Erector spinae plane block for postoperative pain and recovery in hepatectomy
A randomized controlled trial

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Abstract
Background: The randomized controlled trial aimed to examine the efficacy of preoperative ultrasound-guided erector spinae plane (ESP) block combined with ropivacaine in patients undergoing hepatectomy.

Methods: A total of 60 patients were randomized to ESP block group receiving ropivacaine (Group A) and control group (Group B), n = 30 per group. Visual analog scale (VAS) was recorded in both the groups during rest and movement at the various time intervals. Both the groups were also compared for time to initial anal exhaust, analgesic usage, early postoperative complications and side-effects, walk distance after the operation, time to out-of-bed activity, and duration of hospital stay.

Results: No significant differences were observed in the demographic characteristics. For group A, when compared to group B, VAS scores during rest and movement within post-operative 24 hours were decreased, the time of first anus exhaust and ambulation were earlier, analgesic consumption and the incidence of postoperative nausea, vomiting and headache was reduced, the duration of hospital stay were shorter with longer walk distance.

Conclusion: ESP block combined with ropivacaine treatment effectively reduced early postoperative pain and improved recovery after hepatectomy.

Abbreviations: ASA = American Society of Anesthesiology, BIS = bispectral index, BMI = body mass index, CPSP = chronic post-surgical pain, CVP = central venous pressure, ECG = electrocardiogram, ESP = erector spinae plane, IBP = invasive blood pressure, MMA = multimodal analgesia, NIBP = noninvasive blood pressure, PACU = post-anaesthesia care unit, SD = standard deviation, SpO2 = pulse oxygen saturation, SVV = stroke volume variation, VAS = visual analog scale.

Keywords: erector spinae plane block, hepatectomy, postoperative pain, ropivacaine

1. Introduction

Pain is an unpleasant sensation and emotional experience caused by actual or potential tissue damage. In 1995 Presidential Address to the American Pain Society, pain was recognized as the 5th vital sign.[1] Typically, pain is divided into 2 general categories: acute pain and chronic pain according to pain duration. Acute pain is associated with surgical trauma, tissue injury, or disease states, which persists less than 1 month, while chronic pain is defined as pain lasting beyond tissue healing time, generally taken to be 3 months.[2,3] Open abdominal surgery often results in postsurgical pain that lasts a few days, and the incidence of chronic post-surgical pain (CPSP) ranged from 5% to 50%.[4] A US survey which included 300 participants who underwent surgery within 5 years concluded that 86% subjects experienced postoperative pain, and approximately 70% cases experienced adverse effects caused by analgesic medications.[5] Liver cancer remains the fifth most common malignancy and the leading cause of cancer-related death worldwide.[6] Until now, hepatectomy is the most effective treatment method for liver cancer.[7] However, the postoperative pain is a common clinical problem caused by open incision, which is the main focus of clinical research.

The risk factors of postoperative pain after open surgery mainly included preoperative factors such as preoperative pain scores and mental state, and surgical techniques.[8] Abdominal incision trauma induces a strong stress response, which in turn results in the release of proinflammatory cytokines, leading to postoperative pain via direct stimulation of nociceptors, or peripheral nerve activation. Postoperative pain also aggravates the intestinal paralysis and nausea, leads to organ dysfunction, increases the incidence of postoperative complications, affects the recovery of patients and extends the postoperative rehabilitation time.[9] Hence, if the postoperative pain cannot be effectively controlled, chronic pain might be induced, which will seriously affect the postoperative recovery.
It is widely accepted that the combined administration of opioids with non-steroidal anti-inflammatory drugs can produce additive or supra-additive analgesic effects. However, abundant studies provide strong evidence that the analgesic effects of this analgesic strategy on hepatectomy and postoperative recovery are still not ideal, due to higher incidence of adverse reactions such as nausea, vomiting, and pruritus.\(^{[10]}\) In recent years, regional nerve block has been widely used in clinical practices as the basis of multimodal analgesia (MMA). Erector spinae plane (ESP) block is a newly defined regional anesthesia technique. Compelling evidence has delineated the local anesthetic effects of ultrasound-guided ESP block on the management of breast surgery,\(^{[11]}\) thoracotomy,\(^{[12]}\) and horacic vertebra surgery.\(^{[13]}\) Furthermore, its use for other indications, such as neuropathic pain resulting from rib fractures has recently been reported.\(^{[14]}\)

The purpose of this randomized, controlled study was to evaluate the analgesic and postoperative recovery effects of ESP block in patients undergoing partial hepatectomy.

