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Effects of Thoracic Paravertebral Block on Nociceptive Levels After Skin Incision During Video-Assisted Thoracoscopic Surgery

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Background: Regional anesthesia provides excellent analgesic effects after surgery. However, the effects of regional anesthesia on nociceptive levels during surgery under general anesthesia have not been quantitatively evaluated. To reveal the effects of thoracic paravertebral block (PVB) on nociceptive levels after skin incision during general anesthesia, we performed a retrospective cohort study in patients without serious preoperative conditions or comorbidities undergoing elective video-assisted thoracoscopic surgery (VATS). Nociceptive levels during general anesthesia were calculated using our previously determined Nociceptive Response (NR) equation, which utilizes common hemodynamic parameters.





Material/Methods: Data on 77 adult patients who underwent VATS from May 2018 to August 2018 were retrospectively obtained from our institutional database. We then performed propensity score matching between patients who received thoracic PVB (PVB group: n=29) and those who did not (Control group: n=48). The averaged values of systolic blood pressure (SBP), heart rate (HR), perfusion index (PI), bispectral index (BIS), and NR from 10 to 5 minutes before skin incision (T0), 5 to 10 minutes (T1), 10 to 15 minutes (T2), 15 to 20 minutes (T3), and 20 to 25 minutes after skin incision (T4), were calculated.

Results: Twenty-four propensity score-matched patients in each group were analyzed. Mean NR values at T1 and T2 in the PVB group were significantly lower than those in the Control group. SBP, HR, PI, and BIS, however, showed no significant differences between the 2 groups, except for SBP at T2.

Conclusions: Thoracic PVB prevented an increase in NR values, which quantitatively represent nociceptive levels under general anesthesia, in patients undergoing VATS.

MeSH Keywords: **Anesthesia, Conduction • Nociception • Thoracic Surgery, Video-Assisted**

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Background

Nociceptive stimulation activates peripheral nociceptors, inducing autonomic responses [1–3]. Surgical invasion, which activates peripheral nociceptors, also induces autonomic responses, including increases in blood pressure, heart rate and pupillary diameter, and decrease in peripheral blood flow, even under general anesthesia. Several devices have been developed that use these autonomic parameters to monitor nociceptive balance during surgery under general anesthesia [4,5]. Regional anesthesia, which blocks nerve impulse transmission, reportedly suppresses autonomic responses induced by skin incision under general anesthesia [6–8]. However, the effects of regional anesthesia on nociceptive levels after skin incision have not been evaluated.

Thoracic paravertebral block (PVB) is an effective anesthetic method for postoperative analgesia after thoracic surgery [9,10]. Although most anesthesiologists believe that thoracic PVB combined with general anesthesia provides superior analgesia and improves hemodynamic stability after skin incision during thoracic surgery, no quantitative assessments have been performed for the effects of thoracic PVB on intraoperative nociceptive levels.

Recently, we developed the Nociceptive Response (NR) equation, which utilizes the hemodynamic parameters of heart rate (HR), systolic blood pressure (SBP), and perfusion index (PI) to evaluate nociceptive levels under general anesthesia [11]. To reveal the effects of thoracic PVB on nociceptive levels after skin incision, we performed a retrospective cohort study with propensity score-matched analysis of adult patients without serious preoperative conditions or comorbidities undergoing elective video-assisted thoracoscopic surgery (VATS).

Material and Methods

This retrospective cohort study was approved by the Ethics Committee of Hyogo College of Medicine (#2566). We obtained clinical data on adult patients who underwent elective VATS for lung cancer at Hyogo College of Medicine Hospital between May 2018 and August 2018. Eligibility criteria for the present study were: age older than 20 years, American Society of Anesthesiologists-physical status (ASA-PS) I-II, and serum C-reactive protein (CRP) concentration before surgery <0.3 mg·dL⁻¹.

Perioperative management

None of the patients received premedication. General anesthesia was induced with propofol (1.5 mg/kg), fentanyl (2 µg/kg), and rocuronium (0.9 mg/kg), followed by insertion

of a double-lumen endotracheal tube for airway control and cannulation of the radial artery for direct measurement of arterial blood pressure. Anesthesia was maintained with total intravenous anesthesia (TIVA), using a continuous infusion of remifentanyl and propofol with additional injections of fentanyl and rocuronium. The remifentanyl infusion rate was conventionally adjusted to maintain mean blood pressure within a range of $\pm 20\%$ of the pre-anesthesia level. Bispectral index (BIS) was maintained between 40 and 60 by adjusting the target dose of propofol. Mechanical ventilation was performed to maintain normocapnia (end-tidal carbon dioxide range 35–40 mmHg). After surgery, a continuous infusion of intravenous fentanyl was routinely administered until postoperative day (POD) 1 for postoperative analgesia.

