Analysis of unexpected conversion to thoracotomy during thoracoscopic lobectomy in resectable lung cancer

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Analysis of unexpected conversion to thoracotomy during thoracoscopic lobectomy in resectable lung cancer

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December, 2014. Chun Sung Byun

<TABLE OF CONTENTS>

LIST OF TABLES

ABSTRACT

Analysis of unexpected conversion to thoracotomy during thoracoscopic lobectomy in resectable lung cancer

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Since anatomical lung resection by video-assisted thoracoscopic surgery (VATS) was first introduced, VATS has played a major role in resectable lung cancer. However, conversion to thoracotomy is a major concern, since unexpected thoracotomy increases the risk of potential adverse outcomes. Therefore, we compared patients converted to thoracotomy to non-converted controls and identified the risk factors for thoracotomy conversion.

Between January 2005 and December 2013, 69 of 1110 VATS lobectomies for resectable lung cancer required unexpected conversion to thoracotomy. Each converted case was individually matched to three randomly-selected non-converted controls based on date of operation, type of operation and pathologic TNM stage.

The most common cause of conversion was fibrocalcified lymph node, found in 28 patients (40.6%), followed by vascular injury in 20 (29.0%), tumor invasion or extension in 11 (15.9%), pleural adhesion in 5 (7.2%), incomplete inter-lobar fissure in 3 (4.3%) and failure of single lung ventilation in 2 (2.9%). There were no significant differences in the rate of postoperative complications and in-hospital deaths between the two

groups. However, respiratory complications such as acute respiratory distress syndrome, pneumonia and atelectasis were significantly more common in the conversion group (p=0.012). Also, the conversion group had increased operating time, higher blood loss and prolonged intensive care unit (ICU) stay. The independent risk factors for thoracotomy conversion were age ≥65 years, FEV1 <1.8 L/sec, and the presence of fibrocalcified lymph node on preoperative chest computed tomography.

Unexpected conversion to thoracotomy during VATS lobectomy in resectable lung cancer does not appear to increase surgical mortality and morbidity. However, with high risk patients, the surgeon requires careful selection for VATS candidate. Also, if needed, the decision to convert must be made promptly to reduce the operation time, blood loss, ICU stay and possible critical respiratory complications in VATS lobectomy.

Key words : video-assisted thoracoscopic surgery, lobectomy, thoracotomy, conversion, lymph node

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I. INTRODUCTION

Over the past 60 years, the standard surgical treatment for early stage lung cancer has been lobectomy via posterolateral thoracotomy.[1] Since the introduction of video-assisted thoracoscopic surgery (VATS) in the 1990s, VATS has played a major role in lobectomy for resectable lung cancer.[2,3] VATS lobectomy is thought to be many advantages than lobectomy under thoracotomy in terms of postoperative pain,[4] postoperative recovery,[5] preservation of pulmonary function,[6] immune surveillance[7] and surgical complications.[8] In addition, according to oncologic studies, VATS lobectomy is equivalence to thoracotomy in terms of overall survival and recurrence rate.[9,10] Despite these advantages, there is always a possibility of conversion to thoracotomy during VATS lobectomy.[11] The technical difficulties of VATS lobectomy are mainly due to inexperience with manipulating the thoracoscopic instruments in small wounds and at limited camera angles. Regarding the difficulty of VATS lobectomy, the rate of unexpected conversion to thoracotomy in lung cancer patients has been reported to range from around 2.5% to 23%.[10,12,13] Unexpected intraoperative conversion can have adverse

consequences, as it increases operating times, involves extra lung manipulation, increases the risk of injury to adjacent tissues and increases the risk of blood loss.[14] Thus, we conducted this matched case-control study to identify the preoperative clinical risk factors associated with unexpected conversion in order to make more efficient patient selection for VATS lobectomy in lung cancer and minimize the associated adverse outcomes.

