

Original Research Article

Safety and clinical outcomes of regional anaesthesia in Chinese patients with non-small cell lung cancer undergoing non-intubated lobectomy

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Abstract

Purpose: To determine the safety and clinical outcomes of epidural anaesthesia (EA) relative to internal intercostal nerve block (INB) in Chinese patients with non-small cell lung cancer (NSCLC) who were undergoing non-intubated thoracoscopic lobectomy.

Methods: Chinese patients with NSCLC (stage I or II) with no evidence of metastasis were given either EA or INB, with equal number of patients in both groups. The peri-operative outcomes determined were duration of anaesthesia/duration of surgery, SpO₂/PaCO₂ levels, cases of hypotension, and blood loss. The post-operative outcome indices measured were pain score (determined using visual analogue scale (VAS)), post-operative complications, chest drainage, duration of hospital stay, and deaths/mortality. Multiple regression analysis was used to confirm the results obtained in this study by adjusting potential covariates. Peri-operative and post-operative complications were compared between the two groups. The results obtained from 220 patients were subjected to statistical analysis.

Results: Peri-operative results showed that patients who underwent INB had shorter duration of anaesthesia (12.3 vs 31.4 min, $p < 0.05$) and shorter duration of surgery (164.4 vs 197.2 min, $p < 0.05$) than patients who underwent EA for non-intubated lobectomy. Post-operative results showed that patients who underwent INB had significantly lower number of post-operative complications than those who received EA (29 vs 44 %, $p < 0.05$). The most common post-operative complications among patients in both treatment groups were nausea, vomiting, emphysema and pulmonary complications. Patients who underwent INB had shorter hospital stay than those who underwent EA (5.1 vs 7.5 days, $p < 0.05$). These results were confirmed through multiple regression analysis.

Conclusion: These findings favour the use of INB for regional anaesthesia in NSCLC patients undergoing non-intubated lobectomy.

Keywords: Internal intercostal nerve block, Epidural anaesthesia, Non-small cell lung cancer, Lobectomy, Post-operative, Pre-operative

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INTRODUCTION

Non-small cell lung cancer (NSCLC) is one of the common causes of mortality worldwide [1]. Currently, surgical intervention is the only treatment option used in the management of lung cancer (LC). However, 20 to 30 % of patients with advanced stage Ic develop relapse, in spite of surgical removal of cancerous tissue [2]. Lung lobectomy (LL) is one of the standard surgical interventions for the management of patients with early-stage (stage I or stage II) NSCLC [3,4]. It has been observed that after lobectomy, the chances of survival in patients with NSCLC are more than 80 % [3,4]. Moreover, it has been reported that non-intubated thoracoscopic lobectomy has more benefits than tracheal intubation procedure [5]. The potential benefits of using non-intubated thoracoscopic lobectomy include lower incidence of sore throat, rapid recovery, lower complications, and shorter hospital stay [5,6]. Epidural anaesthesia (EA), with or without conscious sedation, has been used in thoracic surgeries in the past decades [5-7].

Moreover, intercostal nerve block (INB) technique is currently being used for thoracic surgeries [5-7].

This study was designed on the basis of the hypothesis that, for non-intubated thoracoscopic lobectomy, INB technique of anaesthesia results in better clinical outcome, and could be a better alternative to EA, in view of EA-induced complications. In China, there are no studies yet on the safety and clinical outcomes of EA, relative to INB in patients with NSCLC undergoing non-intubated thoracoscopic lobectomy. Therefore, the present study was designed to determine the safety and clinical outcomes of EA, relative to INB in Chinese patients with NSCLC who were undergoing non-intubated thoracoscopic lobectomy.

METHODS

Patients and ethics

Chinese NSCLC patients (stage I or stage II) with no evidence of metastasis, who were undergoing lobectomy, and who met the American Society of Anaesthesiologists (ASA) I and II criteria, were enrolled. Written informed consent was obtained from each enrolled patient. The study was initiated after obtaining ethical approval from the institutional ethics committee of Jiaotong

University (approval no. = IRB/XJU/19-3763/Jun-19). The procedures used in the study were in line with the ethical principles laid down in the Helsinki Declaration and its later amendments [8]. Patients with a history of severe renal impairment, liver disease, lung disease, and thyroid disease were excluded. Moreover, patients with any other pathology likely to affect the outcome of study, and patients who received concomitant and contra-indicated medications, as well as patients undergoing any other form of surgery, were excluded.

