



Thoracoscopic lymphadenectomy via multiportal approach: a narrative review

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Objective: This review article outlines the results and the actual technique of lymphadenectomy using video-assisted thoracoscopic surgery (VATS), with a particular focus on the multiportal approach.

Background: Lymphadenectomy plays an important role in the surgical treatment of lung cancer and is considered a cornerstone in assessing the stage and prognosis. Lymph node metastasis is an important factor in determining postoperative strategies and influences the outcome of cancer treatment. Nevertheless, there is no unanimous agreement on the role and technique of lymphadenectomy. Even the major societies of thoracic surgery and oncology have proposed different strategies, advice, and guidelines on this issue. The use of VATS for the treatment of lung cancer is increasing worldwide. Since the introduction of VATS, several studies have demonstrated that this minimally invasive approach is feasible, safe, oncologically efficient, and has several advantages over conventional open thoracotomy surgery, particularly for early-stage lung cancer. However, there is insufficient evidence for lymphadenectomy using a minimally invasive approach, which is often reported to be inferior to open thoracic surgery.

Methods: We reviewed a PubMed search for the latest relevant literature on lymphadenectomy for non-small cell lung cancer.

Conclusions: The goal of oncologic surgery is to ensure the longest possible survival rate. All these techniques have been extensively studied for long-term oncologic outcomes, including overall survival, disease-free survival, and recurrence rates. Future discussions of the “perfect lymphadenectomy” should focus more on other issues that have been discussed, such as the number of lymph nodes to be harvested, the most appropriate sites for analysis depending on the type of surgery and the location of the disease, and less on the comparison of the efficiency of different surgical approaches.

Keywords: Lung cancer; lymphadenectomy; video-assisted thoracoscopic surgery (VATS); multiportal approach

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Introduction

“Radical lobectomy,” proposed by Cahan in 1960, emphasizes the importance of systematic dissection of the regional lymph nodes and is a procedure that is distinct

from simple lobectomy (1). The regional lymph nodes refer to the interlobar, hilar, and mediastinal lymph nodes to which cancer cells could spread from the primary tumor; “lymphadenectomy” or “lymph node dissection” refers to

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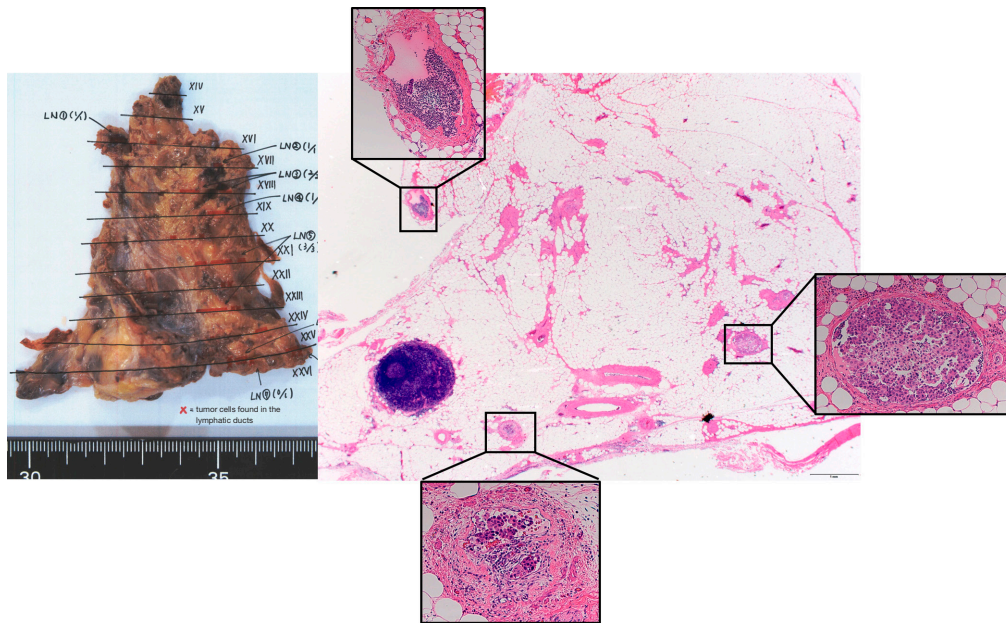


