# What is the best pain control after thoracic surgery?

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Thoracotomy induces severe postoperative pain, which can cause respiratory complications, such as hypoxia, atelectasis, and pulmonary infections (1). In addition, inadequate pain control can lead to post-thoracotomy pain syndrome, which may continue for many years (2-4); thus, appropriate pain management is essential after surgery. The most common pain management after chest surgery is epidural analgesia (EPI). EPI is clearly effective in managing the pain; however, it still has contraindications and a risk of severe complications. In addition, the reported failure rates of EPI are as high as 12% (5), and the effects of this analgesia vary among patients. Furthermore, in respiratory surgery, videoassisted thoracic surgery (VATS), a less invasive procedure, has been adopted, and local nerve blocks that cause few side effects are widely used for perioperative pain control. It is debatable whether EPI will be the best option in the future.

Ghee *et al.* reported a study in which they investigated whether intercostal nerve block (ICNB), administered via an implanted subpleural catheter, was superior to intraoperative incision site injection (ISI) in terms of analgesia for VATS (6). The hypothesis of this study was that there would be an improvement in postoperative pain management after thoracoscopic surgery in patients treated with a subpleural, tunneled catheter that provided continuous infusion of a local anesthetic. However, their results did not show any objective differences between the subpleural catheter and the intraoperative ISI groups that would justify routine use of tunneled subpleural catheters after VATS. Furthermore, these techniques were comparable in terms of the effects on the postoperative clinical course, and no significant differences were observed in parameters such as the length of hospital stay and return to work. We would like to discuss this topic further in terms of an ideal management of postoperative pain after thoracic surgery.

In this study by Ghee et al., 86 patients were randomized into the subpleural catheter or intraoperative ISI groups in a 1:1 fashion, and underwent thoracoscopic surgery using 2 incisions by VATS approaches: a 5- to 12-mm camera port incision at the eighth intercostal space (ICS), posterior axillary line; and a 3- to 4-cm incision in the fifth or sixth ICS, anterior axillary line (6). All patients had standardized anesthetic delivery and postoperative pain control. All pain scores were assessed on a visual analog scale ranging from 0 to 10, where 0 represents no pain and 10 represents severe pain. Consequently, there were no significant differences in average daily pain scores (all P values  $\geq 0.06$ ). There was no significant difference in the 2 groups' usage of narcotics (P=0.23), acetaminophen (P=0.23), or nonsteroidal anti-inflammatory drugs (P=0.57) over time, based on a linear mixed model analysis. Length of hospital stay and the results of 30-day postoperative surveys were not significantly different between the subpleural catheter and intraoperative ISI groups.

Several studies have reported that, after VATS or open thoracic surgery, patients receiving ICNB experienced better pain control than patients who did not receive ICNB (7,8). However, no study had compared the analgesic effects of ICNB with those of other techniques. This study, which was a randomized study with a high evidence level, demonstrated the absence of any significant differences between the subpleural catheter and intraoperative ISI groups. On the other hand, the following points can be regarded as the limitations of this study: (I) the sample size was small (n=42 or 43 in either arm), and the study design lacks statistical power; (II) local infiltration at the incision site was chosen as the control method in this study. This method is generally not as effective as other methods of pain control after thoracic surgery; the gold standard of pain management for thoracic incisions has been placement of a thoracic epidural catheter or paravertebral blocks (PVBs); (III) because the analgesic effects of these techniques after thoracotomy, instead of VATS, were not assessed, the results of this study are less generalizable.

However, the most important implication of the results of this study is that at least in VATS, good pain control can be achieved by local infiltration anesthesia at the incision sites, which is a much simpler and less expensive method than continuous infusion of ICNB via an implanted subpleural catheter. In this context, if only VATS is targeted, comparative studies on PVB versus ISI, EPI versus ISI, etc. will be important in future.

In this study, bupivacaine was continuously infused via a catheter or injected one-shot into the incision sites. Appropriate concentrations and dosages of drugs used also needs to be investigated further in future studies. The drugs used for nerve blocks are commonly long-acting local anesthetics, among which bupivacaine, ropivacaine, lidocaine, levobupivacaine, etc., are frequently used. Recently, liposome bupivacaine, which is a local anesthetic preparation contained in a multilamellar vesicle, was developed, approved by the United States Food and Drug Administration in 2011, and released in the United States in 2012. Although this preparation is currently approved for clinical use only for postoperative local infiltration anesthesia, some reports have indicated that a single injection of liposomal bupivacaine for ICNB exerted an analgesic effect comparable to that of EPI for 72-96 hours after surgery (9). It is expected that development of new local anesthetics will lead to realization of a more effective nerve block in future.

