ORIGINAL ARTICLE

Comparison of the Effects of Ultrasound-guided Erector Spinae Plane Block and Wound Infiltration on Perioperative Opioid Consumption and Postoperative Pain in Thoracotomy

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Abstract

Objective: To compare the effects of preoperative ultrasound-guided erector spinae plane block (ESPB) and preoperative wound infiltration on perioperative opioid consumption and postoperative pain in thoracotomy.
Study Design: Randomised controlled trial.
Place and Duration of Study: Department of Anesthesiology, Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, from October 2018 to April 2019.
Methodology: Sixty adult patients undergoing open esophagectomy were allocated randomly into two groups: experimental group (ultrasound-guided ESPB group, n = 30) and control group (wound infiltration group, n = 30). In ultrasound-guided ESPB group (group EB), ESPB with 20 ml of 0.5% ropivacaine was performed at the level of thoracic 5 transverse process. Whereas, in wound infiltration group (group WI), 20 ml of 0.5% ropivacaine was injected subcutaneously along the marked line of skin incision for surgery and chest tube placement. The perioperative opioid consumption, pain scores at rest and during coughing immediately after surgery, at postoperative day (POD) 1 and POD 2, consumption of rescue analgesic tramadol and postoperative opioid-related adverse events were all assessed.
Results: Compared with group WI, the intraoperative and postoperative opioid consumptions, postoperative tramadol consumption were significantly less in group EB ($p < 0.05$). Moreover, the postoperative pain scores immediately after surgery, at POD 1 and POD 2, were all lower in group EB compared to group WI ($p < 0.05$). Significantly, the postoperative incidence of nausea and vomiting was lower in group EB than that in group WI ($p = 0.021$).
Conclusion: Compared to wound infiltration with local anesthetics, preoperative ultrasound-guided ESPB could significantly reduce perioperative opioid consumption, provide a better postoperative analgesia and reduce opioid-related adverse events in thoracotomy.

Key Words: *Thoracotomy, Erector spinae plane block, Wound infiltration, Opioid consumption, Postoperative pain, Opioid-related adverse events.*

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INTRODUCTION

At present, opioids are the most widely used perioperative analgesics for surgeries, especially for stressful major surgeries, such as open esophagectomy.[1] However, high-dose opioid results in severe nausea, vomiting, pruritus, constipation; and even life-threatening complications, such as respiratory depression.[1] Thus, in order to avoid high-dose opioid, use of regional nerve block technique as an adjunct to general anesthesia is considered to be an effective option.[2] Conventionally, thoracic epidural block is the gold standard for thoracotomy pain.[3] However, the postoperative hypotension and urinary retention caused by epidural block and coagulation concerns for placement and removal are always potential risks to be considered in clinical practice.[3] Moreover, the reported failure rate of thoracic epidural block is as high as 12%[4]; and the analgesic effect of this technique varies among different patients.[4] Therefore, there continues to be growing interest in seeking more safer and simpler regional nerve block techniques for thoracotomy.

The erector spinae plane block (ESPB) is a novel truncal interfascial plane block, which is first found effective in

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treating thoracic neuropathic pain.[5] In a recent randomised clinical research by single-dose injection of local anesthetics deep into the erector spinae muscle, the ESPB could effectively alleviate acute postoperative pain following thoracotomy.[6] The significant advantage of ESPB is that, under the ultrasound guidance, it becomes a safe and simple effective regional nerve block technique.[5] Wound infiltration with local anesthetics is a very simple and effective local analgesic technique.[7,8] As a previous randomised trial reported, wound infiltration with ropivacaine could significantly reduce postoperative pain and postoperative analgesic consumptions in thoracotomy.[9]

To the authors' best knowledge, until now, no randomised, controlled, clinical study has been conducted to compare the effects of preoperative ultrasound-guided ESPB and wound infiltration with local anesthetics on perioperative opioid consumption and postoperative pain in thoracotomy.

The aim of this study was to compare the effects of ultrasound-guided ESPB and wound infiltration with local anesthetics on intraoperative and postoperative opioid consumptions, postoperative pain and post-operative opioid-related adverse events in thoracotomy.