2. Materials and methods

2.1. Patients

A total of 60 patients who underwent partial hepatectomy were consecutively recruited from Linyi Central Hospital between October 2016 to March 2018 after obtaining the Institutional Ethics Committee clearance and written informed consent from all patients. All patients who met the inclusion criteria were included during the study period. Patients aged 20 to 65 years and weighing 38 to 84 kg with American Society of Anesthesiologists (ASA) physical status I-II were included in this study. The exclusion criteria included infection of the skin at the site of the needle puncture, coagulopathy, morbid obesity, hypersensitivity to local anesthetic drugs, serious heart and lung diseases, liver and kidney dysfunction, or mental diseases. All patients were randomized to receive ultrasound-guided ESP block (Group A, n = 30) or no intervention (Group B, n = 30). The flowchart of the study is presented in Figure 1. All experimental protocols were approved by the Ethics Committee of the Second Hospital of Linyi Central Hospital.

2.2. ESP block administration

Patients received no premedication. Preoperative ESP blocks were performed in the operating room prior to induction of general anesthesia. After applying standard American Society of Anesthesiology (ASA) monitoring and supplemental oxygen, intravenous midazolam (0.03 mg/kg; Jiangsu Nhwa Pharmaceutical Co., Ltd., Jiangsu, China) was administered as an anxiolytic. The patient was turned into the right lateral position. In the ESP group, ultrasound-guided bilateral single-injection ESP blocks at the level of T8 transverse process were performed as previously described using the following systematic three-step protocol.

1. The T8 vertebral level was identified via ultrasound by counting down from the first rib, and marked on the skin. A high-frequency linear-array transducer was placed in a transverse orientation to identify the T8 transverse process and then rotated into a longitudinal parasagittal orientation over its tip.

2. The left ESP block was performed first. A 22 G, 100 mm ehogenic needle was inserted in-plane in a cranial to caudal direction to contact the T8 transverse process. Correct needle tip position was confirmed by a linear pattern of injectate spread lifting the erector spinae muscle off the transverse process; 20 ml 0.5% ropivacaine (Guangdong Jiabo Pharmaceutical Co., Ltd.) was injected at this point.

3. The right ESP block was performed in an identical manner without repositioning the patient. The total amount of administered local anesthetics was 40 ml.

2.3. Intraoperative management

Immediately following completion of ESP blocks, patients were returned to the supine position and general anesthesia was induced with 0.03 mg/kg midazolam (Jiangsu Nhwa Pharmaceutical Co., Ltd., Jiangsu, China), 0.5 μg/kg sufentanil (Yichang Humanwell Pharmaceutical Co., Ltd., Hubei, China), 0.2 mg/kg cisatracurium besylate (Jiangsu Hengrui Pharmaceutical Co., Ltd., Jiangsu, China) and 0.3 mg/kg etomidate (Jiangsu Nhwa Pharmaceutical Co., Ltd.) followed by tracheal intubation. Anaesthesia was maintained with 1% to 3% isoflurane (Hebei Nine Sent Pharmaceutical Co., Ltd., Hebei, China), 2 to 4 mg/kg/ hours propofol (Guangdong Jiabo Pharmaceutical Co., Ltd., Guangdong, China) and 5 to 10 mg cisatracurium besylate.

2.4. Surgical procedure

A narrative overview of the pure laparoscopic donor right hepatectomy surgical technique used at our institution has been previously published. Briefly, 5 trocar ports were placed as follows: 1 12 mm port receiving a 30° optical device at the umbilicus; 2 12 mm operative trocars, 1 at the subcostal margin in the right midaxillary line and 1 in the midline between the umbilicus and xiphoid process; and 2 5 mm trocars for instrumental assistance, placed along the subcostal margin in the left mid-clavicular line and in the subxiphoid region. Ultrasound observation was followed by parenchymal sectioning using an ultrasonic dissector (Sonido; Medtronic, Minneapolis, MN, USA) and a cavitrion ultrasonic surgical aspirator (CUSA Excel; Integra LifeSciences, Plainsboro, NJ, USA). The major hepatic veins were saved for reconstruction. After completion of parenchymal dissection, the remnant bile duct stump was sutured. The hepatic graft was removed through a 12 to 14 cm Pfannenstiel incision in the suprapubic area. Surgeons did not perform local anesthetic wound infiltration of any of the surgical incisions.
Table 1
Demographic and pathological data of patients.

