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Pre-emptive local analgesia in video-assisted thoracic surgery sympathectomy☆

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Abstract

Objective: Our goal is to determine whether infiltration with a short-acting local anaesthetic such as lidocaine before the surgical incision has a pre-emptive effect on postoperative pain intensity and on incidence of paraesthesia in patients undergoing standard thoracoscopic sympathectomy for palmar hyperhidrosis. **Material and methods:** This prospective study includes a consecutive series of 18 patients undergoing bilateral standard thoracoscopic sympathectomy for palmar hyperhidrosis during January 2005—December 2007. Each patient enrolled in the study was randomised to receive pre-incisional lidocaine with epinephrine infiltration of the wounds on the one side, and normal saline solution on the other. The identical surgery was performed on each side to allow patients to act as their own controls. Then, the side which received local analgesia was compared with the control side with regard to pain control and paraesthesia after 4, 24 and 168 h postoperatively. The patients and investigators were both blinded concerning the side randomised to receive pre-emptive local analgesia (PLA). **Results:** We found that patients reported significantly less pain on the side treated with pre-emptive local anaesthesia in contrast to the control side 4 and 24 h after surgery ($p = 0.001$ and $p = 0.004$, respectively). However, that difference decreased with time and was no longer significant 168 h following surgery ($p = 0.156$). Regarding the paraesthesia, the incidence was higher in the control side than the PLA side at 4, 24 and 168 h postoperatively, but the difference was not statistically significant. A total of 17 of 18 (94%) patients noted a change in palmar hyperhidrosis status after surgery. **Conclusion:** Our study shows that the pre-injection of local anaesthetic before standard thoracoscopic sympathectomy suppresses the local pain mediators, hence resulting in significantly less pain in the first postoperative 24 h but not thereafter. The clinical impact of the procedure is the possibility of early discharge to home and early return to work with potential economical benefits. However, because of the small number of patients, further studies are needed to corroborate our results.

Keywords: Pre-emptive analgesia; Video-assisted thoracic surgery; Sympathectomy

1. Introduction

The pain that accompanies thoracic surgery is notable for its intensity and duration. Thoracotomy is one of the most painful surgical procedures known, with multiple sources of nociceptor, including the surgical incision, the disruption of ribs, intercostal nerves, the pleural inflammation, the pulmonary parenchymal damage and the presence of post-operative intercostal drains [1]. Video-assisted thoracic surgery (VATS) has been developed as an alternative approach to thoracotomy for a variety of diagnostic and therapeutic operations, including pleurodesis for spontaneous pneumothorax, lung biopsy, excision of benign mediastinal tumours and thoracic sympathectomy allowing equally effective surgery with significantly less morbidity [2]. However, VATS is not without its attendant complications, and recent observations have quantified associated residual and neurological sequelae [3]. In an attempt to reduce these complications, conventional VATS has been developed to include smaller working ports and instrumentation as well as fewer incisions [4,5]. On the other hand, despite the advance in analgesic procedures, the ideal postoperative analgesic regimen following the VATS procedure remains an open issue. Thoracic epidural analgesia, the gold standard for the control of pain, may be somewhat oversized for many thoracoscopic procedures while continuous infusion of systemic non-steroidal anti-inflammatory (NSAI) drugs and/or of opioids have collateral effects, including respiratory depression, gastrointestinal problems and bleeding [1]. According to the promising results reported in other surgical procedures including hysterectomy [6], reduction mammoplasty [7], hernia operations [8] and laparoscopic cholecystectomy [9],

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recently Sihoe et al. [10] have reported that pre-emptive wound infiltration with a local anaesthetic reduces the postoperative wound pain following needlescope-VATS (n-VATS) sympathectomy for palmar hyperhidrosis. The concept of pre-emptive analgesia has gained popularity following experimental work, demonstrating that early control of pain can alter its subsequent evolution as well as the recognition that nociception produces important physiological responses, even in adequately anaesthetised individuals, and the understanding that for many individuals the minimisation of pain can improve clinical outcomes [11]. The pre-emptive analgesia is based on the intuitive idea that if pain is treated before the injury occurs, the nociceptive system will perceive less pain than if analgesia is given after the injury has already occurred. The preoperative administration of analgesic will modify the afferent nociceptive barrage from the site of injury, thus preventing the development of central sensitisation and hyperalgesia [12].

