Original Article

Non-intubated video-assisted thoracoscopic lung biopsy for interstitial lung disease: a single-center experience

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Background: The mortality and morbidity associated with video-assisted thoracoscopic (VATS) lung biopsy for interstitial lung disease (ILD) are not negligible. We evaluated whether non-intubated VATS lung biopsy, which avoids intubation and general anesthesia, can be safely performed in ILD subjects.

Methods: This retrospective study compared the incidence of complications and surgical mortality between 25 consecutive intubated subjects and 10 non-intubated subjects (a total of 35 consecutive subjects) at a single institution.

Results: No major surgical complications or deaths were reported in either group, and non-intubated VATS biopsies were safely performed in subjects with relatively low carbon monoxide diffusing capacity (P=0.08) or poor American Society of Anesthesiologists physical status scores (ASA) (P=0.02).

Conclusions: These preliminary results suggest that non-intubated VATS lung biopsy is a safe and feasible option in patients with ILD.

Keywords: Interstitial lung disease (ILD); lung biopsy; video-assisted thoracoscopic (VATS); non-intubated video-assisted thoracic surgery; minimally invasive surgery

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Introduction

Surgical lung biopsy plays an important role in providing pathological findings in patients with interstitial lung disease (ILD) (1). A recent study of approximately 12,000 surgical lung biopsies from the Nationwide Inpatient Sample revealed that in-hospital mortality after surgery was 1.7% for elective procedures and 16.0% for non-elective procedures (2). The mortality and morbidity associated with surgical lung biopsy for ILD are not negligible (3,4). Acute exacerbation of ILD generally has a very poor prognosis (5), and acute exacerbation of ILD after biopsy is one of the major causes of mortality. The etiology of acute exacerbation of ILD remains unclear. The typical video-assisted thoracoscopic (VATS) procedure is performed under general anesthesia with positive mechanical ventilation, which is thought to trigger or worsen acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) (6-9).

Non-intubated VATS is another option for lung biopsy in ILD. As the VATS technique and anesthetic technology have evolved, the use of non-intubated VATS has become

widely accepted in thoracic surgery. Reports have described applications in wedge resection, segmentectomy, lobectomy, and bronchoplasty. And several studies reported safety and feasibility of non-intubated VATS biopsy in patients with undetermined ILD (10-12). Non-intubated VATS is known to have fewer postoperative complications and faster recovery times than typical VATS, because it does not use muscle relaxants, double lumen tube intubation, and injuries from positive pressure ventilation (13-15). Therefore, we hypothesized that non-intubated thoracic surgery would decrease postoperative complications. The aim of our study was to assess the feasibility and safety of non-intubated VATS lung biopsy.

Methods

Study population

This study was approved by the institutional review board. The need for individual patient consent was waived. We retrospectively analyzed ILD subjects undergoing VATS lung biopsy at a single institution between January 2016 and June 2016. The inclusion criteria were subjects aged >20 years with chest CT findings of ILD. Exclusion criteria included preoperative ICU hospitalization, preoperative ALI, hemodynamic instability, and redo thoracotomy. A total of 35 consecutive subjects were included for the analysis and divided into two groups—an intubated group (n=25) and a non-intubated group (n=10). The allocation of a patient to each group was determined according to the preference of each surgeon and the consent of the patient. And the exact diagnosis was not known before operation and confirmed by postoperative pathological results. Early outcome data including intraoperative and postoperative variables were compared between the groups.

Surgical procedure

Intubated group

VATS was performed in intubated subjects under general anesthesia. In the operating room, the standard monitoring devices including electrocardiography (EKG), pulse oximeter, end-tidal carbon dioxide ($ETCO_2$) were applied. Endotracheal intubation was performed via the routine double-lumen endotracheal intubation procedure. An arterial catheter was placed in the radial artery opposite the surgical site for invasive arterial blood pressure monitoring. A 5.5- or 10.5-mm camera port and one 5.5-mm instrumentation port were inserted. A thorough assessment of the pleura and lung surface was made, and wedge resection was performed with an Endo GIA 60–4.8 mm endoscopic stapler (Covidien Endo GIA Universal Roticulator). At the end of the procedure, one of the chest tubes was left in situ.

