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Lung Cancer (HA Wakelee, Section Editor)

Updates on Minimally Invasive Surgery in Non-Small Cell Lung Cancer

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Opinion statement

Video-assisted thoracic surgery (VATS) has become widely used since the 1990s and has become a standard treatment approach mainly for early-stage non-small cell lung cancer. The few randomized controlled trials providing evidence of the effectiveness of VATS lobectomy at present are supported by a large number of propensity-matched studies, several high-quality meta-analyses, and outcome studies. These studies provide comprehensive data demonstrating the lower morbidity, shorter chest tube duration, and shorter hospital stay of VATS than thoracotomy during the postoperative course. Moreover, VATS shows equivalent oncological outcome as thoracotomy and therefore should be performed for lobectomy as much as possible. Importantly, VATS has recently been applied to advanced cases and previously contraindicated complex procedures such as bronchoplasty and chest wall resection. Attention has also been paid to reduced port surgery performed by frontier surgeons. Thus, the indications of VATS have seen a significant expansion. This major development logically negates any hesitation to change to the VATS technique as any doubt will likely constrain its wider applications. Preparation of scientific learning environments is necessary and should be actively pursued to adopt new skills instead of debating between the choice of "VATS or open."

Introduction

Computed tomography has become commonly used in routine practice, enabling the more frequent detection of early-stage lung cancers. Currently, the standard treatment for early-stage lung cancer is surgery. Recently, video-assisted thoracic surgery (VATS) has been widely used as a less invasive procedure. In 2015, 26,188 lung cancer operations by VATS were performed in Japan, which corresponded to 64.4% of

the entire operations (40,687 cases) [1]. Since the first description of VATS lobectomy in the early 1990s, its potential advantages include a smaller incision, minimal chest wall damage, and less postoperative pain. Moreover, several studies have demonstrated the benefits of VATS over conventional thoracotomy for early-stage lung cancer, such as shorter length of hospital stay, lower rate of complications, and no significant difference in the survival rate [2–6]. Presently, VATS is considered a routine surgical procedure used not only for early-stage lung cancer but also for advanced cancer and some complicated surgical procedures. The aims of this article are to describe the present status of and consensus on minimal invasive surgery and to discuss the future of VATS and other surgical systems on the basis of collected scientific data.

Standardization of VATS

There are two kinds of "VATS," namely, hybrid VATS [7] and complete VATS [8]. These terms have not yet been standardized to date. In hybrid VATS, the surgeon makes a small thoracotomy (8–10 cm) and employs both direct vision from the incision and video monitor imaging. In complete VATS, the surgeon makes three or four small incisions without rib spreading and visualizes only the video monitor during the operation. Cancer and Leukemia Group B (CALGB) 39,802 was the first prospective, multi-institution study to examine a standardized VATS lobectomy for early-stage lung cancer in 2007. In the same year, Swanson et al. established the definition of VATS lobectomy in a prospective, multi-institutional study. The definition written below has been recognized as the standard definition to date:

1) No rib spreading
2) Incision with a maximum length of 8 cm for removal of the specimen
3) Individual dissection of the vein, arteries, and airway for the lobe in question
4) Standard node sampling or dissection

The endpoint of this study was the feasibility of VATS lobectomy based on the above-mentioned definition for early-stage lung cancer. Of the 111 (86.5%) stage I patients, 96 were successfully operated with a low complication rate and a short chest tube duration [8].

Short-term postoperative outcome

There are a large number of articles on VATS that are classified into large database analyses with unmatched comparisons, meta-analyses, propensity-matched studies, and a few small randomized controlled trials. The results of representative reports are summarized in Table 1.

Whitson et al. reported a meta-analysis comparing 3114 VATS cases and 3256 thoracotomy cases from 39 publications [2]. The overall complication rates significantly favored the VATS group (16.4% vs 31.2%; $P = 0.018$); thus, VATS lobectomy for patients with early-stage lung cancers shows a lower morbidity. Yan et al. also published the results of a meta-analysis based on 21 studies (2 randomized and 19 nonrandomized studies) [3]. A total of 1391 patients who underwent VATS lobectomy and 1250 patients who received thoracotomy were compared. There were no significant differences in postoperative air leakage

Table 1. Representative propensity-matched analyses showing the benefits of VATS compared with thoracotomy in terms of reduced overall postoperative complications

