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Effect of the number of negative lymph nodes removed on the survival and recurrence rate patients with non-small-cell lung cancer undergoing surgery

A multicenter retrospective cohort study

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Abstract

The role of the number of negative lymph nodes (NLNs) removed on survival and tumor recurrence after surgery in patients with non-small-cell lung cancer (NSCLC) is still unclear. This study aimed to evaluate the effect of the number of NLNs on overall survival (OS), recurrence-free survival (RFS), and recurrence rate of patients with NSCLC after surgery. This multicenter retrospective cohort study examined the medical profile of 1002 patients with a definite diagnosis of NSCLC who underwent surgery between 2021 and 2023 at one of our medical centers. Patients with NSCLC were classified into 4 groups based on the number of NLNs removed during surgery as follows. I: <10 (196 patients); II: 10 to 19 (341 patients); III: 20 to 30 (267 patients); and IV: >30 NLN (198 patients). The patients' demographics, tumor characteristics, and pathological findings were obtained by reviewing their medical records. The 5-year survival rate was 36.1%. The OS rate in groups I, II, III, and IV patients was 14%, 25%, 33%, and 43%, respectively (log-rank = 161.2, $P = .001$). Also, the RFS rate in patients of groups V/III was significantly higher than in groups I/II ($P < .05$). Multivariate analysis showed that the OS rate in group V and II patients was significantly higher than the other 2 groups (I and II). In addition, age > 65 years, comorbidity, tumor size > 3, advanced tumor stage, presence of metastasis, lymph node ratio > 0.3, total lobectomy, central tumor, and no adjuvant chemotherapy are significantly associated with decreased OS rate of patients with NSCLC. The increase in the number of NLNs removed during surgery was associated with an increase in the OS and RFS rates. Attention to this number can be a key factor in improving the survival prediction of patients with NSCLC.

Abbreviations: DFS = disease-free survival, LNR = lymph node ratio, NLN = negative lymph node, NSCLC = non-small-cell lung cancer, OS = overall survival, RFS = recurrence-free survival, SCLC = small-cell lung cancer, TNM = tumor-node-metastasis.

Keywords: five-year survival rate, lung cancer, negative lymph nodes, non-small-cell lung cancer, surgery

1. Introduction

Lung cancer, a global health concern, is on the rise. The World Cancer Report 2020 reveals that it constituted 11.4% of all cancer cases (2.2 million) and 18% of all cancer deaths (1.79 million deaths), which makes it one of the significant causes of cancer deaths.[1,2] This burden is particularly pronounced in developing countries, where 58% of cases and 61% of cancer-related deaths are because of lung cancer.[3] Despite the progress made in health and treatment approaches, the persistent challenge of diagnosing lung cancer at an advanced stage underscores the need for further advancements.[2] The 5-year overall survival rate, estimated

MB and FD contributed to this article equally.

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The data that support the findings of this study are available from a third party, but restrictions apply to the availability of these data, which were used under license for the current study, and so are not publicly available. Data are available from the authors upon reasonable request and with permission of the third party.

This study was approved by the ethics committee of Iran and the University of Medical Science. All methods were carried out in accordance with relevant guidelines and regulations. The need for informed consent was waived by the Ethics Committee/Institutional Review Board of (Iran University of Medical Science).

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at 17%, could be significantly improved with better early detection and treatment.[2] For non-small-cell lung cancer (NSCLC), the 5-year overall survival rate varies from 68% in patients with stage IB to 0% to 10% in those with stage IVA/IVB, highlighting the potential for progress in this area.[4] The number of resected lymph nodes, the number of negative lymph nodes (NLNs), the ratio of involved nodes to resected nodes (lymph node ratio [LNR]), and the chance of registering positive lymph nodes are factors affecting the prognosis of cancer.[5–11] Evaluating lymph nodes is vital to lung cancer medical care.[12] Examining the lymph node staging (N stage) to assess lymph nodes is crucial in treating and diagnosing lung cancer.[13]