The applicability of thoracic PVB was determined by the anesthesiologists in charge. After induction of general anesthesia, patients were placed in the lateral decubitus position on a surgical table to perform thoracic PVB. The skin was cleaned using antiseptic iodine, and an ultrasonography probe (L18-4 Linear Probe, SONIMAGE HS1, Konica Minolta, Tokyo, Japan) was positioned to visualize the spinous and transverse processes of the vertebra and the costa at the appropriate vertebral level. Under appropriate visualization, ultrasound-guided thoracic PVB was performed using a single injection of 20 mL of 0.25% levobupivacaine. Depression of the pleura was considered to indicate successful injection of the analgesic agent. The operation was started 15–20 minutes after thoracic PVB was performed.

Data collection

Information on serum concentrations of CRP before surgery, and numerical rating scale (NRS) scores for maximum postoperative pain on the day of surgery (POD0) and on POD1, were obtained from our institutional medical records. The normal range for CRP at our institution is below 0.3 mg/dL. The NR value was calculated using the following hemodynamic equation: $NR = -1 + 2 / (1 + \exp(-0.01HR - 0.02SBP + 0.17PI))$ [11]. We installed the equation of NR on our institutional anesthesia information managing system (ORSYS, PHILIPS, Amsterdam, Netherlands). Hence, in addition to SBP, HR, PI, and BIS, the NR was also recorded every minute. The averaged values of NR data from 10 to 5 minutes before skin incision (T0), 5 to 10 minutes after skin incision (T1), 10 to 15 minutes after skin incision (T2), 15 to 20 minutes after skin incision (T3), and 20 to 25 minutes after skin incision (T4) were retrospectively obtained from the data-search software (Vi-Pros, Dowell, Sapporo, Japan). The averaged values of SBP, HR, PI, and BIS during the observation period of interest of 10 minutes before skin incision to 25 minutes after skin incision were also obtained at the same time (T0, T1, T2, T3, and T4).

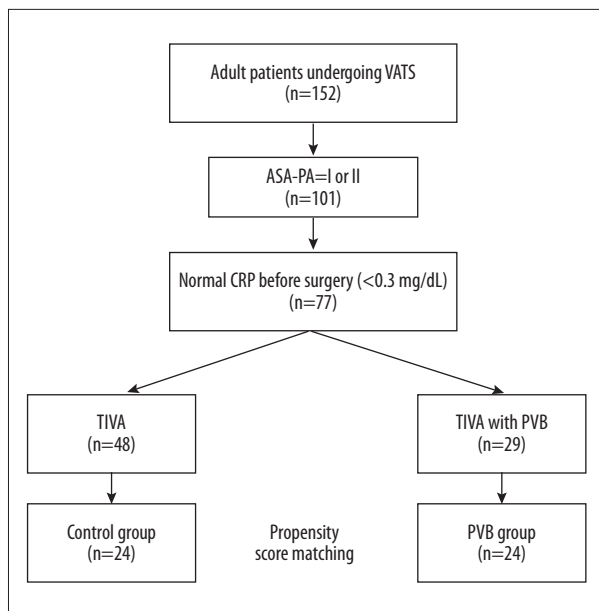


Figure 1. Diagram showing patient inclusion in this study. ASA-PS – American Society of Anesthesiologists – physical status; CRP – C-reactive protein; TIVA – total intravenous anesthesia; PVB – paravertebral block; VATS – video-assisted thoracoscopic surgery.

The averaged values of SBP, HR, PI, NR, and BIS from the start to the end of surgery (mean SBP, mean HR, mean PI, mean NR, and mean BIS throughout surgery) were also obtained. Mean NR throughout surgery was conceived to correspond to the intraoperative nociceptive level.

Statistical analyses

All statistical testing was performed using IBM SPSS Statistics 24 software (IBM Corp., Chicago, IL, USA). We performed propensity score matching of patients who did and did not receive thoracic PVB (PVB group and Control group, respectively). Propensity score was calculated by logistic regression analysis

Table 1. Patient demographics and perioperative data before propensity score matching.