Thus, we have focussed on this argument in the aim of the present study, which is to determine whether pre-emptive local analgesia (PLA) has an effect to reduce acute postoperative pain following standard-VATS (s-VATS) sympathectomy, in view of n-VATS being considered less painful than the s-VATS procedure [4,5]. Furthermore, in PLA, we used a short-acting local anaesthetic such as lidocaine to differentiate better if the analgesic effect on postoperative pain is due to a pre-emptive rather than to a local effect of anaesthetic.

2. Materials and methods

2.1. Patients and study design

This prospective, double-blinded, randomised study included a consecutive series of 18 patients undergoing bilateral VATS sympathectomy for palmar hyperhidrosis during January 2005–December 2007. There were six male and 12 female patients. The mean age of the patients was 27.9 ± 7.57 years (range: 21–41 years). The patients were offered surgery after they were previously deemed intolerant or failed medical therapy for their symptoms. The patients received a detailed consultation to evaluate personal, professional and social handicaps related to palmar hyperhidrosis. A preoperative X-ray was performed to exclude lung or pleural disorders. Exclusion criteria included a history of any of the following conditions: other thoracic surgery performed before VATS sympathectomy, requirement of chest drainage for management of postoperative air leakage or pleural effusion, chronic pain condition, current use of analgesic medications, contraindications to the use of NSAI or allergy to lidocaine. The patients enrolled in the study were injected with local anaesthetic at the randomised side before the trocars were inserted. A table of random numbers was used to generate a randomised schedule as to which side of each patient would be assigned to receive PLA. An envelope containing the side assignment (and the order of lidocaine and saline infusion) was prepared, sealed and numbered for each patient. On the morning of surgery, one of the investigators opened the envelope and prepared two identical 20-ml syringes that were labelled for each side. This investigator had no further involvement with the study. Two different solutions were used: one containing 2% lidocaine and epinephrine, and another filled with normal saline and epinephrine. These syringes were numbered and coded, and the code (recorded by the anaesthesiologist) was not broken until after all the pain data were collected. Because the contents of both sets of syringes were colourless and odourless, the surgical team, the data collector and the patient were unaware of which side PLA was received. Following operation, the side which received local anaesthesia was then compared with the control site for controlling of pain and paraesthesia at different time points after the operation (4, 24 and 168 h). The patients and investigators were both blinded concerning the side having been randomised to receive PLA. Identical surgery was performed on each side of the chest, allowing the patients to act as their own controls and to minimise confounding factors, thus increasing the power of the study. The protocol of this study was approved by the Hospital Ethics Committee of the Second University of Naples, and written informed consent was obtained in all the cases before entering the study.

2.2. Operative procedure

Selective bilateral sympathectomy was performed in a one-stage procedure. All surgical procedures were performed by the same surgeon (one of the authors, M.S.). General anaesthesia using single-lung ventilation technique was applied in all the patients. A slight degree of cranial elevation and the lateral thoracotomy position helps the lungs to drop away from the operating site exposing the sympathetic chain. The patient was placed on the operating table in a semi-sitting position with arms in abduction. Immediately after the induction of anaesthesia, the surgeon opened the randomisation envelopes. On the side randomised for PLA, local infiltration with 2% lidocaine and epinephrine was injected at each port 5 min before the incision. The first port was placed in the third or fourth intercostal space below and anterior to the inferior angle of the scapula. A 10-mm 0° telescope was passed through this port. Two additional ports of 5 mm were, respectively, placed for instrumentation at the level of the third and fourth intercostal spaces in the anterior axillary line. The maximum dose of lidocaine or of the placebo was 10 ml for all the three ports. During operation, we avoided torquing the camera or instruments in the ports, which could compress the intercostal nerves, causing damage. If the operation turned out to be unidentical on both sides, then the patient was excluded from the study. The sympathetic chain was identified at the level of the crossing of the fourth, third and second costal heads. The parietal pleura were opened. The thoracodorsal sympathetic trunk at the T3 level was resected by diathermy until the T2 level. We have been careful during the diathermal incision of the pleura to minimise surgical trauma. All procedures were completed by insertion of a 16 F chest tube through a trocar, and the lung was re-inflated under visual control. The chest tube was aspirated while the anaesthesiologist ventilated the patient manually, exerting continuous positive pressure for a few seconds, to prevent pneumothorax before the drain was subsequently removed. Intramuscular diclofenac was administered every 4–6 h postoperatively according to the

patients request if the pain became intolerable. The patients were discharged the day after the operation.