N stage is a multistage and challenging approach, and factors related to the tumor, such as size, location of the umbilicus and involved lobe, and radiological suspicion, affect it. Therefore, pathological gonadal evaluation is preferred over clinical evaluation.[14,15] The difference in the number of isolated and positive lymph nodes equals the number of NLNs. Evaluating the number of NLNs can reduce the possibility of earlier hidden lesions. The results of the studies indicate that the number of NLNs helps determine the prognosis of cancers.[11,16,17] The importance of the number of NLNs in esophageal thoracic carcinoma, gallbladder cancer, and breast cancer has been shown.[17–21] However, few studies have investigated this issue regarding lung cancer.[19] The results of previous studies have shown a correlation between the number of examined lymph nodes and long-term survival.[22–28] The results of several studies indicate that patients with positive lymph nodes have a higher probability of recurrence.[29] Time to recurrence was crucially longer for patients with NLN.[30] Limited studies have investigated the effect of the NLNs on the survival rate of patients with NSCLC. The survival rate of patients with NSCLC is different based on their demographic characteristics and race.[31,32] According to our knowledge, no study in Iran has investigated the effect of NLN count in patients with NSCLC after surgery. This study aimed to evaluate the impact of the NLNs resected on the survival and recurrence rates of patients with NSCLC after surgery.

2. Materials and methods

2.1. Study design

This retrospective study was approved by the ethics committee of Iran University of Medical Sciences. In this multicenter retrospective cohort study, the medical profile of 1452 patients with different stages of NSCLC who underwent surgery between 2012 and 2023 in 1 of the 3 therapeutic centers affiliated to the Iran University of Medical Sciences was reviewed. Available patients were randomly sampled from among the patients who met the inclusion criteria. Finally, 1002 consecutive patients were examined to investigate the effect of removed NSCLC and other factors on survival rate and tumor recurrence after surgery. The definitive diagnosis of the tumor was based on pathological findings and was made by an oncologist.

On the basis of the number of removed NLNs, patients were divided into 4 groups, including patients with <10, 10 to 19, 20 to 30, and <30. The sensitivity and specificity of this classification have been confirmed by Wang et al.[33]

2.2. Selection of samples

The inclusion criteria for this study were: definitive diagnosis of NSCLC based on biopsy and pathological findings, NSCLC undergoing surgical treatment, patients with at least 6 months of follow-up, knowing the final status (dead or alive or recurrence), and completion of patient's medical records. Small-cell lung cancer (SCLC), receiving chemotherapy or radiotherapy before surgery, tumors metastasized to the lung from other organs, concurrently suffering from other tumors, or receiving treatment for other tumors were defined as exclusion criteria.

The NSCLC was classified using the tumor-node-metastasis (TNM) staging system, which takes into account the size of the tumor (<3/>3 cm), the number of nodules, the number of involved lymph nodes (2 < vs >2), and whether there is metastasis present (positive/negative for other organs).To confirm the reliability of the data characteristics, the patient's medical profile was reevaluated independently by an oncologist and a pathologist regarding tumor stage classification and other characteristics. Agreement between 2 raters was confirmed with a Kappa coefficient equal to 0.93 for the classification of tumor characteristics.

2.3. Data collection

The researcher extracted all patient data using a checklist referring to the patients' files. Demographic and clinical characteristics of patients included (age, gender, average follow-up, BMI, education and history of smoking, underlying diseases, and family history of lung cancer). Tumor characteristics and pathological findings of patients included (primary location of the tumor, histology, stage, size, presence of metastasis to other organs, LNR, and number of positive and NLNs removed).

2.4. Primary observation outcome

Study outcomes were defined as overall survival (OS) rate, recurrence-free survival (RFS), and tumor recurrence. The findings were compared in 4 subgroups with removed NLNs. OS was defined as the time interval between surgery and death. In cases where the patient's final status (dead or alive) was not known at the last follow-up, a phone call with the patient's family was used.

2.5. Sample size calculation

The adequate sample size for this study, with an estimated effect size of 0.26, for the difference in survival rates of patients with NSCLC based on NLNs based on the study by Wang et al,[33]with alpha error 5% and 90% power was estimated by an epidemiologist of 511 patients using G Power version 3.1 software.