Author (ref)	No. of matched pair	Operative mortality (%) Stage	VATS	Thoracotomy	*P* value	Complications (%) VATS	Thoracotomy	*P* value
Nwogu [9]	175	I, II	1.7	1.7	NS	14.9	25.1	< 0.0001
Paul [5]	1281	Majority I, II	0.9	1	1	26.2	34.7	< 0.001
Scott [10]	VATS 66 Thoracotomy 686	T1, T2, N0, N1	0	1.6	1	27.3	47.8	0.44
Flores [11]	313	Majority I	0.3	0.3	1	24	30	0.05
Falcoz [12••]	2721	Majority I, II	1	1.9	0.02	29.1	31.7	0.036

Author (ref)	Chest drainage (days) VATS	Thoracotomy	*P* value	Length of stay (median, days) VATS	Thoracotomy	*P* value	Factors favoring VATS
Nwogu [9]	3.3	5	< 0.0001	4	6	< 0.0001	LOS, CD, complications
Paul [5]	3	4	< 0.0001	4	6	< 0.0001	LOS, CD, complications (arrythmia, reintubation)
Scott [10]	1.5%, > 7	10.8%, > 7	0.029	4.5	7	< 0.001	Operation time, LOS, CD, complications (atelectasis)
Flores [11]				5	7	0.001	LOS, complications
Falcoz [12••]				6	8	0.0003	LOS, hospital death, complications (atelectasis, ventilation, wound infection)

duration ($P = 0.71$), arrhythmia ($P = 0.86$), pneumonia ($P = 0.09$), and mortality ($P = 0.49$) between VATS and thoracotomy. These two representative meta-analyses suggest that VATS lobectomy is a feasible and safe procedure for selected patients compared with the conventional thoracotomy approach.

Scott et al. performed a secondary analysis of the American College of Surgeons Oncology Group (ACOSOG) Z0030 clinical trial, in which the primary object was designed to evaluate the survival of lymph node sampling versus mediastinal lymph node dissection in patients undergoing complete resection of early-stage lung cancer [13]. Scott et al. used propensity score stratification in 752 patients (66 VATS and 686 thoracotomy) to compare the relative morbidity of VATS lobectomy with that of thoracotomy. Patients undergoing VATS lobectomy had significantly less atelectasis (0% vs 6.3%; $P = 0.035$), less frequent chest drainage duration longer than 7 days (1.5% vs 10.8%; $P = 0.029$), and shorter length of hospital stay (mean, 5 days vs 7 days; $P < 0.001$). The postoperative mortality rate was not significantly different (VATS 0% vs thoracotomy 1.6%; $P = 1.0$) [10].

CALGB 31001 compared the outcome of lobectomies for stages I and II lung cancer between VATS and open procedures. The primary endpoint was the length of hospital stay. The secondary endpoints were discharge condition, overall post-operative complications, and disease-free survival. Propensity-matched analysis of 175 patients from the VATS group and 175 patients from the thoracotomy group revealed that the mean hospital stay was significantly shorter in the VATS group (5.4 days vs 8.0 days; $P < 0.0001$) and that the chest tube duration was also significantly shorter in the VATS group (3.3 days vs 5.0 days; $P < 0.001$). VATS had significantly less complications than thoracotomy (14.9% vs 25.1%; $P < 0.001$) [9•]. Several representative propensity-matched analyses data showed the benefits of VATS compared with thoracotomy in terms of reduced overall postoperative complications such as less pain, less prolonged air leakage, arrhythmia, and pneumonia (Table 1).

Oncological outcome

There were two randomized studies comparing the performance of VATS lobectomy and thoracotomy. Kirby et al. randomized 61 stage I lung cancer patients into 2 groups and showed reduction of postoperative complications in the VATS group (6% vs 16%), but no significant decrease in the duration of chest tube drainage and length of hospital stay [14]. Sugi et al. randomized 100 stage IA lung cancer patients into the VATS lobectomy and thoracotomy groups but found no significant differences in recurrence and survival. The 5-year survival rates of the VATS and open thoracotomy groups were 90% and 85%, respectively [15].

Whitson et al. showed that VATS lobectomy was associated with an improved 4-year survival rate [2]. Yan et al. showed that VATS had a relative risk of 0.66 of the all-cause mortality at 5 years (95% confidence interval (CI), 0.45–0.97; $P = 0.04$) compared with thoracotomy, and the relative systemic recurrence risk of VATS was 0.57 (95% CI, 0.34–0.95; $P = 0.03$) [3].

The propensity-matched analysis of the ACOSOG Z0030 cohort showed that the overall survival (OS) was not significantly different between VATS ($n = 66$) and open lobectomy ($n = 686$). The 5-year survival rates of VATS and open surgery were 71.6% and 65.9%, respectively ($P = 0.36$). There was no significant difference in the 5-year disease-free survival between VATS (75.2%) and open

lobectomy (69.2%) ($P = 0.55$) [16].