2.3. Pain assessment

Before surgery, the patients were shown how to complete a pain questionnaire, which they retained and completed after surgery. Pain assessment was carried out using two upgraded vertical visual analogue scales (VASs), one for each operation side. The upper margin of the scale had a score of zero, representing no pain, and the lower margin a score of 10, representing the worst pain imaginable. The patients were asked to complete the VAS on the left side of the page for their left-sided pain and on the right side of the page for their right-sided pain. Pain scores were recorded at each of the following times: 4, 24 and 168 h after surgery. All pain questionnaires were completed independently by the patients and posted back to the authors.

2.4. Paraesthaesia assessment

The presence of paraesthesia was valuated using the descriptions employed by Sihoe, who demonstrated that the most common characteristics for paraesthesia were 'pins and needles', a sensation of 'abnormal swelling' and 'numbness' [10]. Thus, the patient completed a single questionnaire by placing the letters L (left), R (right) or R + L (both sides) beside the words ('pins and needles', 'abnormal swelling' and 'numbness'), which described the sensation which they experienced at each of the following times: 4, 24 and 168 h after surgery.

Patients were also asked to subjectively grade the severity of any paraesthesia on a 4-point analogue scale and the difference between the PLA side and the control side. We regard paraesthesia severity of 1 on the 4-point scale to be 'mild', 2 to be 'moderate' and 3 to be 'severe'. All paraesthesia questionnaires were completed independently by the patients and posted back to the authors.

2.5. Other data

Finally, all study patients were scheduled for follow-up either by visits or through mail at 1 and 12 months after operation. Patients were asked to rate their operative outcome of the procedure (1 for no change, 2 for satisfactory and 3 to denote a significant improvement) and its impact on their quality of life.

2.6. Statistical analysis

Results are reported as means with standard deviations for continuous variables and as percentages for categorical variables. Intensity of postoperative pain for both sides measured by VAS (from 0 to 10) was summarised by median (range) and compared by the Wilcoxon rank-sum test. Scores of residual neuralgia were analysed by the Wilcoxon rank-sum test. A value of p less than 0.05 was considered statistically significant. MedCalc® statistical (MedCalc Software, Mariakerke, Belgium) software was used for statistical analysis.

Table 1
Comparing intensity of pain on PLA side versus control side in the post operatory. Data are presented as mean ± standard deviation and as median (range). Wilcoxon rank-sum test is used for statistical analysis.

Time (h)	PLA side	Control side	p-value
4	2.7 ± 0.8 3 (2.0–3.0)	4.0 ± 1.2 4 (3.0–5.0)	0.001
24	2.5 ± 0.7 2 (2.0–3.0)	3.5 ± 1.5 3 (2.0–3.0)	0.004
168	1.8 ± 0.7 2 (1.0–2.0)	2.1 ± 0.8 2 (2.0–3.0)	0.10

3. Results

All the enrolled patients concluded the study. No conversion to open technique was necessary and there was no operative mortality. The average actual operating time was about 15 min for each side. No postoperative complications were recorded and the mean length of stay in the hospital was 1.38 ± 0.14 days (range 1–3 days).

3.1. Pain

Table 1 shows the mean and the median pain scores on the 10-point VAS scale (0 equals no pain, 10 equals the worst imaginable pain). At 4 and 24 h postoperatively, the PLA side showed a lower intensity of pain than the control side with statistically significant difference ($p = 0.001$ and $p = 0.004$, respectively). At 168 h postoperatively, we registered a trend for reduced pain on the PLA side with respect to the control side but the difference is not statistically significant ($p = 0.156$). The results are shown graphically in Fig. 1.

