The Pattern of Contrast Dye through the Thoracic Paravertebral Catheter Does Not Predict Analgesic Efficacy after Breast Cancer Surgery: A Prospective Cohort Study

Yuko Yamada, Kumiko Tanabe*, Noritaka Yoshimura, Shinobu Yamaguchi, Kiyoshi Nagase, Hiroki Iida

Department of Anesthesiology and Pain Medicine, Gifu University Graduate School of Medicine, Gifu, Japan
Email: *kumiko-t@m2.gyao.ne.jp


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Abstract

Purpose: We examined whether or not the spreading pattern of contrast dye through the catheter into the thoracic paravertebral space (TPVS) was associated with acute post-operative pain relief after breast cancer surgery. Methods: Sixty patients were recruited. After surgery, patients received thoracic paravertebral block (TPVB). The catheter was inserted within the TPVS, and radiographic contrast dye was injected through the catheter. Based on the main spreading patterns of the dye, the patients were divided into a cloud-like (spreading to the posterior compartment of the TPVS) or a longitudinal spread group (spreading to the anterior compartment of the TPVS). The primary endpoint of the study was pain intensity by numeric rating scale (NRS) and additional analgesic requirements within 12 h after surgery. Results: In 22 patients, the spread of contrast dye was not noted in the PVS. Of the 38 eligible patients, 9 patients were assigned to the cloud-like spread group, 28 patients to the longitudinal spread group and 1 patient was excluded. There were no significant differences in the NRS between the two groups both at rest and on moving. No significant differences were found in the frequency of requiring additional analgesics. Conclusions: There is no marked difference in the analgesic efficacy after breast cancer surgery based on the spread of the contrast dye to the posterior or anterior compartment of the TPVS. We should not insert the needle deeply within the TPVS, as the risk of the migration of catheters into the pleural space can be quite high.

Keywords

Breast Cancer, Postoperative Pain, Thoracic Paravertebral Block
1. Introduction

Thoracic paravertebral block (TPVB) is performed via the injection of local anesthetic (LA) into the thoracic paravertebral space (TPVS) [1]. The TPVS is a wedge-shaped area bordered by the vertebral body, intervertebral disks or intervertebral foramina medially; the superior costotransverse ligament (SCTL), the transverse process, or ribs posteriorly; and the parietal pleura anteriorly [2]. It contains the intercostal spinal nerves, the spinal dorsal rami and ventral rami, the rami communicants, the sympathetic chain, intercostal vessels, and fatty tissue [1]. The TPVS is divided into posterior (dorsal) and anterior (ventral) spaces by the endothoracic fascia [3] [4]. TPVB provides ipsilateral, segmental, somatic, and sympathetic nerve blockade in multiple thoracic dermatomes and has been used in pain management for acute or chronic pain of unilateral origin from the chest or upper abdomen [5]. TPVB provides advantages in controlling acute postoperative pain, which when uncontrolled is related to the development of chronic pain after breast surgery or thoracic surgery [6] [7]. The rate of complications, such as symptomatic hypotension, bradycardia, postoperative nausea and vomiting, and urinary retention, is lower for PVB than for central neuraxial blocks [8]. One of the major complications related to TPVB is a pleural puncture, with an incidence of 1.1% [9]. Ultrasound-guided TPVB has become a popular technique for postoperative pain management [7]. Using ultrasound allows us to preview the paravertebral anatomy and enables us to observe the spread of the injected local anesthetics [6]. Furthermore, ultrasound imaging of the needle and the pleura during the procedure may reduce the risk of pleural puncture [10].

The injection of LA into the posterior or anterior compartment of the TPVS results in a cloud-like or a longitudinal segmental spreading image of contrast dye [4]. However, the LA distribution within the TPVS is highly variable, and the analgesic effect is unpredictable [2]. No studies have examined the relationship between the pattern of the spread of LA and the analgesic efficacy after surgery.

We designed a prospective study to evaluate the spreading pattern of contrast dye through the catheter into the TPVS in patients undergoing breast cancer surgery and investigated whether or not the pattern was related to the degree of acute post-operative pain. The primary endpoint of the study was to assess postoperative analgesia (pain intensity using a numeric rating scale (NRS) and additional analgesic requirements) within 12 h after surgery.

