Zhaoming and Zhenfa
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REVIEW

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Lymph node evaluation and surgical procedure selection for non-small cell lung cancer

Gao Zhaoming[1,2,3] and Zhang Zhenfa[2,3*]

Abstract

Lymph node metastasis is a common mode of metastasis in non-small cell lung cancer (NSCLC). Correct lymph node staging is crucial to the selection of treatment and the assessment of the prognosis of patients, and the selection of appropriate lymph node resection can prolong the survival of patients and reduce surgical trauma.In this review, the preoperative lymph node evaluation methods and the common intraoperative lymph node resection methods of NSCLC are reviewed, and the advantages and disadvantages of each method are compared. The purpose of this review is to summarize the latest research progress in the evaluation and resection of NSCLC lymph nodes, so as to select appropriate evaluation and resection methods in clinical work.

Keywords Non-small cell lung cancer, Lymph node metastasis, Lymphadenectomy, Lymph node assessment

According to the global cancer statistics in 2020, lung cancer is the leading cause of cancer-related death [1]. Surgical resection is still the main treatment for early stage lung cancer, and lobectomy plus mediastinal lymph node dissection is the standard surgical method for non-small-cell lung cancer (NSCLC) [2]. Lymphatic metastasis is one of the main ways of lung cancer metastasis and an important factor affecting the stage and prognosis of lung cancer. Patients with positive lymph node (LN) metastases have a higher risk of disease recurrence; Thus, LN involvement is one of the most important determinants of prognosis and treatment strategy in patients with resectable NSCLC. Identification of LN involvement and determination of disease degree by LN sampling or dissection plays an important role in accurate lymph node staging.We conducted a comprehensive literature search in the PubMed database, utilizing the keywords "lung cancer" and "lymph node". The retrieved literature was then screened based on title and abstract. Additionally, we reviewed the reference lists of the included studies to identify additional relevant articles. The initial literature search was performed in March 2023, and upon manuscript revision, it was supplemented with literature published between April 2023 and November 2023.

*Correspondence:
Zhang Zhenfa
67396727@qq.com
[1] Department of Thoracic Surgery, Binzhou People's Hospital, Shandong First Medical University, Binzhou, China
[2] Tianjin Medical University Cancer Institute and Hospital, Tianjin, China
[3] National Clinical Research Center for Cancer, Tianjin Medical University Cancer Institute and Hospital, Tianjin, China

1 Evaluation of mediastinal lymph nodes

Preoperative lymph node evaluation was divided into noninvasive evaluation and invasive evaluation. Noninvasive evaluation included Computed Tomography(CT) scanning, magnetic resonance imaging(MRI) and Positron emission tomography/computed tomography (PET-CT) imaging, while invasive evaluation included mediastinoscopy, bronchoscopy, thoracoscopy and other invasive techniques. Intraoperative lymph node evaluation methods mainly include: mediastinal lymph node sampling and mediastinal lymph node dissection [3].