METHODOLOGY

This single centre, randomised, controlled clinical study was approved by the Institutional Ethics Committee of National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (NCC201804009), and registered on ClinicalTrials.gov (ChiCTR1800016583). The written informed consent was obtained from every patient. Patients with infections at the site of injection for ultrasound-guided ESPB or wound infiltration; neuropathy; coagulation disorders; morbid obesity (body mass index $\geq$40 kg/m^2); allergy to ropivacaine; greater than first-degree heart block; bradycardia (heart rate <60 bpm); pregnancy; clinically significant cardiovascular, pulmonary, hepatic or renal diseases; psychiatric illnesses that would interfere with assessment of pain score and those given a painkiller within one week before surgery were excluded from this study. Initially seventy-two patients with lower thoracic esophageal cancer, American Society of Anesthesiologists (ASA) physical status I and II, aged 30 to 65 years and selected for open thoracic surgery (Sweet procedure) were recruited in this study. All patients were able to communicate well and understood how to evaluate their pain score.

In order to eliminate potential confounders from surgeons, all open thoracic surgeries were performed by the same experienced surgical team. All patients were randomly allocated into the following two groups using a computer-generated random number table: experimental group (ultrasound-guided ESPB group) and control group (wound infiltration group). The group allocation numbers were concealed in sealed opaque envelopes that were opened after enrollment of the patients. In ultrasound-guided ESPB group (group EB), the preoperative ultrasound-guided ESPB with 20 ml of 0.5% ropivacaine was performed ipsilaterally before the general anesthesia induction. In wound infiltration group (group WI), after general anesthesia induction, 20 ml of 0.5% ropivacaine was injected subcutaneously along the marked line of skin incision for surgery and chest tube placement 30 mins before skin incision. After wound infiltration, the injectate was confirmed to be in the subcutaneous tissue by ultrasonography. During preoperative interview, patients were taught how to evaluate their pain score by the numerical pain rating scale (NRS). The flowchart of this study protocol is shown in Figure 1.

On arrival at the operating room, routine monitoring for esophagectomy, including electrocardiography, invasive blood pressure, and pulse oxygen saturation (SpO2), were done. In group EB, before general anesthesia induction, the patient was placed in a right lateral decubitus position and a high-frequency linear ultrasound transducer (GE LOGIQe, Wauwatosa, Wisconsin) was placed in a longitudinal orientation 3 cm lateral to the thoracic (T) 5 spinous process. Then three muscles were identified superficial to the hyperechoic transverse process shadow as follows: trapezius, rhomboid major, and erector spinae (Figure 2). Under the ultrasound guided, an 8-cm 22-gauge block needle (Contiplex; B Braun, Melsungen, Germany) was inserted in-plane in a caudad-to-cephalad direction until the tip laid in the surface of the transverse process. Correct needle tip position was confirmed by visualising linear fluid spread that separated the erector spinae muscle from the transverse process. Then, 20 ml of 0.5% ropivacaine was injected deep to the erector spinae muscle (Figure 2). The assessment of cutaneous sensory block by pinprick was performed 30 minutes later. Also, the complications caused by puncture procedure of ESPB, including hematoma and pneumothorax, were assessed and recorded. After confirmation and assessment of the sensory block to pinprick, the general anesthesia induction was initiated.

In both groups, the general anesthesia was inducted with 2 mg/kg of propofol, 0.3 μg/kg of sufentanil, 0.2 mg/kg of cisatracurium. Then, the general anesthesia was maintained by inhaling 2.5%-3.0% sevoflurane (1.3-1.5 MAC) to keep the bispectral index (BIS) value between 40 and 60. The one-lung ventilation was initiated when the operation was started. A posterolateral incision in the sixth intercostal space on the left side of the chest was made to dissociate the esophagus and clear the way to access the lymph nodes in the thoracic region. The diaphragm was opened for dissociation of the stomach to clear the way for access to the abdominal lymph nodes. The anastomosis was performed at the top of the