2. Materials and Methods

The institutional review board at the Gifu University Hospital (Gifu, Japan) approved the protocol for this prospective cohort study. This study was registered with the University Hospital Medical Information Network (study ID: UMIN000011610) as a clinical trial registry. Informed consent for this study was obtained from all patients. We recruited 60 patients who underwent unilateral breast cancer surgery without reconstruction from June 2015 to January 2016. Exclusion criteria were as follows: American Society of Anesthesiologists Physi-
cal Status 4; age < 20 years; allergy to local anesthetics or contrast dye; hepatic or renal failure; coagulopathy; prior thoracotomy on the ipsilateral side; no spread of the contrast dye within the PVS by thoracic X-ray (pleural space, epidural space, intercostal space, not detectable).

All patients received standard general anesthesia with standard monitoring. Anesthesia was induced with thiopental or propofol and maintained with sevoflurane or propofol. After the operation, the patients received real-time out-of-plane TPVB. Briefly, the patients were placed in a lateral decubitus position. The needle entry site was marked 2.5 cm laterally from the midpoint of the spinous process at the level of thoracic vertebra 3. A 3 - 11 MHz linear array probe (Phillips SONOS 5500; Philips Medical Systems, Andover, MA, USA) was parasagitally positioned to the spinous processes. According to a previous study [2], the distances from the skin to the transverse process and the pleura were measured using an ultrasound transducer tilted slightly laterally. An 18 G Tuohy needle was attached via an extension tube to a syringe with normal saline. The Tuohy needle was inserted perpendicularly to the intertransverse space. The beveled edge of the Tuohy needle was faced cranially. After the needle tip penetrated the SCTL, a small dose of saline was injected. When anterior movement of the pleura was observed by the injection of saline, the tip of the needle was identified inside the PVS. An end-hole 20 G polyethylene catheter (Hakko Medical, Japan) was inserted up to 3 cm from the needle tip and confirmed negative blood or air aspiration. The Tuohy needle was removed and the catheter was secured to the skin with a tape (IV3000™, Smith & Nephew). Ropivacaine (0.33%; 25 ml) was injected into the TPVS after a test of 3 ml of 1.5% lidocaine with epinephrine 1:200,000. The volume of injectate into the PVS is routine dosage in our institution at a single level. The patients were placed in a supine position. Then, 5 ml of radiographic contrast dye (Iopamiron 370 mg·ml⁻¹; Bayer, Leverkusen, Germany) diluted 2-fold with normal saline was injected through the catheter, and X-rays were taken immediately. The catheters were connected to a patient-controlled analgesia (PCA) pump, and the infusion of 0.2% ropivacaine was initiated (basal rate of 3 ml·h⁻¹ and bolus volume 3 ml).

An independent anesthesiologist assessed the spreading patterns of contrast dye and the location of the tip of the catheter by thoracic X-ray. The spreading patterns were assessed by the main spread of contrast dye within the TPVS and divided into two types as described in a previous report [4]: a cloud-like spreading pattern or a longitudinal spreading pattern. The TPVS is separated by endo-thoracic fascia into an anterior and posterior compartment. Injection of radio contrast dye into the posterior compartment results in a cloud-like spreading pattern, whereas into the anterior compartment results in a longitudinal spreading pattern [4]. Cloud-like spreading patterns show a limited segmental distribution not parallel to the spine (Figure 1(A)). Longitudinal spreading patterns show a longitudinal, cranio-caudal distribution of contrast dye parallel to the spine (Figure 1(B)). Additional spreading patterns as prevertebral, epidural, or contralateral spreading were also assessed.
Figure 1. Representative contrast dye pattern. (A) Cloud-like spreading pattern: a relative segmental spread was shown. (B) Longitudinal spreading pattern: multisegmental longitudinal spread parallel to the spine along with spread around the intercostal space was shown. Based on the spreading patterns of (A) or (B), we confirmed the correct catheter placement in the TPVS. Black arrows indicate the spread of contrast dye.