Treatment and procedure

Subjects who met the eligibility criteria were enrolled and were given either EA or INB, with equal number of patients in the two treatment groups. Intravenous fentanyl (50 – 100 mg) was administered to all patients as pre-anaesthesia medication. Each enrolled patient was thoroughly monitored. Carbon dioxide (end-tidal) was measured by inserting a detector into the nostril. Bispectral index (BIS) sensor was used to monitor the depth of anaesthesia.

For patients undergoing non-intubated lobectomy using EA, lidocaine (2 %) was administered in the T5/T6 thoracic region with epidural catheter so as to attain T2-T9 sensory block.

Moreover, sedation was attained by intravenous propofol administration to a Ramsay sedation score of III, with BIS values between 40 and 60. Intravenous fentanyl (25mg) was administered. For the patients undergoing non-intubated lobectomy using INB, a thoracoscopy port was created with 2 % lidocaine. Intercostal nerve block (from 3rd to 8th nerve) was produced with 0.5 % bupivacaine using a thoracoscope. A vagal block was used to prevent coughing during the procedure. Air leaks were checked using positive-pressure mask ventilation technique after discontinuing propofol. Each patient was asked to take a deep breath and cough in order to re-expand the collapsed lung following surgical intervention. In situations where the study drug was not efficacious, the patients were transferred from regional anaesthesia to general anaesthesia via intubation, at the discretion of the attending surgeon, and in consultation with the anaesthesiologist.

As a part of postoperative care, each patient was managed using either 0.1 % bupivacaine and fentanyl (1.25 mg/ml) administered via continuous epidural infusion, or using intravenous (*iv*) injection of morphine (1 mg/mL) as patient-controlled analgesia for 48-72 h.

Patients who refused to use patient-controlled analgesia were managed using 5 mg morphine via intramuscular (*im*) injection every 4 -6 h, as and when required, for the relief of post-operative pain. Chest radiography was done after surgical procedure. The chest tube was detached if no air leak was observed (with drainage of < 200 mL per 24-h period). All postoperative difficulties that required medical support were recorded.

Assessment of efficacy and safety

Peri- and post-operative outcomes were determined. The indexes of peri-operative outcome were duration of anaesthesia/duration of surgery, SpO₂/PaCO₂ levels, cases of hypotension, and blood loss. The post-operative outcomes measured were pain score (determined using VAS), post-operative complications, chest drainage, duration of hospital stay, and number of deaths/mortality. Multiple regression analysis was used to confirm the results obtained in this study via adjustment of potential covariates. Safety was assessed in terms of peri-operative ad post-operative complications in the two groups.

Statistical analysis

No formal sample size calculation was performed since the present investigation was designed as a pilot study. Quantitative data (normal data) were analysed using unpaired *t*-test, whereas quantitative data (non-normal data) were analysed using Mann Whitney test. Quantitative data are presented as mean ± SD, whereas categorical data are expressed as percentage/proportion of patients, and were analysed using Fisher exact test/Chi-squared test. Significant differences were assumed at *p* < 0.05.

RESULTS

Patients' profile

A total of 210 Chinese NSCLC patients who satisfied all the eligibility criteria were enrolled in this study. The characteristics of the enrolled patients are presented in Table 1. Demography and baseline characteristics were similar in the two treatment groups.

Peri-operative results showed that patients who underwent INB had shorter duration of anaesthesia and shorter surgical duration than

patients who underwent EA for non-intubated lobectomy (Table 2). In addition, the duration of surgery intervention was significantly lower in patients who underwent INB than in those who underwent EA. Arterial CO₂ and SaO₂ during each lung ventilation were safe and within clinically acceptable range, and there were no statistically and clinically significant differences in these parameters between the two treatment groups. Moreover, conversion from regional anaesthesia to general anaesthesia via intubation was required in only 1 subject in each group. The incidence of hypotension was significantly lower in patients who underwent INB than in patients who underwent EA. In addition, blood loss and fluid administration were significantly lower in patients who underwent INB than in those who underwent EA. These results indicate more favourable peri-operative clinical outcome in patients who underwent INB than in patients subjected to EA.