2.6. Statistical analysis

The data analysis utilized Stata 17 software. A log-rank test was employed to compare the survival rate of essential variables, clinical parameters, and tumor characteristics. Continuous variables were reported as mean ± SD and categorical variables were reported as numbers (%). The survival function was estimated using the Kaplan–Meier product limit estimator. Variables with a P value of <.15 in the univariate analysis were included in the Cox multivariate analysis. Multiple Cox regression with a stepwise backward selection variable strategy was used to assess the adjusted associations of the covariates and time to event. Cox multivariate regression analysis was utilized to control the effect of stage and other tumor characteristics on patient survival. The adjusted hazard ratio in the 95% confidence interval was used to determine the variables predicting survival. A statistically significant level was considered with a P value <.05.

3. Results

3.1. Baseline characteristics and outcomes

The average age of the patients was 63.1 ± 3.4 years (range: 41–91 years). The median age of patients was 66 years. A total of 613 (61.2%) patients were male. Regarding the level of education of the patients, 73% of the patients had less than a diploma. Almost 52% of patients had a history of smoking. The overall average body mass index was 24.3 ± 1.9 kg/m^2. Regarding the primary location of the tumor, 66% of the tumors were peripheral. Histologically, adenoma–carcinoma was the most common type of tumor. The median follow-up was 19.3 months (interquartile range: 15.5–23.1). The overall mean survival was 35.1 months after surgery. In terms of disease stage, the majority of patients were in stages I and II. In 80% of patients, the number of involved lymph nodes was more than 2 in 80% of patients. Metastasis was reported in 209 (32.7%) cases. Regarding NLNs, <10 NLNs were removed in 19.6% of patients. A total of 10 to 19 nodes were removed in 34% of patients (Table 1).

3.2. Univariate analysis finding

Overall, the 5- and 3-year survival rates of patients with NSCLC were 36.1% and 49.6%, respectively (Fig. 1). Univariate analysis showed that the OS rate in patients ≥65 years was significantly lower than in patients <65. The OS rate of patients was significantly lower in patients with NSCLC with comorbidities and treated with pneumonectomy compared to those without comorbidity (log-rank = 11.2, $P = .001$) and treated with lobectomy (log-rank = 7.1, $P = .021$) Also, the survival rate of the patients was related to the characteristics of the tumor. The survival rate was significantly lower in patients with a higher tumor stage (>II vs <II), tumor size > 3 vs <3 cm, LNR > 0.3, tumor location (central vs peripheral), number of involved lymph nodes > 2, pathological stage > II, and the number of removed NLNs (negative and positive). At the same time, adjuvant chemotherapy after surgery was associated with improved patient survival (Table 2).

OS and RFS rates significantly differed based on the number of NLNs resected. The OS rate in patients with the number of removed NLNs < 10, 10 to 19, 20 to 30, and >30 was 14%, 25%, 33%, and 43%, respectively (log-rank = 161.2, $P = .001$) (Fig. 2A). The RFS rates in patients with the number of removed NLNs <10, 10 to 19, 20 to 30, and >30 were 11%, 21%, 26%, and 37%, respectively (log-rank = 138.5, $P = .001$) (Fig. 2B).

3.3. Comparison of demographic and tumor characteristics based on the number of NLNs removed

The recurrence rate of tumors in patients with the number of NLNs <10, 10 to 19, 20 to 30, and >30 was 90.8%, 91.2%, 71.9%, and 61.1%, respectively, which is statistically significant. Also, the presence of metastasis and LNR > 0.3 in the group with the number of removed NLNs > 20 was significantly lower than in the group with the number of NLNs < 20 ($P < .005$). No significant correlation was observed between the number of NLNs removed group with demographic characteristics and other tumor characteristics ($P > .05$) (Table 3).

3.4. Cox multivariate analysis finding

Multivariate Cox analysis showed that, adjusted for other variables, the number of removed NLNs was significantly associated with the 5-year survival of patients. The survival rate in patients whose number of removed NLNs was >30 or between 20 and 30 was significantly better than the other 2 groups. In addition, age, comorbidity, tumor size, tumor stage, metastasis, LNR, type of pulmonary lobectomy, tumor location, and tumor

Table 1

Demographic and pathological characteristics of patients with NSCLC.

