

Original Article

Chest tube insertion is one important factor leading to intercostal nerve impairment in thoracic surgery

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Abstract

Objectives: Chest tube insertion seems to be one important factor leading to intercostal nerve impairment. The purpose of this prospective study was to objectively evaluate intercostal nerve damage using current perception threshold testing in association with chest tube insertion.

Methods: Sixteen patients were enrolled in this study. Intercostal nerve function was assessed with a series of 2000-Hz ($A\beta$ fiber), 250-Hz ($A\delta$ fiber), and 5-Hz (C fiber) stimuli using current perception threshold testing (Neurometer CPT/C[®]). Current perception threshold values at chest tube insertion were measured before surgery, during chest tube insertion and after removal of the chest tube. Intensities of ongoing pain were also assessed using a numeric rating scale (0 – 10).

Results: Current perception thresholds at each frequency after surgery were significantly higher than before surgery. Numeric rating scale scores for pain were significantly reduced from 3.3 to 1.9 after removal of the chest tube ($p=0.004$). The correlation between current perception threshold value at 2000 Hz and intensity of ongoing pain was marginally significant ($p=0.058$).

Conclusions: This is the first study to objectively evaluate intercostal nerve damage at chest tube insertion. The results confirmed that chest tube insertion has clearly deleterious effects on intercostal nerve function.

Introduction

Post-thoracotomy pain syndrome (PTPS) is well established as a clinically important entity after thoracotomy, with persistent pain reported in 30-40% of patients [1]. PTPS is defined by the International Association for Study of Pain (IASP) as ‘Pain that recurs or persists along a thoracotomy scar at least 2 months following a surgical procedure’ [2]. Many articles have been reported from the perspective of preoperative factors, intraoperative factors [3], and anaesthetic factors to reduce PTPS. Above all, video-assisted thoracic surgery (VATS) has been widely accepted and applied for almost all thoracic surgeries, given the reduced invasiveness to patients and equivalent or favourable surgical results compared to conventional thoracotomy [4]. VATS has thus also been expected to decrease post-thoracotomy pain.

On the other hand, Kato et al. [5] described a patient with severe neuropathic pain induced by ligation of an intercostal nerve after chest tube insertion for secondary pneumothorax. This was a relatively rare case, but we have often encountered patients who, even after VATS, suffer from continuous post-thoracotomy pain around the chest tube insertion scar. However, most articles have focused solely on the thoracotomy site. Few reports have examined the influence of chest tube insertion. Moreover, a key problem with researching post-thoracotomy pain has been the lack of objective tools to measure pain.

We have already evaluated intercostal nerve damage by current perception threshold (CPT) using the Neurometer CPT/C[®] (Neurotron, Baltimore, MD, USA) to objectively assess nerve function, confirming that VATS is a useful procedure to reduce PTPS without using metal retractors that may damage the intercostal nerves [6]. CPT testing can evaluate sensory nerve fibers quantitatively and selectively. CPT values with 2000-, 250-, and 5-Hz stimuli indicate the functions of A β , A δ , and C fibers, respectively. A β fibers are large myelinated fibers

responsible for touch and pressure sensation. A δ fibers are small myelinated fibers responsible for sharp pain. C fibers are unmyelinated fibers responsible for sensing temperature and dull pain [7, 8].

The purpose of the present prospective study was to objectively evaluate intercostal nerve damage associated with chest tube insertion following lung cancer surgery using CPT testing. Correlations between CPT values and intensities of ongoing pain were also assessed.

Patients and methods

Patients

The study was performed at Nagasaki University Hospital from June 2012 to October 2012. Local ethics committee approval was obtained prior to commencement of the study (Approval number: 12052809). All patients provided written informed consent. A total of 16 patients (7 men, 9 women; mean age, 69.1 years) participated in this study. All patients had primary lung cancer. Patients who underwent pneumonectomy or chest wall resection, or who had a history of prior thoracotomy were excluded from this study.

Surgical technique for lung cancer and management of chest tube.

All VATS procedures were performed by visualization through a television monitor only and the procedure was performed without metal retractors using the wound retraction system (WR) (Alexis Wound Retractor[®]; Applied Medical, Rancho Santa Margarita, CA, USA), with an incision length within 4 cm length to remove the lung from the chest cavity. Standardized three-port placements (Thoracoport[®], 11.5 mm; Nippon Covidien, JAPAN) were used regardless of the resected lobe and segment. Once metal retractors were applied, or even if metal retractors were not used but a skin incision more than 7 cm was made, the procedure

was defined as thoracotomy for the purposes of this study.