1.1 Noninvasive evaluation of mediastinal lymph nodes

CT is currently the most commonly used non-invasive means to detect lymph node metastasis of lung cancer. Lymph node short-axis diameter ≥ 10 mm on CT images is usually used as a positive standard, combined with the size, density and other signs of the primary tumor to determine whether lymph node metastasis occurs [4–6], with an accuracy of about 60%. The sensitivity and specificity were 57% and 82%, respectively. Its positive predictive value (PPV) and negative predictive value (NPV) were 62% and 87%, respectively [7]. Electron density derived from dual-energy CT may help diagnose metastatic lymph nodes in NSCLC [8]. On the basis of conventional CT morphological diagnosis, energy spectrum CT imaging technology adds functional analysis, which can be used for quantitative analysis of lymph node metastasis of non-small cell lung cancer, so as to facilitate clinical qualitative evaluation of lymph node metastasis [9]. with the development of radiomics, deep learning and other technologies, models of mining the image information of enlarged lymph node regions further improve the diagnostic accuracy [10–14]. Positron emission tomography (PET) determines the presence of lymph node metastasis by tumor metabolism. Generally, maximum standard uptake value(SUVmax)≥2.5 (or 3) is used as the critical value for determining lymph node metastasis [15, 16]. The combination of multiple parameters is more helpful to improve the diagnosis rate [17–19]. The sensitivity and specificity of PET for diagnosing mediastinal lymph node metastasis are 80% and 88%. Its PPV was 75% and NPV was 91% [5]. It has been reported that the highest accuracy of PET/CT in evaluating lung cancer lymph node metastasis can reach 91.8%, and its accuracy, sensitivity, PPV and NPV are all higher than those of CT or PET [20]. Even patients with NSCLC with PET-CT-defined occult nodal metastasis (ONMs) have a better surgical prognosis than those with significant lymph node metastases [21]. Although PET is highly sensitive to the detection of hilar and mediastinal lymph node metastasis, it can also show obvious concentration in the presence of other high metabolic lesions (such as inflammation, tuberculosis, etc.) and elevated blood sugar, and the detection rate of PET for small lesions is low [22, 23]. A recent study showed that PET-CT had limited staging ability for mediastinal lymph nodes, and recommended histological examination for PET-positive N2 patients to avoid false positive results [24]. Advances in MRI technology have allowed rapid acquisition of high-quality imaging [25]. Diffusion-weighted Imaging (DWI) provides excellent tissue contrast and is superior to PET in mediastinal lymph node assessment, reducing false positive rates [26, 27]. In a meta-analysis, the accuracy of DWI and PET-CT was evaluated. The pooled sensitivity of DWI was 0.95 (95%CI 0.85–0.98), significantly better than PET-CT 0.89 (95%CI 0.85–0.91) [28]. In recent years, positron emission tomography/magnetic resonance imaging (PET/MRI) has been clinically used to diagnose NSCLC. One study has shown that PET/MRI preoperative staging is superior to CT in diagnosing hilar and mediastinal lymph node metastases [29]. To date, however, there have been no large prospective studies comparing the value of DWI and PET in evaluating lymph node metastasis.

1.2 Invasive evaluation of mediastinal lymph nodes

Although the traditional transbronchial needle aspiration (TBNA) technique has been available for many years, only a small number (10–15%) of pulmonologists use it to evaluate mediastinal lymph node staging in patients with resectable stage I -- III lung cancer. The main reason for its underuse is its dependence on lymph node size (> 15–20 mm short axis in CT scans) and operator skill. A meta-analysis reported that the sensitivity of conventional TBNA in clinical N2 disease was 78% [30]. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is currently the main invasive method for lymph node staging of lung cancer, and is considered as the first-line invasive method for lymph node evaluation [31, 32]. EBUS-TBNA can display lymph nodes in 2 groups, 4 groups, 7 groups, 10 groups, 11 groups and even 12 groups, with sensitivity and specificity of 81–89% and 100%, respectively [30]. A retrospective study showed that the overall accuracy and negative predictive value of EBUS-TBNA in determining mediastinal lymph node staging could reach 88.2% and 90.9% [33]. 19-G needles can provide more adequate tissue samples for immunohistochemical examination and gene mutation detection [34]. Real-time cytopathological intervention (RTCI) and rapid on-site evaluation (ROSE) were applied to tissue specimens punctured by EBUS-TBNA to improve diagnostic efficiency [35]. Transesophageal ultrasound-guided fine needle aspiration (EUS-FAN) can show lymph nodes in groups 4 L, 7, 8 and 9, with sensitivity and specificity of 83–89% and 100%, respectively [30]. EUS-FAN supplements other techniques because some LN (stations 8 and 9) cannot be reached by EBUS-TBNA or mediastinoscopy [36, 37]. EBUS-TBNA combined with EUS-FAN can more comprehensively evaluate mediastinal lymph node and improve the sensitivity of mediastinal lymph node staging. Meta-analysis reported that the sensitivity of EBUS-TBNA combined with EUS-FAN for mediastinal lymph node staging was 86–91%, and the specificity was 100% [30, 38]. Cervical mediastinoscopy allows complete dissection of the ipsilateral and contralateral mediastinal lymph nodes. It has been the gold standard for invasive staging in potentially operable lung cancer patients for many years, with 75–78% sensitivity and 100% specificity for mediastinal lymph node staging. Video-assisted mediastinoscopic lymphadenectomy (VAMLA) and transcervical extended mediastinal lymphadenectomy (TEMLA)are new mediastinal lymph node staging methods introduced after 2000. Although the accuracy of mediastinal staging during lymph node dissection is undoubtedly increased compared to lymph node biopsy, these techniques are associated with higher morbidity and mortality, so the European Society of Thoracic Surgeons(ESTS) are not recommended except in clinical trials [36]. Several studies have compared the role of EBUS-TBNA and mediastinoscopy in determining mediastinal lymph node metastasis, suggesting that mediastinoscopy should be added for further diagnosis in patients diagnosed with negative N2 by EBUS [39–41]. However, other studies have reached different conclusions [42]. A randomized clinical trial has shown that confirmatory mediastinoscopy after negative systematic endosonography can be ignored in patients with resectable NSCLC if 8% is selected as a noninferiority margin in unforeseen N2 [43]. Video-assisted thoracoscopic surgery (VATS) can reach nearly every mediastinal node site, but it is more invasive than cervical mediastinoscopy (VATS requires dual lumen intubation) and is limited by pleural adhesions and cannot evaluate contralatoral lymph nodes at the same time. When enlarged PET-positive lymph nodes are at station 5 or 6, these lymph nodes cannot be biopsied by routine mediastinoscopy and E(B)US-FNA. The left VATS are a surgical procedure for obtaining large tissue samples [44, 45].