For additional analgesia, 3 ml 0.2% ropivacaine into the PVS using PCA pump or intravenous flurbiprofen axetil in 50 mg was administered upon patients request. The primary endpoint of the study was to assess postoperative analgesia (pain intensity using a NRS and additional analgesic requirements) within 12 h after surgery.

2.1. Measurement

The postoperative pain intensity was assessed using a NRS (0, no pain; 10, worst pain imaged). The NRS was measured at rest and on moving at 1, 6, and 12 h after surgery. Additional analgesics at 12 h after surgery were recorded. The incidence of hypotension and postoperative nausea and vomiting was also recorded. Patients, surgeons, nurses and data collectors were all blinded to the allocation throughout the study. The independent anesthesiologist who assessed the spreading pattern of the contrast dye and anesthesiologists performing the paravertebral catheter placement were not blinded to the allocation. However, they were not involved in postoperative pain assessment.

2.2. Statistical Analyses

We performed statistical analysis using the SPSS® software program, version 23 (SPSS Inc., Chicago, IL, USA). Continuous data were presented as the mean ± standard deviation (SD). Categorical data were described using frequencies. Data were statistically analyzed by the χ² test and t-test for scale variables. P < 0.05 was defined as statistically significant. A two-way repeated measures analysis of variance (ANOVA) was performed to compare the NRS in the cloud-like spread group with that in the longitudinal spread group. We set a type I error estimate of 5% (alpha = 0.05) and a power (1-beta) of 80%. The sample size estimation was based on the assumption that the difference in the mean NRS between the two groups would be 2.5, and the SD of both groups would be 2.5 based on a previous report [11]; as such, 34 patients were determined to be necessary. We
estimated that a minimum of 34 patients would be required to have 80% power for detecting a significant between-group difference in mean NRS score. According to the previous study [2], the tip of the catheter into the TPVS was highly displaced during catheterization and 40% of the catheters were not in the paravertebral space. To compensate for unforeseen dropouts and potentially higher than expected catheter migration, we planned to enroll 60 patients.

3. Results

A total of 60 patients were recruited for the study (Figure 2). In all of patients, the tip of the needle was identified inside the PVS by visualizing the anterior movement of the pleura on ultrasound. None of the patients experienced an increase in heart rate or blood pressure after injection of a test of 3 ml of 1.5% lidocaine with epinephrine 1:200,000 through the PVB catheter. None of the patients had radiological evidence of pneumothorax. In 22 patients, the spread of contrast dye through the PVB catheters was not noted in the PVS (11 cases in the pleural space, 2 cases in the epidural space, 7 cases in the intercostal space, and 2 cases in unknown spaces). The rate of PVB catheter migration outside of the PVS was 36.7%. The other 38 patients were confirmed to have the catheter correctly positioned in the TPVS. Of the 38 patients, 1 was excludes because she required reoperation for bleeding from the surgical site within 12 h postoperatively.

Of the 37 eligible patients, nine patients (24.3%) were assigned to the cloud-like spread group and 28 (75.7%) to the longitudinal spread group. The typical spreading patterns are shown (Figure 1). The demographics variables and the surgical procedures did not differ significantly (Table 1). No signs of prevertebral, epidural or contralateral spread were identified in either group by X-ray. With the longitudinal spreading pattern, the distribution to the intercostal spaces was significantly greater than with the cloud-like spreading pattern (the number of mean intercostal space 1.1 vs. 0.1, p < 0.01) (Table 2).

The postoperative pain intensity using NRS was compared between the cloud-like spread group and longitudinal spread group by repeated-measures ANOVA. There were no significant differences in the NRS between the two groups both at rest (p = 0.72) and on moving (p = 0.6) within 12 h after surgery (Figure 3). No significant differences were found in the frequency of requiring additional analgesics within 12 h after surgery between the 2 groups (Table 3). Hypotension requiring treatment did not occur in either group. There was no significant difference in the incidence of postoperative nausea and vomiting between the two groups at 1 h (p = 0.56) and 6 h (p = 0.38) after surgery (Table 3).

4. Discussion

The association between the spreading pattern of LA within the TPVS and postoperative analgesic efficacy has been unclear [12] [13]. Previous studies have shown that both cloud-like spread and longitudinal spread are consistent with
### Table 1. Patients’ characteristics.

