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CURRENT TOPICS REVIEW ARTICLE

Video-assisted thoracoscopic surgery lobectomy for non-small cell lung cancer

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Abstract
Since 1990s, video-assisted thoracoscopic surgery (VATS) lobectomy has become a standard procedure for early-stage non-small cell lung cancer. However, VATS lobectomies are less common, and no randomized controlled trial of VATS versus conventional open lobectomy for early-stage lung cancer has been performed in Japan. Furthermore, VATS lobectomy procedures are not standardized in Japan, and may vary by institution or by practitioner, which complicates their evaluation. Although VATS procedures (such as pneumonectomy, bronchoplasty, and chest wall resection) have been reportedly performed for patients with advanced disease, whether VATS could be a standard modality for advanced lung cancer is unclear from an oncological perspective. Until recently, VATS lobectomies commonly used three or four ports to conduct systemic lymph node dissection; however, VATS lobectomies with reduced port have been recently reported. This article reviews current trends in VATS lobectomy procedures.

Keywords Non-small cell lung cancer · Video-assisted thoracoscopic surgery · Lobectomy

Introduction

Lobectomy with systemic lymph node dissection has been the standard treatment for patients with stage I or II non-small cell lung cancer (NSCLC) since the 1960 [1]. Although VATS lobectomy for primary lung cancer is increasingly accepted as a minimally invasive surgery, it is now widely performed with a lack of clear evidence. According to the Japanese Association for Thoracic Surgery (JATS) 2013 Annual Report 2013 [2], of 37,008 operations for primary lung cancer, limited resection by wedge resection or segmentectomy was performed in 8771 (23.7%) cases, lobectomy in 27,469 (74.2%) cases and pneumonectomy in 559 (1.5%) cases. VATS procedures comprised 70.8% of total lung cancer surgeries, including 4,270 (86.2%) of wedge resections, 2,800 (73.4%) of segmentectomies, 18,929 (68.9%) of lobectomy, and 82 (14.7%) of pneumonectomies. However, these data come from practitioners' self-assessments. In fact, the proportion of actual VATS pneumonectomies are lower than reported, due to the lack of consensus definition for VATS. VATS may be indicated for advance cases by sufficiently skilled surgeons. This review article discusses the current state and recent trends of VATS lobectomy.

Definition of VATS lobectomy

In 2007, Swanson et al. [3] reported a prospective, multi-institution feasibility study of VATS lobectomy, in which they defined VATS lobectomy as one 4–8-cm access and two 0.5-cm port incisions that permitted videoscopic guidance and traditional hilar dissection without rib spreading. However, in Japan, VATS lobectomy has not been defined.

Masuda et al. [4] reported that the Committee for Scientific Affairs in JATS changed their method of surveying general thoracic surgery in 2014. JATS started to collect the number of procedures in general thoracic surgery using the database in National Clinical Database (NCD) registry. Before 2013, JATS's recording guidelines for scientific investigations stated that mini-thoracotomy wounds for thoracoscopic lobectomy should be no longer than 8 cm, following Swanson's proposal. However, between 2014 and 2015, NCD registry did not limit skin incision length in VATS procedures. NCD guidelines required surgeons to choose among complete VATS procedure, hybrid VATS using both thoracotomy and VATS, and conventional

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thoracotomy without VATS. As a result, the reported proportion of VATS procedures at that time was higher than actually performed. Therefore, in 2016, the NCD registry again limited incision length to no longer than about 8 cm. However, even now, the Japanese VATS definition does not clarify whether or not VATS should use only monitor visualization.

Advantage of VATS lobectomy

Decreased invasiveness

Although several retrospective studies have shown VATS lobectomy to be a safe procedure with low complication rates [5–7], they are not as statistically robust as a randomized controlled trial (RCT). Summary of the trials regarding surgical invasiveness of VATS are shown in Table 1. When VATS lobectomies began to be widely used, Kirby et al. [8] reported an RCT in which VATS (25 cases) and muscle-sparing thoracotomy (30 cases) showed no significant differences in operating time, intraoperative blood loss, duration of chest tube drainage, or length of hospital stay, but thoracotomy showed significantly longer air leakage. They concluded that VATS lobectomy was not associated with a significant decrease in the duration of chest drainage, length of hospital stay, post-thoracotomy pain, or, in this group of patients, a faster recovery time and return to work. However, their sample size was too small.

Whitson et al. [9] reported a meta-analysis in 2008 comparing 6370 patients (3114 VATS cases and 3256 thoracotomy cases) from 39 publications, in which overall complication rates significantly favored the VATS group (16.4 vs 31.2%; $P=0.018$), as did annual survival rates. They concluded that VATS lobectomy for patients with early-stage NSCLC is appears to favor lower morbidity and improved survival rates compared with lobectomy performed by thoracotomy.