1.3 Selection of mediastinal lymph node evaluation methods

The selection of lymph node evaluation methods was described in ESTS guidelines of the European Society of Thoracic Surgeons [36]. The criteria are as follows: (1) For patients with no suspicious lymph nodes found on CT or PET, tumor $\leq$ 3 cm, and tumor located outside the lung 1/3, surgery can be performed directly. Otherwise, invasive staging is appropriate for lymph nodes with enlarged or PET positive, centrally located tumors, or N1 disease. (2) For tumors > 3 cm and negative PET-CT results, negative EBUS-TBNA should be confirmed by mediastinoscopy. Video - assisted mediastinoscopy is superior to traditional mediastinoscopy. (3) Routine biopsies should be performed at least five lymph node sites (2R, 2 L, 4R, 4 L, and 7). Biopsies of Stations 10R and 10 L should be performed when subsequent treatment strategies need to be determined. For left-side tumors, biopsies should also be performed at stations 5 and 6 if treatment strategies are changed. Biopsies should be performed at the lower mediastinal lymph node sites (8 and 9) if extra-capsular lymph node lesions are suspected [46].

2 The methods of lymph node dissection

2.1 Surgical methods of lymph node resection

Lymph node dissection is of great significance to determine pathological stage, adjuvant therapy and prognosis assessment. With the application of CT in physical examination, more and more early lung cancers have been found. The lymph node metastasis rate of these early lung cancers is low, and it is difficult to determine whether the patients with lung cancer have mediastinal lymph node metastasis before surgery. Therefore, mediastinal lymph node dissection of NSCLC has always been controversial, and there are many different intraoperative lymph node management methods. such as systematic lymph nodes dissection (SLND), lymph nodes sampling (LNS), lobe-specific lymph nodes dissection (L-SLND), etc.They have their own applicable indications and scope of dissection, and there is no consensus on how to choose the treatment method during surgery [47]. Some scholars have suggested that sentinel lymph node (SLN) detection has greater intraoperative utility in non-mediastinal lymph node dissection, especially in sublobectomy [48]. Given that the sentinel node is the theoretical first site of nodal disease, intraoperative evaluation of the sentinel node can quickly confirm the N0 status and thus identify sublobectomy candidates [49], and has shown good clinical results [50]. However, due to the heterogeneity of the method and the lack of multi-center prospective data, it is difficult to be widely used in clinical practice [48].