	Control group n=48	PVB group n=29	P
Age (yrs)	71.6±9.5	62.8±14.0	0.007**
BMI (kg/m ²)	22.7±3.1	21.7±1.7	0.434
Female/Male	19/29	11/18	0.885
ASA-PS I/II	7/41	5/24	0.700
Preoperative CRP level (mg/dL ⁻¹)	0.08±0.08	0.10±0.12	0.348
Duration of surgery (min)	108.2±47.0	126.0±62.8	0.161
Mean SBP throughout surgery (mmHg)	114.8 [109.7–118.3]	110.1 [104.1–113.1]	0.010**
Mean HR throughout surgery (beats/min ⁻¹)	66.4 [60.5–74.1]	67.3 [59.9–72.0]	0.801
Mean PI throughout surgery	1.98 [1.29–2.51]	1.60 [1.09–2.14]	0.122
Mean NR throughout surgery	0.856 [0.830–0.884]	0.850 [0.825–0.871]	0.294
Mean BIS throughout surgery	43.9 [41.4–47.2]	45.0 [43.1–48.3]	0.341
Continuous dose of propofol (mg/kg ⁻¹ /min ⁻¹)	0.09±0.03	0.09±0.03	0.512
Continuous dose of remifentanyl (µg/kg ⁻¹ /min ⁻¹)	0.18±0.06	0.14±0.05	0.006**
Total amount of fentanyl (µg/kg ⁻¹)	6.25±2.13	6.21±2.50	0.942
NRS score for postoperative pain on POD0	5.0 [4.0–7.0]	4.0 [1.8–6.5]	0.132
NRS score for postoperative pain on POD1	5.0 [3.3–6.0]	5.0 [3.0–5.0]	0.284

Data are presented as mean ± standard deviation (SD) or median [25–75 percentile]. PVB – paravertebral block; BMI – body mass index; ASA-PS – American Society of Anesthesiologists-physical status; BIS – bispectral index; CRP – C-reactive protein; HR – heart rate; NR – Nociceptive Response; NRS – numerical rating scale; PI – perfusion index; POD – postoperative day; SBP – systolic blood pressure. * P<0.05, ** P<0.01 versus Control group.

Table 2. Patient demographics and perioperative data after propensity score matching.

	Control group n=24	PVB group n=24	P
Age (yrs)	67.1±10.2	67.2±10.6	0.976
BMI (kg/m ²)	21.9±2.9	22.2±2.6	0.672
Female/Male	9/15	8/16	0.846
ASA-PS I/II	5/19	3/21	0.477
Preoperative CRP level (mg/dL ⁻¹)	0.07±0.08	0.12±0.13	0.381
Duration of surgery (min)	102.3±42.3	125.2±65.7	0.159
Mean SBP throughout surgery (mmHg)	115.4 [107.2–119.9]	109.6 [101.2–112.1]	0.035*
Mean HR throughout surgery (beats/min ⁻¹)	69.2 [60.5–75.7]	65.4 [59.4–71.0]	0.131
Mean PI throughout surgery	1.51 [1.12–2.00]	1.76 [1.10–2.20]	0.766
Mean NR throughout surgery	0.870 [0.844–0.887]	0.843 [0.810–0.862]	0.015**
Mean BIS throughout surgery	44.3 [41.5–47.5]	44.9 [40.8–48.0]	0.699
Continuous dose of propofol (mg/kg ⁻¹ /min ⁻¹)	0.10±0.04	0.08±0.04	0.242
Continuous dose of remifentanyl (µg/kg ⁻¹ /min ⁻¹)	0.19±0.07	0.13±0.05	0.001**
Total amount of fentanyl (µg/kg ⁻¹)	6.64±2.34	5.95±2.24	0.312
NRS score for postoperative pain on POD0	5.0 [4.0–7.0]	3.0 [1.3–5.0]	0.036*
NRS score for postoperative pain on POD1	5.0 [3.3–5.8]	3.0 [1.3–5.0]	0.369

Data are presented as mean ± standard deviation (SD) or median [25–75 percentile]. PVB – paravertebral block; BMI – body mass index; ASA-PS – American Society of Anesthesiologists-physical status; BIS – bispectral index; CRP – C-reactive protein; HR – heart rate; NR – Nociceptive Response; NRS – numerical rating scale; PI – perfusion index; POD – postoperative day; SBP – systolic blood pressure. * $P < 0.05$, ** $P < 0.01$ versus Control group.

using age, gender and body mass index (BMI) as independent variables. Patients in the PVB group whose propensity scores deviated by more than 0.02 from those in the Control group were considered unmatched. The un-paired *t*-test was used to compare continuous variables, and the chi-square test was used to compare nominal variables between 2 groups. The Kruskal-Wallis test, followed by the Mann-Whitney U test with Bonferroni correction, was used to compare ordinal variables between the 2 groups. A value of $P < 0.05$ was considered statistically significant, and after a Bonferroni adjustment, $P < 0.005$ was considered significant when 10 parameters were tested ($0.05/10 = 0.005$).