In thoracotomy, which causes severe postoperative pain, EPI is the standard technique for postoperative analgesia. Studies comparing EPI with postoperative analgesia with opioids have revealed that EPI is associated with a higher analgesic effect and a lower incidence of side effects (4). For patients without any contraindications, EPI may be the first-choice technique for postoperative analgesia (4). In fact, anesthetic management for thoracic surgery is currently performed with general anesthesia combined with EPI in many institutions. Regarding drugs used for EPI, a combination of local anesthetics and opioids is recommended. Recently, PVB has been reported as an alternative to EPI (3,10-13). PVB involves injecting local anesthetics into the paravertebral space (where the spinal nerve emerges from the intervertebral foramen) (14). This technique can block unilateral multisegmental spinal and sympathetic nerves (15). Many previous studies have demonstrated that PVB has analgesic effects equivalent to EPI and has a lower incidence of side effects, such as nausea, vomiting, hypotension, and urinary retention (3,4,16-19). The major difference between PVB and EPI is that PVB mainly blocks the sympathetic and sensory nerves on only one side (3,4,20). Compared with EPI, PVB is associated with a lower risk of urinary retention and a lower hypotensive effect (3,4). Even in cases of hematoma, PVB is considered to have a wider safety margin because the paravertebral space expands (19).

The PVB techniques include an approach of inserting the nerve-block needle from the back and an approach from the surgical field. The dorsal approach is associated with the risk of pneumothorax (21), and the technique using the loss-of-resistance method has not been widely adopted. In recent years, a technique performed under the guidance of ultrasonography has been reported (20). Because it is expected to improve the safety and reliability of PVB, this technique may be widely adopted in future. On the other hand, the approach from the surgical field allows catheter placement and injection of local anesthetics under direct vision in thoracotomy or via thoracoscopic monitoring. Because the lungs are collapsed, there is almost no risk of pneumothorax, and this technique rarely fails. Thus, this insertion skill is recommended in thoracotomy or thoracoscopic surgery.

For analgesia after lung surgery, regional anesthesia, such as EPI, PVB, or ICNB, is used. It generally has a high analgesic effect and causes few side effects. Compared with intravenous anesthesia, regional anesthesia has the advantages of a lower incidence of respiratory complications and less need of additional analgesics (22). On the other hand, analgesia via intravenous injection of opioids is applicable to all patients because the risk of hemorrhagic complications does not need to be considered. However, side effects, such as nausea, vomiting, and respiratory depression, occur occasionally after surgery, and adequate analgesic effects are not achieved in some cases. In recent

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years, an anesthetic technique using multimodal analgesia, which combines analgesics with different mechanisms of action, has been recommended to achieve maximal analgesia and to reduce side effects to the minimum.

Post-thoracotomy pain is multifactorial and is considered to be associated with the intercostal, sympathetic, vagus, and phrenic nerves (23). ICNB blocks the intercostal nerves, and PVB and EPI appear to block the intercostal and sympathetic nerves. The vagus and phrenic nerves cannot be blocked by regional anesthesia. Thus, unless opioids or nonsteroidal anti-inflammatory drugs are concomitantly administered, visceral pain will increase, and no satisfactory analgesia can be achieved. For this reason, multimodal analgesic strategies, which combine different techniques, such as combined application of regional anesthetics with different action mechanisms, local infiltration anesthesia for the surgical wounds (ISI), and opioid intravenous patientcontrolled analgesia, appear to be useful. Because clinical data on multimodal analgesic treatment are still insufficient, acceleration of clinical studies on this issue is urgently needed.

In our institution, we have applied a combination of epidural and PVBs after thoracic surgery to reduce pain more effectively. Our study demonstrated the safety and feasibility of the combination method of EPI and PVB (24). Acute pain after thoracic surgery was adequately controlled using double analgesic regimens, including EPI and PVBs, suggesting an alternative to conventional modalities of EPI alone or PVB alone (24). In 2011, Wildgaard et al. showed promising results with well-controlled postoperative pain in a series of patients treated with PVBs in combination with a catheter placed along a single intercostal neurovascular bundle after VATS (25). Thus, with the objective of ultimate analgesia and minimum adverse effects, an important future study focus would be comparison of multimodality and monomodality, such as PVB + ISI versus PVB alone, epidural block (EPI) + ICNB versus EPI alone, and EPI + PVB + ISI versus EPI alone. Not to be argued, the total daily dosage of local anesthetics in multimodal treatment should be considered cautiously.

There is a lack of large-scale reliable study data on postoperative analgesia because of differences among institutions or researchers in terms of surgical approaches (e.g., thoracotomy and VATS); the number, location, and length of surgical wounds; injection methods for local anesthesia; types (potency), concentrations, injection routes, doses, and injection duration of anesthetics used for nerve block; types and dose of postoperative analgesics; etc. Therefore, clinically relevant large-scale studies, adjusted in terms of differences in techniques and study designs, need to be promoted. The optimum pain management strategy for thoracic surgery will limit the usage of narcotic pain medications, leading to improved pulmonary function and quicker return to normal activity of daily life. Moreover, effective pain management not only contributes to patient satisfaction but may also be associated with improvement in the safety of lung surgery and therapeutic outcomes. In addition, future studies that evaluate other systems to deliver prolonged local anesthetic effects may demonstrate a more effective mechanism for pain management.

Less invasive surgery, that is, surgery performed with fewer or smaller surgical wounds, is made possible by recent technological advances. However, the term "less invasiveness" essentially means that the surgical burden on patients is reduced to the minimum. Considering not only the improvement in surgical approaches, but also the advances in terms of anesthesia and analgesia for surgical wounds, respiratory surgeons should seek genuine "less invasive" surgery.

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#### Footnote

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