Effects of Intermittent Bolus Paravertebral Block On Analgesia and Recovery in Open Hepatectomy: A Retrospective, Cohort Study.

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Abstract

Background

Experiences of paravertebral block use in hepatectomy were limited. We aimed to investigate the effects of intermittent bolus paravertebral block on analgesia and recovery in hepatectomy.

Methods

We selected patients receiving two types of analgesia programs, with matched age, sex and body mass index from a prospective perioperative analgesia and nerve block database: (1) PVB: intermittent bolus paravertebral block (0.5% ropivacaine 25ml before surgery plus 0.125ml•kg^{-1} 0.2% ropivacaine bolus per hour after surgery) and self-controlled intravenous bolus morphine pump till postoperative 48 hours; (2) control: self-controlled intravenous bolus morphine pump till postoperative 48 hours. The baseline, operation, and postoperative analgesia and recovery data were compared between groups.

Results

Thirty-eight patients in each group were included in the analysis. Intraoperatively, PVB group used less sevoflurane (difference −0.1 (-0.2, 0.0) %, \(P=0.019\)) and more ephedrine (\(U=986, P=0.004\)) and crystalloid (\(U=936, P=0.024\)) than control group. The mean arterial pressure in PVB group was lower than that in control group (difference −4mmHg, 95%CI -8~0mmHg, \(P=0.031\)) but similar to its baseline level (difference 2, 95%CI -1~5, \(P=0.153\)). Postoperatively, PVB group had lower cumulative morphine consumption at postoperative 2 (\(U=371.5, P<0.001\)), 4 (\(U=349.5, P<0.001\)), 12 (\(U=342.0, P<0.001\)), 24 (\(U=338.5, P<0.001\)) and 48 (\(U=392.5, P=0.001\)) hour, lower pain numerical rating scale score at rest at postoperative 0 (\(U=299.5, P<0.001\)), 2 (\(U=355.5, P<0.001\)) and 4 (\(U=332.0, P<0.001\)) hour, and on movement at postoperative 0 (\(U=269.5, P<0.001\)), 2 (\(U=405.0, P=0.001\)), 4 (\(U=382.5, P<0.001\)) and 12 (\(U=1179.5, P=0.003\)) hour than control group. PVB group also had lower rescue analgesia rates (OR 0.29, 95%CI 0.08~1.00, \(P=0.044\)), higher emergence satisfaction (5 (4, 5) vs 4 (4, 5), \(P=0.018\)) and lower drowsiness score (0 (0,1) vs 1(0,1), \(P=0.007\)) than control group. Three months postoperatively, PVB group had lower rates of hypoesthesia (OR 0.28 (0.11, 0.75), \(P=0.009\)), numbness (OR 0.26 (0.07, 0.88), \(P=0.024\)) and sleep disorder (OR 0.84 (0.73, 0.97), \(P=0.025\)) than control group.

Conclusions

Intermittent bolus paravertebral block provided anesthetics- and opioids-sparing effects, and enhanced recovery both in hospital and after discharge in patients receiving hepatectomy.

Background
Paravertebral block has been used as an effective perioperative analgesia approach in many types of surgeries, including thoracic, breast, cardiac and abdominal surgeries.\(^1\) It provides good pain relief with less intravenous opioids consumption. Compared to epidural analgesia, paravertebral block carries a lower risk of multiple complications, including hypotension, nausea, vomiting, pruritus and urinary retention.\(^2,6\)

Although various paravertebral block approaches and drug delivery programs have been studied, some clinical problems remain controversial or unsolved. Conflict results were drawn in studies comparing continuous and intermittent bolus drug infusion programs,\(^7,8\) and the effects of paravertebral block on preventing chronic postoperative pain remain unclear.\(^9,10\)

Open hepatectomy for hepatic tumor often causes severe postoperative pain due to its large incision and extensive surgical damage. Cases of paravertebral block use in hepatectomy have been reported,\(^11,12\) but clinical studies were limited.\(^13,14\) And we failed to identify studies reporting the effects of intermittent bolus paravertebral block on intraoperative management, and postoperative analgesia and recovery after discharge in patients receiving hepatectomy as far as searched.