Results

A total of 152 patients were assessed for eligibility, from among whom 77 patients were selected. After propensity score matching, 24 patients who did not receive thoracic PVB (Control group) and 24 patients who received thoracic PVB (PVB group) were selected (Figure 1). Although there were significant differences in age between the 2 groups before propensity score

matching (Table 1), no significant difference was observed after matching (Table 2).

Comparisons of NR, SBP, HR, PI, and BIS between before and after skin incision

NR values at T1, T2, and T3, and SBP and HR values at T1 and T2 were significantly higher than their respective values at T0 in the Control group. The PI value at T1 and T2 was significantly lower than that at T0 in the Control group. In the PVB group, on the other hand, SBP, HR, PI, and NR after skin incision were not significantly different compared to those before skin incision. Thoracic PVB improved hemodynamic stability after skin incision. BIS values from T1 to T4 were not significantly different compared to the values at T0 in both groups (Figure 2).

Comparisons of NR, SBP, HR, PI, and BIS between Control group and PVR group

Although NR values before skin incision (T0) were not significantly different between the Control group and the PVB group,

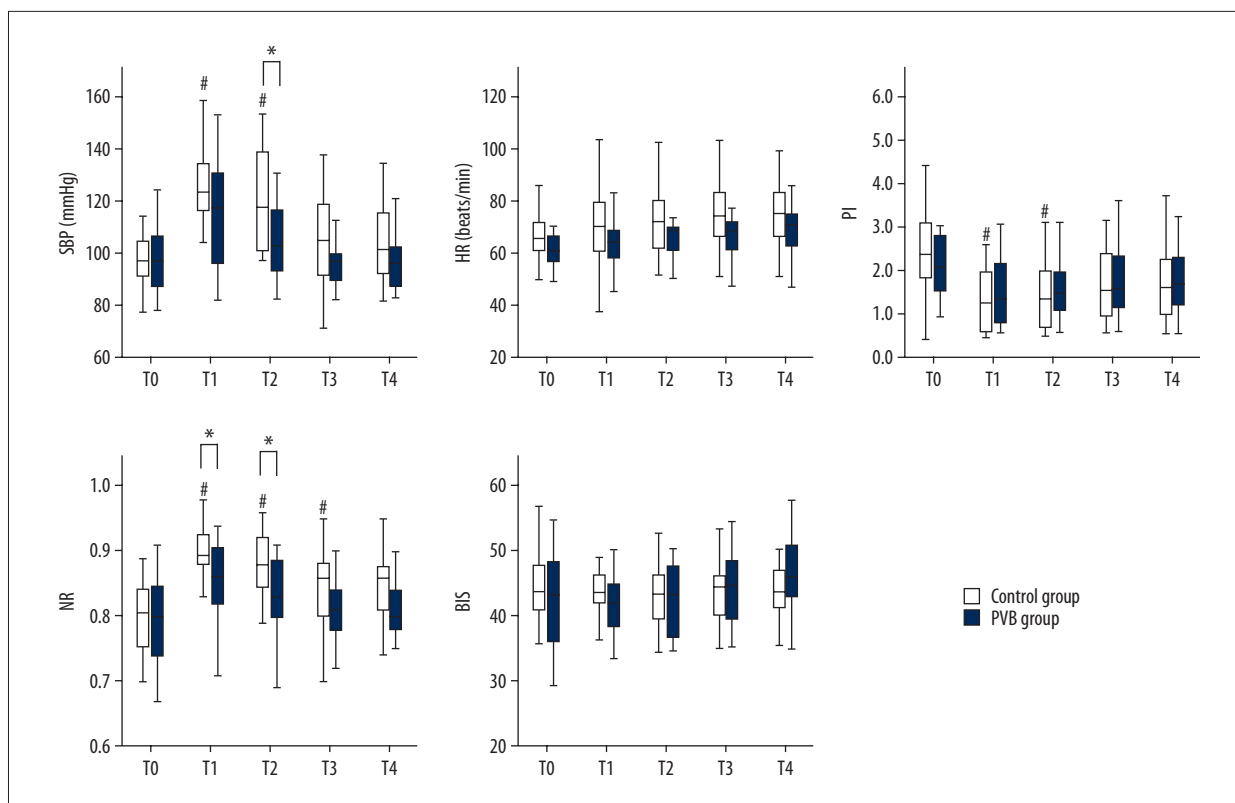


Figure 2. Comparison of SBP, HR, PI, NR, and BIS between the Control group and the PVB group at the 5 observation periods. T0 – 10 to 5 minutes before skin incision, T1 – 5 to 10 minutes after skin incision, T2 – 10 to 15 minutes after skin incision, T3 – 15 to 20 minutes after skin incision and T4 – 20 to 25 minutes after skin incision. * $P < 0.005$ versus Control group, # $P < 0.005$ versus T0; Kruskal-Wallis test, followed by Mann-Whitney U test. SBP – systolic blood pressure; HR – heart rate; PI – perfusion index; NR – Nociceptive Response; BIS – bispectral index.

they were significantly lower in the PVB group than the Control group at T1 and T2. Thoracic PVB suppressed nociceptive levels after skin incision. The SBP value was only significantly lower at T2 in the PVB group compared to the Control group. HR, PI, and BIS were not significantly different between the 2 groups from T0 to T4 (Figure 2).

Intraoperative nociceptive levels

After matching, the mean NR throughout surgery, doses of continuous remifentanyl infusion, and NRS score for postoperative pain on POD0 in the PVB group were significantly lower than those in the Control group (Table 2). Thoracic PVB suppressed nociceptive levels throughout surgery.

Discussion

In the present study, thoracic PVB suppressed the increase in nociceptive levels after skin incision with stabilization of hemodynamic responses in patients undergoing VATS. Thoracic PVB also suppressed intraoperative nociceptive levels, as quantified