II. MATERIALS AND METHODS

1. Data Collection and Patient Groups

We reviewed the medical records of 1673 patients with primary lung cancer who underwent pulmonary resection at Severance Hospital from January 2005 to December 2013. Exclusion criteria were patients with a planned thoracotomy approach, those with a sublobar resection through VATS, those with an advanced lung cancer stage (≥IIIB), those with a neoadjuvant chemo- or radiotherapy history and those with a prior cancer history. Overall, 1110 patients underwent complete pulmonary resection through an initial VATS approach. Of these patients, 69 patients required unexpected conversion to thoracotomy. Each thoracotomy conversion cases were individually matched to three randomly-selected non-converted controls to compare outcomes and identify the independent risk factors for thoracotomy conversion. Matching was performed based on the date of operation (±3 months), type of operation and pathologic TNM stage, which were chosen to reduce treatment selection bias and to reduce the effects of confounding factors. To identify the preoperative clinical risk factors for thoracotomy conversion, we chose the pathologic TNM stage as a matching parameter. It is because that preoperative clinical TNM stage was often changed in pathologic TNM stage after surgery. The control group was selected according to published guidelines on matched case-control studies.[15] Pathological lung cancer staging was based on the 2009 TNM classification system.[16] Fibrocalcified interlobar or hilar lymph nodes in the resected lobe were identified by preoperative chest computed tomography (CT) and metastatic interlobar or hilar lymph nodes were also identified by preoperative positron emission tomography (PET) scan.

2. Statistical Analysis

All statistical analysis was performed using Statistical Analysis System

version 9.2 (SAS Institute, North Carolina, USA). The student's t-test or the nonparametric Wilcoxon's rank-sum test was used to determine significant differences between the conversion and non-conversion groups. Categorical variables were described as proportions and compared using χ^2-test or Fisher's exact test, depending on the sample size. All risk factors found to be significantly associated ($p<0.05$) with thoracotomy conversion by univariate analysis were then entered into a multivariable conditional logistic regression model. Odds ratios (OR) and 95% confidence interval (CI) were used to estimate the association between conversion and these risk factors.

3. Ethics Statement

The institutional review board of Yonsei University College of Medicine approved this retrospective matched case-control study (4-2014-0689). The board waived the need for informed consent.

III. RESULTS

1. The causes of thoracotomy conversion

From January 2005 to December 2013, 1110 patients underwent planned VATS lobectomy, and of these, 69 (6.2%) patients underwent conversion to thoracotomy. The causes of conversion were as follows: severe fibrocalcified lymph node around the bronchus or vessel in 28 patients (40.6%), uncontrolled bleeding due to intraoperative vascular injury in 20 (29.0%), tumor invasion or extension in 11 (15.9%), dense pleural adhesion in 5 (7.2%), incomplete inter-lobar fissures in 3 (4.3%), and failure of single lung ventilation in 2 (2.9%) (Table 1).

Table 1. The underlying causes of unexpected thoracotomy conversion

	N (%)
Severe fibrocalcified lymph node	28 (40.6)
Uncontrolled bleeding	20 (29.0)
Tumor invasion or extension	11 (15.9)
Dense pleural adhesion	5 (7.2)
Incomplete inter-lobar fissure	3 (4.3)
Failure of single lung ventilation	2 (2.9)

2. Comparison of the preoperative clinical data and outcomes

The univariate analysis of the preoperative clinical data revealed that older age at operation, a history of pulmonary tuberculosis, current chronic obstructive lung disease (COPD), more pack-years of smoking, low forced expiratory volume in one second (FEV1) and the presence of fibrocalcified lymph node were significantly related to conversion to thoracotomy (Table 2).

Postoperative results of the conversion and non-conversion groups differed with respect to mean operating time (222.0 vs. 150.9 min, $p<0.001$), mean estimated blood loss (692.75 vs. 227.54 ml, $p<0.001$) and mean postoperative intensive care unit (ICU) stay (3.25 vs. 1.39 days, $p=0.047$) (Table 3). Rate of postoperative complications ($p=0.199$) and in-hospital deaths ($p=0.261$) were not significantly different between the two groups. However, respiratory complications, such as, acute respiratory distress syndrome (ARDS), pneumonia and atelectasis were significantly higher in conversion group compared to the non-conversion group (7.4% vs 1.4%, $p=0.017$).

Table 2. Patient preoperative clinical data in the conversion and non- conversion groups

	Conversion (n=69)	Non-conversion (n=207)	p value
Age (year)	67.6 ± 7.9	62.5 ± 10.4	0.009*
Male	43 (62.3)	113 (54.6)	0.145
BMI (kg/m^2)	26.4 ± 8.1	26.1 ±7.5	0.862
History of tuberculosis	20 (29.0)	18 (8.7)	0.029*
Current COPD	7 (10.1)	6 (2.9)	0.049*
Current smoker	34 (49.3)	77 (37.2)	0.183
Smoking pack-years	22.6 ± 28.2	14.7 ± 23.8	0.042*
FEV1 (L/sec)	2.18 ± 0.62	2.47 ± 0.66	0.023*
Tumor size (cm)	3.3 ± 1.7	2.9 ± 1.6	0.269
Tumor location			0.409
Right upper	24 (34.8)	58 (28.0)	
Right middle	7 (10.1)	26 (12.6)	
Right lower	15 (21.7)	51 (24.6)	
Left upper	15 (21.7)	40 (19.3)	
Left lower	8 (11.6)	32 (15.5)	
Fibrocalcified LN†	24 (34.8)	19 (9.2)	<0.001*
Metastatic LN†	11 (15.9)	14 (6.8)	0.276

Data are presented as the number (%) or mean ± standard deviation.