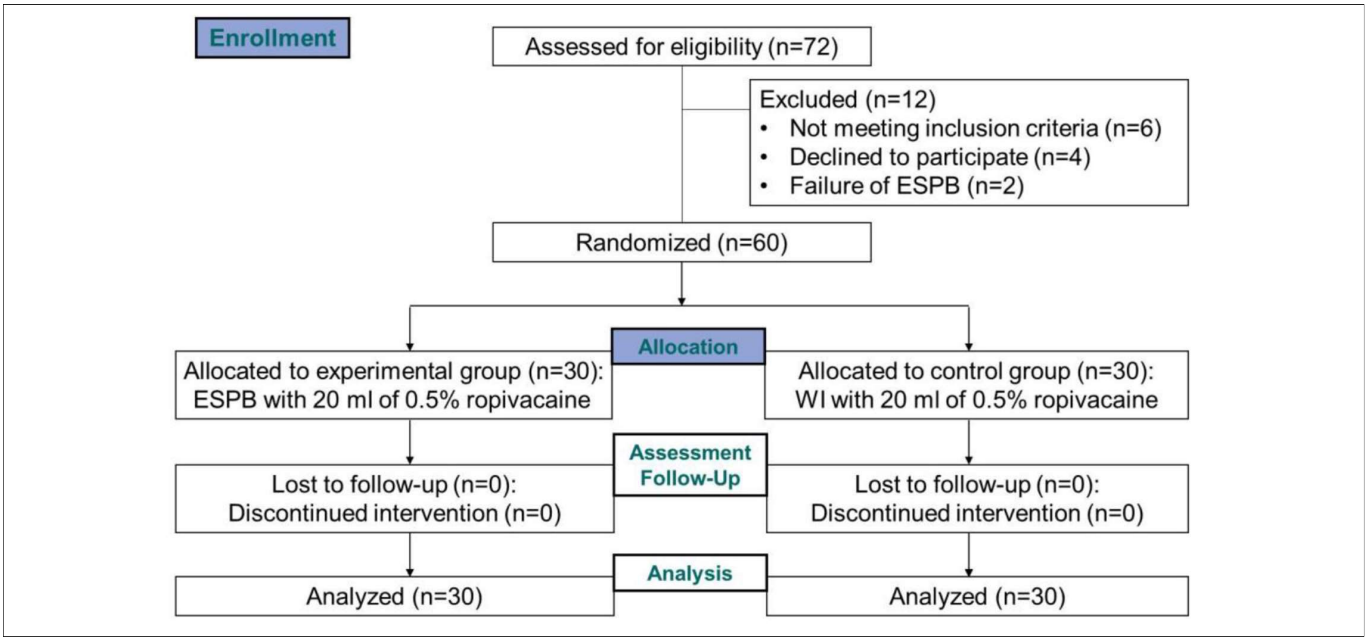

Figure 1: Consort flow diagram of this study.

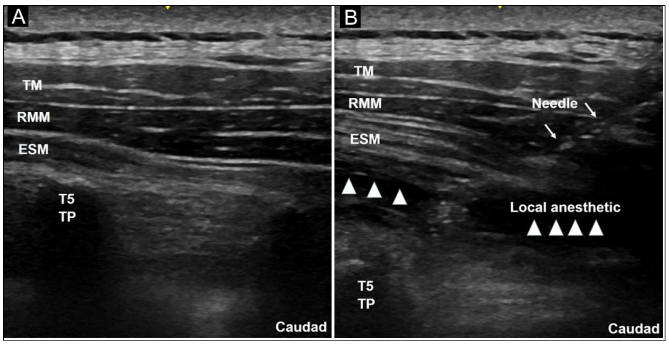

Figure 2: The ultrasound-guided ESPB performed deep to the erector spinae muscle (ESM) in a patient in the right lateral decubitus position. (A) Ultrasound imaging of the ESM at the level of the fifth thoracic vertebra. (B) Injection of ropivacaine into the interfascial plane deep to ESM produced a visible fluid spread (white solid triangles) beneath the ESM.
TM = Trapezius; RMM = Rhomboid major; ESM = Erector spinae muscle; T5 = The fifth thoracic vertebra; TP = Transverse process.

thorax. During the surgical procedure, 0.2 μg/kg of sufentanil was administered intravenously in both groups when the systolic arterial pressure exceeded 120% of the preoperative value or the heart rate exceeded 100 bpm. This dose was repeated every 10 minutes until the blood pressure or heart rate returned to the required limits. The consumption of sufentanil during general anesthesia in each group was recorded, and cisatracurium was administrated as required. At the conclusion of surgical procedure, a chest drain was placed, and the patient controlled intravenous analgesia (PCIA) infusion was initiated. Morphine was the opioid of choice for PCIA unless the patient had allergic reaction or other contraindications. Secondary alternatives included fentanyl or sufentanil. The initial recommended starting dose settings included: no basal rate and 2 mg every 10 minutes of demand dosing. After the operation, the patient was transferred to the postanesthesia care unit (PACU). The numerical pain rating scale (NRS) was used to assess patient-reported pain at rest and during coughing immediately after surgery, at postoperative day (POD) 1 and POD 2. When the NRS was more than 3 at rest or during coughing, the demand dosing of PCIA was given. If the NRS was still more than 3, 100 mg of intravenous tramadol was given as a rescue analgesic. For every patient, the consumption of morphine and tramadol for postoperative analgesia was recorded. Opioid-related adverse events after the operation, such as respiratory depression, nausea, vomiting, pruritus and uroschesis were also recorded.

