



The effects of lymph node dissection techniques on the survival of geriatric patients with non-small cell lung cancer

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Abstract

Background: Lymph nodes are the most important prognostic factors in lung cancer. Controversy still continues on lymph nodes prognosis. This study aims to evaluate the effects of lymph node dissection techniques on survival in geriatric patients.

Methods: The study was conducted retrospectively in patients who were operated on for non-small cell lung cancer (NSCLC) between 2007 and 2016. Lobe-specific lymph node dissection (LsLND) was performed in 77 patients, while complete (systematic) lymph node dissection (SLND) was performed in 206 patients.

Results: A total of 283 patients were included in the study, of which 258 were male (91.2%) and 25 were female (8.8%). The median age of the patients was 69 years (IQR: 65-84). The mean survival time of the patients was 46 months, and the 5-year survival rate was 38.9%. The survival rate in pN2 disease was 15.6%, while the survival rate in pN0 disease was 46%. While the 5-year survival rate was 34.4% in patients who underwent lobe-specific lymph node sampling, it was 40.5% in patients who underwent systematic lymph node dissection (p=0.147).

Conclusions: As a result of our study, no difference was found in terms of survival between lobe-specific lymph node dissection or systematic lymph node dissection in the geriatric age group. Especially pN2 disease, histopathological, and resection width were observed among the most important prognostic factors affecting survival. Therefore, we think lobe-specific lymph node sampling may be preferred instead of performing complete-systematic lymph node dissection in advanced ages because of less morbidity.

Keywords: Carcinoma, Non-Small-Cell Lung, Survival Rate, Prognosis, Lymph Nodes.

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INTRODUCTION

Lung cancers remain the leading cause of cancer-related mortality (1,2). In therapy, surgery has been accepted as the main procedure for the early stages. Surgical treatment is particularly avoided in elderly patients with lung cancer. The fragility of vascular structures of the elderly, the loss of elasticity of lung parenchyma, and high comorbidities are the main reasons for surgeons to avoid surgical treatments. However, patients over 75 years old are compared with younger ages, and it is seen that curative lung resection has been performed 22% less than elderly patients(3).

Today, there have been ongoing debates about lymph nodes which are one of the most crucial prognostic factors in lung cancer. It can be seen that there are different views and approaches in the literature related to the issue. There has not been a clear consensus about lymph node dissection, especially in the geriatric age group yet (4-6). While some suggest that it increases the complications and does not have an effect on survival and due to this reason, they offer simple lymph node dissection; some others think that complete lymph node dissection will increase the chance of survival of the patient.

In this study, our aim was to evaluate the effects of lymph node dissection techniques on the survival of geriatric patients.

MATERIALS AND METHODS

This study has been retrospectively conducted with patients who had operations due to non-small cell lung cancer (NSCLC) between 2007 and 2016. Patients with mortality, patients who received neoadjuvant therapy, and patients whose data cannot be reached have been excluded from the study. Two hundred eighty-three patients with NSCLC are evaluated in this study. The geriatric group is defined as over 65 years old in the study. All patients in the study are required a thoracic CT in order to evaluate the preoperative tumor localization. Positron emission tomography and cranial magnetic resonance imaging have been used to evaluate distant metastases. Respiratory function tests and carbon monoxide diffusion capacity (DLCO) have been used so as to evaluate respiratory capacities. As all the patients are geriatric, they have been examined by cardiology pre-operatively.

The lymph node dissections of the patients in the study are evaluated in two groups. While lobe-specific lymph node dissection has been performed in 77 patients (LN1), complete (systematic) lymph node dissection has been performed in 206 patients (LN2). The lymph node dissection techniques have been accepted as defined by Watanabe (7).

This study was approved by the clinical research ethics committee of the Health Sciences University, Yedikule Chest Diseases and Thoracic Surgery Training and Research Hospital (Date: 29.07.2021 number: 2021/141) and written consent was obtained from all patients participating in the study.

Statistical Method:

Statistical analyses were done by using IBM SPSS Windows 22.0. While numeric variables were determined by mean±standard deviation and median (min-max), categorical variables were determined by number and percentage. Kaplan Meier analysis was used to evaluate the survival rate, and log-rank analysis was used to compare factors. In this study, the level of significance was accepted as $p<0.05$.