Scott et al. [10] reported a secondary analysis of data from the American College of Surgeons Oncology Group Z0030 randomized clinical trial. Data from 964 participants in ACOSOG Z0030 trial were used to construct propensity scores for VATS versus open lobectomy. A total of 752 patients (66 VATS and 686 open procedures) were analyzed on the basis of propensity score stratification. Median operative time was shorter for VATS lobectomy (VATS 117.5 min versus open 171.5 min; $P<0.001$). Patients undergoing VATS had less atelectasis requiring bronchoscopy (0 vs 6.3%; $P=0.035$), fewer chest tubes draining greater than 7 days (1.5 vs 10.8%; $P=0.029$), and shorter median length of stay (5 days versus 7 days; $P<0.001$). Fewer patients who underwent VATS (27.8%) experienced at least 1 complication than did open group (47.8%; $P=0.005$). Operative mortality was similar (VATS 0% vs open 1.6%; $P=1.000$). They concluded that VATS lobectomy may offer advantages in terms of decreased length of stay and overall fewer complications.

The CALGB 31,001 study, a multi-center analysis [11], compared outcomes between VATS and thoracotomy for early-stage NSCLC. Propensity-matched analysis from 350 eligible patients ($n=175$ for both groups) showed that in the VATS group, mean hospital stay was shorter (5.4 versus 8.0 days, $P<0.0001$) and incidence of surgical complication was lower (14.9 vs 25.1%, $P<0.0001$).

A propensity-matched analysis [12] from the European Society of Thoracic Surgeons database compared the outcome following VATS versus open lobectomy. Propensity-matched analysis from 5,442 eligible patients ($n=2721$ for both groups) showed that, compared with open procedures, the VATS group had significantly lower rates of overall complications (VATS 29.1%, open 31.7%, $P=0.0357$) and major cardiopulmonary complications (VATS 15.9%,

Table 1 Summary of the trials regarding surgical invasiveness

Study (year)	Design	No. of patients VATS	Open	Clinical stage	Significant factor
Kirby [8] (1995)	RCT	25	30	I	CD, LOS, pain
Whitson [9] (2008)	Retrospecitve (Meta-analysis)	3114	3256	ND	Complication rate; 16.4% vs. 31.2% ($P=0.018$)
ACOSOG Z0030 [10] (2010)	RCT	66	686	I–II	Operation time, atelectasis, CD, LOS, complications
CALGB 31,001 [11] (2015)	Retrospecitve (Propensity-matched)	175	175	I–II	LOS, complications
ESTS [12] (2016)	Retrospecitve (propensity-matched)	2721	2721	ND	LOS, complications, in hospital death
Bendixen [13] (2016)	RCT	102	99	I	Pain (NRS), QOL

ACOSOG American College of Surgeons Oncology Group, *CALGB* Cancer and Leukem ia Group B, *ESTS* Europian S ociety of thoracic surgeon, *RCT* randomised controlled trial, *ND* not described, *CD* chest drainage, *LOS* length of stay, *QOL* quality of life, *NRS* numerical rating scale

open 19.6%, $P=0.0094$). Postoperative hospital stay was 2 days shorter in VATS group (VATS 7.8 days versus open 9.8 days, $P=0.0003$). In terms of outcome at hospital discharge, there were 27 deaths in the VATS group (1%) versus 50 in the open group (1.9%, $P=0.0201$). They concluded that lobectomy performed through VATS is associated with a lower incidence of complications compared with thoracotomy. Many case-control studies have been reported, but there are few reports showing a high evidence in terms of the RCT. However, in 2016, an RCT from Denmark [13] that compared postoperative pain and quality of life after VATS lobectomies ($n=102$) and open lobectomies (anterolateral thoracotomy; $n=99$) performed from October 2008 to August 2014 for early-stage lung cancer showed the VATS group had lower incidences of significant pain (Numeric Rating Scale [NRS] ≥ 3) in the first 24 h after surgery for the VATS group (VATS 38%, open 63%, $P=0.0012$) and of relevant pain episodes (NRS ≥ 3) during the 52-week follow-up period ($P<0.0001$); and postoperative quality of life was significantly better according to the EuroQol 5 Dimensions questionnaire ($P=0.014$), but not statistically different according to the European Organization for Research and Treatment of Cancer 30-item questionnaire ($P=0.130$).

Although prospective RCTs are uncommon, VATS lobectomies are generally considered to be less invasive than thoracotomy. In fact, even in thoracotomies, shorter incisions are favored, as. they have some advantages for the patient after lobectomies.