The primary study endpoint was intraoperative sufentanil consumption. The dermatomal level of sensory block by ultrasound-guided ESPB, the pain scores immediately after surgery, at POD 1 and POD 2, the postoperative consumptions of morphine and tramadol, the incidence of postoperative opioid-related adverse events were used as the secondary endpoint.

Based on the result of previous study,[10] excluding 0.2 μg/kg of sufentanil for induction, the average supplementary consumption of intraoperative sufentanil was 0.261 μg/kg/h for thoracic surgery. On the basis of preliminary experimental data, a 15% reduction of intraoperative sufentanil consumption was considered clinically significant. Under these conditions, by using statistical software PASS (NCSS, LLC), a sample size of 24 patients was calculated with 90% power at a two-sided alpha level of 0.05. Ultimately, we recruited 30 patients in each group for a total of 60 patients considering possible dropouts.

Continuous variables were presented as means ± standard deviation or median (25^{th} to 75^{th} centiles), and categorical data were presented as number and

percentages. Normality was tested by the Kolmogorov-Smirnov analysis. For appropriate comparisons between the two groups, the Chi-square test, Student t-test, Mann-Whitney U-test, or Fisher exact test was used, if needed. All data were processed by IBM SPSS Statistics 21.0 (IBM Inc., New York, NY). A two-sided p-value less than 0.05 was considered to be statistically significant.

RESULTS

Initially, seventy-two patients were recruited in this study. Six patients in group EB were excluded because they did not meet the inclusion criteria (one patient was known allergy to ropivacaine, three patients had significant cardiovascular diseases, the other two patients were diagnosed with bradycardia); four patients declined to participate in this clinical study; and two patients in group EB were excluded because the failure of ultrasound-guided ESPB. Thus, 60 patients remained for the study.

Table I: Demographic, surgical and anesthetic data.

Demographic, surgical and anesthetic data	Treatment group		Significance
	Group EB (n=30)	Group WI (n=30)	
Sex (male/female)	18/12	17/13	0.793
Age (year)	56.5 ±5.1	56.1 ±4.9	0.739
Weight (kg)	64.7 ±4.2	65.5 ±3.7	0.476
Height (cm)	168.7 ±5.5	169.2 ±4.9	0.694
BMI (kg/m^2)	22.8 ±1.8	22.9 ±1.4	0.822
ASA (I/II)	13/17	15/15	0.796
Duration of surgery (min)	150.9 ±11.9	149.5 ±12.4	0.642
Duration of anesthesia (min)	178.4 ±11.4	179.2 ±13.4	0.796

BMI, body mass index; ASA, American Society of Anesthesiologists.

Table II: Analgesic data, postoperative pain scores and postoperative opioid-related adverse events.

Analgesic data, pain scores and opioid-related adverse events	Treatment group		Significance
	Group EB (n = 30)	Group WI (n = 30)	
Intraoperative sufentanil consumption (μg/kg/h)	0.166 ±0.016	0.274 ±0.019	<0.001
Pain score at rest immediately after surgery (numerical)	1.9 ±1.2	3.6 ±1.5	<0.001
Pain score at rest at POD 1 (numerical)	3.2 ±1.4	4.8 ±1.5	< 0.001
Pain score at rest at POD 2 (numerical)	2.9 ±1.3	4.0 ±1.4	0.003
Pain score during coughing immediately after surgery (numerical)	2.1 ± 1.2	3.8 ±1.5	< 0.001
Pain score during coughing at POD 1 (numerical)	4.5 ±1.9	5.8 ±2.1	0.011
Pain score during coughing at POD 2 (numerical)	4.0 ±1.3	5.3 ±1.5	0.001
Postoperative morphine consumption (mg)	10.4 ±5.2	19.1 ±6.9	<0.001
Tramadol usage (Used/Not used)	3/27	11/19	0.03
Respiratory depression	0	0	-
Nausea and vomiting	2 (6.7%)	10 (33.3%)	0.021
Pruritus	0	0	-
Uroschesis	0	0	-