* $p<0.05$

† Diagnosed by preoperative chest CT or PET scan

BMI: Body mass index, COPD: Chronic obstructive pulmonary disease,

FEV1: Forced expiratory volume in one second, LN: Lymph node

Table 3. Postoperative results between the conversion and non-conversion groups

	Conversion (n=69)	Non-conversion (n=207)	p value
Operation time (minute)	222.0 ±72.7	150.9 ± 66.3	<0.001*
Estimated blood loss (ml)	692.75 ± 664.78	227.54 ± 213.46	<0.001*
Chest tube duration (day)	7.07 ± 3.82	6.25 ± 3.76	0.140
ICU stay (day)	3.25 ± 7.37	1.39 ± 2.85	0.047*
In-hospital stay (day)	9.36 ± 7.29	8.42 ± 7.57	0.397
Complication	8 (11.6)	14 (6.8)	0.199
Respiratory	5 (7.4)	2 (1.4)	0.012*
ARDS	1	0	
Pneumonia	3	2	
Atelectasis	1	0	
Non-respiratory	3 (4.3)	12 (5.8)	0.768
Air leak >7 days	2	5	
Prolonged effusion	1	3	
Atrial fibrillation	0	2	
Chylothorax	0	1	
In-hospital death	2 (2.9)	2 (1.0)	0.261

Data are presented as the number (%) or mean ± standard deviation.

* $p<0.05$

ICU: Intensive care unit, ARDS: Acute respiratory distress syndrome

3. The risk factors for thoracotomy conversion

In univariate analysis of preoperative clinical data, 6 variables were found to be significantly associated with thoracotomy conversion. According to multivariable conditional logistic regression analysis, age ≥65 years (p=0.031), FEV1 <1.8 L/sec (p=0.005) and the presence of fibrocalcified lymph node (p=0.020) were the independent risk factors for conversion to thoracotomy (Table 4). The thresholds for age and FEV1 were determined using receiver operating characteristic (ROC) analysis, which showed an area under the curve of 0.746 for age, and 0.736 for FEV1.

Table 4. Results of conditional logistic regression analysis for the risk factors of unexpected conversion to thoracotomy

	OR	95% CI	p value
Age ≥65 years	1.81	1.06-3.09	0.031*
History of tuberculosis	1.48	0.41-5.33	0.151
Current COPD	1.08	0.25-4.66	0.418
Smoking pack-years	1.02	0.52-2.00	0.953
FEV1 <1.8 L/sec	2.01	1.11-3.63	0.005*
Fibrocalcified LN†	2.67	1.25-4.93	0.020*

* p<0.05

† Diagnosed by preoperative chest CT

OR: Odds ratio, CI: Confidential interval,

COPD: Chronic obstructive pulmonary disease,

FEV1: Forced expiratory volume in one second, LN: Lymph node

IV. DISCUSSION

Since lobectomy of lung disease via VATS was first introduced in 1992, the scope of this procedure has changed over time. With increasing experience in the treatment of lung cancer, VATS has gradually been adopted for use in radical curative lobectomy of lung cancer.[2] Although the technical safety of VATS lobectomy has been widely accepted, there remain a range of situations that cause unexpected conversion to thoracotomy for a variety of reasons.[11] There are some difficulties with the VATS procedure, including the surgeon's discomfort with small wound, narrow video angle and VATS instruments for lung manipulation. Moreover, patient characteristics also make VATS more difficult, such as pleural adhesions, confused inter-pleural fissures, and fibrocalcified lymph nodes. Also oncologic issues such as unintended disruption or dissemination of cancer cells during VATS lobectomy remain a problematic scenario. During the study period, the attending surgeons began performing VATS lobectomy for lung cancer since 2005. There was a relatively high conversion rate in the early period, but with increased experience and confidence using VATS, the conversion rate decreased over time.

