Changes in Pulmonary Function in Lung Cancer Patients After Video-Assisted Thoracic Surgery

Se Joong Kim, MD, PhD, Yeon Joo Lee, MD, Jong Sun Park, MD, PhD, Young-Jae Cho, MD, Sukki Cho, MD, PhD, Ho Il Yoon, MD, PhD, Kwhanmien Kim, MD, PhD, Jae Ho Lee, MD, PhD, Sanghoon Jheon, MD, PhD, and Choon-Taek Lee, MD, PhD

Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, and Department of Thoracic and Cardiovascular Surgery, Seoul National University Bundang Hospital, Gyeonggi-do, Republic of Korea

Background. Video-assisted thoracoscopic surgery (VATS) is widely performed in patients with resectable non-small cell lung cancer. However, it is unknown whether VATS sublobar resection has advantages compared with VATS lobectomy in preserving pulmonary function.

Methods. Three hundred patients with non-small cell lung cancer who underwent VATS were enrolled. Pulmonary function tests were performed three times: preoperatively, and at 3 and 12 months postoperatively. Pulmonary function was compared between the VATS lobectomy group (n = 227) and the VATS sublobar resection group (n = 73).

Results. The VATS sublobar resection group had greater preserved pulmonary function than the VATS lobectomy group at 3 and 12 months postoperatively (p < 0.001). However, a VATS lobectomy of the right upper or right middle lobe revealed no difference in forced vital capacity (−1.21% versus −1.45%; p = 0.88) or the diffusion capacity of carbon monoxide (−3.99% versus −2.45%; p = 0.61) compared with VATS sublobar resection after 12 months. In those who underwent VATS of the right lower lobe, forced expiratory volume in 1 second (−8.60% versus −3.69%; p = 0.12) was not different between the two groups after 12 months. Video-assisted thoracoscopic surgery lobectomy of the left upper or left lower lobe resulted in lower pulmonary function than VATS sublobar resection (p < 0.05).

Conclusions. Patients with non-small cell lung cancer who underwent VATS sublobar resection demonstrated greater pulmonary function than those who underwent VATS lobectomy. However, in right-side VATS lobectomy, some differences dissipated at 1 year.


Accepted for publication July 23, 2014.

Address correspondence to Dr C-T Lee, Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Seoul National University College of Medicine, Seoul National University Bundang Hospital, 173-82, Gumi-Ro, Bundang-gu, Seongnam-si, Gyeonggi-do, 463-707, Republic of Korea; e-mail: ctlee@snu.ac.kr.

Lung cancer is the most common cause of cancer-related death worldwide [1]. Surgery is considered the primary treatment for patients with resectable, early non-small cell lung cancer (NSCLC) [2]. The Lung Cancer Study Group implemented the only randomized study comparing lobectomy and sublobar resection, such as a segmentectomy or wedge resection [3]. The results revealed an increased risk of local recurrence and reduced survival in patients who underwent sublobar resection. Furthermore, there was no advantage in postoperative pulmonary function after sublobar resection. This study established lobectomy as the gold standard treatment for resectable NSCLC.

However, these results have been challenged in recent years. The development of surgical skills and increased identification of small cancers by low-dose computed tomography screening have naturally led surgeons to resect lung parenchyma to a lesser extent [4]. At present it is suggested that sublobar resection can produce comparable recurrence and survival rate results for patients with stage 1A NSCLC [5–7]. Sublobar resection might be favorable in preserving pulmonary function compared with lobectomy [8, 9]. However, changes in pulmonary function according to chronology and the resected lobe have not been previously investigated between the two surgical methods.

Since the early 1990s, video-assisted thoracoscopic surgery (VATS) has been used for several diagnostic procedures and resections of small, peripheral lung nodules [10]. Recently, VATS has gained widespread acceptance for lung cancer surgery [11]. Video-assisted thoracoscopic surgery can be performed through small incisions and results in less postoperative pain, fewer adhesions, and faster recovery [12, 13]. With respect to pulmonary function, VATS lobectomy outperformed open thoracotomy [14–16]. However, it is unknown whether VATS sublobar resection has advantages compared with VATS lobectomy with respect to pulmonary function.

In this study, we compared postoperative pulmonary function between patients who underwent VATS...
lobectomy versus VATS sublobar resection according to chronology and the resected lobe.