3.2. Paraesthesia

In the PLA side, we registered two (11.1%) cases of paraesthesia (range of severity: mild) while three (16.6%) in the control side (range of severity: two mild and one moderate) 4 h postoperatively. At 24 h postoperatively, three (16.6%) cases of paraesthesia (range of severity: two mild and

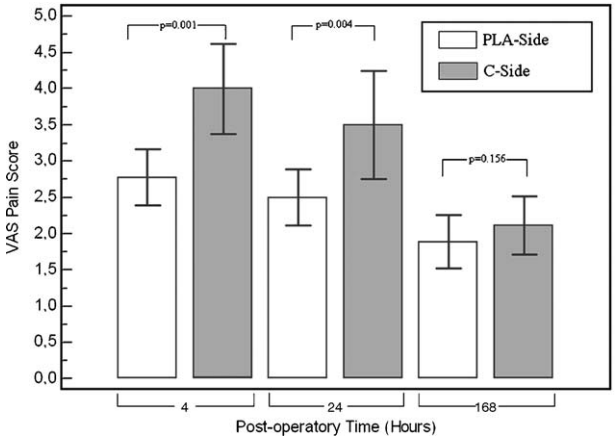

Fig. 1. Graphic compares the intensity of pain at different post operatory points time on the side treated with pre-emptive local analgesia (PLA) versus control side (C side). Intensity of postoperative were summarized by median and compared by Wilcoxon rank-sum test.

one moderate) were found in the PLA side in contrast to five (27.7%) cases (range of severity: two mild, two moderate, and one severe) in the control side. Finally, at 168 h postoperatively, four (22.2%) cases (range of severity: two mild, one moderate, and one severe) and five (27.7%) cases (range of severity: two mild, two moderate, and one severe) of paraesthesia were scheduled in the PLA side and in the control side, respectively. Although the incidence of neurological complaints was higher in the control side than in the PLA side, these differences were not statistically significant at 4, 24 and 168 h postoperatively.

3.3. Other data

A total of 17 out of 18 (94%) patients noted a change in the palmar hyperhidrosis status after surgery. Following discharge, all the patients returned to normal quotidian activity. Compensatory hyperhidrosis was complained by two patients on follow-up (grade 1 in both cases). However, the symptoms were tolerated and no further treatment was sought for them.

4. Discussion

The past few years have seen VATS rapidly becoming the preferred approach for selected surgical procedures, including thoracodorsal sympathectomy [13]. VATS is associated with less postoperative pain, less risk of retained secretions and atelectasia, which permits faster recovery and discharge from the hospital [14]. However, pain after VATS may be significantly extended till the first postoperative day with a potential to delay the early discharge home, and it is not surprising that there are scattered reports in the literature on postoperative pain management following VATS [15,16].

Our study is designed to clarify if PLA may reduce the postoperative pain after s-VATS sympathectomy for palmar hyperhidrosis. Most studies on acute pain illustrate large inter-patient variation in the rating of pain intensity and the main difficulty in comparing the extent of pain is the adequacy of the control group. Many factors such as sex, age, race, anxiety and pain tolerance may alter the level of perceived pain. Thus, the variables encountered when measuring pain in different patients would necessitate a larger group in a study. Considering the small number of patients of our study, and in an attempt to reduce these confounding variables to minimum and to increase the power of the study, we decide to use a study design in which patients act as their own controls. The same surgeon performs all operations and if he judges that the operation is not identical on both sides, the patient is excluded from the study.

The design of our study and the outcome measures used are the same as those of a previous study reported by Sihoe, but with two key differences. First, we evaluate the role of PLA on the reduction of pain of the first operation following s-VATS instead of n-VATS sympathectomy. Sympathectomy for hyperhidrosis using the needlescopic VATS technique has shown clinically excellent results with less postoperative pain and scarring [4,5,12]. Although needlescopic operations may reduce the trauma inflicted on the chest wall and represent the next step in the evolution of VATS, there are still some limitations to its use because of the narrow field of vision, lower resolution and difficulty in maintaining fine control when compared with conventional VATS [17].