|                      | Group A (n = 30) | Group B (n = 30) |
|----------------------|------------------|------------------|
| Male/Female          | 16/14            | 17/13            |
| Age (year)           | 55.4 ± 7.0       | 53.2 ± 7.1       |
| BMI (kg/m²)          | 21.4 ± 1.5       | 22.0 ± 1.9       |
| ASA VI               | 12/18            | 14/16            |
| Child-pugh A/B       | 11/19            | 12/18            |
| Operative time (min) | 217.5 ± 28.6     | 211.0 ± 30.1     |
| Blood loss (ml)      | 271.4 ± 35.5     | 273.7 ± 33.2     |
| Fluid transfusion (ml)| 1962.1 ± 315.7 | 2051.4 ± 274.3  |

Values expressed as mean ± SD.

* Chronic liver disease is classified into Child-Pugh class A to C, Class A, 5-6 points; Class B, 7-9 points; Class C, 10-15 points.

ASA = American Society of Anesthesiology, BMI = body mass index.

2.5. Postoperative management

After surgery, the donors recovering spontaneous breathing were shifted to the post-anesthesia care unit (PACU). Pain intensity was measured using the 10 point visual analog scale (VAS), where 0 denoted no pain and 10 denoted the worst pain experienced. If patients presented with breakthrough pain (VAS ≥ 4 at rest), intravenous morphine (5mg) was administered for relieving pain. If the patient was ineffective after 15 minutes, intravenous fentanyl 25 to 50μg was administered. Postoperative nausea or vomiting was treated with intravenous metoclopramide (10mg). A blinded nurse recorded all PACU data, including opioid consumption, presence or absence of nausea or vomiting, and highest, lowest, and average pain scores during PACU stay.

2.6. Observation indexes

The following parameters were recorded:

1. Baseline characteristics, including sex, age, body mass index (BMI), ASA grade and child-pugh classification;
2. Operation conditions, including operative time, blood loss, and the volume of fluid transfusion;
3. Postoperative pain assessment using VAS at rest and movement at 2 hours, 4 hours, 8 hours, 24 hours, and 48 hours;
4. Postoperative clinical indexes, including time to initial anal exhaust, analgesic usage within postoperative 48 hours, early postoperative complications and side-effects, time to out-of-bed activity, walk distance on the first, second and third days after the operation, duration of hospital stay of patients.

2.7. Statistical analysis

The sample size was calculated based on the non-inferiority hypothesis. The predetermined non-inferiority limit was set to 1 point on the 10-point VAS scale. Based on preliminary analyses (unpublished), an SD of 1.2 was assumed for the VAS distribution. With α = 0.05 and power of 90%, 28 patients were required in each group. Assuming a 10% dropout rate, we decided to enroll 30 patients per group. The primary outcome was analyzed according to the non-inferiority approach. The non-inferiority hypothesis for the primary outcome was tested using the one-sided t test (null hypothesis that the difference in pain scores was ≥1 point vs the alternative hypothesis that the difference in pain scores was < 1 point) under a significance level of 2.5%. The two-sided 95% CI, the upper limit of which was equivalent to the upper limit of the one-sided 97.5% CI of the mean difference in pain scores by treatment, is presented in relation to the predefined non-inferiority limit and null effect.

Data were expressed as mean ± standard deviation (SD). Categorical data were analyzed using Chi-Squared test and independent t test was used to analyze the continuous variables. Statistical analysis was performed using SPSS software version 12.0 (SPSS Inc., Chicago, IL, USA), and a value of P < .05 was considered statistically significant.

3. Results

3.1. Patient baseline characteristics

A total of 60 patients were included in this study and divided into 2 groups of 30 patients, namely, Group A and Group B according to whether they underwent ESP block. As shown in Table 1, both groups were similar with respect to the gender and age. Furthermore, there were no significant differences between the groups in terms of ASA grade, child-pugh classification, operative time, the volume of intraoperative blood loss, and the volume of fluid transfusion.