Non-intubated group

For non-intubated VATS, though some other groups used intercostal blocks or only local anesthesia (11,12), our group used epidural anesthesia. Thoracic epidural catheter was inserted before operation in the pre-anesthesia room and the correct position of catheter was confirmed by test dose and/or fluoroscopy.

In the operating room, monitoring was the same with the intubated group. Four mL of 4% lidocaine nebulization (Nebulizer: PARI, Moosstrasse3, Germany) was applied for 15 minutes to prevent coughing before operation. While the patient was on lidocaine nebulization, the radial artery was cannulated and drug injection for thoracic blockade was started. Three to four mL of the local anesthetic [0.75% ropivacaine (Ropivacaine HCl, HANLIM PHARM)] was administered incrementally through epidural catheter. A total of 13–15 mL of 0.75% ropivacaine (mixed with 50 μg fentanyl) was administered. The final check of the sensory block before operation covered from T3 to T10 after 15 minutes.

Conscious sedation was maintained during operation with a remifentanil (0.0–0.5 mcg/kg/min) or dexmedetomidine (0.3–0.5 mcg/kg/hr) infusion and the dose was titrated to maintain a bispectral index (BIS) of 60–80 during surgery. Five L/min of 100% oxygen was administered via facial mask with $ETCO_2$ monitor line attached to the mask during the operation. In case of low saturation (<95%), the O_2 fraction of facial mask was increased and patient was encouraged to breathe deeply.

A laryngeal mask airway (LMA) and bronchial blocker were prepared in case of conversion to general anesthesia. We used the single incision laparoscopic surgery (SILS) for non-intubated VATS biopsy to decrease patient discomfort and achieve better control of collapse and inflation of the operated lung. This was also effective in reducing coughing by minimizing irritation of the pleura, which can be caused by airflow. The operation started with 4 cm of skin incision on the left 5th intercostal space after enough skin and subcutaneous tissue local infiltration. Then 4 cm uniport utility (Glove port 4220-AS-3, Nelis medical, Korea) was inserted and tissue biopsies were performed. At the time when the scope was inserted, the lung became atelectatic

Table 1 Subject characteristics

Baseline characteristics	Intubated group (n=25)	Non-intubated group (n=10)	P
Age (years)	61.2±6.6	54.0±14.8	0.19
Sex (male, %)	52	60	0.46
Smoking (%)	48	40	0.86
BMI (kg/m^2)	24±3.5	25.14±2.3	0.26
DLCO (%)	66.7±13.6	51.4±20.7	0.08
FEV_1, %	78.9±16.0	70.9±13.1	0.27
ASA classification (3 or 4, %)	16	60	0.02

Data were presented as mean ± standard deviation. DLCO, diffusing capacity of the lungs for carbon monoxide; FEV_1, forced expiratory volume in 1 s; ASA, American Society of Anesthesiologists physical status.

and if not, within first 10 minutes. The lung remained atelectatic until the end of the operation. An intraoperative vagal nerve block was not required because only simple wedge resection was performed.

In both groups, lung biopsy was performed by one or two wedge resections of lung regions deemed radiologically and macroscopically more representative for diagnosis using standard method. At the end of the procedure, one of the chest tubes was left *in situ*.

Postoperative management

All subjects were evaluated via chest radiography every day. Chest tube removal was performed if chest tube drainage was less than 200 mL for 24 hours with sufficient lung recruitment and no air leakage on chest radiography. And subjects were discharged the next day after a chest tube removal if there is no specific medical problem.

Follow-up

Early mortality was defined as mortality within the first 30 days after surgery. ALI was defined according to the following criteria occurring within 7 days after surgery that was unrelated to other documented causes of ALI; (I) acute onset; (II) bilateral infiltration with pulmonary edema; (III) a ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO_2/FiO_2) between 201 and 300 mmHg, regardless of the level of positive end-expiratory pressure. ARDS was included as subcategories of ALI and defined as more severe hypoxemia (PaO_2/FiO_2 ≤200 mmHg).

Statistical analysis

Analyses comparing patient parameters and outcomes by study group included the two sample *t*-test or Mann-Whitney U test for continuous variables, and the χ^2 analysis or the Fisher exact test for categorical variables. A P value less than 0.05 was considered statistically significant. Statistical analysis was carried out using SPSS ver. 21.0 (IBM Corp., Armonk, NY, USA).