Patients and Methods

Patients

A registry and management protocol were started in August 2003 for patients with NSCLC who underwent surgery at Seoul National University Bundang Hospital. Pulmonary function tests (PFTs) were performed at least three times: preoperatively, and at 3 and 12 months postoperatively. From August 2003 to December 2012, 1,799 patients were enrolled in the registry. Among them, 900 patients underwent VATS lobectomy or VATS sublobar resection, which included VATS segmentectomy and VATS wedge resection. We excluded patients with any missing PFT data, a simultaneous resection of more than two lobes, pleurodesis because of pleural effusion or pneumothorax, inhaler use because of chronic obstructive pulmonary disease or asthma, interstitial lung disease or atelectasis on a chest computed tomography, and sustained smoking after VATS. Finally, 300 patients were enrolled (Fig 1). Baseline PFT values were not significantly different between the enrolled patients and those excluded because of missing PFT data.

Video-Assisted Thoracic Surgery

Video-assisted thoracic surgery was performed through three ports. Two incisions were used for a 10-mm thoracoscopic port and a 5-mm surgical instrument port. A utility window was made along the anterior axillary line of the fourth or fifth intercostal space. Rib cutting or rib spreading was not used. Systematic mediastinal lymph node dissection was performed. The choice of surgical approach, such as VATS lobectomy or VATS sublobar resection, was chosen by the surgeon while considering NSCLC stage, tumor size, tumor location, patient age, and pulmonary function.

The Institutional Review Board of Seoul National University Bundang Hospital approved this study (B-1401/234-105).

Fig 1. Study enrollment flow chart.

(CT = computed tomography; ILD = interstitial lung disease; NSCLC = non-small cell lung cancer; PFT = pulmonary function test; VATS = video-assisted thoracoscopic surgery.)
Data Collection
Clinical and demographic data, such as age, sex, medical history, smoking status, pathologic stage according to the International Association for the Study of Lung Cancer (7th edition), histology, tumor size, and tumor location were collected [17]. Pulmonary function tests were performed by spirometry (V62J; Sensor Medics Corp, Yorba Linda, CA) according to American Thoracic Society recommendations [18]. The parameters of the PFT included forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), FEV1/FVC ratio, and diffusion capacity of carbon monoxide (DLCO); both the absolute values and predicted percentages were recorded. Pulmonary function test changes at short-term and long-term follow-up were defined as the differences between preoperative baseline PFT values and postoperative PFT values at 3 or 12 months after VATS, respectively. The percentage differences in pulmonary function were also compared between the two groups at the short-term and long-term follow-up times as follows: baseline values were subtracted from postoperative values, with the result divided by baseline values and multiplied by 100. We also compared PFT changes for each surgical method in the same lobe. That is, PFT changes were evaluated in both groups according to the resected lobe: the right upper lobe (RUL) or right middle lobe (RML), right lower lobe (RLL), left upper lobe, and left lower lobe.

Statistical Analysis
Values are expressed as the mean ± standard deviation, or number and percent. Intergroup differences were compared by an independent samples Student’s t test for continuous variables. In comparisons for percentage differences in pulmonary function at 3 months and 12 months, multiple Student’s t tests were performed. Changes in PFT values between the short-term and long-term follow-up were analyzed by paired Student’s t tests. All probability values were two-sided, with probability values less than 0.05 regarded as significant, except in multiple Student’s t tests. In multiple Student’s t tests, a Bonferroni correction was performed and a probability value less than 0.025 was regarded as significant. The statistical tests were performed using SPSS version 21.0 software (IBM, Inc, Armonk, NY).

Results
Overall Patient Characteristics
Table 1 shows the baseline characteristics of 300 patients. The two groups did not differ significantly with respect to age, sex, smoking status, operative duration, the duration of chest tube, or hospital stay duration. However, adenocarcinoma was significantly more common in the VATS sublobar resection group. Tumor size and NSCLC