**Objectives**

This retrospective, cohort study aimed to evaluate the effects of intermittent bolus paravertebral block on analgesia and recovery of patients receiving open hepatectomy for hepatic tumor. We hypothesized that intermittent bolus paravertebral block reduced postoperative 48 hours cumulative intravenous opioid consumption, without increase of adverse events. Intraoperative management, postoperative analgesia and recovery, and follow-up data were collected and compared between patients receiving and without receiving paravertebral block.

**Methods**

**Study design**

This is a retrospective, cohort study of existing medical data that were prospectively entered into an institutional perioperative analgesia and nerve block database. The hospital’s institutional review board approved the data review (No. S-K 1574), and patient informed consent was waived.

**Participants**

We searched medical records of patients receiving open hepatectomy for hepatic tumor with a J-shaped subcostal incision from Jan 2019 to Dec 2019 in the database. Patients receiving intermittent bolus paravertebral blocks (0.5% ropivacaine 25ml before surgery plus 0.125ml\(\cdot\)kg\(^{-1}\) 0.2% ropivacaine bolus per hour after surgery) and self-controlled intravenous bolus morphine pumps for postoperative 48 hours were recruited into the paravertebral block (PVB) group. Patients receiving only self-controlled intravenous
bolus morphine pumps for postoperative 48 hours, with matched age, sex and body mass index were selected as control group.

Patients comorbid with other pain diseases, received analgesic techniques apart from the studied analgesia program, or failed to complete the analgesia program or follow-up due to reasons that were not related to perioperative analgesia, for instance, postoperative hemorrhage, surgical site infection or self-withdraw, were excluded from the study.

**Baseline data collection**

The hospital’s perioperative analgesia team consisted of a group of experienced anesthesiologists, they provided all kinds of analgesic services to the surgical patients, including preparing analgesia pump, performing nerve blocks, postoperative follow-up and data recording.

Baseline data included age, sex, body mass index, American Society of Anesthesiologist (ASA) classification and preoperative surgical site pain score evaluated by a 11 points-numerical rating scale (NRS). The NRS pain score was evaluated and recorded by the anesthesiologists during preoperative visit, with 0-point indicating no pain and 10-point indicating the maximum degree of insufferable pain. Patients were also educated with a pain control goal of NRS < 4. Laboratory examination data that were collected included preoperative liver, renal and coagulation function and complete blood count.

**Paravertebral block**

In the PVB group, all paravertebral blocks were performed by the perioperative analgesia team members before anesthesia. The paravertebral block was performed using an in-plane approach(15) to insert a 21-gauge 10 cm needle (PlexoLongNanoline; Pajunk Inc, Geisingen, Germany) into the T8 paravertebral space between the internal intercostal membrane and the pleura under the guidance of ultrasonography (CX-50, Philips Inc., USA). After a negative aspiration test, 25 ml of 0.5% ropivacaine was slowly injected into the paravertebral space. Then, a catheter (PlexoLongNanoline; Pajunk Inc, Geisingen, Germany) was inserted through the needle into the paravertebral space with a depth of 1–2 cm, tunneled subcutaneously and secured with Bio-gel to the patients’ back. The catheter was connected to a programmable, portable, electronic infusion pump (Apon ambulatory infusion pump ZZB-I, Jiangsu Apon Medical Technology Co., Ltd.) to deliver a bolus of 0.125 ml•kg\(^{-1}\) 0.2% ropivacaine per hour, commencing immediately after surgery. In the control group, no nerve blocks were performed before or after the surgery.

**Intraoperative data collection**

Both PVB and control groups received general anesthesia with endotracheal intubation. All patients recorded in the studied database adopted similar general anesthesia plan. Induction was performed with intravenous fentanyl, propofol and rocuronium. Anesthesia was maintained with sevoflurane and a 50%O\(_2\)-50%N\(_2\)O mixture to maintain a BIS index within 40–60. All open hepatectomies were performed by the same group of surgeons. The open hepatectomy with a J-shaped incision consisted of a right
subcostal incision with a medial cranial extension to the xiphoid process and a variable right lateral extension with transection of the oblique abdominal musculature.\(^\text{(16)}\)

Intraoperative data that were collected included the baseline and mean value of heart rate and blood pressure, mean sevoflurane concentration, intraoperative medication and fluid volume. All vital signs and sevoflurane concentration were collected by the monitor and ventilator in real-time and transmitted to the database via electronic cables at 5-minute intervals during the surgery. All medications and fluids were recorded by the anesthesiologists during the surgery.