Results

Subject characteristics

The procedures were successfully completed in all 35 subjects. The baseline characteristics of the two groups are summarized in *Table 1*. There were no statistically significant differences in age, sex, smoking status, body mass index (BMI), or forced expiratory volume in 1 second (FEV_1) between the two groups, but the non-intubated group had a significantly higher American Society of Anesthesiologists physical status (ASA) score than that of the intubated group III or at of the intubated group non-intubated group had a significance. The mean preoperative carbon monoxide diffusing capacity (DLCO) of the non-intubated group was 51.4%, which was lower than that of the intubated group (66.7%; P=0.08).

Perioperative data

Perioperative data pertaining to the two groups are summarized in *Tables 2* and *3*. Comparisons between the intubated and non-intubated groups showed no significant differences in operation time, intraoperative blood loss, chest tube dwelling time, overall postoperative chest drainage volume, or hospital stay. However, duration of anesthesia was significantly lower in the non-intubated group (median, 66 min; interquartiles, 62–82) than in the intubated group (median, 83 min; interquartiles, 69–99; P=0.025). And the non-intubated group showed low level of intraoperative saturation and heart rate. Visual analogue scale, systolic blood pressure and heart rate at post anesthesia care unit were also lower in the non-intubated group.

Table 2 Operative results

Variables	Intubated group (n=25)	Non-intubated group (n=10)	P
Surgical duration (min)	37 (26.0–53.0)	33 (28.0–41.0)	0.255
Anesthesia duration (min)	83 (69.0–99.0)	66 (62.0–82.0)	0.025
Conversion to intubation	N/A	0	N/A
Intraoperative blood loss (mL)	30 (10.0–40.0)	30 (17.5–50.0)	0.397
Pleural drainage, total (mL)	150 (72.5–260.0)	225 (142.5–297.5)	0.270
Chest tube dwelling time (days)	2 (1.5–3.0)	2 (2.0–2.25)	0.815
Hospital stay (days)	5 (3.0–5.0)	5 (4.0–9.0)	0.174

Data were presented as median (interquartiles). N/A, not available.

Table 3 Perioperative physiologic data

Variables	Intubated group (n=25)	Non-intubated group (n=10)	P
SpO_2 (%)			
Preoperative	95.9±1.9	94.4±4.1	0.281
Intraoperative	99.9±0.2	97.6±3.1	0.039
PACU	98.2±2.7	97.5±2.4	0.431
POD1	93.4±2.5	92.1±3.6	0.313
Intraoperative (mmHg)			
PaO_2	167.7±104.4	193.2±88.6	0.565
$PaCO_2$	38.9±4.1	41.6±3.2	0.121
Systolic blood pressure (mmHg)			
Preoperative	104.8±9.2	103.8±8.0	0.743
Intraoperative	93.1±9.2	89.3±10.1	0.322
PACU	112.0±13.9	93.3±10.8	0.001
POD1	104.9±11.2	104.6±9.9	0.935
Heart rate (beats/m)			
Preoperative	66.8±8.8	64.5±6.3	0.389
Intraoperative	66.8±10.1	57.1±6.2	0.002
PACU	67.4±13.6	57.7±9.3	0.023
POD1	68.2±10.4	66.7±5.3	0.589
VAS [0–10]			
Preoperative	0.1±0.3	0±0	0.161
PACU	2.4±0.7	1.1±0.9	0.001
POD1	1.7±0.9	1.6±0.7	0.782
Pulmonary hypertension, n	0	1	–

Data were presented as mean ± standard deviation. PACU, post anesthesia care unit; POD1, post-operative day 1; VAS, visual analogue scale.

Postoperative complications

No early mortality or significant complications, including postoperative ALI, prolonged air leak (≥5 days), postoperative bleeding, postoperative pneumonia (within ≤1 month), wound infection, or ICU admission after surgery, occurred in either group.

Histological results

We were able to obtain a final histological diagnosis in all subjects (diagnostic yield 100%). In the intubated group, unusual interstitial pneumonia (UIP, N=11, 44%) was the most common, followed by nonspecific interstitial pneumonia (NSIP, N=8, 32%), organizing pneumonia (N=4, 16%), and granulomatous ILD (N=1, 4%). In the non-intubated group, NSIP was the most common (N=8, 80%), with one subject diagnosed with UIP and one with desquamative interstitial pneumonia (DIP).