Systematic lymph node dissection (SLND): It refers to the formal excision of all tissues with lymph nodes in the mediastinum within the defined anatomical boundaries [3]. In addition to hilum and intrapulmonary lymph nodes, 2R, 4R, 7, 8, 9 groups should be excised in the right lung and 4 L, 5, 6, 7, 8, 9 groups should be excised in the left lung [51, 52]. An article by Darling details the extent of a systematic lymph node dissection: On the right side, all tissue between the phrenic nerve, vagus nerve, right innominate artery and right main bronchus is removed baring the superior vena cava(SVC), trachea, anterolateral aspect of the ascending aorta, right tracheobronchial angle, azygous vein (if not resected) and right main bronchus. Additionally, all the subcarinal tissue is removed baring the right and left main bronchi, and posterior pericardium. Also, the stations 8 and 9 nodes are removed by clearing all the lymph node bearing tissue around the inferior pulmonary vein and esophagus. On the left side, the inferior mediastinal dissection is the same. For the upper mediastinum, all lymph node bearing tissue between the phrenic and vagus nerve is removed down to the left main PA including the subaortic space. The distal left main bronchus is also dissected free of lymph node bearing tissue. Some surgeons also recommend dividing the ligamentum arteriosum to remove all the lymph node tissue on the left main bronchus up to and including the left tracheobronchial angle [3]. SLND has long been considered as a standard treatment for resectable lung cancer, which can improve staging accuracy, achieve better local control and optimize postoperative treatment by identifying latent N2 disease, thus improving postoperative survival [53]. However, SLND increases the incidence of surgical trauma and postoperative complications [54]. A recent study in 2023 showed that with the increase of tumor volume, there was a significant difference in lymph node metastasis in the pure solid nodules group: ≤1 cm, 2.67%; 1.0 to 1.5 cm, 12.46%; 1.5 to 2.0 cm, 21.31% ($P<0.001$). Therefore, the authors recommend that a thorough lymph node dissection is required even in small-volume NSCLC surgery, especially for pure solid tumors ≥ 1 cm [55]. Katsumata,et al. [56]compared the situation of elderly patients with SLND and those without SLND, and found no significant differences in overall survival(OS), cancer-specific survival (CSS), chest drain duration, length of postoperative stay, perioperative complications and other aspects.

Lobe-specific lymph node dissection (L-SLND) : Lymph nodes in specific areas are selectively dissected mainly according to different locations of lesions. The theory is mainly based on the fact that lung cancer tumor cells often transfer to specific lymphatic drainage areas through lymphatic channels. In 2006, L-SLND strategies for early NSCLC were presented in the European Society of Thoracic Surgery (ESTS). The recommended strategies were 2R, 4R, and 7th stops of right upper lobe (RUL) and right middle lobe (RML) tumor sweeps. Right lower lobe (RLL) tumor dissection 4R, 7, 8, 9 stations; Left upper lobe (LUL) tumor dissection 5, 6, 7 stations; Left lower lobe (LLL) tumor dissection 7, 8, 9 stations. However, different strategies of lymph node resection were reported. The basic strategy is RUL cleaning 2R, 4R stations, or including 7 stations. RLL clean stations 7, 8 and 9; LUL sweep 5, 6 stations, or include 4 L, 7 stations; LLL dissection at stations 7, 8 and 9. There are few studies on RML lymph node dissection [53, 57–62]. A recent prospective study validated specific mediastinal LN metastasis patterns in cT1N0 aggressive NSCLC and proposed six new selective lymph node dissection strategies [63]. Current studies have shown that the risk of postoperative complications of L-SLND is significantly lower than that of SLND, and does not affect the long-term survival outcome of patients with early NSCLC. It can be used as an alternative to SLND in the treatment of patients with early NSCLC [64]. However, there are still some controversies about the anatomic range and therapeutic effect of L-SLND, and more similar studies are needed to verify and improve it. It is important to note that although 4 L and 3 A lymph nodes are less frequently mentioned inL-SLND, we should not overlook their role in patient prognosis [65, 66].

Lymph nodes sampling (LNS):Surgical sampling involves the removal of one or more lymph nodes based on preoperative or intraoperative findings that are considered representative. Systematic sampling is the selection of lymph nodes by the surgeon based on predetermined criteria. For right-side lung cancer, systematic sampling would include sites 2R, 4R, 7, 10R, 8R, and 9R. For left-side lung cancer, this would include sites 5, 6, 7, 10 L, 8 L, and 9 L. LNS is suitable for early stage lung cancer, which can reduce surgical trauma and reduce the occurrence of postoperative complications. Takizawa et al. [67]reported that the 5-year OS after systemic lymph node dissection and lymph node sampling in clinical stage I NSCLC was 78.0% and 76.2%, respectively, and there was no statistical difference between them. Stiles et al. [68]believed that wedge resection plus systematic lymph node sampling in stage Ia NSCLC could reduce the local recurrence rate and improve the survival rate, but would not increase the incidence of surgical complications.