**Postoperative data collection**

Both PVB and control groups’ patients received self-controlled intravenous bolus morphine pump (Gemstar, Hospiria Inc., USA) after extubation. Intravenous morphine was given with no background infusion, patient-controlled bolus of 1–2 mg, 5-minute lockout interval and an upper limit of 8 mg per hour. If the patients still complained about pain with the upper limit dose, tramadol was given as rescue analgesia.

Postoperative paravertebral and intravenous analgesia were provided for 48 hours. The perioperative analgesia team members visited the patients and assessed the outcomes in the ward at postoperative 2, 4, 12, 24 and 48 hours and follow-ups were done by telephones at postoperative three months.

Primary outcome was postoperative 48 hours cumulative morphine consumption collected from electronic pump record. Secondary outcomes included: (1) cumulative morphine consumption at postoperative 2, 4, 12 and 24 hours and total number of rescue analgesia; (2) pain NRS score at rest and on movement at postoperative 0, 2, 4, 12, 24 and 48 hours; (3) opioid adverse effects including nausea, vomiting, pruritus, respiratory depression, bowel movement recorded as gas time and urinary retention recorded as Foley catheter removal time; (4) recovery data that were evaluated at postoperative 48 hours included drowsiness, thirsty, cold feeling, cognitive decline and shiver. These indices were evaluated using a 0–3 points Likert scale with 0 point defined as none, 1-point defined as mild, 2-point defined as moderate and 3-point defined as severe. Emergence, analgesia and overall satisfactions were evaluated using a 1–5 points Likert scale with 1-point defined as very unsatisfied, 2-point defined as unsatisfied, 3-point defined as no comments, 4-point defined as satisfied and 5-point defined as very satisfied; (6) length of hospital stay; (7) recovery data that were evaluated at postoperative three months included incidences of hypoesthesia, numbness and pain, pain NRS scores at rest and on movement, pain characteristics including throbbing, aching, pricking and stabbing pain, and the incidence of sleep disorder.

**Statistical analysis**

Study sample size was calculated based on a pilot study of ten patients receiving the studied analgesia program, that were randomly selected from the database via computer. The mean postoperative 48 hours cumulative morphine consumptions were \((16.8 \pm 13.5)\) mg and \((32.7 \pm 19.2)\) mg in the PVB and control
groups, respectively. Thirty-five patients were required in each group to achieve an \( \alpha \) level of 0.01 and \( \beta \) level of 0.9.

Statistical analysis was performed using SPSS for Mac version 23.0 (IBM Corp., Armonk, NY, USA). Normality was tested using the Q-Q plots. Normally distributed variables were expressed as mean \( \pm \) SD, non-normally distributed variables were expressed as median (quartile), and categorical variables were expressed as frequency (percentage). Normally distributed continuous data were analyzed using the students \( t \) test and non-normally distributed continuous data were analyzed using the Mann-Whitney U tests. Categorical data were compared using the Chi-square test when the expected cell counts > 5, otherwise the Fisher's exact test was used. All tests were two-tailed, and a \( P \) value less than 0.05 was considered statistically significant. The Bonferroni correction was performed on the raw \( P \) value where applicable. For the multiple comparison of cumulative morphine consumption and pain score at different time points, the \( P \) values for the 0.05 level of significance were adjusted to 0.01 and 0.008 based on the number of observed time points.

**Results**

A total of 234 patients receiving open hepatectomy were screen and 48 received the studied nerve block program. Five patients were dropped due to PVB catheter dislocation, unplanned secondary surgery and ICU admission. Five patients did not complete the follow-up. Finally, thirty-eight patients in the PVB group were included in the analysis. Another thirty-eight patients receiving only self-controlled intravenous bolus morphine pump with matched age, gender and body mass index were selected from the same database as control group.