Sihoe et al. [10] report the maximal benefits on the pre-treated side at 7-days postoperatively while at the other time points (4 and 24 h, respectively) only a trend for reduced pain on the PLA side was observed with no statistically significant difference compared with the control side. Conversely, in our study, the maximal benefits are seen up to 24 h post-operation and then they progressively decreased. The disparity among the aforementioned studies may be due to the theory that n-VATS is not painful enough to produce a noticeable difference in the first postoperative pain in comparison with the s-VATS technique. The theory of PLA in VATS surgery is that the local anaesthetic injection given before the operation reduces the degree of sensitisation produced in the nervous system by incision, retraction and trocar placement. Noxious stimulation generates reflex by hyperexcitability in the dorsal horn of the spinal cord. This central sensitisation prolongs and increases sensitivity to noxious stimuli. In addition, repetitive torquing of the wounds from surgical instruments generates multiple noxious stimuli, which evoke a progressively escalating response in the spinal cord with further magnification of the pain. Theoretically, there is less risk of injuring the intercostal structures during the insertions of the needlescopic instruments than during insertion of the 5-mm and 10-mm standard instruments. Moreover, the length of the skin incisions is smaller than in conventional VATS with further reduction of surgical trauma. If the noxious stimulations decrease, there are fewer nociceptive impulses, and the theoretical power of PLA may be masked in the first 24 h after the operation.

The clinical implication of our results is that PLA renders these patients pain free when pain would be at its most intense and may help in discharging them the night after the surgery. Yet, PLA would make the s-VATS comparable with n-VATS regarding the degree of first postoperative pain, in view of the fact that n-VATS is preferred by some authors because it is less painful than the s-VATS procedure.

Second, lidocaine instead of bupivacaine was used for PLA. Bupivacaine has a higher lipid solubility, tissue permeability and affinity for sodium channels than lidocaine, resulting in greater anaesthetic potency [18]. As a confirmation of that, for spinal or epidural anaesthesia, a larger concentration of lidocaine than of bupivacaine is required to block nerves. In addition, bupivacaine has a longer duration of action than does lidocaine [19]. Thus, considering the different features of both anaesthetics, we suppose that while using bupivacaine rather than lidocaine, it would be more difficult to find out if the reduction of postoperative pain is due to a pre-emptive effect or due to the simple local effect of the anaesthetic. Although PLA seems to be effective, the question remains: Would postoperative pain in the PLA site have been as equally well managed if the anaesthetic had been given after the incision was made? Bourget et al. [20] compare if PLA yields better post-operative pain control than infiltration of local anaesthetic at the time of wound closure in 200 patients undergoing laparatomy. The results indicate that pain is no better controlled with pre-incisional infiltration than post-incisional infiltration of bupivacaine and the authors raise the question

of the benefit of PLA in long-term postoperative care. In a review of 80 randomised trials including 3761 patients, from which 1964 patients received pre-emptive treatment, 20 trials comparing pre-emptive with post-incision application of peripheral local anaesthetics were analysed. The authors conclude that there is no evidence for improved pain relief with PLA wound infiltration compared with a similar post-incision administration of medications [21]. In the literature, we have not found results of studies involving pre-incisional versus post-incisional local analgesic methods after a thoracic procedure.

However, considering that the half-life of lidocaine is only 1.5–2 h and that we registered significant effect in the control of pain until 24 h after the operation, our data indicates that the benefit seen is due to the pre-emptive blockage of the sensitisation of central nociceptive pathways rather than the simple local effect of lidocaine and confirm that PLA does not simply mean 'before incision'.

On the other hand, the choice of a short-acting anaesthetic as lidocaine instead of a long-acting anaesthetic as bupivacaine may explain why we do not find a significant effect of PLA in controlling pain 24 h postoperatively in contrast to Sihoe's experience. It has also been argued that the effect of PLA should not stop at the end of surgery because nociceptive stimuli continue to be produced by the wounds until they are fully healed [22]. Thus, to achieve a pre-emptive effect, it is likely that the intervention must be effective not only during and immediately after the surgical procedure but also during the postoperative phase. In confirmation of that, some clinical trials have reported PLA failure because of inadequate duration of action of the local anaesthetic [11]. Thus, our result seems to suggest that the failure of regional anaesthesia to block all the input of nociceptors during operation, or early onset of postoperative pain as a result of the use of shorter-acting local anaesthetics, might have contributed to the development of central sensitisation with decrease of the PLA effect following 24 h after the operation. Finally, lidocaine is not as expensive as bupivacaine and the chances of severe complications are less with bupivacaine [23], although these patients are not at higher risk for local anaesthetic toxicity.