Figure 1 Dissected tissue as *en bloc* of the right upper mediastinum. Histopathologically, tumor clusters floating in the lymphatic duct are observed. LN, lymph node.

the procedure in which these lymph nodes are removed *en bloc* (2). Therefore, lymphadenectomy is an important therapeutic component in lung cancer surgery. However, there is still no consensus on the role and technique of lymphadenectomy. Even major societies of thoracic surgery and oncology have proposed different strategies, advice, and guidelines on this issue (2,3).

Since the 1990s, video-assisted thoracoscopic surgery (VATS) lobectomy has become increasingly prevalent and is now a standard surgical approach instead of open thoracotomy (4). VATS has a better cosmetic appearance and faster postoperative recovery than open thoracotomy surgery (5). However, there is insufficient evidence regarding the oncological outcomes, especially for lymphadenectomy, for which it is often reported to be inferior to open thoracic surgery (6-8).

This review article outlines the results and the actual technique of lymphadenectomy by VATS, with a particular focus on the multiportal approach. We present the following article in accordance with the Narrative Review reporting checklist (available at <https://asj.amegroups.com/article/view/10.21037/asj-21-62/rc>).

Methods

The latest relevant literature was searched in PubMed using

the keywords: “lymphadenectomy,” “lung cancer,” and “VATS.” The relevant studies in English were identified, screened, and reviewed by all the authors. Unpublished materials, congress abstracts, and proceedings were not selected. The authors are responsible for all aspects of the work to ensure that any questions relating to the accuracy or completeness of any part of the work are properly investigated and resolved.

Definition of lymphadenectomy

Lymphadenectomy is a procedure in which the lymph nodes to which cancer may have metastasized in an anatomically delineated area are completely removed *en bloc* with the surrounding lymphatic ducts and adipose tissue (2). Meanwhile, piecemeal resection of individual lymph nodes is defined as lymph node sampling, which can be distinguished from lymphadenectomy (2). There are some reports of a technique called “video-assisted mediastinoscopic lymphadenectomy (VAMLA)” (9); however, this technique is lymph node sampling using mediastinoscope, and the term “lymphadenectomy” should not be used. In cases where lymph node metastasis occurs, tumor cells are often found in the lymphatic ducts of the adipose tissue surrounding the lymph nodes (Figure 1). Lymphadenectomy is a more appropriate procedure for

Table 1 Differences in the extent of mediastinal lymphadenectomy between systematic and selective lymphadenectomy in each guideline

Guidelines	Resected lobe					
	Right upper lobe	Right middle lobe	Right lower lobe	Left upper lobe		Left lower lobe
				Upper division	Lingular division	
Systematic						
ESTS guideline		#2R, 4R, 7, 8, 9		#4L, 5, 6, 7, 8, 9		
Japanese ND2a-2	#2R, 4R, 7		#2R, 4R, 7, 8, 9	#4L, 5, 6, 7		#4L, 5, 6, 7, 8, 9
Selective						
ESTS guideline	#2R, 4R, 7		#4R, 7, 8, 9	#5, 6, 7		#7, 8, 9
Japanese ND2a-1	#2R, 4R	Not applicable*	#7, 8, 9	#4L, 5, 6	Not applicable*	#7, 8, 9

*, only for ND2a-2. ESTS, the European Society of Thoracic Surgeons.

lung cancer surgery compared to lymph node sampling.

Types of lymphadenectomy

Lymphadenectomy is classified according to the extent of dissection: (I) up to the hilum, (II) up to the ipsilateral mediastinum, and (III) up to the contralateral mediastinum and neck. Lymphadenectomy up to the ipsilateral mediastinum is the most common.