**Baseline data**

Baseline clinical characteristics were listed in Table 1. The age, sex, body mass index, ASA classification, preoperative pain score, hemoglobin and platelet counts, liver function and coagulation test results were similar between PVB and control groups (all \( P > 0.05 \)).
Table 1
Baseline characteristics of the paravertebral block and control groups.

|                      | PVB group (n = 38) | Control group (n = 38) |
|----------------------|--------------------|------------------------|
| Age (years)          | 55 ± 11            | 56 ± 10                |
| Male (n, %)          | 23, 60.5%          | 23, 60.5%              |
| BMI (kg⋅m⁻²)         | 23.31 ± 3.15       | 23.60 ± 3.62           |
| ASA I/II/III level   | 19/18/1            | 15/22/1                |
| Pain NRS             | 0 (0,1)            | 0 (0, 0)               |
| Hemoglobin (g⋅L⁻¹)   | 139 ± 19           | 141 ± 18               |
| Platelet (x10⁹⋅L⁻¹) | 203 ± 87           | 178 ± 68               |
| ALT (U⋅L⁻¹)          | 31 ± 24            | 31 ± 25                |
| Albumin (g⋅L⁻¹)      | 42 ± 6             | 43 ± 4                 |
| Creatinine (µmol⋅L⁻¹)| 72 ± 16            | 72 ± 14                |
| PT (s)               | 13 ± 1             | 13 ± 1                 |
| APTT (s)             | 29 ± 4             | 28 ± 5                 |

BMI: body mass index; ASA: American Society of Anesthesiologists; NRS: numerical rating scale (0–10 points); ALT: alanine aminotransferase; PT: prothrombin time; APTT: activated prothrombin time.

Intraoperative data

Operation data were listed in Table 2. In PVB group, patients had similar intraoperative mean heart rate (difference 1, 95%CI -2 ~ 4, P = 0.340) and mean arterial pressure (difference 2, 95%CI -1 ~ 5, P = 0.153), compared to their baseline levels. In control group, patients had similar intraoperative mean arterial blood pressure (difference 0, 95%CI -3 ~ 2, P = 0.754) but lower mean heart rate (difference 4, 95%CI 2 ~ 7, P = 0.003) than their baseline levels.
Table 2
Operation data of the paravertebral and control groups.

|                      | PVB group (n = 38) | Control group (n = 38) | D 95% CI / U score | P value |
|----------------------|--------------------|------------------------|--------------------|---------|
| Surgical time (hours)| 2.9 ± 0.9          | 3.0 ± 1.1              | -0.2 (-0.6, 0.3)   | 0.518   |
| Baseline HR (bpm)    | 77 ± 9             | 76 ± 8                 | 2 (-2, 5)          | 0.393   |
| Baseline MAP (mmHg)  | 91 ± 8             | 93 ± 9                 | -2 (-6, 2)         | 0.350   |
| Mean HR (bpm)        | 76 ± 11            | 71 ± 10                | 5 (0, 9)           | 0.053   |
| Mean MBP (mmHg)      | 89 ± 8             | 93 ± 9                 | -4 (-8, 0)         | 0.031*  |
| Mean Sevoflurane (%) | 1.1 ± 0.2          | 1.2 ± 0.2              | -0.1 (-0.2, 0.0)   | 0.019*  |
| Awake time (min)     | 8 ± 5              | 8 ± 5                  | 0 (-2, 2)          | 0.937   |
| Extubation time (min)| 12 ± 6             | 10 ± 6                 | 2 (-1, 4)          | 0.175   |
| Fentanyl (µg)        | 331 ± 107          | 371 ± 125              | -40 (-93, 13)      | 0.140   |
| Ephedrine (mg)       | 6 (6, 16)          | 6 (0, 7)               | 986                | 0.004*  |
| Phenylephrine (ug)   | 0 (0, 25)          | 0 (0, 0)               | 810                | 0.188   |
| Urapidil (mg)        | 0 (0, 0)           | 0 (0, 0)               | 683.5              | 0.301   |
| Atrophin (mg)        | 0 (0, 0)           | 0 (0, 0)               | 645.5              | 0.089   |
| Crystalloid (ml)     | 1800 (1525, 2300)  | 1800 (1300, 1925)      | 936                | 0.024*  |
| Colloid (ml)         | 0 (0, 500)         | 500 (0, 500)           | 675                | 0.595   |
| RBC (U)              | 0 (0, 0)           | 0 (0, 1)               | 702.5              | 0.781   |
| Plasma (ml)          | 0 (0, 0)           | 0 (0, 0)               | 736                | 0.838   |
| Urine (ml)           | 675 (375, 1125)    | 350 (200, 600)         | 1021               | 0.002*  |
| Hemorrhage (ml)      | 275 (100, 400)     | 200 (139, 425)         | 698.5              | 0.805   |
| Crystalloid I/O (ml) | 1175 (800, 1725)   | 1100 (800, 1625)       | 764                | 0.662   |
| Colloid I/O (ml)     | -25 (-100, 625)    | 300 (-116, 400)        | 708                | 0.884   |