In the light of our experience, PLA seems to be an acceptable and effective strategy for reducing the post-operative pain following standard VATS procedure. The infiltration of the operative field with local anaesthetic is very cheap and the required drug is easily available and has few side effects. Furthermore, in today's climate of financial constraints on health-care expenditure, it may be important to consider the economic effect of adopting pre-emptive analgesia into the routine of VATS sympathectomy with the potential of reducing overall postoperative analgesic requirements, of early discharge to home and early return to work. However, some consideration should be formulated to implement PLA effect in the future with the next step of realising day-case surgery for VATS sympathectomy. If PLA controls the pain secondarily to intercostal nerves and to skin, it will not prevent the nociceptive impulse that the pleural structures transmits to the central nervous system in case of pleural damage during sympathectomy using electrocautery, and the mediastinal shift from one-lung ventilation, lung collapse and expansion sequentially, right and left. Thus, Sihoe et al. [10] propose a technique of selective lobar collapse, which is useful to minimise the mediastinal shift from the one-lung ventilation but may not prevent the noxious stimuli originating from pleural damage. Therefore, in view of this consideration, further studies are advocated to evaluate if the pre-emptive pleural cavity analgesia using the instillation of local anaesthetic may minimise the nociceptive impulse from pleural damage caused by electrocautery. Conversely, considering the mechanism of PLA reported above, we believe that this strategy does not work as well in open thoracic as in minimal invasive procedure. Intercostal nerve injury and skin incision are the potential targets of pre-emptive analgesia action but the pain from thoracotomy is secondary to several components including a visceral component that local anaesthesia cannot control. In confirmation, Cerfolio et al. [24] evaluated the use of PLA of the skin before thoracotomy in 119 patients. The patients are prospectively randomised into two groups. One group receives an injection of 1% lidocaine with epinephrine in the planned skin incision just before thoracotomy, and the other group receives an equal amount of saline and epinephrine. Although a trend is noted towards less pain in the lidocaine group during the first three postoperative days, the difference is not statistically significant at 3, 6 and 12 months after the operation. Thus, the authors conclude that the injection of lidocaine and epinephrine in the skin just before thoracotomy does not decrease the amount or type of pain during the hospital stay or at 3, 6 and 12 months after surgery.

Regarding paraesthesia, we do not find any effect for PLA in reduction of neurological sequelae for several factors. Although the incidence of paraesthesia is higher in the PLA side than in the control side, the differences are not significant. Surprisingly, we note that the incidence of paraesthesia tended to increase in relation to the reduction of pain. Probably, the patients are not able to clearly distinguish paraesthesia from postoperative wound pain, especially at 4 and 24 h postoperatively. However, thoracoscopic sympathectomy is a minimal surgical procedure, which is associated with low intensity of paraesthesia in contrast to other procedures, including VATS pleurodesis for pneumothorax. Finally, our study presents some limitations and several critical points may be formulated.

First, we used the three-point scale to assess the patient's perception of operation, but it may be inadequate because there does not have an option for the patients to express dissatisfaction, making it difficult to see how satisfaction correlates with pain, compensatory hyperhidrosis and so on. However, the main limitation in evaluating the results of surgical sympathectomy is the inability to measure objectively the outcome of the subjective nature of all these methods. Many centres have developed different scales or parameters to evaluate the success rate after VATS sympathectomy, none of which is widely used by the others [25].

Second, the lack of significance seen with paraesthesia may be affected by the use of a 4-point scale which is probably less adequate than a 10-point VAS used for the assessment of pain.

Third, recent literature has suggested a potential role for PLA in prevention of chronic incisional pain [1], but we have considered it unnecessary to evaluate this since PLA has not

yielded significant results in controlling pain 24 h post-operatively.

Fourth, although our study may have minimised variables such as age, sex, race and anxiety, it did not eliminate small differences in surgery and hence tissue damage, despite the procedure being carried out by the same surgeon. However, for the small number of cases, we are unable to arrive at a final decision, but only an impression regarding the efficacy of the role of PLA in preventing pain after s-VATS procedure.

5. Conclusion

Our results seem to confirm that the injection of a short-acting local anaesthetic such as lidocaine in the skin just before standard VATS procedure suppresses the local pain mediators, hence resulting in significantly less pain up to 24 h postoperatively. By contrast, it does not seem to decrease the pain 24 h thereafter. However, because of the small number of patients in our study, further studies are required to corroborate our results and to implement PLA for VATS patients in the future.

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