Ipsilateral mediastinal lymphadenectomy is also classified as follows: (I) systematic lymphadenectomy, which is a broad dissection from the superior mediastinum to the inferior mediastinum, and (II) selective lymphadenectomy (lobe-specific lymphadenectomy). While the European Society of Thoracic Surgeons (ESTS) guidelines for systematic lymphadenectomy describe the ranges uniformly for the right and left sides, the Japanese guidelines omit dissection of #8 and #9 for tumors in the upper and middle lobes. In selective lymphadenectomy, only the superior mediastinal nodes (#2R, 4R on the right side; #4L, 5, and 6 on the left side) for upper lobe lung cancer and only the inferior mediastinal nodes (#7, 8, 9) for lower lobe lung cancer are dissected in Japan, which is more limited than the ESTS guidelines (2,10) (Table 1).

According to the International Association for the Study of Lung Cancer (IASLC) staging manual in thoracic oncology, the assessment of six nodes/nodal stations is recommended for proper nodal staging. Moreover, these should include three nodes/stations from the mediastinum, one of which should be subcarinal node #7 and three nodes/stations from the hilum or other N1 locations (11). Therefore, systematic lymphadenectomy is considered the international standard. However, in recent North American

clinical practice, it has been reported that in 83% of cases in which systematic lymphadenectomy was performed, the quality was equivalent to lymph node sampling. With the improvement of radiological technology, the trend is shifting from the era of uniform systematic lymphadenectomy to the era of selective lymphadenectomy according to each case. In Japan, a randomized phase III trial of lobe-specific *vs.* systematic lymphadenectomy for clinical stage I–II non-small cell lung cancer [Japan Clinical Oncology Group (JCOG) 1413] is currently ongoing (12). It will be interesting to determine if the scientific validity of selective lymph node dissection can be proven.

Purpose of lymphadenectomy

Lymphadenectomy plays an important role in the surgical treatment of lung cancer and is a cornerstone in assessing the stage and prognosis of this disease. The expected purpose of this procedure is as follows: (I) an accurate evaluation of the presence or absence of lymph node metastasis, which is beneficial for predicting the prognosis and for the indication of postoperative adjuvant therapy (staging effect), and (II) an improved prognosis by complete resection of metastatic lymph nodes (prognosis improvement effect) (2).

Staging effect

In the American College of Surgeons Oncology Group (ACOSOG) Z0030 trial (13), occult lymph node metastases (unsuspected pN2), which were not noted preoperatively or intraoperatively were identified in 4% of patients in the lymphadenectomy group when compared with the lymph node sampling group. Conversely, there was no increase

in the complications, operative mortality, blood loss, or the length of hospital stay in the lymphadenectomy group, despite a 15-minute increase in the operative time and a 121 mL increase in the total drainage volume, indicating that lymphadenectomy can be performed safely and contributes to a more accurate staging compared with the lymph node sampling group (14).

Prognosis improvement effect

Theoretically, an improved prognosis can be expected when there are lymph node metastases, and the metastases are confined to the dissected lymph nodes with little possibility of systemic dissemination (e.g., pN1, single pN2). Moreover, in the absence of lymph node metastasis (pN0), dissection is the same as resection of a cancer-free area, and there is no prognostic effect of dissection.

In the ACOSOG Z0030 trial, the median survival time in the lymph node sampling group was 8.1 years, compared with 8.5 years in the lymphadenectomy group (the median follow-up time was 6.5 years) (13). The lack of confirmatory evidence for a favorable effect of lymphadenectomy may be due to the following: (I) there was extensive systemic sampling in this study, (II) the majority of lung cancer surgery cases were pN0 cases, and (III) adjuvant chemotherapy was not standardized at the time of conducting this trial. However, scientific validation did not show that lymphadenectomy improved the prognosis.

Thus, although lymphadenectomy is considered the international standard, the established scientific evidence is in terms of staging efficacy, and its therapeutic significance has not been clarified.

Lymphadenectomy by minimally invasive surgery

The appropriate surgical approach for lymphadenectomy in lung cancer remains controversial. Several reports have described that the minimally invasive approach has a lower quality of lymphadenectomy than open thoracotomy (6-8). Meanwhile, no quality indicators of lymphadenectomy have been defined to date; there is still an open debate regarding the quality of nodal evaluation. The nodal upstaging rate and the total number of dissected lymph nodes may be quality indicators of lymphadenectomy (6-8,15,16). However, the quality of lymphadenectomy should be assessed using long-term postoperative outcomes. The evaluation of postoperative recurrence patterns, especially at the site where lymphadenectomy was

performed, is of paramount importance in assessing the quality of lymphadenectomy.

