (dilution 1:200,000) was injected through the catheter to exclude intrathecal placement. After completion of the procedure, the patient was positioned in a supine position. A 5 mL bolus of 0.33% ropivacaine was injected through the catheter followed by the same cold test as QLBA group. An intermittent 5 mL/h bolus injection of 0.33% ropivacaine was administrated through the catheter until the end of surgery depending on patients' vital signs.

Anesthesia protocol and surgery procedure

All patients were placed with the standard preoperative monitor, including electrocardiogram, noninvasive blood pressure, oxygen saturation, invasive radial arterial blood pressure, and bi-spectral index (BIS). Both right central venous access and peripheral venous access were established. After completion of regional anesthesia, 0.05 mg/kg midazolam,

0.5 ug/kg sufentanil, and 2.5 mg/kg propofol were administered intravenously for anesthesia induction. An appropriate type of endotracheal tube was placed by a video laryngoscope following intravenous induction of 1 mg/kg rocuronium and 3 min mask ventilation. Mechanical ventilation was by volume-controlled ventilation mode with the maintenance of respiratory rate of 12–14/min, tidal volume of 7–8 ml/kg, positive end-expiratory pressure of 5 cm H_2O, and end-tidal carbon dioxide 40–50 mm Hg. Intraoperatively, anesthesia was administered with intravenous target-controlled infusion of propofol (2 ug/mL) and remifentanil (3 ng/mL), as well as intermittent infusion of rocuronium as needed. When BIS >60, propofol was given as a bolus at a dose of 0.5 mg/kg, followed by an adjustment in the infusion rate until a BIS value in the range of 40–60 was maintained. Remifentanil was given intravenous bolus at a dose of 0.5 ug/kg, and then the infusion rate was increased in the range of 0.5 ug/kg/h–1 ug/kg/h for hypertension or tachycardia. If the infusion dose exceeded 1 mg/h, vasoactive agents were used. On the contrary, the infusion rate was gradually reduced when hypotension or bradycardia was present. In addition, fluids, atropine, and norepinephrine were given as needed to maintain the fluctuation of mean arterial pressure (MAP) and heart rate within 20% of the baseline value. At the end of each surgery, all patients received 0.5 mg of intravenous palonosetron.

All surgeries were performed by the same surgical team strictly using the same standardized four ports technique: LRG with modified Roux-en-Y anastomosis.[11] After surgery, patients were extubated after completely awake in the postanesthesia care unit.

Postoperative pain management

Postoperatively, the QLBA group received PCIA with 150 ug sufentanil diluted to 100 mL with 0.9% normal saline for 48 h. The infusion was administrated at the rate of 2 mL/h and supplemented by a rescue bolus of 2 mL admixture with a lockout time of 20 min. PCEA was administered with 100 mL of diluted solution containing 20 mL of 1% ropivacaine and 5 mg morphine for the TEA group for 48 h. The pump infuser was set to 2 mL/h for continuous infusion, and a rescue bolus of 2 mL was supplemented with a 20-min lock-out period. 50 mg flurbiprofen was intravenously injected as rescue analgesia if patients reported their Numeric Rating Scale (NRS) score at rest was >3 before removing the patient-controlled analgesia pump.

Outcome measures and data collection

The primary endpoint was the difference in the procedure time between two groups. Secondary endpoints included pain severity during rest and while exercising, which were assessed using the 11-point NRS (0 = no pain to 10 = pain as bad as you can imagine) at 0.5, 2, 6, 12, 24, and 48 h after surgery. Other secondary endpoints contained successful rate of puncture, procedure time, the dermatomes of cold sensory loss at 5 min and 10 min after block, MAP at 5 min and 10 min following block; intraoperative propofol, remifentanil and vasoactive agents consumption; intraoperative fluid blood loss and fluid volume; postoperative extubated time; rescue analgesic incidence during the first 48 h after surgery; duration of urinary catheterization; time to first out-of-bed ambulation after surgery; postoperative hospital stay duration and expense. Complications related to block, including hematoma, pneumothorax, and renal trauma, and adverse events associated with patient control analgesia, such as postoperative dizziness, nausea/vomiting, hypotension, and urinary retention, were also assessed.