RESULTS

In the study, 258 male (91.2%) and 25 female (8.8%) patients were included. The median age of the patients was 69 years (IQR: 65-84). While pneumonectomy was performed on 61 patients (21.6%), lobectomy was performed on 222 patients (78.7%). Also, while right resection was performed on 155 patients (54.8%), left resection was performed on 128 patients (45.2%). The mean diameter of the tumors was found to be 4.5 ± 2.3 centimeters. Systematic (complete) lymph node dissection was performed in 206 patients, and lobe-specific lymph node dissection was performed on 77 patients (27.2%). There were 124 (72.1%) patients with pN0, 58 (73.4%) patients with pN1, and 24 patients (75%) with pN2, who underwent systematic lymph node dissection. Forty-eight (27.9%) patients with pN0, 21 (26.6%) patients with pN1, and 8 patients (25%) with pN2 underwent lobe-specific lymph node dissection ($p=0.934$). Demographic, surgical, and histopathologic properties of the patients are shown in Table 1.

Table 1. Demographic and surgical characteristics of the patients

Variables		n	%
Gender	Male	258	91.2
	Female	25	8.8
Age (Median)	Year	69	
Side	Right	155	54.8
	Left	128	45.2
Operation	Lobectomy	222	78.4
	Pneumonectomy	61	21.6
pN Status	pN0	172	60.8
	pN1	79	27.9
	pN2	32	11.3
Histopathology	Adenocarcinoma	112	39.6
	Squamous Cell Carcinoma	158	55.8
	Other	13	4.6
Stage	I	88	31.1
	II	100	35.3
	III	95	33.6
Lymph Node Dissection Technique	LN1	77	27.2
	LN2	206	72.8

LN-1: lobe-specific lymph node dissection, LN-2: systematic lymph node dissection

The average survival time of the patients were 46 months, and the five-year survival rate was found to be 38.9%. While the five-year survival rate was 26.2% in the pneumonectomy patients, it was 42.4% in lobectomy patients ($p=0.005$). The survival rate was 41.6% in right-operated patients; on the other hand, it was determined as 54.6% in left-operated patients. It was determined that there was no statistically significant difference ($p=0.057$). While pN2 patient survival was 15.6%, pN0 patient survival was detected as 46%. The five-year survival rate was 34.4% in the patients for whom lobe-specific lymph node dissection has been done. On the other hand, the survival rate was determined to be 40.5% in patients for

whom systematic lymph node dissection was performed ($p=0.147$). In the analysis of survival performed by excluding pN2 and pneumonectomy patients, the 5-year survival rate in the LN1 group was 40.7%, while the 5-year survival rate in the LN2 group was 47%. There was no statistically significant difference between the groups ($p=0.135$). Prognostic factors that affect the survival rate are shown in Table 2.

Table 2. Prognostic factors affecting survival

Variables		5 Year Survival (%)	Median Month	% 95 CI	p-Value
Gender	Male	39.2	48	39-52	0.873
	Female	36	46	28-67	
Side	Right	41.6	52	45-58	0.057
	Left	54.6	37	22-51	
Operation	Lobectomy	42.4	50	42-57	0.005
	Pneumonectomy	26.2	26	11-40	
Histopathology	Adeno Carcinoma	35.3	41	32-49	0.008
	Squamous Cell Carcinoma	43.4	52	42-61	
	Other (Large Cell and Adenosquamous cell carcinoma)	15.4	12	0-28	
Lymph node	pN0	46	55	45-64	0.002
	pN1-pN2	27.9	37	25-48	
Lymph Node Dissection Technique	LN1	34.4	40	21-58	0.147
	LN2	40.5	47	39-52	

CI: Confidence Interval, LN-1: lobe-specific lymph node dissection, LN-2: systematic lymph node dissection

Based on the multivariate analysis of factors affecting survival, pN1-N2 status and large cell and adenosquamous cell carcinomas were found as poor prognostic factors. Multivariate analyses of prognostic factors affecting survival rate are shown in Table 3.

Table 3. Multivariate analysis of prognostic factors affecting survival

Variables		HR	%95 CI	p-Value
Operation	Pneumonectomy	1.34	0.9-1.9	0.123
Histopathology	Adenocarcinoma			0.004
	Squamous Cell Carcinoma	0.77	0.5-1.0	0.102
	Other (Large Cell and Adenosquamous cell carcinoma)	2.01	1.1-3.6	0.021
Lymph node	pN1-pN2	1.45	1.0-2.0	0.023

CI: Confidence Interval

DISCUSSION

The situation of the lymph node is one of the most important prognostic factors in lung cancers. Today, systematic lymph node dissection is one of the standard procedures in lung resections. European Society of Thoracic Surgeons (ESTS) suggests systematic lymph node dissection for complete resection to all patients(8). ESTS recommend at least three mediastinal lymph node (at least one of them subcarinal), and at least six lymph node must dissect for systematic lymph node dissection. However, in early lung cancers, radical dissection occurs more complications to the patients. Previous studies have shown that lobe-specific lymph node dissections have been foreseen as more practical than systematic lymph node dissections in lung cancers.