An epidural catheter was placed for each patient and general anaesthesia was induced using propofol and rocuronium. After double lumen endotracheal intubation, the patient was placed in a lateral position. At first, a 0° thoracoscope was introduced through the seventh intercostal space in the anterior axillary line. Systemic mediastinal or hilar lymph node dissection was performed according to clinical stage, performance status, and lymph nodal status of the patient.

A 24-Fr chest tube (Argyle[®], thoracic catheter, straight, 24-Fr/Ch (8.0 mm) ×52 cm; Nippon Covidien) was inserted through the seventh intercostal space where the port was mainly used as a video camera port in both procedures. We closed the chest with pericostal sutures (stitches placed on top of the fourth rib and at the bottom of the fifth rib, to avoid injuring intercostal nerves and vessels). The chest tube was removed as soon as possible on the condition that the total amount of pleural effusion was <200 ml/day, no air leakage had been seen for more than 24 h, and no chylothorax was apparent.

Pain relief

For postoperative pain relief, an epidural catheter was placed according to the site of incision before the induction of general anaesthesia. Ropivacaine (8 mg/h) was given for no longer than 5 days. The epidural catheter was removed simultaneously with the chest tube. We did not perform any intercostal nerve or paravertebral blocks in this study. All patients received oral celecoxib (200 mg), a systemic, non-steroidal anti-inflammatory drug, twice a day for at least 1 week. If the patient was not obtaining good pain relief, a diclofenac sodium suppository (25 mg) was added.

Current perception threshold and the Neurometer CPT/C[®]

The Neurometer CPT/C[®] (Fig 1) produces constant-current sine-wave stimulation at 2000, 250, or 5 Hz. The sine waves at 2000, 250, and 5 Hz correspond to depolarization periods of 0.25, 2, and 100 ms, respectively. The electrical stimulus selectively excites distinct subpopulations of nerve fibers as a function of the sinusoid frequency [9, 10]. Thus, large myelinated A (A β), small myelinated A (A δ), and unmyelinated C (C) nerve fibers are evaluated with a series of 2000-, 250-, and 5-Hz stimuli, respectively. A pair of gold-plated surface electrodes was placed just beside the site of chest tube insertion (Fig 2). The methods of CPT testing were similar to those described previously [6, 11,12].

Patients were also asked to rate the intensity of total ongoing pain (both at the site of thoracotomy and chest tube insertion) using a numerical rating scale (NRS) (0 – 10, with 0 = no pain, 10 = worst pain imaginable). Thus, NRS scores and CPTs were measured before surgery, during chest tube insertion (just before removal of the chest tube) and 7 days after surgery. When chest tube placement was prolonged to more than 7 days, CPT was measured two days after chest tube removal.

Statistical analysis

Differences among groups were determined using the paired T-test for continuous variables. CPT data was analyzed by one-way factorial analysis of variance (ANOVA). A value of $p < 0.05$ was considered statistically significant. Statistical analysis was performed using SAS version 9.2 statistical software (SAS Institute, Cary, NC, USA).

Results

All 16 patients underwent lung resection for clinical stage I primary lung cancer, with 11

cases of lobectomy, 4 cases of segmentectomy, and 1 case of partial resection. Fourth intercostal thoracotomy was performed in 14 cases, and fifth intercostal thoracotomy in 2 cases. All chest tubes were inserted through the seventh intercostal space. The epidural catheter was placed from thoracic vertebral interspace 6 - 7 (11 cases) or 7 - 8 (5 cases) and a catheter advanced 5 cm into the epidural space. None of the patients experienced severe operative or postoperative complications, with the exception of prolonged air leakage in one patient who had removed the chest tube after postoperative day 8 and chylothorax in one patient who was treated using low-fat diet therapy. No drug-related problems or complications were caused by the analgesic procedures. No patients dropped out in this study. Patient demographics and types of surgery are shown in Table 1.