Sample size calculation

PASS software, version 16 (NCSS, LLC., Kaysville, Utah, USA) was used to estimate sample calculation before the conduction of the present randomized controlled trial. Based on our pretest with 20 patients per group, the mean procedure time for QLBA and TEA groups is 12.96 and 15.65 min with standard deviation (SD) in the range of 2.79–6.42, respectively. We would like to generate a sample size for the study with 90% power at two-sided alpha of 5% to reject the null hypothesis of equal procedure time between the two groups. Taking 20% dropouts into account, the sample size is 152 per group to investigate which group has lower procedure time. The consumption of intraoperative propofol, remifentanil (mean ± SD) and the total QoR-40 scores within postoperative 48 h were 1215.26 ± 180.36 vs. 1267.38 ± 137.21, 1.84 ± 0.39 vs. 1.81 ± 0.32 and 168.24 ± 11.6 vs. 180.67 ± 20.9 in QLBA and TEA group, respectively. According to the same criteria, a sample of 83, 150, 75, and patients per group was calculated, compensating for 20% dropouts, respectively. Moreover, we performed a Mann–Whitney–Wilcoxon test instead of *t*-test for equivalence assessment for the NRS scores throughout the postoperative 48-h day between two different analgesia, 55 patients per group were calculated using two means of 3.2 and 3.8, a SD from 0.2 to 1.0 by 0.1 and a Tukey's Lambda distribution with Skewness value of 0.468 and Elongation of − 1.088. Therefore, the final sample size came up with 152 patients per group based on the primary endpoint of the difference in procedure time between two groups.

Statistical analysis

SPSS software, version 22.0 (SPSS Inc., Chicago, IL, USA) Statistical analysis was used for statistical analysis. Statistical significance was defined as $P < 0.05$. Data were described as mean ± SD for normally distributed continuous variables, median ± inter-quartile range for skewed variables, frequency and percentage for categorical variables. Independent *t*-test, Mann–Whitney *U* test, and Chi-square test were employed to compare means, median, and proportions, respectively. A generalized linear mixed model (GLMM) was used for NRS scores after surgery, and the Student–Newman–Keuls multiple comparison *post hoc* test was conducted to differentiate within groups. Intention-to-treat analysis was performed for all variables. Missing data were dealt with multiple imputation.

Results

The consolidated standards of reporting trial diagram of the

study are shown in Figure 1. Among 304 patients whose data were eligible for analysis, nine patients in QLBA group and 11 patients in TEA group deviated from the protocol because of the given reason, as shown in Figure 1. Table 1 shows the demographic characteristics of the 304 patients included in the present study. No significant differences were observed in terms of age, gender, BMI, the ASA score and clinical stage between two groups.