Lymph node dissection and oncological efficacy in VATS lobectomy

Efficacy of lymph node (LN) dissection for lung cancer depends on accurate staging and the likelihood of survival benefit. In the 1990s, some surgeons were concerned that they might not be able to conduct LN dissection at the same level using VATS lobectomy as with thoracotomy; the quality of nodal dissection between the two surgical modalities is still controversial, and is further complicated by lack of consensus on how to evaluate LN dissection (e.g., number of dissected LNs versus upstaging rate [14, 15]). Few RCTs have compared long-term prognosis associated with these procedures. Summary of lymph node dissection and nodal upstage are shown in Table 2.

Sugi et al. [16] reported on an RCT that compared VATS ($n=48$) and conventional ($n=52$) lobectomies for clinical stage IA (T1N0M0) lung cancer, performed between January 1993 and June 1994. The two groups did not significantly differ in mean numbers of dissected hilar LNs (VATS: 8.4 ± 1.0, conventional: 8.2 ± 1.5), or mediastinal nodes (VATS: 13.4 ± 1.7, conventional: 13.0 ± 2.5). They concluded the number of lymph nodes removed by VATS were comparable to those removed by thoracotomy and survival and recurrence were comparable as well.

Palade et al. [17] also reported a small-cohort prospective RCT of VATS ($n=34$) vs open ($n=32$) mediastinal lymphadenectomy for stage I NSCLC that showed the two procedures did not significantly differ in mean numbers of removed LNs per patient, in total or per side (right side—VATS: 24.0 LNs, open: 25.2 LNs, $P=0.98$; left side—VATS: 25.1 LNs, open: 21.1 LN, $P=0.32$). Mediastinal lymph node dissection can be performed as effectively by the VATS approach as by the open thoracotomy.

In contrast, Boffa et al. [18] evaluated LN assessment with VATS or open surgery in 11,531 anatomical resections for stage I lung cancer (including sub-lobar resections). They found the open group had a higher upstaging rate for N0–N1 disease (open: 9.3%, VATS: 6.7%, $P<0.001$), but similar upstaging rates for N1 to N2 disease (open: 5.0%, VATS: 4.9%, $P=0.52$), which they suggested reflected variability in completeness of peribronchial and hilar LN dissections.

In 2016, a propensity-matched analysis of nodal upstaging from the Society of Thoracic Surgeons (STS) General Thoracic Surgery Database showed that although nodal upstaging was more common in the open group (open: 12.8%, VATS: 10.3%, $P<0.001$) [15]. For sub-group of patients whose number of lymph nodes examined was ≥ 7, propensity maching revealed that nodal upstaging remained more common following open ($n=2825$) versus VATS ($n=2825$) (14.0 versus 12.1%, $P=0.03$). However, for

Table 2 Summary of the trials of lympn node dissection and nodal upstages

Study (year)	Design	No. of patients VATS	Open	Clinical stage	Results
Sugi [16] (2000)	RCT	48	52	IA	No. of dissected LNs, OS, and recurrence we are comparable
Plade [17] (2013)	RCT	34	32	I	No. of removed LN was comparable
STS [15] (2016)	Retrospective (Propensity-mattched)	2825	2825	I	nodal upstage VATS 12.1% vs. Open 14.0% ($P=0.03$) in an Academic/research facility, 10.5% vs. 12.2% ($P=0.08$)

STS society of thoracic surgeons, *RCT* randomised controlled trial, *no*. number, *LNs* lympn nodes, *OS* overall survival

patients who were treated in academic or research facilities, the difference in nodal upstaging was no longer significant between open ($n=2008$) versus VATS ($n=2008$) approach (12.2 versus 10.5%, $P=0.08$). They concluded that nodal upstaging was affected by facility type, which may be a surrogate for minimally invasive expertise.

Further prospective RCTs that compare VATS and conventional thoracotomy for early-stage lung cancer are unlikely to occur, as VATS has already become the standard approach for early-stage cases.