<table>
<thead>
<tr>
<th>Variable</th>
<th>VATS Lobectomy (n = 227, 75.7%)</th>
<th>VATS Sublobar Resection (n = 73, 24.3%)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>63.1 ± 10.1</td>
<td>62.0 ± 11.7</td>
<td>0.45</td>
</tr>
<tr>
<td>Women</td>
<td>122 (53.7)</td>
<td>30 (41.1)</td>
<td>0.08</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td>0.21</td>
</tr>
<tr>
<td>Current smoker</td>
<td>42 (18.5)</td>
<td>10 (13.7)</td>
<td></td>
</tr>
<tr>
<td>Former smoker</td>
<td>55 (24.2)</td>
<td>25 (34.2)</td>
<td></td>
</tr>
<tr>
<td>Never smoked</td>
<td>130 (57.3)</td>
<td>38 (52.1)</td>
<td></td>
</tr>
<tr>
<td>Lung cancer histology</td>
<td></td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>194 (85.5)</td>
<td>70 (95.9)</td>
<td></td>
</tr>
<tr>
<td>Squamous cell carcinoma</td>
<td>26 (11.5)</td>
<td>3 (4.1)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>7 (3.0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>23.8 ± 2.9</td>
<td>23.8 ± 2.9</td>
<td>0.97</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td>2.58 ± 1.23</td>
<td>1.30 ± 0.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-small cell lung cancer stage</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IA</td>
<td>119 (52.4)</td>
<td>69 (94.5)</td>
<td></td>
</tr>
<tr>
<td>IB</td>
<td>68 (30.0)</td>
<td>2 (2.7)</td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>18 (7.9)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>IIB</td>
<td>4 (1.8)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>IIIA</td>
<td>17 (7.5)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>IIIB</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>1 (0.4)</td>
<td>2 (2.7)</td>
<td></td>
</tr>
<tr>
<td>Adjuvant chemotherapy</td>
<td>38 (16.7)</td>
<td>2 (2.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Operative duration (min)</td>
<td>155.8 ± 46.1</td>
<td>167.5 ± 55.9</td>
<td>0.49</td>
</tr>
<tr>
<td>Duration of chest tube (days)</td>
<td>3.6 ± 2.3</td>
<td>4.1 ± 2.3</td>
<td>0.43</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>5.2 ± 3.3</td>
<td>5.8 ± 2.1</td>
<td>0.19</td>
</tr>
</tbody>
</table>

* Values are n (%) or mean ± standard deviation.

VATS = video-assisted thoracic surgery.
stage were significantly larger and more advanced in the VATS lobectomy group. Both groups had similar baseline PFT values with respect to FVC (L), FEV₁ (L), FEV₁/FVC (%), and DLCO (mL mm Hg⁻¹ min⁻¹). However, baseline FVC (%) and FEV₁ (%) were significantly greater in the VATS lobectomy group (Table 2). Among the 73 VATS sublobar resections, 69 were wedge resections. Because their lung cancers were stage 1A with small-sized pure or mixed ground-glass opacity nodules in the periphery, we believed that a wide wedge resection was sufficient for their treatment. In cases of segmentectomy, only one segment was resected. An R0 resection was performed for 226 (99.6%) patients in the VATS lobectomy group and 71 (97.3%) patients in the VATS sublobar resection group. After VATS sublobar resection, 3 patients died at a median of 37 months. Among them, 2 had another fatal malignancy. One patient initially had stage IV lung cancer and underwent VATS sublobar resection for palliative purpose.

**Pulmonary Function Changes With Time**

At both the short-term and long-term follow-ups, the percentage differences in pulmonary function such as FVC, FEV₁, and DLCO were more significantly decreased in the VATS lobectomy group than in the VATS sublobar resection group (Table 2). Between the short-term and long-term follow-up periods, FVC and DLCO were significantly more improved in the VATS lobectomy group (0.24 ± 0.24 L, and 1.11 ± 2.10 mL mm Hg⁻¹ min⁻¹) than in the VATS sublobar resection group (0.10 ± 0.30 L; p < 0.001; Fig 2A, and 0.37 ± 2.10 mL mm Hg⁻¹ min⁻¹; p = 0.012, respectively). However, during this period, the improvement in FEV₁ was not significantly different between the VATS lobectomy group (0.10 ± 0.18 L) and the VATS sublobar resection group (0.07 ± 0.17 L; p = 0.19).

**Pulmonary Function Changes According to Resected Lobe**

Changes in pulmonary function were compared between the VATS lobectomy group and the VATS sublobar resection group. After VATS of the RUL or RML, FVC, FEV₁, and DLCO were significantly and rapidly decreased in the VATS lobectomy group at the short-term follow-up (all p < 0.05). However, FVC and DLCO were more rapidly improved in the VATS lobectomy group. Finally, there were no significant differences between the groups at the long-term follow-up (Table 3, Fig 2B). After VATS of the RLL, FVC, FEV₁, and DLCO were significantly and rapidly decreased in the VATS lobectomy group at the short-term follow-up (all p < 0.01). Forced vital capacity was significantly lower in the VATS lobectomy group at both the short-term and long-term follow-ups (Fig 2C). However, FEV₁ showed no difference between the groups at the long-term follow-up (Table 3). After VATS of the left upper lobe (Fig 2D) or left lower lobe (Fig 2E), all PFT values were significantly lower in the VATS lobectomy group at both follow-up periods (Table 3). According to the resected lobe, the percentage differences in pulmonary function