As shown in Table 2, the mean of procedure time was significantly lower in the QLBA group compared with the TEA group (13.19 ± 0.78 vs. 15.65 ± 3.49, $P = 0.001$). The successful rate of puncture was higher in QBLA group when compared to TEA group; however, there was no significant difference (100% vs. 90.1%, $P < 0.001$). At 5 after block, the majority in QLBA group and TEA group achieved a loss of cold sensation at dermatomes T8-L1 and T8-T10, respectively. The majority developed a cold sensory block in T5-L1 and T6-T11 at 10 min after QLBA and TEA, respectively. The bar in Figure 3a showed that percentage of cold sensory block on T10 (100% vs. 51.6%, $P < 0.001$), T11 (100% vs. 0%, $P < 0.001$), T12 (96.5% vs. 0%, $P < 0.001$), L1 (69.0% vs. 0%, $P < 0.001$) at 5 min after block and T11 (100% vs. 41.9%, $P < 0.001$), T12 (100% vs. 0%, $P < 0.001$), L1 (100% vs. 0%, $P < 0.001$), L2 (24.1% vs. 0%, $P < 0.001$) at 10 min postblock in QLBA group was significantly more than that in TEA group. In addition, number of dermatomes with loss of cold sensation was significantly larger in QLBA group than that in TEA group at 5 and 10 min after block, respectively (5 [3, 7] vs. 3 [2, 4], $P < 0.001$ and 8 [6, 10] vs. 5 [3, 7], $P < 0.001$) [Figure 3b]. The mean of MAP for QLBA and TEA group was decreased from 89.79 ± 4.71 versus 90.58 ± 5.28 at baseline ($P = 0.540$) to 86.59 ± 4.71 versus 89.06 ± 5.31 at 5 min after block ($P = 0.061$) and 86.59 ± 4.36 versus 81.52 ± 4.74 at 10 min after the block, respectively [Figure 4]. A significant reduction in the mean of MAP was observed in TEA group as compared to the QLBA group at 10 min after block ($P < 0.001$).

Table 1: Baseline characteristics of participating patients

Variables	QLBA group ($n=152$)	TEA group ($n=152$)	*P*
Age (years)	65.07±7.51	66.03±8.29	0.640
Female sex, *n* (%)	52 (34.2)	58 (38.2)	0.551
Height (cm)	164.31±7.27	163.13±8.78	0.574
BMI	22.58±3.12	22.62±2.53	0.957
ASA classification, *n* (%)			
II	98 (64.5)	106 (69.7)	0.393
III	54 (35.5)	46 (30.3)	
Hypertension present, *n* (%)	32 (21.1)	45 (29.6)	0.113
Diabetes present, *n* (%)	36 (23.7)	28 (18.4)	0.325
Coronary heart disease present, *n* (%)	30 (19.7)	43 (28.3)	0.107
Clinical stage, *n* (%)			
I	99 (65.1)	95 (62.5)	0.673
II	29 (19.1)	25 (16.4)	
III	22 (14.5)	29 (19.1)	
IV	2 (1.3)	3 (2.0)	
Lymphadenectomy, *n* (%)			
D1	18 (11.8)	10 (6.6)	0.281
D1+	79 (52.0)	85 (55.9)	
D2	55 (36.2)	57 (37.5)	

BMI: Body mass index, ASA: American Society of Anesthesiologists, QLBA: Anterior quadratus lumborum block, TEA: Thoracic epidural analgesia