Lymphadenectomy via multiport thoracoscopic approach

Comparison with open thoracotomy

Several reports have indicated a higher rate of nodal upstaging after open thoracotomy than after multiportal VATS, suggesting that open thoracotomy could offer a more radical lymphadenectomy than multiportal VATS (6-8). However, we compared multiportal VATS and open thoracotomy, focusing on lymphadenectomy (17). The findings of this study are as follows: First, the effects of the surgical approach did not change the postoperative pathological nodal upstaging rate. Second, the prognoses were not significantly different between multiportal VATS and open thoracotomy. Finally, the recurrence patterns, including recurrences at the site where lymphadenectomy was performed, and post-recurrence overall survival rates between multiportal VATS and open thoracotomy were equal regardless of the pathological N status. Therefore, we confirmed that the quality of lymphadenectomy between multiportal VATS and open thoracotomy is equivalent when a highly experienced surgeon performs it, and several reports support this result (18-20).

Comparison with other minimally invasive approaches

A novel, minimally invasive approach, observed in robotic and uniportal surgeries, can assess an equal number of lymph nodes compared with open thoracotomy (21,22). In addition, it has been reported that these approaches can remove more lymph nodes than multiportal VATS (21). Although both approaches are promising, there are few reports on the long-term oncological outcome, and there may be a bias in the surgical techniques among institutions; therefore, future studies are essential.

Summary

Regardless of the surgical approach, lymphadenectomy should be performed appropriately with the same quality and procedure. If adequate lymphadenectomy is performed, the rate of nodal upstaging and the number of dissected lymph nodes are expected to be the same. Accurate lymphadenectomy may simultaneously achieve accurate

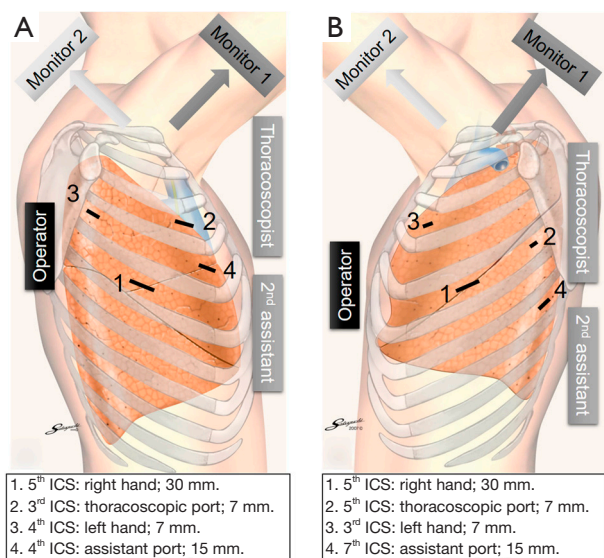


Figure 2 Port placement and confronting upside-down monitor setting (A) right side, (B) left side. Two monitors are set up on the cranial side of the patient, and the monitor for the assistants is placed upside down (Monitor 2). The surgeon stands on the right side of the patient for both right- and left-sided cases and looks at Monitor 1. The thoracoscopist and secondary assistants stand on the left side of the patient and look at Monitor 2. If the thoracoscopist keeps the thoracoscope in a horizontal position, mirror images and disorientation can be avoided. ICS, intercostal space.

lymph node staging and improve survival.

Surgical techniques

In this section, we have described the procedure of lymphadenectomy via multiportal VATS followed at our institute (23,24).

Principles of lymphadenectomy

The procedure of lymphadenectomy requires the understanding of certain important principles, which are as follows, (I) ensuring a good surgical field and not performing surgery with poor vision, (II) achievement of anatomical landmarks, (III) avoiding direct grasping of lymph nodes, and (IV) ligation or clipping of the dissection edge.