At 2000 Hz (Fig 3A), CPT values at chest tube insertion showed a significant increase ($p=0.007$) and increased still further after removal of the chest tube ($p=0.01$) compared to CPT values before surgery. At 250 Hz (Fig 3B), CPT values at chest tube insertion showed a significant increase ($p=0.01$). However, CPT values after removal of the chest tube were marginally decreased compared to at chest tube insertion ($p=0.05$). Similar results were seen at 5 Hz (Fig 3C), with CPT values showing a significant increase at chest tube insertion ($p=0.002$) and decreasing significantly compared to values at chest tube insertion ($p=0.003$).

Mean postoperative pain measured using the NRS (Fig 4) was significantly lower ($p=0.004$) after removal of the chest tube than during insertion of the chest tube. Five of 16 patients (31.3%) complained of more pain at the site of chest tube insertion than from thoracotomy. A marginal correlation was observed between CPT values at 2000 Hz during insertion of the chest tube and after removal and NRS score ($p=0.058$).

Discussion

CPT testing using the Neurometer CPT/C[®] has now seen wide use in various clinical setting associated with quantitative evaluation of sensory function, and its utility and objectivity have been confirmed [13, 14]. However, use of CPT testing related to thoracic surgery has not been reported except in our previous study [6]. We objectively assessed intercostal nerve damage by chest tube insertion in lung cancer surgery using CPT testing because we have encountered some patients who complain of persisting pain around the site of chest tube insertion despite use of VATS. Intercostal nerve damage is well known as a main cause of post-thoracotomy pain. We have previously evaluated intercostal nerve damage by CPT with the Neurometer CPT/C[®], to objectively assess intercostal nerve function and offer the first confirmation that VATS is useful for reducing PTPS [6]. The present study demonstrated that chest tube insertion is also clearly harmful to the intercostal nerves and could result in post-thoracotomy pain.

We have shown in this study that the function of myelinated fibers ($A\beta$ and $A\delta$ fibers) in the intercostal nerve is significantly impaired after insertion of the chest tube. Continuous compression of intercostal nerves by the chest tube is also responsible for elevated CPT values, as previously shown with metal retractors during surgery [6]. We also confirmed that myelinated fibers are sensitive to mechanical compression. On the other hand, unmyelinated C fibers were also seen to be significantly impaired after insertion of the chest tube in this study, even though C fibers were not impaired by metal retractors [6]. Han et al. [14] reported that the degeneration of $A\beta$ and $A\delta$ fibers was more rapid than that of C fibers in patients with diabetic neuropathy. Given these results, C fibers (unmyelinated fibers) seem stronger than $A\beta$ and $A\delta$ fibers (myelinated fibers) in terms of resisting physical stimuli. We do not have a definite cause for this result, but we speculated that continuous chest tube insertion for 3.8 days, as the average duration of chest tube insertion in this study, caused more intercostal nerve damage than use of metal retractors during several hours of lung surgery.

In the present study, the NRS scores decreased significantly after chest tube removal, although this decrease could represent the natural course of wound healing. As we have experienced in daily practice, five of 16 patients (31.3%) complained of more pain at the site of chest tube insertion than at the thoracotomy site. Moreover, two of those five patients (40.0%) had undergone VATS. Surgeons should thus recognize that chest tube insertion could result in more intercostal nerve damage than thoracotomy itself.

We found a marginally significant correlation between CPT values at 2000 Hz during insertion of the chest tube and after removal and NRS. The present results implied that CPT values may be useful for evaluating the intensity of ongoing pain despite surgical procedure, race, age, sex and other factors considered to impact postoperative pain. However, this test did not always correlate with clinical symptoms of pain, because neuropathic pain has been reported to involve both peripheral and central mechanisms. We have previously reported on allodynia and pain of postherpetic neuralgia using CPT and found no correlation between intensities of ongoing pain and CPT values at any frequencies, proposing that postherpetic neuralgia might be a pain syndrome including both peripheral and central mechanisms. [11].

Wildgaard et al. [15] evaluated neurophysiological characterization of PTPS after VATS by using quantitative sensory testing, using thermal and mechanical stimuli. In that study, both PTPS and pain-free patients showed increased sensory thresholds implying the existence of nerve injury, but no significant quantitative differences between PTPS and pain-free patients could be found. These findings suggested that the presence of factors other than intercostal nerve injury was important for PTPS after VATS lobectomy. That report indicated that the cause of neuropathic pain is not simply damage to a single nerve, but involves multi-factorial mechanisms. For example, pregabalin, a derivative of γ -aminobutyric acid, is a drug that binds to Ca^{2+} channels in the nerve presynapses and suppresses release of neural transmitters, thus showing analgesic effects for neuropathic pain [16]. For this reason, pregabalin has now

gained wide use for neuropathic pain, including post-thoracotomy pain. Matsunami et al. [17] reported on four patients who showed significant improvement of chronic pain after thoracotomy with pregabalin administration.