Other outcomes are also summarized in Table 2. Intraoperative consumption of propofol (1116.21 ± 199.76 vs. 1166.45 ± 125.31 ug, $P = 0.245$) and remifentanil (1.83 ± 0.41 vs. 1.81 ± 0.37 ng, $P = 0.988$), intraoperative fluid blood loss 91.38 ± 63.57 vs. 103.87 ± 55.67 mL, ($P = 0.122$) and fluid volume (2100 [1600–2600] vs. 2000 [1500–2500] mL, $P = 0.074$), surgery time (5 [3.5–6.6] vs. 4.8 [4.0–5.6] h, $P = 0.621$) as well as postoperative extubated time (10 [7–13] vs. 11 [8–14] min, $P = 0.604$) were similar between two block groups, but significantly less consumption of vasoactive agents including atropine (0 [0–0] vs. 0.50 [0–1.0] mg, $P < 0.001$) and norepinephrine (0.10 [0–0.20] vs. 0.40 [0–0.80] mg, $P < 0.001$) was observed in QLBA group when compared to TEA group. Postoperatively, both two block modalities did not differ in the percentage of patients requiring rescue analgesia (11.2% vs. 8.6%, $P = 0.565$). GLMM analysis revealed that there were no statistically significant differences when the first 48 h average NRS scores during rest and while exercising were respectively compared between two groups (0.727 [95% confidence interval (CI): 0.545–0.970] vs. 0.802 [95% CI: 0.615–1.045], F = 0.241, $P = 0.624$ during rest and 4.606 [95% CI: 3.895–5.447] vs. 4.567 [95% CI: 3.887–5.364], F = 0.005, $P = 0.942$ while exercising) [Table 2]. Moreover, average NRS scores at 0.5, 2, 6, 12, 24, and 48 h after surgery were similar between two block groups ($P = 0.567$, 0.131, 0.431, 0.156, 0.252, 0.818 during rest and 0.340, 0.833, 0.629, 0.439, 0.728, 0.608 while exercising) [Table 3]. With regard to rehabilitation, there was no significant difference between the two groups in the time to first flatus and eating (2 [1, 3] vs. 2 [1, 3] d, $P = 0.844$ and 7 [5, 9] and 7 [5, 9] d, $P = 0.891$). On the other hand, significantly shorter duration of urinary catheterization and earlier time to out-of-bed ambulation were observed in the QLBA group as compared with TEA group (1.5 [0.5, 2.5] vs. 3 [2, 4] d, $P < 0.001$ and 1 [0, 2] vs. 3 [2, 4] d, $P < 0.001$). Moreover, patients in the QLBA group had less length of hospital stay and expense than patients in TEA group; however, it did not differ significantly (10 [8, 12] vs. 11 [9, 13] d, $P = 0.885$; 47676.07 ± 4251.68 vs. 48469.23 ± 6703.78 ￥, $P = 0.584$).

The presence of block-related severe complications, including hematoma, organ injury, and pneumothorax, was not observed in both two block groups. Postoperative nausea/vomiting (PONV) was found in 21.7% of patients in QLBA group and 16.4% of patients in TEA group, but a significant difference was not observed ($P = 0.307$). Significantly higher incidence of hypotension with symptoms of dizziness, headache and palpitations, as well as urinary retention, occurred in TEA group than that in QLBA group (5.9% vs. 39.4%, $P < 0.001$ and 0 vs. 21.7%, $P < 0.001$).

Table 2: Comparison between anterior quadratus lumborum block group and thoracic epidural analgesia group on primary, some secondary outcomes and side effects

Outcome	QLBA group (n=152)	TEA group (n=152)	χ^2/Z/t	P
Time of block procedure (min)	7.99±0.78	14.65±3.42	−10.221	<0.001
Successful rate of puncture, *n* (%)	152/152 (100.0)	137/152 (90.1)	15.779	<0.001
Intraoperative outcomes			1.770	0.413
Propofol dosage (g)	1116.21±199.76	1166.45±125.31	−1.175	0.245
Remifentanil dosage (ng)	1.83±0.41	1.81±0.37	0.181	0.988
Atropine dosage (mg)	0 (0–0)	0.50 (0–1.0)	−3.636	<0.001
Norepinephrine dosage (mg)	0.10 (0–0.20)	0.40 (0–0.80)	−6.288	<0.001
Blood loss (mL)	91.38±63.57	103.87±55.67	−1.548	0.122
Fluid infusion (mL)	2100 (1600–2600)	2000 (1500–2500)	−1.784	
Surgery time (h)	5 (3.5–6.6)	4.8 (4.0–5.6)	−0.494	0.621
Postoperative outcomes				
Extubated time (min)	10 (7–13)	11 (8–14)	−0.519	0.604
Incidence of rescue analgesic, *n* (%)	17/152 (11.2)	13/152 (8.6)	0.592	0.565
Duration of urinary catheterization (day)	1.5 (0.5–2.5)	3 (2–4)	−3.653	<0.001
Time to first out-of-bed ambulation (day)	1 (0–2)	3 (2–4)	−4.864	<0.001
Time to first flatus (day)	2 (1–3)	2 (1–3)	−0.197	0.844
Time to first eat (day)	7 (5–9)	7 (5–9)	−0.138	0.891
Hospital stay duration (day)	10 (8–12)	11 (9–13)	−0.144	0.885
Hospitalization expense (￥)	47,676.07±4251.68	48,469.23±6703.78	1.797	0.584
Nausea/vomiting, *n* (%)	33/152 (21.7)	25/152 (16.4)	1.364	0.307
Hypotension, *n* (%)	9/152 (5.9)	56/152 (39.4)	47.888	<0.001
Urinary retention, *n* (%)	0	33/152 (21.7)	37.018	<0.001