3.2. Postoperative outcome

The primary outcome was postoperative pain determined by VAS scores on movement and at rest. The postoperative pain scores at rest and movement were significantly lower in group A than in group B at 2 hours, 4 hours, 8 hours, 24 hours, and 24 hours after operation (all P < .05; Table 2). There was no significant difference in VAS score between this 2 groups at 48 hours rest and movement after surgery (P > .05; Table 2). The secondary outcomes included time to initial anal exhaust, analgesic consumption, side effects, and complications associated with postoperative pain management. As presented in Table 3, the initial anal exhaust time were earlier in group A than in group B after surgery. Analgesic consumption and the incidences of nausea/vomiting and headache in group A postoperative 48 hours were significantly less than that in group B. (all P < .05).

Table 2
Comparison of VAS during movement and rest.

|                | Groups     | 2h   | 4h   | 8h   | 24h  | 48h  |
|----------------|------------|------|------|------|------|------|
| Movement       | A (n=30)   | 2.5 ± 0.5∗ | 2.1 ± 0.4∗ | 2.0 ± 0.5∗ | 1.8 ± 0.5∗ | 1.6 ± 0.4 |
|                | B (n=30)   | 4.0 ± 0.7 | 3.8 ± 0.6 | 3.2 ± 0.5 | 2.8 ± 0.4 | 1.7 ± 0.3 |
| Rest           | A (n=30)   | 2.1 ± 0.3∗ | 2.0 ± 0.3∗ | 1.5 ± 0.3∗ | 1.4 ± 0.3∗ | 1.2 ± 0.2 |
|                | B (n=30)   | 3.7 ± 0.5 | 3.5 ± 0.4 | 3.0 ± 0.6 | 2.5 ± 0.4 | 1.3 ± 0.2 |

Values expressed as mean ± SD.

∗ P < .05 vs group B.

VAS = visual analogue score.
Collectively, ESP block markedly reduced postoperative pain score, complications, and side effects associated with hepatotomy.

3.3. Postoperative recovery
As shown in Table 4, painless walking distance was improved in group A relative to group B on the first, second and third days after the operation (P < .05). Additionally, the time for out of bed activity of group A was earlier, and the duration of postoperative hospital stay in group A was shorter compared to group B (all P < .05). Taken together, these findings suggested that the ESP block program significantly promoted patients recovery.

4. Discussion
Postoperative pain is a major cause of chronic pain, which would result in disability and lower quality of life, leading to poor outcomes. To the best of our knowledge, intravenous opioid analgesia, and epidural analgesia are conventional strategies for the management of perioperative pain.[15,16] Although epidural analgesia is effective in pain control, it provokes higher hospital charges and incidence of urinary tract infections, and hemodynamic instability as well as longer hospital stay, which may represent major disadvantages.[17,18] The aim of the study was to determine the duration of analgesia of ESP block, quality of analgesia as assessed by VAS scores and to note the surgical outcomes, which follow opioid usage. The results of the present trial indicated that ESP block with ropivacaine infusion strengthened the analgesic effects of ropivacaine, reduced fentanyl consumption, and improved postoperative recovery without severe adverse events in patients undergoing hepatotomy.

Regional anesthesia is one of the successful tools against severe postoperative pain. When used successfully, truncal nerve blocks may offer great analgesic efficacy, which are associated with a higher risk profile. The transversus abdominus plane (TAP) block is often incorporated into the multimodal analgesia regimens for surgical patients undergoing abdominal and gynecological procedures. Rectus sheath blocks (RSB) were originally introduced to help relax the anterior abdominal wall during surgery and as an adjunct pain therapy. With the development of ultrasound guided techniques, RSB now have a more ubiquitous role and have been shown to decrease postoperative pain and opioid consumption.[19] However, one of the limitations of RSB is its inability to provide visceral analgesia. Paravertebral nerve block with perineural local anesthetic is usually was recently reported to effectively relieve postoperative pain after hepatectomy and reduce opioid dosage.[20] Previously, Forero et al.[21] described the successful use of continuous ESP block as a rescue analgesic technique for postthoracotomy analgesia in a patient with failed thoracic epidural analgesia, which also reduced opioid-related adverse reactions. Alpaparmak et al.[22] showed that ultrasound-guided ESP block could more effectively reduced postoperative tramadol consumption and pain scores than TAP block after laparoscopic cholecystectomy (LC) surgery, suggesting that although TAP is a well-studied plane block, ESP block seems like an effective analgesia technique for LC. Ropivacaine used in this study is a new long-acting aminoamide local anesthetic with low systemic toxicity, which is characterized by motor nerve and sensory nerve separate block. Abdul et al.[23] found that the effectiveness of 2 different concentrations of ropivacaine (0.5% versus 0.2%) given via TAP block was comparable in providing postoperative analgesia for patients undergoing appendectomy. Patients who received 0.5 ml/kg of ropivacaine 0.5% patients required a significantly less amount of additional intravenous fentanyl. Thus, it is reasonable to select 0.5% ropivacaine (20 ml) for ESP block at level T9 according to the research results of Forero et al.[21] In this study, ultrasound guided-single ESP block was selected to evaluate its effectiveness in postoperative pain after open liver resection. In the current research, we observed that the VAS scores were significantly decreased in ESP block group at rest and during movement within postoperative 24 hours as compared to the control group. The average analgesic consumption in ESP block group within postoperative 48 hours was 100 μg, which was lower compared to patients in the control group, where the consumption was 155 μg, resulting in higher incidence of nausea/vomiting and headache in ESP block group. No serious adverse effects, such as respiratory depression or haemodynamic instability were noted in either of the groups. These findings demonstrated that preoperative ESP block can effectively reduce the requirement of postoperative analgesic drugs and the incidence of adverse reactions, which was consistent with a previous study conducted by Murouchi et al.[24] However, conflicting studies were recently stated by Kang et al.[24] showing that bilateral single-injection