PVB: paravertebral block, D: difference, CI: confidential interval, HR: heart rate, MBP: mean blood pressure, RBC: red blood cell, I/O: difference between input and output.

* P < 0.05, significant difference.
Intraoperatively, PVB group had lower mean arterial blood pressure (difference − 4mmHg, 95%CI -8 ~ 0mmHg, \( P = 0.031 \)), used less sevoflurane (difference − 0.1%, 95%CI -0.2 ~ 0.0%, \( P = 0.019 \)) but more ephedrine (U = 986, \( P = 0.004 \)) than control group. Other medications used were similar between groups (all \( P > 0.05 \)). The PVB group also received more crystalloid (U = 936, \( P = 0.024 \)) than control group, but the overall input minus output volumes were similar between groups due to a higher urine output volume (U = 1021, \( P = 0.024 \)) of the PVB group. The volumes of colloid infusion, blood products transfusion and hemorrhage were similar between groups (all \( P > 0.05 \)).

**Postoperative data**

Postoperative analgesia data were listed in Table 3 and depicted in Fig. 1–3. The cumulative morphine consumptions at postoperative 2 (U = 371.5, \( P < 0.001 \)), 4 (U = 349.5, \( P < 0.001 \)), 12 (U = 342.0, \( P < 0.001 \)), 24 (U = 338.5, \( P < 0.001 \)) and 48 (U = 392.5, \( P = 0.001 \)) hours were lower in the PVB group than control group. Rescue analgesia rate was also lower in the PVB group than control group (OR 0.29, 95%CI 0.08 ~ 1.00, \( P = 0.044 \)).
Table 3
Postoperative cumulative morphine consumption and pain NRS score at rest and on movement of the paravertebral block and control group at different time points.

| Time points | PVB group (n = 38) | Control group (n = 38) | U score | P value |
|-------------|--------------------|------------------------|---------|---------|
| **Morphine (mg)** | | | | |
| 2h | 1.5 (1.0, 2.3) | 4.5 (1.5, 6.0) | 371.5 | < 0.001* |
| 4h | 1.8 (1.5, 4.5) | 6.0 (3.0, 9.0) | 349.5 | < 0.001* |
| 12h | 5.3 (1.5, 12.0) | 12.5 (7.1, 21.3) | 342.0 | < 0.001* |
| 24h | 10.0 (4.5, 18.0) | 19.8 (13.1, 33.4) | 338.5 | < 0.001* |
| 48h | 15.8 (5.6, 28.5) | 26.5 (17.8, 45.8) | 393.5 | 0.001* |
| **NRS At rest** | | | | |
| 0h | 0 (0, 0) | 3 (0, 5) | 299.5 | < 0.001** |
| 2h | 2 (0, 3) | 3 (3, 5) | 355.5 | < 0.001** |
| 4h | 2 (0, 3) | 3 (2, 4) | 332.0 | < 0.001** |
| 12h | 2 (2, 3) | 3 (2, 3) | 1310.0 | 0.104 |
| 24h | 2 (1, 3) | 2 (2, 3) | 1376.5 | 0.352 |
| 48h | 1 (0, 2) | 1 (0,2) | 1400.0 | 0.495 |
| **NRS On movement** | | | | |
| 0h | 0 (0, 1) | 4 (3, 6) | 269.5 | < 0.001** |
| 2h | 3 (1, 4) | 4 (3, 6) | 405.0 | 0.001** |
| 4h | 3 (1, 4) | 4 (3, 5) | 382.5 | < 0.001** |
| 12h | 3 (2, 4) | 4 (3, 5) | 1179.5 | 0.003** |
| 24h | 4 (2, 5) | 4 (3, 5) | 1420.0 | 0.650 |
| 48h | 2 (2, 3) | 3 (2, 4) | 1300.0 | 0.081 |