QLBA: Anterior quadratus lumborum block, TEA: Thoracic epidural analgesia

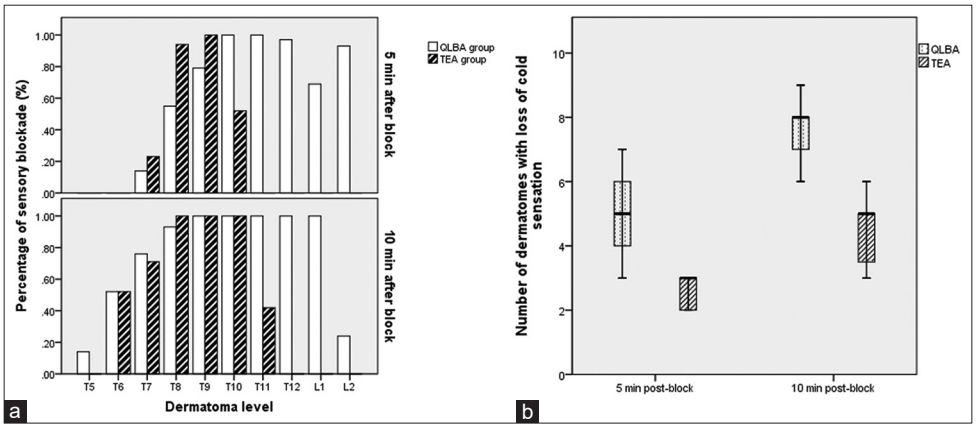

Figure 3: (a) Percentage of loss of cold sensation at each dermatome observed at 5 and 10 min after block. Significantly wider sensory block area was achieved in the QLBA group in comparison with the TEA group at 5-and 10-min postblock, respectively. T = Thoracic; L = Lumbar. (b) Statistical box plot shows the number of dermatomes with sensory blockade over time. *P < 0.001. QLBA: Thoracic epidural analgesia, TEA: Thoracic epidural analgesia

Discussion

To the best of our knowledge, the present study was the first randomized controlled trial to estimate the analgesic efficacy and benefits of US-guided bilateral QLBA at the supra-LAL in combination with PCIA as MMA protocol for LRG. The results were consistent with our hypothesis that this new technique not only demonstrated an equivalent efficacy of analgesia as the conventional TEA but also had some advantages of shorter procedure time, higher successful rate of puncture, less influence on intraoperative hemodynamic variables as well as reduced adverse events associated with postoperative analgesia to enhance recovery after surgery.

Minimally invasive laparoscopic technology has been widely used since it was first applied to radical gastrectomy in 1994, which could reduce intraoperative trauma and improve quality of life owing to less postoperative complication compared with the conventional open surgery.[12] Nevertheless, this laparoscopic method is associated with longer procedure time and more complicated operation with the establishment of carbon dioxide pneumoperitoneum. Hence, it requires

Table 3: Numeric Rating Scale scores during rest and while exercising during the first 48 h postoperation in intention-to-treat analysis

Group	NRS scores during rest (mean±SD)				NRS scores while exercising (mean±SD)			
	Mean (95% CI)	Contrast estimate (95% CI)	*F*	*P*	Mean (95% CI)	Contrast estimate (95% CI)	*F*	*P*
QLBA group (*n*=152)	0.727 (0.545–0.970)	−0.074 (−0.373–0.224)	0.241	0.624	4.606 (3.895–5.447)	0.039 (−1.027–1.106)	0.005	0.942
TEA group (*n*=152)	0.802 (0.615–1.045)				4.567 (3.887–5.364)			