2.2 Number of lymph nodes dissected

The minimum number of lymph nodes removed is still controversial. It has been suggested that postoperative patient survival is associated with the number of lymph nodes dissected, and that improved Disease Free Survivall(DFS)and OS are associated with a larger number of lymph nodes sampled. Systematic node sampling and systematic lymph node dissection were associated with improved survival compared with random node sampling. The number of lymph nodes dissected determines more accurate lymph node staging and facilitates subsequent treatment [69, 70]. Zhou et al. [71]suggested that lymph node sampling with more than 3 stations could significantly improve the overall survival rate in early NSCLC. Raymond et al. [72] analyzed that patients with 18 to 21 lymph nodes examined had the lowest risk of death. Matthew et al. [73] compared the overall survival between groups by dividing pN into 8 groups and found that examining at least 10 lymph nodes was associated with the greatest increase in pN0 survival. This demonstrates the value of more thorough removal of N1 nodes, and it is proposed therefore examination of at least 10 nodes and sampling from a minimum of 3 mediastinal stations should be required. The Cancer Committee of the American College of Surgeons (ACS) has issued a quality measure recommending that at least 10 regional lymph node samples be taken in patients with early NSCLC, regardless of the extent of excision [74]. However, a retrospective study of 102,225 patients with stage I/II NSCLC who underwent surgical treatment in the NCDB database found that survival after lobectomy was positively correlated with 4 LN samples (3 for wedge resection), but in most cases the ideal number of samples may be 5 LN [75]. Results of the SCAT-SLCG trial [76] showed that the number of lymph nodes removed was associated with better prognosis. Extensive lymph node resection may be beneficial for patients, but high numbers may not be achieved due to anatomical differences between individuals [77]. A Study have compared the number of positive lymph nodes (NPLN), the number of negative lymph nodes (NNLN), the number of dissected lymph nodes (NDLN), the lymph node ratio (LNR), the chain of lymph nodes, the log odds of positive lymph nodes (LODDS) and the number of lymph node sites involved in region-based classification.Only LODDS was found to be superior in pN0 heterogeneity elimination, so they considered LODDS might be superior before establishing a criterion for the minimum number of lymph nodes removed [78]. JIN et al. [79]also confirmed that LODDs had the best prognostic performance in predicting LCSS and OS in IIIA-N2 stage diseases. WANG et al. [80] confirmed that compared with AJCC N stage descriptors, LODDS showed better predictive power for NSCLC patients undergoing surgery after receiving neoadjuvant therapy. Recent studies have also confirmed that LNR is associated with postoperative survival [81, 82].

2.3 Comparison of clinical value of different lymph node dissection methods

Comparison of lymph node dissection (LND) and lymph node sampling (LNS). Compared with LNS, LND can obtain more lymph nodes, which is conducive to the postoperative pathological stage, the formulation of postoperative adjuvant therapy, the improvement of local control rate, and the improvement of lung cancer survival rate. However, LND prolongs the operation time and hospital stay, and increases the perioperative complications. A 2017 review of five randomized controlled studies found that LND, compared with LNS, improved overall survival, but also increased complications such as chylothorax, bleeding, and nerve injury [83]. The Z0030 trial [54] conducted by the American College of Surgical Oncologists Group (ACOSOG) showed that systematic lymph node dissection increased the average operative time by only 14 min compared with systematic lymph node sampling. The average postoperative drainage volume increased by 200 ml, and the length of hospitalization increased by 1 day. A 2019 retrospective study showed that mediastinal lymph node dissection yielded more nodes (12.2VS8.5, $P<0.001$) and node stations (6.3VS5.2, $P<0.001$) than mediastinal lymph node sampling, and that 12.3% of patients had an nodal upstaging of N2 after lymph node dissection. However, only 2.3% of patients with elevated N2 stage after lymph node sampling, suggesting that mediastinal lymph node dissection can better stage postoperative patients than sampling. However, at the same time, lymph node dissection has a longer operation time, more drainage volume and longer hospital stay, but the study did not mention the influence of lymph node dissection and lymph node sampling on DFS and OS [84].