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline Values</th>
<th>Short-Term Follow-Up (Mean % Differences)</th>
<th>Long-Term Follow-Up (Mean % Differences)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>3.36 ± 0.76</td>
<td>106.1 ± 14.55</td>
<td>106.5 ± 18.94</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>2.44 ± 0.55</td>
<td>2.00 ± 0.74</td>
<td>2.10 ± 1.04</td>
</tr>
<tr>
<td>DLCO (%/C0)</td>
<td>7.31 ± 8.48</td>
<td>105.9 ± 18.4</td>
<td>105.5 ± 18.9</td>
</tr>
<tr>
<td>DLCO (mL/C0)</td>
<td>18.7 ± 4.4</td>
<td>18.7 ± 4.4</td>
<td>18.7 ± 4.4</td>
</tr>
<tr>
<td>FEV₁/FVC (%)</td>
<td>73.1 ± 10.1</td>
<td>100.1 ± 18.9</td>
<td>100.1 ± 18.9</td>
</tr>
</tbody>
</table>

*Table 2. Percentage Differences in Pulmonary Function Testsa*  

---

FVC = forced vital capacity; FEV₁ = forced expiratory volume in 1 second; DLCO = diffusion capacity of carbon monoxide; VATS = video-assisted thoracoscopic surgery; FEV₁/FVC = forced expiratory volume in 1 second/forced vital capacity. 

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---

---
Comment

Video-assisted thoracoscopic surgery sublobar resection was superior to VATS lobectomy for the preservation of pulmonary function. Video-assisted thoracoscopic surgery has fewer destructive properties than open thoracotomy [14]. Video-assisted thoracoscopic surgery is associated with less pain, low morbidity and mortality, and earlier recovery compared with open thoracotomy [19, 20]. The National Comprehensive Cancer Network guidelines also recommend VATS for resectable NSCLC [2]. However, there was no study comparing pulmonary function between VATS lobectomy and VATS sublobar resection. Previous studies compared lobectomy with sublobar resection without using VATS and found conflicting results. Some studies, performed before the year 2000, showed no significant difference in pulmonary function between lobectomy and sublobar resection [3, 21]. Other more-recent studies demonstrated that sublobar resection resulted in more favorable pulmonary function than lobectomy [8, 9, 22]. Although these studies did not use VATS, the results were similar to those of our study. Recent advances in operative techniques, instruments, and postoperative management might have contributed to the improvement of pulmonary function after sublobar resection.

To evaluate changes in pulmonary function, we chose to analyze PFTs from 3 and 12 months postoperatively. Because many patients sustained postoperative pain for 1 to 2 months, real pulmonary function could not be evaluated. Therefore, we decided to check postoperative PFTs at 3 months for short-term follow-up. After 12 months, pulmonary function showed somewhat of a plateau; thus, we decided to check PFTs at 12 months for long-term follow-up. Although pulmonary function was better in the VATS sublobar resection group, the VATS lobectomy group showed greater improvements in FVC and DLco between 3 and 12 months. After lobectomy, the remaining lobe in the mainly ipsilateral and partially contralateral lung expands and somewhat compensates for the resected lobe [23]. This expansion of the remaining lung leads to a gradual increase in lung volume; therefore, the FVC in the VATS lobectomy group was more rapidly improved than in the VATS sublobar resection group [24]. The expansion also occurred in vascular tissues; thus, the ventilation–perfusion ratio was improved [25]. Our results showed a more rapid improvement of DLco in the VATS lobectomy group. Although both groups demonstrated improved FEV1 with time, the degree of improvement in FEV1 was not different between the two groups. Lobectomy inevitably leads to displacement of the remaining lobe. Such displacement could cause bronchial angulation, a narrowed airway, and increased airway resistance [26]. As FEV1 is an indicator of airway resistance, the VATS lobectomy group did not show greater improvements in FEV1 [18].