QLBA: Anterior quadratus lumborum block, TEA: Thoracic epidural analgesia, NRS: Numeric Rating Scale, SD: Standard deviation, CI: Confidence interval, NRS: Numeric rating scale

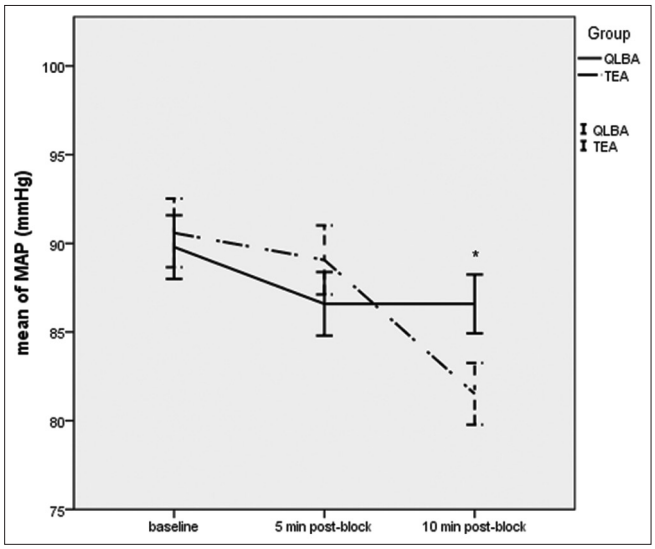

Figure 4: The changes of mean arterial pressure before and after each procedure in two groups. Significant difference was observed between two groups at 10 min after block. *$P < 0.001$. MAP: Mean arterial pressure, QLBA: Thoracic epidural analgesia, TEA: Thoracic epidural analgesia

adequate intraoperative anesthesia and sedation. In addition, moderate-to-severe acute pain due to utility incision and visceral inflammatory reaction remains a crucial problem after surgery, which would cause immobility and decreased intestinal function to inhibit postoperative recovery. Therefore, it is critical to take optimal perioperative analgesic strategies for LRG.

Systematic review with high-quality evidence has shown that epidural analgesia accelerates the recovery of gastrointestinal function due to a reduction in opioid administration, a blockade of sympathetic innervation, and a direct effect of systemic local anesthetics.[13] However, the performance of TEA has an ambagious learning curve in clinical practice, and its application is limited by some contraindications, including coagulation disorders, thoracic spinal deformity, and severe respiratory or cardiac disease. Previous study has reported a failure rate up to 32% in the performance of TEA, and there is a possibility of malposition of the catheter in the spinal space, resulting in severe postoperative neurologic deficits.[14,15] According to our results, failed TEA occurred in 10.5% of patients, which was predefined as failure to insert a puncture needle at the thoracic epidural space at 2cn attempt at the same entry point, although our anesthesiologists had expertise in this technique. Furthermore, the management of PCEA requires expertise across several domains of care, prolapse of the epidural catheter was observed in one patient in TEA group and resulted in inadequate postoperative analgesia. On the other hand, epidural analgesia, especially using a high concentration of LA is also associated with the risk of developing postoperative PONV, hypotension, and urinary retention, which were all observed in our TEA group. Considering the strong analgesic effect and inevitable adverse events of TEA, it is questionable whether TEA with PCEA is necessary for minimally invasive laparoscopic gastrectomy.