Table 1: Demography and baseline characteristic of Chinese patients with early-stage NSCLC patients undergoing non-intubated thoracoscopic lobectomy

Variable	EA Group (N=110)	INB Group (N=110)	P-value
Age (years)	57.2±3.1	59.4±4.2	>0.05
BMI (kg/m ²)	27.2±1.3	26.6±2.1	>0.05
Gender (M/F)	75/35	70/40	>0.05
Waist (in cm)	112.3±4.1	113.1±7.1	>0.05
SBP (mmHg)	123.43±5.1	121.2±3.2	>0.05
DBP (mmHg)	85.2±3.1	81.1±2.3	>0.05
Hypertension (% of patients)	53.1	45.7	>0.05
DM (% of pts)	74	78.3	>0.05
Smoking, %	89	87	>0.05
FVC, % anticipated	112±6.3	111±5.3	>0.05
FVC, % anticipated	114±5.2	112±7.2	>0.05
ASA class			
I	21	23	
II	49	46	>0.05
III	30	31	
Tumor size, cm	1.4±0.6	1.5±0.9	>0.05
Lobe (%)			
Upper (Rt)	21	20	
Middle (Rt)	19	18	
Lower (Rt)	11	12	>0.05
Upper (Lt)	19	15	
Lower (Lt)	30	35	

Values expressed as mean ± SD for numerical variable, and % of patients for categorical variables

Table 2: Peri-operative results in the two groups of patients

Variable	EA Group (n=110)	INB Group (n=110)	P-value
Induction duration (min)	31.4±14.2	12.3±6.2	<0.05
Surgical duration (min)	197.2±12.8	164.4±8.2	<0.05
Operating duration (min)	258.3±32.5	201.3±18.5	<0.05
SpO ₂ (lowest, %)	96.4±3.2	95.2±3.8	>0.05
SpO ₂ less than 90% (% of patients with lowest)	14	7	<0.05
End-tidal carbon dioxide	48.2±5.2	47.1±4.3	>0.05
PaCO ₂ during one-lung ventilation	46.5±4.7	45.8±4.3	>0.05
PaO ₂ during one-lung ventilation	123.3±14.3	126.8±18.3	>0.05
Persistent hypotension (% of patients)	63	43	<0.05
Conversion to intubation/thoracotomy (% of patients)	1/0	1/0	>0.05
Fluid volume administered (mL)	1783.8±238.4	1163.8±122.1	<0.05
Blood loss (mL)	106.8±40	49.8±12	<0.05

Values expressed as mean ±SD for numerical variable, and as % patients reported (for categorical variables). Values of P based on categorical variables were calculated using Chi-square test, whereas p values based on numerical variable was calculated using Mann Whitney test

Post-operative results showed that the patients who underwent INB had significantly lower number of post-operative complications than patients who underwent EA for non-intubated lobectomy (Table 3). The most common post-operative complications among the patients in the two treatment groups were nausea, vomiting, emphysema and pulmonary complications, all of which were mild. There was no statistically significant difference between the two groups, with regard to post-operative complications. Moreover, the severity of post-operative pain was numerically lower in the patients who underwent INB than in patients who underwent EA for non-intubated lobectomy. However, there was no statistically significant difference in VAS scores between the two groups. The patients who underwent INB had significantly less post-operative chest drainage than those subjected to EA for non-intubated lobectomy ($p < 0.05$). A similar trend of results was observed for duration of hospital stay. Patients who underwent INB had shorter hospital stay than patients who underwent EA for non-intubated lobectomy. These results indicate more favourable peri-operative clinical outcome in patients who were underwent INB than in those who underwent EA.

Multiple regression analysis was performed to confirm the findings of present study by adjusting potential covariates such as age, gender, history of relevant concomitant diseases, smoking history and pre-operative pulmonary function (Table 4). The results of regression analysis were similar to those of primary analysis which favoured the use of INB as regional anaesthesia in NSCLC patients undergoing non-intubated lobectomy. Post-operatively, INB was also associated with shorter length of hospital stay and duration of chest drainage, when compared to EA.

Table 3: Postoperative complications in the two groups of patients

Variable	EA Group (n=110)	INB Group (n=110)	P-value
Complications			
Nausea and vomiting	13	9	
Neurological symptoms	2	1	>0.05
Air leak for more than 5 days	9	5	
Emphysema	12	9	
Pulmonary related complications	9	6	
CVS related complications	3	2	
Total (%)	44%	29%	<0.05
VAS score, pain severity			
Day 1	1.9±1.4	1.8±1.3	>0.05
Day 2	1.7±1.1	1.6±1.2	>0.05
Chest drainage, days	3.7±2.8	2.2±1.1	<0.05
Hospital stay, days	7.5±3.1	5.1±2.1	<0.05
Deaths/mortality	0	0	NA

Values are expressed as mean ± SD for numerical variable, and as % patients reported (for categorical variables). Values of p based on categorical variables were calculated using Chi-square test, whereas p value based on numerical variable was calculated with Mann Whitney test

DISCUSSION

Surgery serves an important role in the management of NSCLC. However, 20 to 30% of subjects at advanced stage of NSCLC develop relapse in spite of surgical removal of cancerous cells [2,3]. Lung lobectomy is one of standard surgical interventions for the management of early-stage lung cancer [1]. In China, safety and clinical outcomes of regional anaesthesia in NSCLC patients undergoing non-intubated lobectomy are not well established.