Port replacement

At our institution, thoracoscopic lobectomy with systematic

lymphadenectomy is performed via multiport (four ports: 7, 7, 15, and 30 mm) while routinely confronting an upside-down monitor setting (Figure 2). Two monitors are set up on the cranial side of the patient, and the monitor for the assistants is placed upside down. The surgeon stands on the right side of the patient, and the thoracoscopic assistant and secondary assistant stand on the left side of the patient in all cases. During the operation, the secondary assistant provides the surgeon with a better view of the surgical site by placing two instruments using a 15 mm incision. The thoracoscopic assistant places a 7 mm port and can visualize all the structures in the chest cavity with a 5 mm 30° rigid thoracoscope. For the surgeon, a 30 mm utility incision is made, and a 7 mm port is inserted for the surgeon’s left hand. In this setting, the surgeon can freely use both hands and perform sharp dissection using scissors.

Right mediastinal lymphadenectomy via four-port VATS

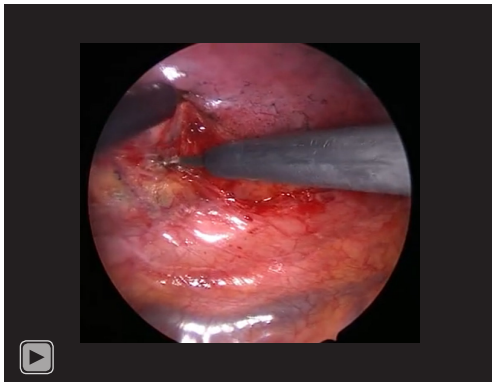
In the case of right upper lobectomy, a 30 mm utility incision for the surgeon’s right hand is made on the posterior axillary line in the 5th-intercostal space (ICS). A 15 mm incision for the secondary assistant is made on the anterior axillary line in the 4th-ICS. Two 7 mm ports are placed: one in the 3rd-ICS for the thoracoscope and one in the 3rd-ICS for the surgeon’s left hand (Figure 2A). In the case of right middle or lower lobectomy, each port uses one ICS below.

Subcarinal zone (#7)

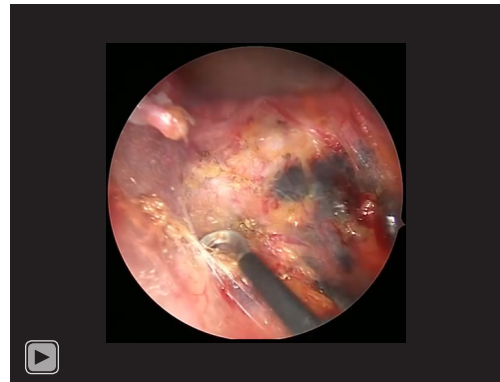
The space between the upper and lower pulmonary veins is lifted. The right vagus nerve is identified. Subsequently, the #7 lymph nodes are sequentially dissected from the pericardium and esophagus, and the left main bronchus is identified. The #7 lymph nodes are dissected from the left and right main bronchi. Finally, the #7 lymph nodes are clipped and divided from the top of the carina (Video 1).

Upper zone (#2R, #4R)

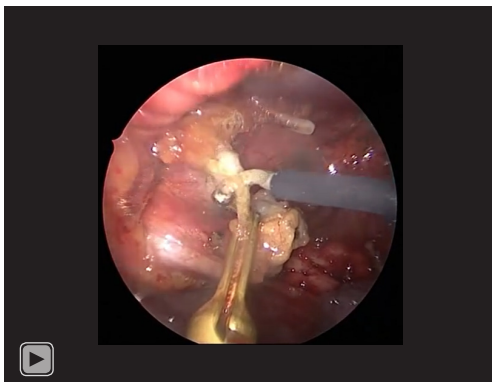
The pleura is incised at the anterior border of the vagus nerve to expose the entire length, and the distal side of the right brachiocephalic artery is identified. The anterior margin is dissected from the right lateral margin of the trachea. Subsequently, the pleura on the superior vena cava is incised, dorsal to the phrenic nerve. The pericardium at the cranial of the azygos vein is exposed, dissect upward, and the proximal side of the right brachiocephalic artery is identified. The thymus is divided and the tissue along



Video 1 Right subcarinal (#7) lymphadenectomy.