Discussion

As a small sized pilot study, we could not confirm whether non-intubated lung biopsy reduces acute exacerbation of ILD compared to normal VATS lung biopsy. However, this study demonstrated the safety and feasibility of non-intubated VATS lung biopsy in ILD subjects.

General anesthesia with double lumen tube intubation was previously considered essential in VATS. However, to reduce complications related to intubation or mechanical ventilation, non-intubated VATS is increasingly being performed in selected patients (16). Non-intubated surgery reduces intubation-related complications compared to conventional VATS surgery under general anesthesia. In addition, as muscle relaxants are not required and the amount of anesthetic drug used during the operation is lower, non-intubated surgery enables early ambulation after the operation and minimizes respiratory muscle weakness and digestive system dysfunction (17). Therefore, recovery is accelerated after non-intubated surgery. This reduces the duration and costs of hospital stays (18,19).

We applied non-intubated VATS for ILD lung biopsy. ILD is relatively rare, and few reports are available on the epidemiology of ILDs. Karakatsani *et al.* reported that the estimated annual incidence of ILDs is 4.63 per 100,000 and that the prevalence is 17.3 per 100,000 in Greece (20). Surgical lung biopsy may be required for the diagnosis of ILD. However, because of the morbidity and mortality associated with VATS for ILD, biopsy is not always safe (21-24). According to one single center study (21), among patients who underwent VATS lung biopsy between 1998 and 2004, the 60-day mortality rate was 3 in 68 (4.4%). All three patients were cases of UIP. Two of these patients underwent postmortem examination, and both had diffuse alveolar damage on a background of UIP, consistent with acute exacerbation of UIP. The relationship between positive pressure ventilation and acute exacerbation of ILD has not been clearly elucidated, but postoperative ALI is related to ventilator-induced lung injury (25). In addition, life-threatening pneumothorax was caused by bulla rupture during intubated thoracoscopic lung surgery with a large bulla on the contralateral side (26). Therefore, non-intubated VATS without positive pressure ventilation may eliminate one of the potential triggers of acute exacerbation of ILD after lung biopsy. Several studies demonstrated safety and feasibility of non-intubated VATS lung biopsy in ILD subjects (10-12).

In the current study, a 100% diagnostic success was achieved. Guidelines suggest that more than one specimen should be collected when biopsy is performed (1). After careful examination via high-resolution computed tomography (HRCT), the location of the wedge resection was decided considering the extent and distribution of the lesion. When the wedge resection was performed, the lesion was resected to a size sufficient to include some of the healthy tissue. However, strict standardization of the method used for specimen resection among surgeons is limited.

For limitations, as the total number of subjects was low, it was not possible to meaningfully compare the incidence of death or major complications between the two groups. Additional limitation is the comparability of the groups. Although it was not intentional, there were meaningful differences between the study groups in ASA score and pathological diagnosis. These differences as well as the short time lapse of recruitment of the entire cohort may suggest bias from patient allocation. The patient allocation was decided by surgeons and preference expressed by the patient. Notably, however, their collective outcome was not different. This suggests that non-intubated VATS may be an option in patients with poor lung function for whom general anesthesia is contraindicated.

In the current study, we inserted chest tubes in all subjects. However, as chest tubes cause pain and is closely related to the hospitalization period, chest tubeless VATS lung biopsy can be considered (27). Recent studies have

also introduced chest tubeless non-intubated VATS. Guilin Peng *et al.* reported 43 patients with ILD who underwent chest tubeless non-intubated VATS lung biopsy (11). In such cases, it may be possible to perform the biopsy as an outpatient procedure.

Conclusions

In this study, we successfully performed non-intubated VATS lung biopsy with a facial mask, epidural anesthesia, and conscious sedation. We demonstrated that non-intubated VATS lung biopsy is a safe and feasible procedure even in subjects with high ASA score and poor DLCO. This procedure also resulted in excellent diagnostic yield without any morbidity or mortality. Notably, these preliminary results have to be confirmed by a larger study to assess the long-term effects and diagnostic rate of this less-invasive surgical strategy.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: This study was approved by the ethics board of Samsung Medical Center (approval number: 2017-09-070). The need for individual patient consent was waived.

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