PVB: paravertebral block, h: hours, NRS: numerical rating scale

* P < 0.01, significant difference after bonferroni correction, ** P < 0.008, significant difference after bonferroni correction.

The pain NRS scores at rest were lower in the PVB group than control group at postoperative 0 (U = 299.5, P < 0.001), 2 (U = 355.5, P < 0.001) and 4 (U = 332.0, P < 0.001) hours, but similar between groups at postoperative 12 (U = 1310.0, P < 0.001), 24 (U = 1376.5, P < 0.001) and 48 (U = 1400.0, P < 0.001) hours.
The pain NRS scores on movement were lower in the PVB group than control group at postoperative 0 (U = 269.5, \( P < 0.001 \)), 2 (U = 405.0, \( P = 0.001 \)), 4 (U = 382.5, \( P < 0.001 \)) and 12 (U = 1179.5, \( P = 0.003 \)) hours, but similar between groups at postoperative 24 (U = 1420.0, \( P = 0.650 \)) and 48 (U = 1300.0, \( P = 0.081 \)) hours.

Postoperative recovery data during hospital stay and three months after discharge were listed in Tables 4 & 5. At postoperative 48 hours, the PVB group had lower drowsiness score (U = 492.5, \( P = 0.007 \)) and higher emergence satisfaction (U = 923.5, \( P = 0.018 \)) than control group. Other recovery data including nausea, vomiting, pruritus, respiratory depression, bowel movement, Foley catheter removal, thirsty, cold feeling, cognitive decline, shiver, analgesia and overall satisfaction, and the length of hospital stay were similar between groups (all \( P > 0.05 \)).
Table 4
In-hospital recovery data of the paravertebral block and control group.

|                                | PVB group (n = 38) | Control group (n = 38) | OR / D 95% CI /U score | P value |
|--------------------------------|-------------------|------------------------|------------------------|---------|
| Rescue analgesia (n, %)        | 4, 10.5%          | 11, 28.9%              | 0.29 (0.08, 1.00)      | 0.044*  |
| Nausea (n, %)                  | 23, 60.5%         | 18, 47.4%              | 1.70 (0.69, 4.23)      | 0.250   |
| Vomiting (n, %)                | 4, 10.5%          | 8, 21.0%               | 2.27 (0.62, 8.29)      | 0.208   |
| Pruritus (n, %)                | 3, 7.9%           | 3, 7.9%                | 1.00 (0.19, 5.30)      | 1.000   |
| Respiratory depression (n, %)  | 7, 18.4%          | 14, 36.8%              | 0.39 (0.14, 1.11)      | 0.073   |
| Bowel movement (hours)         | 60 ± 28           | 60 ± 21                | 0 (-11, 11)            | 0.979   |
| Foley catheter removal (hours)| 41 ± 22           | 46 ± 23                | -5 (-16, 5)            | 0.314   |
| Drowsiness (points)            | 0 (0, 1)          | 1 (0, 1)               | 492.5                  | 0.007*  |
| Thirsty (points)               | 1 (1, 2)          | 1 (1, 2)               | 707.5                  | 0.875   |
| Feel cold (points)             | 0 (0, 0)          | 0 (0, 0)               | 665.0                  | 0.237   |
| Cognitive decline (points)     | 0 (0, 0)          | 0 (0, 0)               | 703.0                  | 0.317   |
| Shiver (points)                | 0 (0, 0)          | 0 (0, 0)               | 722.0                  | 0.999   |
| Emergence satisfaction (points)| 5 (4, 5)          | 4 (4, 5)               | 923.5                  | 0.018*  |
| Analgesia satisfaction (points)| 4 (4, 5)          | 4 (4, 4)               | 838.0                  | 0.167   |
| Overall satisfaction (points)  | 5 (4, 5)          | 4 (4, 5)               | 832.5                  | 0.187   |
| Hospital stay (days)           | 9 ± 5             | 10 ± 4                 | -1 (-3, 1)             | 0.202   |