Video 3 Left subcarinal (#7) lymphadenectomy.



Video 2 Right upper and lower paratracheal (#2R, 4R) lymphadenectomy.

the superior border of the right brachiocephalic artery is dissected, and the upper end of the dissection is determined. The lower end of the dissection is the main trunk of the pulmonary artery. Dissection is continued upward while clipping the left border of the trachea (*Video 2*).

Left mediastinal lymphadenectomy via four-port VATS

For left upper lobectomy, a 30 mm utility incision for the surgeon's right hand is made in the 5th-ICS. A 15 mm incision for the secondary assistant is made in the 7th-ICS. Two 7 mm ports are placed: one in the 5th-ICS for the thoracoscope and one in the 3rd-ICS for the surgeon's left hand (*Figure 2B*). For left lower lobectomy, each port will be placed one ICS below as on the right side.

Subcarinal zone (#7)

After the conventional hilar lymphadenectomy, we

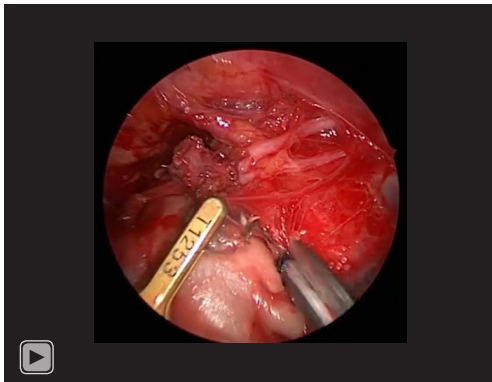
lift the left main bronchus and stump of the left lower pulmonary vein using a thread and specially modified muscle retractor that may be inserted through a 15 mm incision. Consequently, the entire subcarinal area may be viewed posteriorly. Subsequently, the #7 lymph nodes are sequentially dissected from the esophagus and pericardium. The right vagus nerve may be identified, followed by the right main bronchus. The #7 lymph nodes are dissected from the right and left main bronchi. Finally, the #7 lymph nodes are clipped and divided from the top of the carina (*Video 3*).

Upper zone (#4L) and AP zone (#5, #6)

The secondary assistant retracts the lung anteriorly. The mediastinal pleura of the dorsal side is incised just in front of the aorta, and the bronchial arteries, directly branching from the aorta, are divided with a surgical energy device. The left main bronchus is dissected cranially using scissors. The vagus nerve is exposed, and the left recurrent laryngeal nerve is dissected distally. Dissection of the posterior area of the nodal packet, including the #4L lymph nodes and surrounding structures, such as the left main bronchus, aortic arch, vagus nerve, and left recurrent laryngeal nerve, is completed before approaching the hilar structures. The #4L lymphadenectomy is straightforward because the left recurrent laryngeal nerve has already been dissected, and only the anterior area of the #4L remains to be dissected (*Video 4*).

Major complications related to lymphadenectomy

We reviewed 1,398 lung cancer patients who underwent radical lobectomy or more extensive pulmonary resection



Video 4 Left lower paratracheal (#4L), subaortic (#5), and para-aortic (#6) lymphadenectomy.

with mediastinal lymphadenectomy between 2010 and 2020 at our institute. Major postoperative complications related to lymphadenectomy were as follows: chylothorax in five, transient recurrent laryngeal nerve paralysis in 11, and bronchopleural fistula in four patients; morbidity rate of 1.4%. The results were considered to be acceptable.

Conclusions

The goal of oncologic surgery is to ensure the longest possible survival rate. All these techniques have been extensively studied in terms of long-term oncologic outcomes, including overall survival, disease-free survival, and recurrence rates. Future discussions of the “perfect lymphadenectomy” are required to focus more on other issues that have been discussed, such as the number of lymph nodes to be harvested, the most appropriate sites for analysis depending on the type of surgery and the location of the disease, and less on the comparison of the efficiency of different surgical approaches.

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