Moreover, several genetic approaches have attempted to identify the intensity of postoperative pain. Lee et al. [18] reported that catecholamine-O-methyltransferase polymorphisms are associated with postoperative pain intensity after elective surgery. Moreover, Ochroch et al. [19] identified haplotypes of the μ -opioid receptor (OPMR1) that predicted increases in self-reported pain on postoperative day 3 after thoracotomy. We hope that the detailed mechanisms underlying post-thoracotomy pain will be resolved in the near future and 'tailor-made' pain control will move a step closer.

However, it is realistic for surgeons to find other effective methods to reduce intercostal nerve damage by chest tube insertion in daily life. As recently developed silastic flexible drains, Blake[®] drains (Ethicon, Somerville, NJ, USA) are available and expected to address the disadvantage of conventional drains in terms of rigidity and thickness. Nakamura et al. [20] have used these new drains in 420 cases of thoracic surgery. The drains functioned efficiently even under situations of postoperative bleeding, prolonged air leakage, and chylothorax. Moreover, the most important point in that study was that no patients complained of discomfort resulting from drain placement. They concluded that Blake drains represent an acceptable option for general thoracic surgery. Thus, it may be worthwhile to assess intercostal nerve damage using thinner, softer drains, such as the Blake drain, using CPT testing. Use of such drains could alleviate pain around the site of chest tube insertion. However, Clark et al. [21] reported encountering life-threatening hypovolemic shock in patients after thoracic surgery associated with non-functioning small-sized silastic drains. Moreover, we have experienced several clinical cases of severe subcutaneous emphysema with Blake drains that did not appropriately drain the air from the chest cavity, especially in

patients with severe emphysematous lung. Sakakura et al. [22] reported not only on the efficiency of Blake drains, but also on their disadvantages. In that study, insufficient air evacuation was seen in some cases compared to conventional drains and suction was considered warranted when air leakage occurred. Although we sometimes use it in partial resection of primary or metastatic lung cancers, mediastinal tumours, or spontaneous pneumothorax, we do not always use suction in lung cancer surgery.

This present study had three main limitations. First, the sample population was very small and obtained from a single institution. Small samples sometimes affect the statistical accuracy. Second, the site of chest tube insertion was also used as a video camera port, where the scope was usually heavily manipulated during surgical procedures. We thus cannot exclude the possibility of effects on physical oppression. Third, we cannot discriminate the pure intercostal nerve damage with chest tube insertion from the retractor's damage itself because we included both VATS and thoracotomy approaches. Future studies are needed to address these limitations.

Conclusion

This represents the first report to assess intercostal nerve damage after chest tube insertion during lung cancer surgery using CPT testing. The present study demonstrated that chest tube insertion has negative effects on the intercostal nerve, as seen for metal retractors during thoracotomy. Attention needs to be paid not only to the thoracotomy wound, but also to the chest tube in reducing pain.

Acknowledgments

None

Conflict of interest statement

Miyazaki and other co-authors have no conflict of interest.

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Figure legends

Fig. 1. Neurometer CPT/C[®] for measurement of current perception threshold (CPT) values.

Fig. 2. The experiments were carried out with patients in a supine position in an isolated room. A pair of gold-plated surface electrodes was placed just beside the site of chest tube insertion.

Fig. 3. The transition of CPT values at 2000 (A), 250 (B), and 5 (C) Hz in the intercostal nerve associated with the influence of chest tube insertion.

A) CPT values at 2000 Hz during insertion and after removal of the chest tube were significantly higher than before surgery ($p=0.007$, 0.01 , respectively).

B) CPT values at 250 Hz were significantly higher during insertion than before surgery ($p=0.01$). CPT values after removal of the chest tube were not significantly decreased compared to CPT values at chest tube insertion ($p=0.05$).