VATS lobectomy for advanced lung cancer

Initially, VATS lobectomy for lung cancer was indicated for early-stage disease. After gaining experience and skill with VATS, some surgeons pioneered VATS procedures for advanced cases, such as bronchoplasty, vascular sleeve resections, and chest wall resection. In 2007, Nakanishi [19] reported early experiences with VATS bronchoplasty, including a VATS sleeve and four VATS wedge lobectomies, successfully performed without no major complications. He noted that positioning of mini-thoracotomy and other access ports, suture management, and secure tightened techniques were important. Huang et al. [20] reported their experiences with 118 complete VATS bronchial sleeve lobectomies performed from January 2008 to February 2015. Operations lasted 118–223 min, including 15–42 min for bronchial anastomosis. One patient died of massive hemoptysis after anastomotic leakage on the 15th postoperative day, and another had acute pneumonia, however, no operative complication was reported for the remaining 116 patients. Zhou et al. [21] analyzed 51 sleeve lobectomies (10 by VATS, 41 by thoracotomy) in patients with NSCLC. VATS patients had a longer surgery (VATS 226 ± 37 min versus thoracotomy 166 ± 40 min, $P<0.001$) but a shorter postoperative hospital stay (VATS 11.6 ± 2.8 days versus thoracotomy 16.1 ± 4.9 days, $P=0.01$). The two groups did not differ in pathologic stage, histologic results, blood loss, ICU stay, amount or duration of chest drainage, numbers or distributions of dissected LNs, or complication rate. Median overall survival (OS) was 3.2 years for both groups ($P=0.58$), with a median follow-up: 34 months for both groups. They concluded that VATS sleeve lobectomy is technically feasible and safe compared with thoracotomy but deserves further investigation in a large series. Although some cases [22–25] of angioplasty (including double-sleeve resection) and chest wall resection have been reported, these procedures are uncommon.

Although complex resections for advanced lung cancer are technically well described, follow-up data are insufficient and oncological efficacy is unclear. These are complex, technically demanding procedures with a steep learning curve, and should only be done by skilled surgeons with experience in both VATS and open surgeries.

New VATS lobectomy approaches

Initially, VATS lobectomies used multiple ports. In 2004, Rocco et al. [26] reported successfully using a single-port VATS technique for diagnosis and treatment. In 2011, Gonzales-Rivas et al. [27–29] adapted the single-port VATS to VATS lobectomies. Since then, he has demonstrated the use of single-port VATS for more complex surgeries, such as bronchoplasty, double-sleeve resection, and pneumonectomy. Dai et al. [30] showed the results of a propensity-matched analysis between single-port and two-port VATS ($n=63$ for both, conducted from January 2013 to June 2015). The single-port VATS group had significantly less blood loss, less pain (visual analogue scale on POD 1 and POD 3), and higher satisfaction score than did the two-port VATS group, with lower morbidity (single port: 3.2%, two-port: 9.5%; $P=0.273$), respectively. No deaths occurred in either groups during the follow-up period. They concluded that a single-port VATS lobectomy is safe and feasible for treating NSCLC, with lower blood loss and postoperative pain, and higher patient satisfaction, than two-port VATS.

In contrast, Borro et al. [31] reported the results of comparative study of survival following VATS lobectomy for lung cancer by single-port ($n=140$) vs. multi-port ($n=146$) approaches. They analyzed age, sex, comorbidities, current smoker, respiratory function, surgical approach, TNM and pathological stage, histologic type, neoadjuvant or co-adjuvant chemotherapy, relapse and metastasis time, with the main aim of evaluating OS and disease-free survival, especially with regard to 2–3-versus 1-port approach. Global survival rates were 1-year: 88.1%; 4-year: 67.6%. In this retrospective study, survival was significantly lower for patients after single-port VATS than after multiple-port VATS (5-year OS for stage I disease—multiple-port: 80.6%, single-port: 43.1%, $P=0.036$; 3-year OS for T2 disease—multiple-port: 75.0%, single-port: 47.0%, $P=0.029$). In multivariate analysis, single-port surgery was associated with a higher risk of death (HR = 1.78). They concluded that the single-port technique might be challenge for lung malignancies, and recommended RCTs to characterize the role this technique has in lung cancer surgery.

In traditional thoracoscopic surgery, instruments and thoracoscope enter the thoracic cavity through 2–4 operating ports on the lateral chest wall, often leading to chronic postoperative pain and numbness. Even single-port VATS could also cause similar problems.

Liu et al. [32] reported a subxiphoid uniportal VATS left upper lobectomy in 2014. This approach involves making a single incision in the subxiphoid area and creating a tunnel into the thorax. The technique does not involve intercostal incisions, thereby avoiding potential injury to the intercostal nerves and subsequent intercostal neuralgia. Song et al. [33] reported the results of 105 subxiphoid uniportal VATS

lobectomies since August 2014 (10.5% complication rate, with significantly lower average pain scores [$P < 0.001$] at 8 h, post-operative days 1, 2, and 3 and day before discharge than in the control group [standard intercostal uniportal VATS]).

In the International Society of Minimally Invasive Cardiothoracic Surgery 2007 consensus statement by the American College of Chest Physicians' 2007 evidence-based clinical practice guidelines [34], and by the National Comprehensive Cancer Network 2010 guidelines [35], VATS lobectomy was recommended as an acceptable procedure for the treatment of clinical stage I NSCLC. Recently, well-designed large-scale RCTs that compared VATS and open lobectomies have been reported. However, as minimally invasive oncological procedures become more widely used, their feasibility, indications and outcomes will warrant ongoing study.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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