<table>
<thead>
<tr>
<th>Pattern of contrast dye spreading</th>
<th>Cloud-like</th>
<th>Longitudinal</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>9</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD), year</td>
<td>55.4 (9.8)</td>
<td>53.4 (12.8)</td>
<td>0.66</td>
</tr>
<tr>
<td>BMI (SD), kg/m²</td>
<td>23.2 (3.1)</td>
<td>22.3 (3.1)</td>
<td>0.48</td>
</tr>
<tr>
<td>ASA-PS I:II:III, n</td>
<td>5:4:0</td>
<td>19:9:0</td>
<td>0.80</td>
</tr>
<tr>
<td>Surgery time, min</td>
<td>139.8 (54.8)</td>
<td>129.7 (49.5)</td>
<td>0.65</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
<td>0.56</td>
</tr>
<tr>
<td>Mastectomy + SNB, n</td>
<td>5</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Mastectomy + AND, n</td>
<td>3</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Partial mastectomy + SNB, n</td>
<td>1</td>
<td>11</td>
<td></td>
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<tr>
<td>Partial mastectomy + AND, n</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as the mean (SD) or numbers (n). BMI: body mass index, SD: standard deviation, ASA-PS: American Society of Anesthesiologist-Physical Status, SNB: sentinel lymph node biopsy, AND: axillary lymph node dissection.

### Table 2. The number of paravertebral segments, intercostal segments and thoracic levels covered by contrast dye within TPVS.

<table>
<thead>
<tr>
<th>Pattern of contrast dye spreading</th>
<th>Paravertebral segments</th>
<th>Intercostal segments</th>
<th>Thoracic levels overlaid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cloud-like, n = 9</td>
<td>0</td>
<td>0.1 (0 - 1)</td>
<td>2.3 (1 - 3)</td>
</tr>
<tr>
<td>Longitudinal, n = 28</td>
<td>2.6 (1 - 5)</td>
<td>1.1 (0 - 2)</td>
<td>0</td>
</tr>
</tbody>
</table>

P value <0.01

The cranio-caudal spread of contrast dye in a longitudinal spread group was shown as paravertebral segments. The additional intercostal spread in both of two groups were shown as intercostal segments. The limited segmental spread of contrast dye in a cloud-like spread group was shown as thoracic levels overlaid. Data are presented as the mean (range).

### Table 3. Intraoperative fentanyl consumption, frequency of rescue and incidence of side effects.

<table>
<thead>
<tr>
<th>Pattern of contrast dye spreading</th>
<th>Intraoperative fentanyl consumption (μg)</th>
<th>Frequency of additional analgesics within 12 h after surgery</th>
<th>Incidence of side effects, n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cloud-like (n = 9)</td>
<td>Longitudinal (n = 28)</td>
<td>Hypotension</td>
</tr>
<tr>
<td></td>
<td>94.4 (15.7)</td>
<td>91.1 (26.9)</td>
<td>0icum</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PONV 1 h after surgery</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>PONV 6 h after surgery</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

P value 0.66

Data are presented as the mean (SD) or numbers (n). N/A: not applicable, PCA: patient-controlled anesthesia, NSAID: nonsteroidal anti-inflammatory drug, PONV: postoperative nausea and vomiting, SD: standard deviation.
The NRS at rest (a) or on moving (b) at 1, 6 and 12 h after surgery. The white box indicates the cloud-like spread group and the black box indicates the longitudinal spread group. Horizontal lines indicate medians; boxes indicate IQRs; and whiskers indicate ranges. There were no significant differences between the two groups (repeated-measures ANOVA).

adequate block after renal surgery [14]. However, it has been suggested that successful TPVB shows a longitudinal multisegmental spread with relatively little intercostal spread [4]. The findings of our study showed that patients with longitudinal segmental spreading had similar pain intensity scores to those with cloud-like spreading patterns. This indicates that the analgesic effect of TPVB cannot be predicted from the spread pattern of LA within the PVS.