In the present study, the most common cause of conversion was the presence of fibrocalcified lymph node around the bronchus or vessel, which occurred in 28 patients (40.6%), followed by uncontrolled bleeding in 20 patients (29.0%). These results are consistent with those of other studies.[17-19] Importantly, fibrocalcified lymph node may be predictable on preoperative chest CT. There are few studies estimating the role of CT scan in determining the surgical approach for lobectomy. According to Park et al.,[19] 41% of conversions were due to hilar nodal anthracofibrosis, and when the authors retrospectively reviewed the CT scans, hilar fibrocalcified lymph nodes were found in 71% of conversion patients. Also, Mason et al.[20] evaluated the role of chest CT for predicting complications associated with VATS, and demonstrated that pleural

thickening and lymph node calcifications detected by CT predicted surgical difficulties.

The second cause of conversion, and the most serious complications for surgeons, was massive hemorrhage from pulmonary vessels. Dense lymph nodes and hilar structure adhesions increase the risk of vascular injury, requiring conversion to thoracotomy. In such cases, vessels dissection can be difficult and the risk of vascular injury high, even during thoracotomy. However, with advanced VATS skills and experience in thoracoscopic suturing, conversion can often be avoided when minor to moderate bleeding from the pulmonary vessels is encountered.

In the present study, 11 conversions by oncologic cause were due to bronchus or vascular invasion from tumor in 4 patients, chest wall invasion in 1 patient, and lymph node metastasis confirmed by intraoperative frozen result in 6 patients. Interestingly, univariate analysis showed that there were no significant differences between the conversion and non-conversion groups with respect to tumor size and tumor location. But, in a view of tumor size, the surgeon tended to select small tumor size patients for VATS candidate than those who planned thoracotomy. So this tendency may result no significant differences between two groups. The oncologic cause of conversion also can be predictable by preoperative PET scan, which showed a high probability of lymphatic metastasis in the 6 frozen positive cases. However, the decision to convert depended solely on the surgeon's preference, and it remains questionable whether VATS lobectomy is suitable for lung cancer patients with metastatic lymph nodes.[21] Watanabe et al.[22] revealed that VATS lobectomy outcomes were similar to those of thoracotomy for clinical N0 but postoperative pathological N2 patients. Long-term outcome is another important consideration when evaluating the safety and feasibility of conversion patients. However, we did not compare tumor recurrence or overall survival in the conversion and non-conversion groups. Additional causes of conversion such as pleural

adhesion and incomplete inter-lobar fissure can be predictable when patients had a previous pulmonary tuberculosis history or COPD or pneumoconiosis. However, single lung ventilation problems were difficult to predict on preoperative evaluation.

According to univariate analysis, the risk factors for conversion to thoracotomy were older age at operation, a history of tuberculosis, current COPD, more pack-years of smoking, low FEV1 and the presence of fibrocalcified lymph node by preoperative chest CT. However, multivariable analysis revealed that the independent risk factors for conversion were age $\geq$65 years, FEV <1.8 L/sec and the presence of preoperatively identified fibrocalcified lymph node. Old age may result in a decline in functional reserves and an increase in comorbidities, and these factors reflect the vulnerability of patient during VATS lobectomy.[23] Furthermore, low lung function in spirometry infers the presence of obstructive lung disease such as emphysema. The presence of dense fibrocalcified lymph node may be attributed to the patient's history of pulmonary tuberculosis or pneumoconiosis, which contributes to an increased risk of vascular injury during surgery. Therefore these three independent risk factors, which reflect the complicated condition of pulmonary structure, elevate the risk for thoracotomy conversion during VATS lobectomy.

Patients who encounter unexpected conversion to thoracotomy are most likely suffer prolonged operating time, increased lung manipulations, increased risk of injury to adjacent tissue and massive blood loss, which could all adversely affect surgical outcomes.[14] Although the efficacy and safety of VATS lobectomy in lung cancer has been certified by many authors, there are few studies exploring conversion that reported no significant increase in mortality or morbidity.[19,24] In Table 3, the conversion group showed more blood loss, prolonged operation time and increased ICU stay. Increased blood loss is potentially harmful to patients with shock and the need for transfusion.