As an emerging regional block, QLB has been administrated before surgery in patients undergoing general anesthesia (GA) with the effect of suppressing pain reflex, reducing intraoperative anesthetic consumption, and providing effective postoperative analgesia. Since the first description of a US-guided QLB to inject LA adjacent to the QL muscle with the goal of anesthetizing the thoracolumbar nerves by Blanco *et al*., the technique has been increasing used.[16] The exact mechanism of QLB for analgesia has not been fully clarified. Nevertheless, the three-layered thoracolumbar fascia provides a potential pathway for the spread of LA from the abdominal to the thoracic cavity and paravertebral space to achieve both somatic and visceral analgesia effects according to the elaborating trunk sonoanatomy.[17,18] It has been proved that in the anterior QLB, LA is applied anterior to QL muscle leading to spread of LA through the thoracic paravertebral space to block the somatic, the celiac ganglion or thoracic sympathetic trunk of lower thoracic segments. Elsharkawy *et al*. reported an in-plane US-guided subcostal anterior QLB near to the 12th rib, and their cadaveric study demonstrated that the anterior approach produced broader coverage of the lower to mid-thoracic region, resulting in a reliable loss of dermatomal sensation to cold test from T6-7 to L1-2, when compared with the posterior QLB.[19] Whereas, this conventional approach for QLB has some defects in clinical practice. It usually takes 20–30 min to get the analgesia effect with anterior QLB, because LA spreads from the fascia space around QL muscle to the thoracic paravertebral space through the posterior pathway of arcuate ligaments requires time.[20] In addition, the success rate will be reduced when it is difficult to identify the anterior thoracolumbar fascia from the posterior renal fascia and the investing fascia of QL muscle using US scan, especially in obese or elderly patients.[9] All these above-mentioned limitations may result in an unstable anesthetic effect. To meet the growing demands for

rapid onset of reliable analgesia efficacy, a novel pathway of anterior QLB under US guidance was proposed by Li *et al*. in 2020. This technique is a slight modification of the subcostal QLB, which may be attributed to the shorter pathway for LA to spread toward the low thoracic paravertebral space since it is directly injected anterior to QL muscle at the supra-LAL and circumvents the obstacle of the medial and LAL.[20] Shi *et al*. estimated dermatomal coverage of single-injection US-guided parasagittal approach to anterior QLB block at the supra-LAL. Their data showed that at 5 and 10 min after block, the patients respectively achieved the sensory block of dermatomes T9-T12 and T7-L1, which indicated the rapid onset with reliable dermatomal coverage.[10] LRG is usually performed with an incision at the midline and multiple endoscopic operation holes at the bilateral abdominal wall, which requires bilateral sensory block ranges of T5 to T12. Therefore, this innovative parasagittal technique was bilaterally performed for QLBA group in the present study, and the injection site was moved up above the LAL among the 12th rib, the TP of L2, and the lateral aspect of the TP of L1, which allowed LA to diffuse faster into the lower thoracic paravertebral space in comparison with conventional approaches. Our results were consistent with the action mechanism of the QLBA at the supra-LAL, the highest and lowest level of sensory block were T7 and L2 at 5 min and T5 and L2 at 10 min after block. All patients respectively reported the complete loss of dermatomal sensation to cold test from T6 to L1 and T4 to L2 at 5 and 10 min after block, which suggested this approach was suitable for intraoperative anesthesia of LRG. In addition, the fluctuation of MAP after block was significantly lower in QLBA group as opposed to TEA group, which illustrated that although a wider dermatome of sensory block was achieved, QLBA approach had less influence on hemodynamic changes when compared with the conventional neuraxial anesthesia. Moreover, a higher successful rate of puncture as well as a shorter procedure time were observed in QLBA group based on the clear anatomical features under US scanning when compared with those in TEA group. This result indicated that a simple anatomy without complex fascial interspace structures and high imaging quality under US scanning could be achieved when performing the anterior QLB at the supra-LAL using this paramedian long-axis technique, which made it easier to achieve success.