PVB: paravertebral block, OR: odds ratio, D: difference, CI: confidential interval

* P< 0.05, significant difference.
Table 5
Postoperative three months recovery data of the paravertebral block and control group.

|                          | PVB group (n = 38) | Control group (n = 38) | OR 95% CI / U score | P value |
|--------------------------|--------------------|------------------------|---------------------|---------|
| Hypoesthesia (n, %)      | 9, 23.7%           | 20, 52.6%              | 0.28 (0.11, 0.75)   | 0.009*  |
| Numbness (n, %)          | 4, 10.5%           | 12, 31.6%              | 0.26 (0.07, 0.88)   | 0.024*  |
| Pain (n, %)              | 18, 47.4%          | 15, 39.5%              | 1.38 (0.56, 3.43)   | 0.488   |
| NRS at rest (points)     | 0 (0, 3)           | 0 (0,1)                | 838.5               | 0.156   |
| NRS on movement (points) | 1 (0, 3)           | 1 (0, 3)               | 712.0               | 0.911   |
| Throbbing pain (n, %)    | 3, 7.9%            | 1, 2.6%                | 3.17 (0.32, 31.952) | 0.615   |
| Aching pain (n, %)       | 0, 0%              | 2, 5.3%                | 0.95 (0.88, 1.02)   | 0.493   |
| Pricking pain (n, %)     | 6, 15.8%           | 10, 26.3%              | 0.53 (0.17, 1.63)   | 0.260   |
| Stabbing pain (n, %)     | 5, 13.2%           | 2, 5.3%                | 2.73 (0.50, 15.03)  | 0.430   |
| Sleep disorder (n, %)    | 0, 0%              | 6, 15.8%               | 0.84 (0.73, 0.97)   | 0.025*  |

PVB: paravertebral block, D: difference, CI: confidential interval, NRS: numerical rating scale

* P< 0.05, significant difference.

At postoperative three months, PVB group patients experienced less hypoesthesia (OR 0.28, 95% CI 0.11 ~ 0.75, P = 0.009), numbness (OR 0.26, 95% CI 0.07 ~ 0.88, P = 0.024) and sleep disorder (OR 0.84, 95% CI 0.73 ~ 0.97, P = 0.025) than control group patients. Other recovery data including the incidence, severity and characteristics of pain were similar between groups (all P> 0.05).

**Discussion**

This study showed that perioperative intermittent bolus paravertebral block in patients receiving hepatectomy provided good anesthetics- and opioids-sparing effects, and enhanced postoperative recovery both in-hospital and three months after discharge. The study results showed that intermittent bolus paravertebral block could reduce intraoperative sevoflurane consumption and postoperative intravenous opioid consumption up to 48 hours after hepatectomy, and provided better analgesia at rest and on movement up to postoperative 4 and 12 hours, respectively. Patients receiving paravertebral block also had lower drowsiness score, higher emergence satisfaction during hospital stay, and lower incidences of hypoesthesia, numbness and sleep disorder three months after discharge.
Intermittent bolus paravertebral block could reduce postoperative intravenous morphine consumption for 48 hours in patients receiving hepatectomy. While early studies on thoracic surgery showed superior analgesic effects of continuous infusion than intermittent bolus infusion,(4) three recent studies suggested that analgesics delivered in intermittent bolus modality provided comparable or even superior pain relief, and wider dermatome spreads of sensory block than analgesics delivered in continuous infusion modality.(7, 8, 17) Our study used an intermittent bolus paravertebral block program initiated preoperatively on patients receiving hepatectomy for hepatic tumor. Compared to Chen et al's thoracic paravertebral block study starting with an initial dose of 10 mL 0.2% ropivacaine administered at the completion of right lobe hepatectomy and followed by a continuous infusion of 0.2% ropivacaine at 6 mL·h⁻¹ for 24 hours postoperatively, we administered an initial dose of 25 mL 0.5% ropivacaine preoperatively and followed by 0.125mL·kg⁻¹·h⁻¹ 0.2% ropivacaine bolus infusion for 48 hours postoperatively. The results showed that at postoperative 24 hours, the cumulative intravenous morphine consumption reduced by 21% in Chen et al's study and reduced by 50% in our study. This suggested that the analgesic programme we used provided a better opioid-sparing effect than the programme described by Chen et al. (13)