Sugi et al. have stated that among the patients for whom systematic lymph node dissection has been performed, the morbidity is higher than the ones for whom sampling has been done, and they also notified that a longer time is required intraoperatively (9). Particularly, they have stated that the operation time has been prolonged in systematic lymph node dissections on the left. There have been many publications from Japan that report that the best way to detect the metastasis rate (N-positive) in cancers is performed systematic lymph node dissection. Especially in peripheral tumors, it is a 10-25% possibility to see lymph node metastasis, and for this reason, systematic lymph node dissection is required to correct staging (9,10).On the other hand, Gajra et al.(11) have detected a difference between random sampling lymph node dissection and

systematic lymph node dissection related to the survival of the patients. While the five-year survival rate is 56.4% in random sampling lymph node dissections, it has been 83.3% in systematic lymph node dissections. Besides, the selective lymph node dissection technique has been a more prioritized choice in minimally invasive surgeries (12,13). Especially, there have been some approaches that support using this technique not to increase morbidity among elderly patients. However, this approach is not accepted as a standard technique. Also, Hokage has stated that the survival rates of subcarinal lymph node metastasis positive upper lobe tumors have a worse course than isolated upper mediastinal lymph node metastasis. For this reason, Aokage does not recommend a selective lymph node dissection technique (14). Similarly, Ichinose and Okada have also determined that subcarinal lymph nodes have a worse course than superior mediastinal lymph nodes related to survival rates (15,16). Tulay et al. (17), they stated that intraoperative sentinel lymph node mapping would provide better information about the lymphatic drainage of the tumor, assist the surgeon in performing a better lymphadenectomy, and enable the detection of occult and micrometastatic disease for non-small cell lung cancer. Also, Turna et al.(18) mentioned sentinel lymph node is also defined as the most common involved of mediastinal lymph node station or stations for each pulmonary lobe. 96.5% of the patients of the right upper lobe tumors have lower paratracheal lymph nodes. In our study, we recommend removing sentinel lymph nodes at the lobe-specific lymph node dissection.

In this study, a statistical difference has not been detected between systematic lymph node dissection technique and lobe-specific lymph node dissection technique. While the five-year survival rate has been 40.5% in systematic lymph node dissection, it has been 34.4% in lobe-specific lymph node dissection technique.

In this study, it has been found out that the most important factor that affects the survival of geriatric patients is the width of resection, large cell carcinoma, and pN2. While the five-year survival rate of the patients for whom pN0 is detected is 46%, this rate is 27.9% for whom pN1-2 is detected. In their study, Sezen et al. have not been found out a relation between the resection type and survival rates(19). It has been found out that while the five-year survival rate of the patients with lobectomy is 44.6%, it is 23.4% in the patients with pneumonectomy. It is thought that there has been a statistically non-significant result in this study due to the low number of patients. Besides, Li et al. have been detected that the survival rate of patients with lobectomy

is higher than the ones with pneumonectomy. It has been observed that the five-year survival rate is 25.7% for the patients with lobectomy, and it is 7.3% for the patients with pneumonectomy ($p < 0.001$, HR:1.96) (4).

This is a retrospective study by definition, and also there might be a bias due to the low number of patient groups that are included in the study. The limitation increases because the number of women patients is also low. Moreover, it is a single-center study, and a lack of disease-free survival analysis might cause limitations.

In this study, the lack of clinical staging data also creates bias. In our clinical practice, we don't have any consensus about systematic lymph node dissection and lobe-specific lymph node dissection techniques. The surgeons' preference for the lymph node dissection technique can cause heterogeneity in the study. Also, in this study, our aim is to evaluate the long-term results of the lymph node dissection. However, we didn't evaluate short-term outcomes in this study; for this reason, this increases the selection bias of the study.

In this study, as a result, it has been found out that there is no difference between lobe-specific lymph node dissection and systematic lymph node dissection in geriatric patients in terms of survival rates. It has been observed that pN2 disease, histopathology, and the type of resection are the most important prognostic factors that affect the survival rates. Although ESTS recommended systematic lymph node dissection for lung cancer; we think that both surgical techniques can be applied to elderly patients since there is no difference in survival rates between lymph node dissection techniques. However, multi-centered and prospective studies are still required.

Declarations

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