by the averaged value of NR from the start to the end of surgery (mean NR throughout surgery), with reduction of the dose of remifentanyl used for continuous infusion.

To assess nociceptive levels during general anesthesia, most anesthesiologists depend on intuition and experience based on changes in hemodynamic responses. However, hemodynamic responses, such as HR, blood pressure, and peripheral blood flow indices, are affected by various other factors in addition to nociceptive levels [3,5]. In our previous study, NR values were better able to reflect differences in nociceptive levels after skin incision between laparoscopic and open abdominal surgeries than SBP, HR, and PI [11]. Further, they could also differentiate between the Control group and PVB group in the present study. This might be because changes in SBP, HR, and PI are incorporated into the NR equation, which varies less than SBP, HR, and PI during surgery, by using an exponential function [11]. Therefore, NR reflects nociceptive levels better than do individual autonomic responses induced by nociceptive stimulation.

Previously, analgesic effects of regional anesthesia during surgery under general anesthesia was evaluated by the reduction of total amount of intraoperative opioid requirement [12]. Although several monitoring devices have been designed to evaluate nociceptive levels during general anesthesia [3–5], no study has shown significant differences in nociceptive levels with and without peripheral nerve blocks. Recently, Teerth et al. reported the effects of scalp block or incision-site infiltration on intraoperative fentanyl consumption in patients undergoing craniotomy when fentanyl was administered according to the changes in analgesia nociception index (ANI). They found that scalp block reduced fentanyl consumption compared to incision-site infiltration [13]. On the other hand, in the present study, the continuous dose of remifentanyl was adjusted according to changes in blood pressure, and we found that thoracic PVB suppressed nociceptive levels during VATS with reduction of the remifentanyl infusion rate and SBP. Monitoring of nociceptive levels under general anesthesia can, thus, be used both as an index of opioid dose, and to provide objective information on the effect of regional anesthesia.

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A limitation of this study was that the small number of patients included, as many patients were excluded due to a high ASA-PS class and high CRP level preoperatively. Nevertheless, the results still indicated statistical significance.

Conclusions

Thoracic PVB suppresses nociceptive levels not only at the skin incision, but also throughout surgery, in patients undergoing VATS under general anesthesia. The NR value provides an objective assessment tool for the evaluation of the analgesic effects of regional anesthesia under general anesthesia.

Conflict of interest

None.