Paravertebral block also had an impact on intraoperative hemodynamics and anesthetic management. Previous study on mastectomy showed that paravertebral block helped maintain a higher heart rate and shorter duration of mean aterial pressure < 55mmHg, with reduced intraoperative sevoflurane and opioids consumption, and similar ephedrine doses.(18) Study on thoracoscopic surgery revealed lower intraoperative opioids consumption in the paravertebral block group than placebo group, but changes of heart rate and blood pressure were not reported.(19) Our study on patients receiving hepatectomy showed that the mean arterial pressure in the PVB group was lower than that in the control group, but similar to patient's baseline level. As for intraoperative management, a lower sevoflurane and higher ephedrine and crystalloid consumption were noted in the PVB group than control group. Though no difference in fentanyl consumption was detected between groups, lower pain scores both at rest and on movement at postoperative 0 hour were achieved in PVB group. These results showed that paravertebral block reduced anesthetic dose and provided better intraoperative analgesia. Although induced slight hemodynamic instability, it could be easily corrected with prompt intraoperative management, including the use of vasoactive agents and increase of fluid infusion.

Although two studies have been conducted to investigate the perioperative analgesia effects of paravertebral block on hepatectomy,(13, 14) we failed to find reports on chronic postoperative pain and recovery after discharge in this group of patients, as far as searched. The reported effects of paravertebral block on chronic postoperative pain in other types of surgeries were controversial.(9, 20) While one study on patients receiving mastectomy suggested that paravertebral block could not reduce the incidence of chronic pain at postoperative 3 and 6 months, but reduced the pain score and improved their overall health related quality of life,(21) the other study suggested that preemptive paravertebral block reduced the prevalence of chronic postoperative pain one year after mastectomy, regardless of whether axillary dissection was performed.(22) Study on thoracotomy suggested that paravertebral block
could not reduce chronic postoperative pain. (23) Our study found that paravertebral block did not affect the incidence, severity and characteristics of pain, but reduced the incidence of hypoesthesia, numbness and sleep disorder three months after hepatectomy. Possible explanations might be reduced central sensitization due to nerve block, which should be applied as early as possible. (21) Further studies with larger sample size and longer follow-up time are required to fully illustrate this issue.

This study has several limitations. Firstly, although all data were prospectively entered into the database, this study remains a retrospective review of the experiences of a single center and suffers from all of the shortcomings of this type of study. Secondly, the unique clinical profile of patients from a single medical center may not be generalizable to other clinical situations. Further extensive multicenter studies are required to validate our findings.

**Conclusions**

In conclusion, intermittent bolus paravertebral block provides good anesthetics- and opioids-sparing effects, and enhanced recovery both in hospital and after discharge in patients receiving hepatectomy for hepatic tumor.

**List Of Abbreviations**

- PVB: paravertebral block
- NRS: numerical rating scale
- ICU: intensive care unit
- BMI: body mass index
- ASA: American Society of Anesthesiologists
- ALT: alanine aminotransferase
- PT: prothrombin time
- APTT: activated prothrombin time.

**Declarations**

**Ethics approval and consent to participate:** This study was approved by the institutional review board (No. S-K1574) of Peking Union Medical College Hospital. No informed consent was required, because the
data are anonymized.

Consent for publication: Not applicable.

Availability of data and materials: The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Authors’ contributions: WJ and CXL designed the study, WJ & ZZY & CXL collected the data, WJ & ZYL analysed the data, WJ drafted the manuscript, HYG & MYL & SXT revised the manuscript.

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**Figures**

Figure 1

Postoperative cumulative morphine consumption at different time points.
Figure 2

Postoperative pain numerical rating scale at rest at different time points.
Figure 3

Postoperative pain numerical rating scale on movement at different time points.