There were no significant differences in demographic and surgical data between the two groups (Table I). The sufentanil consumption during the surgery was significantly lower in group EB than that in group WI (Table II). Compared with group WI, the pain scores at rest or during coughing evaluated by NRS immediately after surgery, at POD 1 and POD 2, were all significantly lower in group EB (Table II). Compared with group WI, the postoperative morphine consumption was significantly lower in group EB (Table II). Moreover, the tramadol used for rescue analgesia was significantly less in group EB than that in group WI (Table II). After the surgery, no respiratory depression, pruritus or uroschesis was observed in either group (Table II). Compared with group WI, the incidence of postoperative nausea and vomiting in group EB was much lower (Table II).

Successful ultrasound-guided ESPB was accomplished in 30 patients in group EB. A sensory loss to pinprick from T3 to T9 over the entire posterolateral aspect of the left hemithorax, extending anteriorly to the midclavicular line was obtained in 16 patients. A sensory block over the T2 to T8 dermatomes was obtained in 10 patients. There was an area of blocked sensation to pinprick extending from T2 to T9 in a cephalocaudal direction in 4 patients (Figure 3). No complications related to ultrasound-guided ESPB technique and local anesthetic toxicity were observed in group EB. Moreover, no complications related to local anesthetic toxicity were observed in group WI.

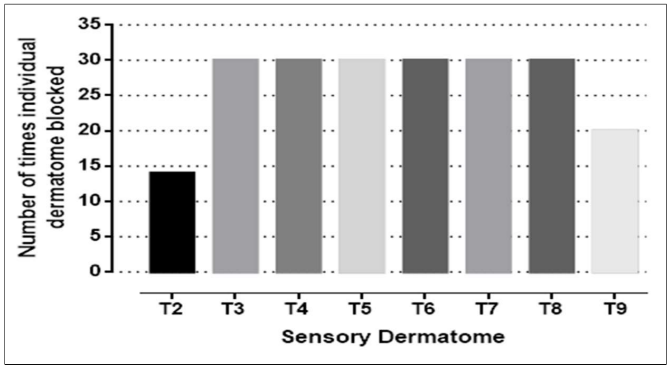

Figure 3: Bar graph showing the number of times each individual sensory dermatome was blocked (Y-axis), X-axis represents sensory dermatomes range from T2-T9.
Abbreviations: T2, Second thoracic vertebra; T3, Third thoracic vertebra; T4, Fourth thoracic vertebra; T5, Fifth thoracic vertebra; T6, Sixth thoracic vertebra; T7, Seventh thoracic vertebra; T8, Eighth thoracic vertebra; T9, Ninth thoracic vertebra.

DISCUSSION

As shown in the present study, ultrasound-guided ESPB induced a sensory loss to pinprick from T2 to T9 in the left hemithorax. In a recent clinical report, Adhikary *et al.*[11] showed that 20 ml of 0.5% ropivacaine injected *via* ESPB at T5 spinous process could provide sensory block between the T3 to T9 dermatomes, which was similar to the result of this study. The ESPB, first described by Forero *et al*. in 2016, was found to be effective in analgesia for thoracic neuropathic pain.[5] As

a previous cadaveric study found, at the exit from each intervertebral foramen, that the upper thoracic spinal nerve split into a ventral and dorsal ramus.[5] After passing through the costotransverse foramen, the dorsal ramus ran posteriorly and ascended into the deep plane of the erector spinae muscle. The ventral ramus extended laterally as the intercostal nerve and travelled deep to the internal intercostal membrane. Ultimately, the nerve branch which innervated the lateral and partial anterior thoracic wall arose from it.[5,12] Based on the above-mentioned cadaveric investigation, the ultrasound-guided ESPB was performed in this study. Previously, several studies found that 20 ml of local anesthetics injected through ESPB could provide effective sensory block to pinprick from T2 to T9.[5,13,14] In order to cover enough dermatomes, 20 ml of 0.5% ropivacaine was used in this study. In addition, in several previous clinical reports, the analgesic effect of ESPB was assessed only 20 minutes after the injection of ropivacaine.[15,16] In this study, in order to make sure that the analgesic effect of ESPB has fully emerged, the sensory block to pinprick was assessed at 30 minutes after ropivacaine injection.