Nwongu et al. reported a hazard ratio of 1.15 (95% CI, 0.85–1.55; $P = 0.36$) for disease-free survival of VATS versus thoracotomy and 1.27 (95% CI, 0.92–1.76; $P = 0.15$) for OS [9•].

A large number of studies have provided strong lines of evidence that the minimally invasive approach is oncologically equivalent to open surgery without a significant difference in the survival rate [17, 18]. However, there is still room for debate in terms of lymph node dissection. D'Amico et al. evaluated the mean number of mediastinal lymph nodes dissected in patients who underwent lobectomy (VATS, 199; thoracotomy, 189) and found that the number of N2 lymph node stations dissected was not significantly different between VATS ($n = 3.15$) and thoracotomy ($n = 2.91$) [6]. Scott et al. also reported that the mean number of lymph nodes retrieved was not significantly different between VATS (15 nodes) and thoracotomy (19 nodes) ($P = 0.147$) [10].

Boffa et al. analyzed 11,531 clinical stage I lung cancer operations (7137 thoracotomy, 4394 VATS), and pathological nodal upstaging was observed more frequently in the thoracotomy group than in the VATS group (14.3% vs 11.6%; $P < 0.001$). Hilar or peribronchial nodal metastases were identified more often in the thoracotomy group than in the VATS group (54% vs 42%; $P = 0.002$); thus, complete hilar and peribronchial lymph node dissection must be improved in the VATS approach [19].

Specialized VATS technique and robotic surgery

Although the non-small cell lung cancer (NSCLC) patient selection criteria for VATS vary among surgeons, VATS has been limited to patients with small, peripherally located tumors, without evidence of lymph node metastasis. With the rapid progression in the use of VATS techniques and the accumulation of experience, the choice of VATS has become comparable to that of traditional thoracotomy lobectomy [20]. In fact, the indications of VATS have expanded to complex procedures such as segmentectomy [21–23] or sleeve resection [24–26], and these indications are currently more pressing issues for treating advanced lung cancer.

Huang et al. reported the results of 118 VATS bronchial sleeve lobectomies. Two serious postoperative complications (i.e., anastomosis failure and pneumonia) were reported, but the remaining patients did not have major morbidity [24]. Recently, considerable attention has been paid to single-port VATS lobectomy. Vannucci et al. started and extensively performed single-port VATS [25•] and also demonstrated its use for bronchoplasty and double-sleeve resection [26]. The VATS approach for bronchial sleeve resections and bronchovascular double sleeve resections involves complex minimally invasive resections. Although VATS has been demonstrated to be technically feasible, these procedures should be limited to experienced surgeons. Tumors invading the chest wall and superior sulcus can also be indicated for the VATS approach in selected patients [27]. Most of the procedure is performed using VATS, and thoracotomy can be minimized in the extent of chest wall resection. Almost all lung cancers even in the advanced stage can be technically resected by VATS. However, thoracic surgeons should evaluate the operative indication in terms of both resectability and oncological result.

Notably, the number of robotic surgery for lung cancer has also been gradually increasing. In a previous study, a total of 470 clinical stage I NSCLC patients (172

robotic surgery, 141 VATS, and 157 open thoracotomy) were matched by propensity score and compared in terms of survival and postoperative course. Patients undergoing minimally invasive approaches had significantly shorter median length of hospital stay (4 days for robotic vs 4 days for VATS vs 5 days for open thoracotomy; $P < 0.001$). The 5-year OS rates of the robotic, VATS, and open matched groups were 77.6%, 73.5%, and 77.9%, respectively, with no significant difference. These surgical approaches were not associated with OS [28].

Oh et al. compared the short-term results of lobectomy by these surgical approaches using propensity-matched analysis. This involved robotic lobectomy versus open lobectomy with 2775 pairs and robotic lobectomy versus VATS with 2951 pairs. The robotic group showed a lower complication rate, a shorter hospital stay, and a lower mortality rate than the open lobectomy group. Compared with the VATS lobectomy group, the robotic group showed less complications and a shorter hospital stay [29]. Although robotic lung cancer surgery is presently performed only in limited institutes, it is definitely a very promising procedure and would become widely used if a new cost-effective generation system is developed.

Conclusion

Both VATS and open lobectomy are well-established approaches to lobectomy for lung cancer. Importantly, a large amount of data show that VATS results in long-term survival, decreased rate of complications and length of stay, and decreased operative mortality—at least in experienced institutions and in appropriately selected patients. Nevertheless, it is clear that both VATS resection and open resection for lung cancer have a particular role and that they should be viewed as complementary rather than competitive approaches.

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Compliance with Ethical Standards

Conflict of Interest

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