Table 4: Data on regression analysis

Variable	EA vs INB Odd ratio	95% CI	P- value
Complications (peri- and postoperative)	0.65	(0.3 to 1.23)	>0.05
Hemodynamic intrusions	0.52	(0.3 to 1.23)	>0.05
Effect size/difference (EA-INB)			
Anaesthesia duration (min)	-19.1	(-23.2 to -13.9)	<0.05
Surgical duration (min)	-32.8	(-45.2 to -18.3)	<0.05
Fluid administered (mL)	-620	(-845.2 to -697.3)	<0.05
Blood loss (mL)	-57	(-78.2 to -49.3)	<0.05
Chest drainage (days)	-1.5	(-2.2 to -1.3)	<0.05
Hospital stay (days)	-2.4	(-3.2 to -1.9)	<0.05

The present study is the first investigation that evaluated the safety and clinical outcomes of regional anaesthesia in Chinese NSCLC patients undergoing non-intubated lobectomy.

The results obtained showed that non-intubated thoracoscopic lobectomy using INB and EA is effective and safe in Chinese NSCLC patients. A comparison of both methods revealed that INB was simpler and faster than EA for performing non-intubated thoracoscopic lobectomy in Chinese patients with NSCLC. Moreover, INB produced significantly greater reduction in overall duration of surgical procedure than EA. Significantly lower volume of blood loss was observed in INB group than in EA group. This indicates that the patients who received INB had better stability of hemodynamic parameters, resulting in decreased requirement for fluid supplementation. Furthermore, INB was associated with shorter length of hospital stay, when compared to EA. Overall, INB was a better alternative to EA for Chinese NSCLC patients undergoing non-intubated thoracoscopic lobectomy. Results from multiple regression analysis also confirmed the finding of the present study after adjusting potential covariates such as age, gender, history of relevant concomitant diseases, smoking history and preoperative pulmonary function.

The results of this study in Chinese NSCLC patients are consistent with those of previous studies which indicate that thoracoscopic lobectomy for NSCLC using regional anaesthesia is an effective and safe therapeutic option, similar to standard technique of general anaesthesia via intubation [7,9,10]. Moreover, the results of the present study are consistent with the findings in a published study which demonstrated the safety and effectiveness of INB and EA in Taiwanese NSCLC patients

undergoing non-intubated thoracoscopic lobectomy [9,10].

In this study, INB was simple and fast, and it produced better clinical outcome in terms of hemodynamic stability. Moreover, INB was suitable for non-intubated lobectomy for early-stage NSCLC, and it improved operating room efficiency. The only disadvantage of INB was that while it produced limited perioperative analgesia, EA resulted in extensive perioperative analgesia. The key shortcomings of the EA technique were the requirement for a skilled a surgeon, and its time-consuming nature. In addition, it had higher risk of neurological side effects than INB.

It is a well-known fact that intercostal nerves can be visualized easily using thoracoscopy, and appropriate anaesthesia can be achieved with the use of low dose of local anaesthetic drug injected under the parietal pleura without the risk of needle injury. In practical terms, the simplicity and accuracy of INB make it a better choice as regional anaesthesia for thoracoscopic lobectomy in NSCLC patients since it induces rapid anaesthesia. The incidence of hypotension was significantly higher in patients who received EA than in those who received INB. The higher incidence of hypotension in EA group could possibly be due to sympathetic block. Moreover, the patients who underwent INB required lower volume of fluid replacement than those subjected to EA.

Overall, the findings of the present study have shown that INB and EA are effective and safe in NSCLC patients undergoing non-intubated lobectomy. However, based on peri- and postoperative clinical outcomes, the results favour the use of INB as regional anaesthesia in NSCLC patients undergoing non-intubated lobectomy. Post-operatively, INB was also associated with shorter length of hospital stay

and shorter duration of chest drainage than EA. The results of the present preliminary study necessitate confirmation through a large clinical trial among NSCLC patients across globe.

Limitations of the study

The findings of the present trial cannot to be generalized to the Chinese population since the study was conducted at a single study centre in China. A large clinical trial with appropriate sample size is needed to confirm the present findings.

CONCLUSION

The findings of the present study show that INB and EA are effective and safe as regional anaesthesia in NSCLC patients undergoing non-intubated lobectomy. However, based on peri- and post-operative clinical outcomes, the results favour the use of INB as regional anaesthesia in NSCLC patients undergoing non-intubated lobectomy.

DECLARATIONS

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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