Additionally, a prolonged operation time with extra lung manipulation may increase the duration of the ICU stay and risk of postoperative complications. Although no significant intergroup differences were found for postoperative complications or in-hospital death rate in the present study, the conversion group did show increased respiratory complications compared to the non-conversion group. These results could have been influenced by poor preoperative patients' characteristics (such as old age, history of tuberculosis, current COPD, and poor pulmonary function on spirometry) in the conversion group, but prolonged operation time with extra lung manipulation during thoracotomy conversion may have aggravated the outcomes. Also, two deaths in the conversion group were due to ARDS and pneumonia, respectively. To avoid these adverse respiratory complications after unexpected thoracotomy conversion, we recommend that surgeons make an effort to identify the VATS candidates' preoperative risk factors in order to reduce unexpected thoracotomy conversion. Identifying these risk factors may help surgeons to select appropriate patients for VATS. Mortality in the non-conversion group was 1.0% (2 of 207), and these two deaths occurred during the early period of VATS performed at our institution and the patients had several preoperative co-morbidities. Subsequently, no surgical mortality after VATS lobectomy was seen in the non-conversion group, which is more consistent with the published results on the safety of a VATS lobectomy.[10,25]

Our study has several limitations. First, due to the limited number of conversion cases, comparing the outcomes of the unexpected conversion and non-conversion cases was performed with low power. Second, we used a matching to make the patient groups comparable according to the confounders. Although residual confounding may still exist, our study findings have implications for assessing potential strategies for selecting high risk VATS lobectomy candidate.

V. CONCLUSION

Unexpected conversion to thoracotomy during VATS lobectomy in lung cancer does not appear to increase surgical mortality and morbidity. However, in order to consider the risk factors for thoracotomy conversion, the surgeon requires careful preoperative surveillance of VATS candidate. When VATS lobectomy becomes too difficult, the decision to convert must be made promptly to reduce the operating time, blood loss, ICU stay and possible critical respiratory complications.

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ABSTRACT(IN KOREAN)

절제 가능한 폐암의 흉강경 폐엽 절제술 도중 예기치 않은 개흉술 전환의 분석

<지도교수 정 경 영 >

연세대학교 대학원 의학과

변 천 성

흉강경을 이용한 폐엽 절제술이 처음 소개된 이후에 흉강경은 폐암수술에서 많은 역할을 하게 되었다. 그러나 흉강경 수술 도중 발생하는 예기치 않은 개흉술 전환은 환자에게 잠재적인 부작용을 초래할 수 있다. 이 연구에서는 흉강경 수술 환자에서 예기치 않게 개흉술로 전환한 환자들을 전환하지 않은 환자군과 비교하였고, 이러한 개흉술 전환의 위험인자를 규명하고자 하였다.

2005년부터 2013년까지 총 1110명의 절제 가능한 폐암환자에서 흉강경 폐엽 절제술을 시행하였고, 이중 69명에서 예기치 않은 개흉술로의 전환이 발생하였다. 각각의 개흉술 전환 환자들에 대한 대조군으로 수술 시기, 수술 방법 및 병리학적 폐암 병기를 기준으로 매칭하여 흉강경으로 수술을 완료한 3배의 대조군 환자들을 선정하였다.

개흉술 전환의 가장 많은 원인으로는 섬유석회화된 림프절이 28명 (40.6%), 폐혈관 손상이 20명 (29.0%), 종양의 침윤 또는 주위 침범이 11명 (15.9%), 흉막 유착이 5명 (7.2%), 불완전한 엽간열이 3명 (4.3%) 그리고 수술 중 일측 폐환기의 실패가 2명이었다 (2.9%). 수술 후 합병증 발생 수는 두 그룹간 차이가 없었으며 수술 후 사망자 수도 유의한 차이가 없었다. 하지만 합병증 중 호흡기 관련 합병증의 발생

빈도만 비교하였을 때는, 개흉술 전환 그룹에서 유의하게 발생 수가 많았다 (p=0.012). 또한, 개흉술 전환 그룹에서 수술 시간, 출혈량 그리고 중환자실 재원 기간의 증가를 보였다. 예기치 않은 개흉술 전환의 독립적인 위험 인자는 65세 이상의 나이, 1초간 강제호기량이 1.8 L/sec 미만, 수술 전 흉부 컴퓨터 단층촬영에서 관찰되는 섬유석회화된 림프절이었다.

절제 가능한 폐암의 흉강경 폐엽 절제술 도중 예기치 않은 개흉술 전환은 수술 사망률과 이환율을 악화시키지 않았다. 그러나 개흉술 전환의 위험도가 높은 환자들을 수술 전에 잘 선별하고, 필요 시 개흉술로의 전환을 신속하게 결정해야, 수술 시간, 출혈량, 중환자실 재원 기간을 줄이고 수술 후 발생할 수 있는 치명적인 호흡기 합병증을 감소할 수 있다.

핵심되는 말 : 흉강경, 폐엽 절제술, 개흉술, 전환, 림프절