C) CPT values at 5 Hz during insertion were significantly higher than before surgery ($p=0.002$). CPT values after removal of the chest tube were significantly decreased compared to CPT values at chest tube insertion ($p=0.003$).

CPT, current perception threshold; Before, before surgery; Insertion, during insertion of the chest tube; After, after chest tube removal.

Fig. 4. NRS after removal of the chest tube was significantly lower than that during chest tube insertion ($p=0.004$). NRS, numeric rating scale; Insertion, during insertion chest tube; After, after chest tube removal.



Figure 1



Figure 2

2000 Hz

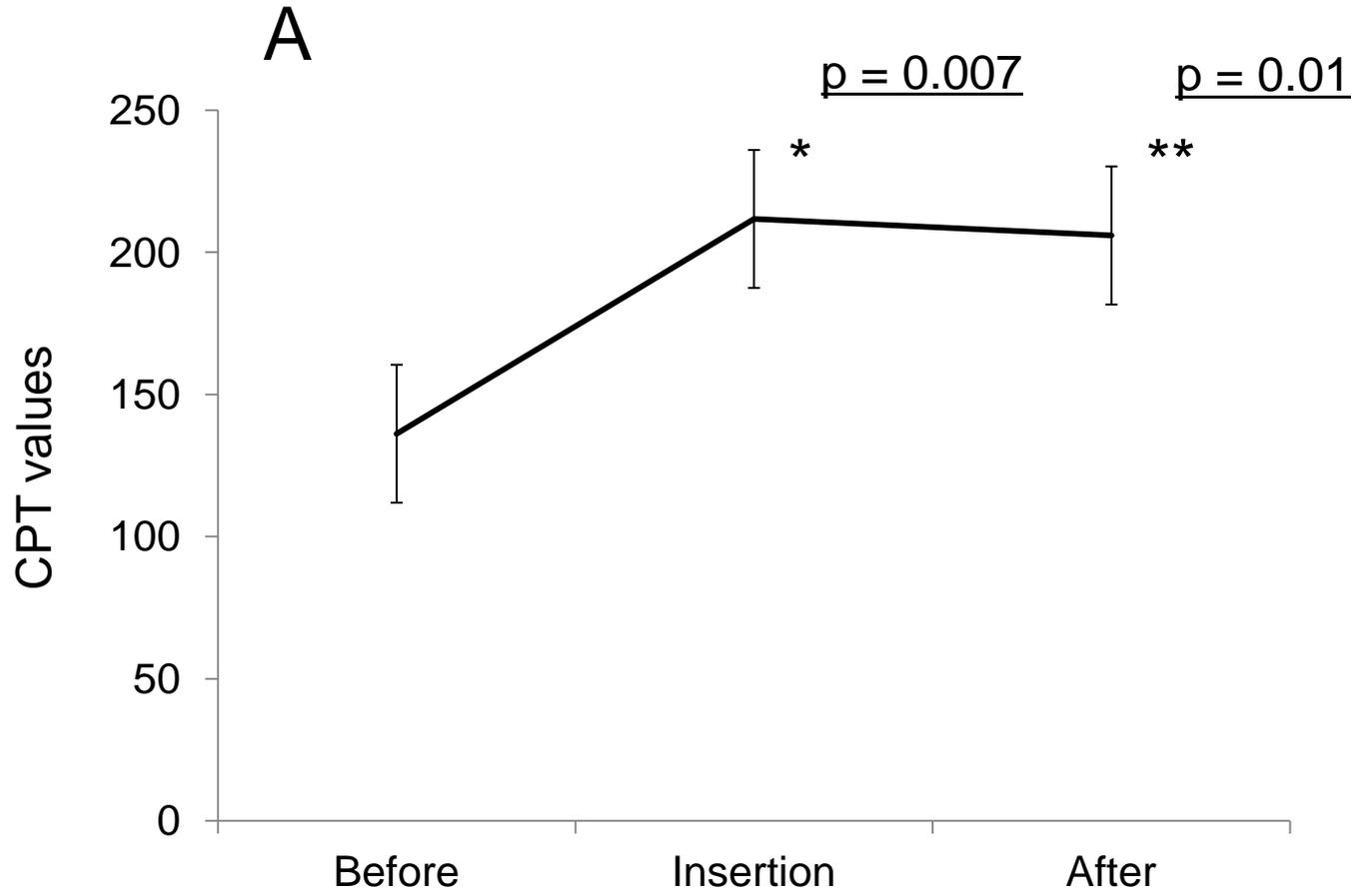