There is controversy about whether LND can improve the survival of early-stage non-small cell lung cancer. Izbicki et al. found no difference in OS between mediastinal lymph node dissection and mediastinal lymph node sampling, but the disease-free recurrence rate was indeed superior to LND. In subgroup analysis, there was no difference between patients with no lymph node involvement or extensive N2 involvement. MLND can prolong OS and relapse-free survival(RFS)in patients with regional lymph node involvement [2]. But in a large prospective randomized trial that included 532 clinical stage I-IIIA patients (471 available for final analysis), the LND anatomical group (49 months) showed an improvement in 5-year overall survival compared to the LNS group (37 months). In addition, systemic and local recurrences were reduced in the LND group [85]. In the ECOG 3590 trial, although multistage N2 was identified in 30% of LND patients compared to 12% of patients with MLNS ($p=0.001$), However, the LND group had a higher survival rate (66.4 months vs. 24.5 months $p<0.001$), although the survival benefit was limited to RUL tumors [86]. Based on these studies, LND appears to offer a survival advantage to patients with advanced disease or who do not have any preoperative evaluation of mediastinal lymph nodes. However, the value of LND in patients with early stage disease is less clear [3]. The American Society of Surgical Oncology (ACOSOG) Z0030 trial answered the question of whether adding formal lymph node dissection to systematic sampling improves survival in early-stage non-small cell lung cancer. Eligible patients had T1 or T2 tumors and underwent rigorous systematic mediastinal lymph node sampling before randomization. Patients were then randomly assigned to formal lymph node dissection or no further lymph node evaluation. The frequency of occult N2 was 4% in the lymph node dissection group, but overall survival was not statistically significant between the systematic sampling and systematic dissection groups. It should be emphasized that all patients underwent systematic mediastinal lymph node sampling. In addition, randomized anterior hilar lymph nodes were negative in all patients. Finally, only patients

Table 1 Comparison of lymph node dissection and lymph node sampling

First author	Zhao [84]	Dong [87]	Meredith A. Ray [89]	Shen-Tu [88]
year	2019	2015	2020	2017
Patient group	558(279LND, 279LNS)	711(317LND, 394LNS)	1942(358LND, 120LNS., 1464 neither)	317(161LND, 156LNS)
Participants	cl-IIIa	cl	T1 or T2, N0 or non-hilar N1	cl
Surgical method	VATS	RATS was excluded	Open, VATs, RATS.	Not mentioned
Research type	Retrospective cohort	meta-analysis	Retrospective cohort	Retrospective cohort
N2(number)	LND:11.17 LNS:8.50 $P<0.001$	Not mentioned	LND:8 LNS:7 Neither: 3 $P<0.001$	Not mentioned
N2(station)	LND:6.12 LNS:5.17 $P<0.001$	Not mentioned	LND:5 LNS:4 Neither: 2 $P<0.001$	Not mentioned
Operation time(minutes)	LND:128 LNS:114 $P<0.001$	Not mentioned	LND:109 LNS:159.5 Neither: 141 $P<0.001$	Not mentioned
Blood loss (ml)	LND:100 LNS:100 $P=0.160$	Not mentioned	Not mentioned	Not mentioned
Drainage volume (ml)	LND:920 LNS:720 $P<0.001$	Not mentioned	Not mentioned	Not mentioned
Drainage time (days)	Not mentioned	Not mentioned	LND: 3 LNS: 3 Neither: 4 $P<0.001$	Not mentioned
Length of stay (days)	LND:6 LNS:5 $P<0.001$	Not mentioned	LND:4 LNS:5 Neither:6 $P<0.001$	Not mentioned
Technical complication	LND:9 LNS:0	Not mentioned	LND[a]:182(51%) LNS[a]:50(42%) Neither[a]:708(48%) $P=0.2197$	Not mentioned
Functional complication	LND:17 LNS:14 $P=0.579$	Not mentioned		Not mentioned

Table 1 (continued)

First author	Zhao [84]	Dong [87]	Meredith A. Ray [89]	Shen-Tu [88]
Survival analysis	Not mentioned	There was no significant difference in 1-year survival rate. The 3-year and 5-year survival rates were different ($p = 0.03, p = 0.004$).	Median survival was 59 months in the LND group and 34 months in the LNS group, $p < 0.001$	The median survival time of LND group was 154.67 months, which was better than that of LNS group (124.67 months).
Conclusion	LND should be an integral part of minimally invasive and open surgery for NSCLC, especially in patients with higher clinical N categories and more invasive histology.	LND is necessary for routine staging of early NSCLC. LND does improve long-term survival in patients with early (pathological stage I) NSCLC.	Compared with LNS, lobectomy (pneumonectomy) combined with LND can improve the survival rate of resectable NSCLC.	Compared with LNS, LND is associated with better survival in patients with early NSCLC.