Furthermore, the improvement of pulmonary function was variable according to the resected lobe. Video-assisted thoracoscopic surgery lobectomy of the RUL or RML showed greater improvements in FVC and DLco. These parameters reached levels similar to those in the VATS sublobar resection group after 12 months postoperatively. The volume of the RUL or RML is relatively low compared with that of the other lobes. Therefore, the expansion of the remaining lobe could compensate for the resected lobe over the course of time. However, as we previously reported [26], after lobectomy...
Table 3. Percentage Differences in Pulmonary Function After VATS at 1 Yeara

<table>
<thead>
<tr>
<th>Variable</th>
<th>LLL</th>
<th>VATS Sublobar (n=29)</th>
<th>VATS Lobectomy (n=60)</th>
<th>VATS Sublobar (n=41)</th>
<th>VATS Lobectomy (n=91)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>−2.45 ± 12.42</td>
<td>8.07 ± 13.22</td>
<td>−0.67 ± 8.60</td>
<td>0.12 ± 6.20</td>
<td>0.02 ± 5.27</td>
<td>0.01</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>9.96 ± 14.42</td>
<td>8.60 ± 13.62</td>
<td>0.67 ± 6.70</td>
<td>0.12 ± 11.96</td>
<td>0.02 ± 10.24</td>
<td>0.004</td>
</tr>
<tr>
<td>DLCO (mL/mm Hg)</td>
<td>3.33 ± 14.34</td>
<td>8.74 ± 13.32</td>
<td>0.88 ± 6.37</td>
<td>0.02 ± 6.37</td>
<td>0.00 ± 5.27</td>
<td>0.001</td>
</tr>
<tr>
<td>DLCO (% of predicted value)</td>
<td>3.33 ± 14.34</td>
<td>8.74 ± 13.32</td>
<td>0.88 ± 6.37</td>
<td>0.02 ± 6.37</td>
<td>0.00 ± 5.27</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation.

Of note, this is the first study comparing pulmonary function between VATS lobectomy and VATS sublobar resection. Previous studies compared pulmonary function between lobectomy and sublobar resection without using VATS [3, 8, 9, 21]. We also analyzed pulmonary function according to the resected lobe. However, previous studies had small sample sizes and were obliged to analyze only upper lobe resection or lower lobe resection groups [21, 27].

The present study has several limitations. First, we could not measure the exact volume of each lobe. Postoperative volume changes could be assessed by Cavalieri’s principle [28]. However, the method is not simple, and the analysis of a large population might be impossible. Although we could not directly evaluate gradual lung volume changes after VATS, a previous study clearly demonstrated expansion of the remaining lung leading to a gradual increase in lung volume [23]. Second, because of the strict inclusion criteria, a relatively large number of patients were excluded. Especially, many patients were excluded because they had missing 3- or 12-month follow-up PFTs. Third, in the baseline characteristics, NSCLC stage was more advanced and tumor size was larger in the VATS lobectomy group. Adjuvant chemotherapy was also more frequently performed in the VATS lobectomy group. These discrepancies might have negative effects on pulmonary function. Fourth, our enrolled patients sustained good pulmonary function postoperatively. Therefore, they might not reflect the situation of patients with high-risk marginal pulmonary function.

In conclusion, patients with NSCLC who underwent VATS sublobar resection showed greater pulmonary function than those who underwent VATS lobectomy. However, some parameters of pulmonary function after right-side VATS lobectomy reached those after VATS sublobar resection at 1 year postoperatively. Because lobectomy showed a better prognosis than sublobar resection, except for patients with stage IA disease [3, 20, 29], clinicians should consider these results when determining the surgical method, especially in high-risk...
patients. More large-scale, multicenter studies are warranted to verify these findings.

References

INVITED COMMENTARY

In 1995, the landmark study written by Ginsberg and Rubinstein [1] for the Lung Cancer Study Group evaluating the efficacy of a lobectomy versus limited resection set the stage for the ensuing two decades. In recent years, it has become standard practice for parenchymal resection of small nodules (ideally anatomic segmentectomy) to be performed with video-assisted thoracoscopic surgery (VATS). The VATS approach has emerged as a superior approach to early-stage NSCLC [2]. The published benefits of VATS have been an improved oncologic outcome, less pain and morbidity, and improved pulmonary function. As instrumentation and technique improved, VATS resections became more commonplace, with the lobectomy being the treatment of early-stage NSCLC.

As proficiency was attained with VATS techniques, the role of sublobar resections (ideally anatomic segmentectomy for small nodules) has been revisited with concomitant improvements in imaging, critical care, and pulmonary medicine. These improvements extended the benefits of surgical resection for high-risk, frail patients, once thought to have limited physical or pulmonary function. As the approach to surgically treating early-stage NSCLC, especially in high-risk patients, a multicenter, large-scale study to further elucidate these effects would be beneficial.

Bryan A. Whitson, MD, PhD
Department of Surgery
The Ohio State University Wexner Medical Center
N-813 Doan Hall
410 W 10th Ave
Columbus, OH 43210
e-mail: bryan.whitson@osumc.edu

References