According to the previous literature, 62 patients who underwent laparoscopic donor nephrectomy were randomized to receive bilateral QLB using 0.25% bupivacaine and intraoperative fentanyl requirement was not significantly different between the QLB group and the epidural group (50 [34.66–83.08] vs. 50 [40.73–101.21] ug, P = 0.442). Whereas, ephedrine requirement was higher in the epidural group in comparison with the QLB group (0 [1.37–9.59] vs. 10 [5.48–14.39] mg, P = 0.026). In addition, the mean dosage of bupivacaine used in the QLB group was significantly lower than that used in the epidural group (200.00 ± 0.00 vs. 253.19 ± 11.12, P < 0.001). We also advocate that intraoperative consumption of propofol and remifentanil were significantly comparable between the QLBA and TEA groups; however, intraoperative requirements of atropine and norepinephrine were significantly lower in the QLBA group than those in the TEA group during our observation. These coincident results illustrated that the QLBA technique had less influence on changes in intraoperative hemodynamic variables in comparison with TEA.

As postoperative analgesia, PCIA may be the preferred modality due to safe and effective analgesia and recovery after laparoscopic gastrectomy.[6] Recent evidence suggests that the combined use of QLB and PCIA is a viable alternative approach for perioperative analgesia in LRG.[21] Several previous studies demonstrated that QLB could produce effective and long-lasting analgesia from 6 to 48 h after surgery.[22,23] We found that NRS pain scores at rest and during exercising at each time point in 48 h after recovery from anesthesia were comparable between QLBA and TEA approach [Figure 3]. The 48-h incidence of rescue analgesia was not significantly different between the two groups. These above-mentioned results suggested that MMA using combinations of QLBA and PCIA had comparable analgesic effects with continuous TEA for the 48 h after LRG.

As is well known, the volume and dose of LA used in conventional QLB is large, and a considerable part is deposited in the lumbar fascia space, leading to LA poisoning such as a metallic taste, tinnitus, dizziness, and tachycardia/bradycardia as well as motor blockade. However, if LA was directly injected into the anterior of QL muscle at the supra-LAL, the tension of LAL would result in a full diffusion of LA toward the effect site with less caudally leaky in the lumbar fascial space.[20,24] Therefore, no presence of LA poisoning and motor weakness was observed in the QLBA group. Based on our results, no incidence of pneumothorax and Admakiewicz artery injury occurred in the QLBA group, which emphasized the benefit of using US as the tool for guiding block.[25,26] When considered along with the aforementioned unfavorable adverse events related to postoperative epidural analgesia, it has been reported that temporary hemodynamic instability might occur due to the sympathetic blockage of epidural analgesia, which may slow down ambulation and even recovery from surgery.[27] Moreover, early removal of the urinary catheter is recommended because longer urinary catheterization can delay mobilization and recovery after surgery.[28] According to our observations, we were not aware of any incidence of hypotension and urinary retention in the QLBA group. Therefore, the time to removal of the urinary catheter and first out-of-bed activity was significantly shortened in the QLBA group as opposed to TEA group, which might enhance recovery after surgery. Therefore, shorter lengths of postoperative hospital stay and less hospital expense were subsequently observed in the QLBA group in comparison with that in the TEA group (P < 0.05).

There were some limitations. First, the anesthesiologists could not be blinded to the analgesia method, and patients failed to be blinded due to the insertion of the catheter for PCEA, which might lead to the biased postoperative outcomes. Second, NRS scores, first time to flatus and activity which was adopted to evaluate postoperative pain intensity and function recovery

were highly subjective. Third, standard GA without regional block was not included in the present study for placebo control, which needed to be improved in further studies with a large sample.

As an emerging regional block, US-guided bilateral QLBA at the supra-LAL combined with postoperative PCIA was shown to provide the comparable perioperative analgesia as the conventional TEA. Besides, compared with neuraxial anesthesia, there were some advantages including technical simplicity with shorter procedure time, wider anesthetized dermatomes, less influence on intraoperative hemodynamic variables, fewer postoperative adverse events, and improved several sensible parameters of postoperative recovery.

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Conflicts of interest

There are no conflicts of interest.

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