TPVS is a semi-enclosed area that communicates with the multilevel paravertebral space, intercostal space, epidural space, and the sympathetic chain [5] [15]. The analgesic efficacy of a TPVB is obtained by extending LA to the continuous space via the TPVS [2]. The TPVS is separated by the endothoracic fascia into an anterior and posterior compartment [3] [4]. The injection of contrast dye into the posterior compartment results in a cloud-like spreading pattern,
whereas the injection into the anterior compartment results in a longitudinal multisegmental spreading pattern [4]. While the endothoracic fascia does not form a definitive tissue layer, making it difficult to identify by ultrasound [14], our results showed that the injected LA did not travel much through septation.

One of the problems associated with TPVB is catheter misplacement. The use of a nerve stimulator or ultrasound for performing PVB results in higher success rates and reduce rates of complications [7]. However, there is the possibility of the risk of misplacement of the catheter tip [4] [16]. The tip of the catheter within the TPVS is highly displaced during catheterization. According to the human cadaveric studies [2], catheter migration occurred in 40% - 45% of cases after easy puncture to PVS. Half cases had difficulty advancing the catheter within the PVS [2]. One of the complications associated with catheter misplacement of TPVB is pleural puncture [7] [17]. The rate of catheter misplacement intrathoracically was 3.2% in a cadaver study using ultrasound in the transverse plane [2], and 8.9% in patients using ultrasound in the sagittal plane [6]. In the present study, we found that the catheters accidentally punctured the parietal pleura in 11 patients (18.3%). The incidence of accidental pleural puncture by using ultrasound might be higher than by using a landmark technique (3%) [16]. Because an ultrasound-guided technique provides direct visualization of the PVS during needle manipulation, we were able to insert the needle more deeply under the SCTL to an anterior compartment of the TPVS and more closely to the pleura than using the classical technique.

Injection made in the dorsal part of the TPVS results in cloud-like spread with very limited distribution to adjacent segments. In the present study, the numbers of thoracic levels overlaid in cloud-like spread were relatively smaller than the numbers of paravertebral segments in longitudinal spread. The volume to cover paravertebral segments was found to be 0.033 ml-kg⁻¹-segment⁻¹. However, it is still unclear whether there is the correlation between spread and dose [15].

We also found that there was no relationship between the LA spreading pattern within the TPVS and the postoperative analgesic efficacy. Therefore, there is no need to insert the needle deeply into the anterior compartment of PVS after penetrating the SCTL. When we use the approach involving the insertion of the Tuohy needle and the catheter tangentially to the pleura [18], we must always consider the risk of accidental pleural puncture by the catheter and try not to insert the needle any deeper than necessary.

**Limitation**

There are several limitations in the present study. First, we did not evaluate the patients without spread of PVS. The catheter tips were misplaced in the epidural space, pleural space and intercostal space. Because the injection of local anesthetics through the misplaced catheters have analgesic efficacy in clinical use, we should also assess the patients without spread of PVS. However, we focused on the accurate location of the tip of the catheter within PVS and tried to figure out
the analgesic effect in two different classic spread patterns. Therefore, we did not take into account the patients without spread in the PVS. Next, we also should have confirmed analgesic efficacy by sensory block measurement after PVB. The breast areas must be anaesthetized from T1 till T5 for major breast surgery including the axillary lymph node dissection [19]. In our present study, single-injection through the catheter following continuous TPVB could not provide complete analgesia in either spread group. It might be one of the reasons that the patients who had different spreading patterns had the similar pain. Then, we did not observe the posterior spread of contrast dye in the PVS by the lateral view of X-ray. The posterior spread may be the spread into the erector spinae plane. In our present report, there is the possibility that the cloud-like spread worked as the erector spinae block for pain management [20]. Finally, we calculated the sample size that is necessary to reach that power (α = 0.05, β = 0.8). However, given that this was a prospective cohort study, it was inevitable that proportion of the eligible population in the two groups was not equal.

5. Conclusion
There is no marked difference in the analgesic efficacy after breast cancer surgery when LA spreads to the posterior compartment or anterior compartment of the TPVS. We should not insert the needle deeply under the SCTL using an out-of-plane approach, as the risk of the migration of the catheter may be high.

Conflicts of Interest
The authors declare no conflicts of interest regarding the publication of this paper.

References