In this study, the intraoperative and postoperative opioid consumptions in group EB were significantly less compared with those in group WI, which indicated that the ESPB could provide effective perioperative analgesia for thoracotomy. Therefore, the ESPB could provide a significant opioid-sparing effect in patients undergoing thoracotomy. Although opioids were widely used for perioperative analgesia in esophageal surgery, high-dose opioid use was reported to be significantly associated with an increased risk of recurrence in esophageal squamous cell carcinoma (ESCC).[17] It was confirmed that the μ-opioid receptor expressed in ESCC cells.[18] Moreover, the μ-opioid receptor 1 expression in ESCC cells was associated with lymph node metastasis of ESCC patients.[18] Consequently, by opioid-sparing effect, the ESPB probably provided potential benefits in cancer therapy for patients with esophageal cancer.

The thoracotomy was found to be able to cause intense stress responses proportionate to both visceral damage and skin incision pain.[19] Previous study found that wound infiltration with local anesthetics could block parietal afferent signals from incision injury.[20] However, it was deemed to have weak inhibiting effect on the afferent noxious stimuli from visceral pain caused by surgical operation.[20] In contrast, in a cadaveric investigation, Forero *et al.* found that the local anesthetics injected *via* ESPB could penetrate into the immediate vicinity of dorsal and ventral rami of the spinal nerve roots.[5] Based on the above-mentioned research results, the authors hypothesised that the ESPB could prevent afferent neural stimuli from reaching the central nervous system and inhibit efferent activation of the sympathetic nervous system. Ultimately, the ESPB could effectively reduce the pain caused by both visceral damage and skin incision, which contributed to the opioid-sparing effect of ESPB in this study. As shown in this study, compared with group WI, the pain scores at rest and during coughing immediately after surgery, at POD 1 and POD 2 were significantly lower in group EB. Moreover, compared with group WI, the postoperative consumptions of morphine and tramadol were significantly lower in group EB. These results suggested that 20 ml of 0.5% ropivacaine injected by preoperative ESPB at T5 level could provide effective analgesia in the postoperative period.

As found in this study, the incidence of postoperative nausea and vomiting in group EB was significantly lower than that in group WI, which indicated that the ESPB could markedly reduce the incidence of opioid-related adverse events after thoracotomy. Previous research has demonstrated that opioids could induce nausea and vomiting by activating opioid receptors in the chemoreceptor trigger zone, vestibular apparatus and gastrointestinal tract; and the severity degree of nausea and vomiting was positively correlated to the consumption of opioids.[21] Therefore, the authors speculated that the ESPB probably reduced the incidence of nausea and vomiting by decreasing perioperative consumption of opioids.

There were several limitations in the present clinical study. First, according to the results of previous studies, only one volume and one concentration of ropivacaine was used for ultrasound-guided ESPB. However, a volume-response or concentration-response study was not performed to obtain the optimal volume and concentration of ropivacaine used in ultrasound guided-ESPB for thoracotomy in order to get a better analgesic effect and less adverse events. Second, only one single bolus of ropivacaine was injected for ultrasound-guided ESPB. However, continuous infusion of ropivacaine for ESPB was not performed. Thus, whether continuous infusion of local anesthetic for ESPB could provide longer postoperative analgesia was not clear. Third, this study was a single center clinical study. The sample size was relatively small; and patients recruited were relatively healthy (American Society of Anesthesiologists I and II). More patients with or without comorbidities are needed to be recruited in future multi-center clinical studies.

CONCLUSION

Compared to wound infiltration with local anesthetics, ultrasound guided-ESPB could significantly reduce perioperative opioid consumption, alleviate postoperative pain, and reduce incidence of postoperative nausea and vomiting in patients undergoing thoracotomy. Therefore, combined ultrasound guided-ESPB with general anesthesia was a recommended multi-mode anesthesia regimen for thoracotomy.

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ETHICAL APPROVAL:
Ethics Committee of National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College (NCC201804009), and registered on ClinicalTrials.gov (ChiCTR1800016583).

PATIENTS' CONSENT:
The written informed consent was obtained from every patient.

CONFLICT OF INTEREST:
Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
QW: Contributed to research design, data acquisition, data analysis, and paper writing.
GZ: Contributed to research design, data acquisition, data analysis and paper writing.
SW: Contributed to data acquisition.
ZH: Contributed to data acquisition.
LS: Contributed to data acquisition and analysis.
HZ: Contributed to research design, data analysis and paper writing.

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