[a] Include all complications

with early stage disease (T1, T2) were eligible. Therefore, the results of ACOSOG Z0030 are not applicable to patients who did not have systematic lymph node sampling prior to resection. Furthermore, the results of ACOSOG Z0030 are not applicable to T3 or T4 tumors, or the presence of suspected or confirmed hilar or N1 disease [3, 52]. A prospective study by J R Izbicki [2] also suggested that the type of lymphadenectomy may not have a significant impact on long-term clinical outcomes in patients without lymph node involvement. However, two studies by Dong [87]and Shen-Tu [88]showed that LND was associated with better survival in patients with early NSCLC compared with LNS. Recent relevant studies are shown in Table 1.

Comparison of lobe-specific lymph node dissection (L-SLND) and systemic lymph node dissection (SLND). A retrospective report of 625 patients with propensity score matching found that 5-year OS was not statistically significant in patients receiving L-SLND (76.0%) compared with patients receiving SLND (71.9%), HR 1.17, $p=0.50$ [61]. In a large retrospective matched study of 5,392 clinical stage I or II patients with non-small cell lung cancer, SLND identified N2 disease outside the L-SLND region in 3.2% of patients. Despite this, the survival rate was not poor in the L-SLND group. Although randomized trials and meta-analyses of SLND versus MLNS have reported survival benefits in favor of MLND, there is no survival advantage for SLND compared to L-SLND [57]. A study by Handa et al. [90] in 2021 showed that SLND may provide better oncology outcomes than lob-specific LND in patients with high metabolism and high SUVmax NSCLC. In this multicenter, propensity score matched study, SLND obtained more metastatic lymph nodes and showed better results in terms of oncology outcomes than L-SLND with radiologically aggressive lung cancer. In addition, due to the characteristics of multiple and skipping lymph nodes in non-small cell lung cancer, studies have reported that L-SLND increases the likelihood of recurrence in patients [91]. However, several retrospective studies [92, 93] have shown detailed patterns of lymph node diffusion in surgically resected NSCLC, and L-SLND is gaining widespread acceptance. In addition, previous retrospective studies [94] have shown that survival and recurrence rates for LND and L-SLND may be the same in early NSCLC. As a result, L-SLND is performed more frequently and has become a more popular surgical option.A 2021 meta-analysis of five retrospective studies and one randomized controlled study compared selective mediastinal lymphadenectomy (SML) to complete mediastinal lymphadenectomy (CML).No statistically significant differences were found in the 1- and 5-year overall survival rates and no significant differences in the 1-, 3-, and 5-year disease-free survival rates between the two groups. There were also no statistically significant differences between the local and distant metastasis. Among the postoperative complications, pneumonia, atelectasis, and prolonged air leak were more common in the CML group ($P<0.05$). So the anthor considered SML was the preferred treatment with less invasiveness for clinical stage I NSCLC [95].

3 The way of lymph node resection

Lymph nodes can be removed by thoracotomy, VATS or Robot-assisted thoracic surgery (RATS). A prospective multicenter study showed that open surgery resulted in more complete lymph node dissection compared with VATS [96]. Another study showed that VATS lobectomies were associated with lower rates of harvesting ≥ 10 LNs, sampling ≥ 5 LN stations, and pathologic nodal upstaging compared with open and RATS lobectomies. Compared with thoracotomy, lobectomy in RATS is associated with a higher sampling rate of ≥ 5 LN stations, but there is no significant difference between open surgery and RATS in the rate of node upgrading or node collection of ≥ 10 nodes [97]. The study by Kneuertz et al. also showed a lower rate of lymph node upstaging with VATS compared to open surgery, but there was no difference between open surgery and RATS [98].Recent studies have shown that the quality of lymph node dissection by RATS is better than that by VATS [99, 100].We also note that studies have come to different conclusions. Reichert et al. found a high rate of lymph node upstaging after VATS in their study of stage I NSCLC [101].

Supplementary Information

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Additional file 1: Supplementary Table. Abbreviation.

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