### Table 3
Comparison of surgical outcomes.

| Index                          | Group A (n = 30) | Group B (n = 30) |
|--------------------------------|------------------|------------------|
| Time to initial anal exhaust (h) | 24.5 ± 4.1       | 41.2 ± 4.4       |
| Analgesic usage (μg)           | 103.1 ± 11.4     | 149.0 ± 6.0      |
| Nausea/vomiting                | 2 (6.7%)         | 8 (26.7%)        |
| Hypotension                    | 2 (6.7%)         | 3 (10.0%)        |
| Respiratory depression         | 0 (0.0%)         | 1 (3.3%)         |
| Headache                       | 3 (10.0%)        | 6 (20.0%)        |
| Pruritus                       | 1 (3.3%)         | 0 (0.0%)         |
| Incision infection             | 6 (20.0%)        | 3 (10.0%)        |

Values expressed as mean ± SD. *P < .05 vs group B.

### Table 4
Comparison of postoperative recovery.

|                         | Painless Walk distance (m) | Time to out-of-bed activity (d) | duration of hospital stay (d) |
|-------------------------|-----------------------------|---------------------------------|------------------------------|
|                         | 1st day                     | 2nd day                         | 3rd day                      |
| Group A (n = 30)        | 130.0 ± 24.4                | 258.9 ± 34.6                    | 432.1 ± 47.8                 |
| Group B (n = 30)        | 108.0 ± 16.0                | 214.3 ± 52.1                    | 341.0 ± 44.9                 |

Time to out of bed activity: 3.8 ± 3.0, 6.3 ± 3.0, 9.3 ± 3.0

Values expressed as mean ± SD. *P < .05 vs group B.
ESP blocks resulted in higher resting pain scores 24 hours postoperatively compared with intrathecal morphine (ITM) in laparoscopic donor hepatectomy. However, the pain intensity with ESP blocks was mild (mean pain scores <3/10) and associated with reduced incidence of postoperative vomiting and pruritus.

However, our study has several limitations. First, a larger sample size in this study would have been more ideal for the statistical significance. Second, we did not have a control group of systemic analgesia alone, which might have better elucidated the true analgesic efficacy of ESP block. Third, there is a risk of bias from lack of patient blinding. Fourth, our results may not be generalizable to other techniques of donor hepatectomy, or to other combinations of multimodal analgesics. The serum concentrations of the drugs administered in the ESP were not estimated. Evaluation of sensory block level was not undertaken, for they were performed in anaesthetized patients. Fifth, consecutive measurement of liver function panel and monitoring was also not mentioned. Sixth, it needs more studies for the fundamental mechanism of ESP block and the effects of block. Finally, our results may similarly only be applicable to the specific single-injection ESP block.

Taken together, we concluded that preoperative ultrasound-guided ESP block combined with ropivacaine administration provides effective analgesia, and also reduces opioid requirement, thereby decreasing opioids-related side-effects and improving the degree of comfort and satisfaction of patients undergoing hepatectomy.

Author contributions
Data curation: Junbao Fu, Guangmeng Zhang.
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