Figure 3A

250 Hz

B



Figure 3B

5 Hz

C



Figure 3C

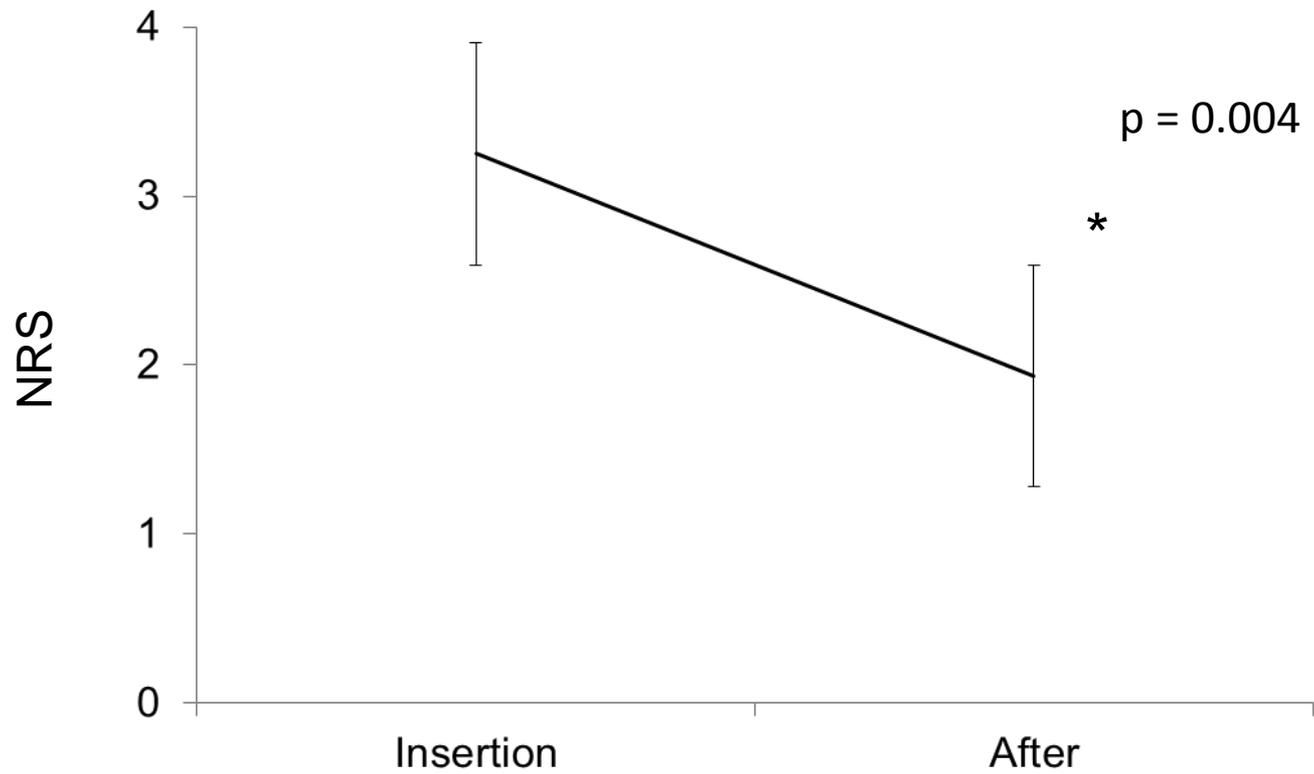


Figure 4

Table 1. Patients characteristics

Number of patients	
Age (year)	70 (54-83) ^a
Gender	
Male	7
Female	9
Methods	
VATS	5
Thoracotomy	11
Length of skin incision (cm)	8 (4-12) ^a
Surgery time (min)	249 (74-349) ^a
Chest tube insertion (day)	3.8 (2-8) ^a
Procedure	
Lobectomy	11
Segmentectomy	4
partial resection	1
Clinical Stage	
IA	13
IB	3
Resected lobe	
Right upper	3
middle	3
lower	3
Left upper	3
lower	4
Lymphnode dissection	
ND2	11
ND1	4
ND0	1

^a Median (minimum- maximum)

VATS = video-assited thoracic surgery

ND = nodal dissection