Variables	1002 Patients with NSCLC
Demographic characteristics	
Age (year) (mean ± SD)	63.1 ± 3.4
Age (year)	
<65	399 (39.8%)
≥65	603 (60.2%)
Sex	
Male	613 (61.2%)
Female	389 (38.8%)
Marital status	
Unmarried	37 (5.8%)
Married	602 (94.2%)
Education	
Illiterate	192 (19.2%)
<Diploma	540 (53.9%)
≥Diploma	270 (26.9%)
BMI (kg/m^2)	24.3 ± 1.9
Family history of lung cancer	
Yes	354 (35.3%)
No	648 (64.7%)
Smoking status	
Yes	521 (52.1%)
No	481 (47.9%)
Comorbidity	
Yes	861 (85.9%)
No	141 (14.1%)
Tumor characteristics	
Tumor location	
Peripheral	672 (67%)
Central	208 (20.8%)
Missing	122 (12.2%)
Tumor type	
Adenoma–carcinoma	652 (65%)
Squamous cell carcinoma	211 (21.1%)
Other and unknown	139 (13.9%)
Positive lymph node count	
<5	711 (70.6%)
≥5	291 (29.4%)
T-stage tumor	
T1	199 (19.9%)
T2	483 (48.2%)
T3	157 (15.7%)
T4	85 (8.5%)
Unknown	78 (7.7%)
Tumor size (cm)	
≤3	448 (44.7%)
>3	358 (35.7%)
Unknown	196 (19.6%)
NLNs	
<10	196 (19.6%)
10–19	341 (34%)
19–30	267 (26.6%)
>30	198 (19.8%)
Metastasis	
Yes	309 (30.8%)
No	693 (70.2%)
Lymph node ratio (%)	
≤0.3	895 (89.3%)
>0.3	107 (10.7%)
Pathological stage	
IIa	151 (15.1%)
IIb	61 (6.1%)
IIIa	706 (70.4%)
Unknown	84 (8.4%)
Mean follow-up (month)	19.3 ± 3.8
Median survival (month)	36.1 + 3.2
Adjuvant chemotherapy	
No	341 (34%)
Yes	661 (66%)
Recurrence rate (yes)	811 (80.9%)

BMI = body mass index, NLN = negative lymph node, NSCLC = non-small-cell lung cancer.

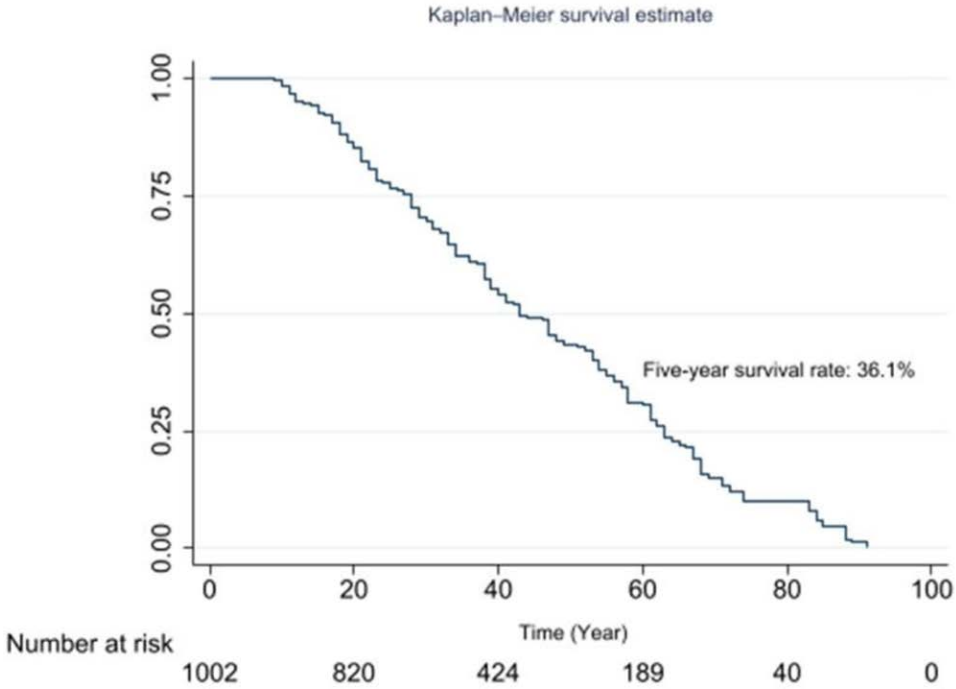

Figure 1. Kaplan–Meier overall 5-year survival of patients.

pathological stage are significantly related to the survival of patients with NSCLC ($P < .05$) (Table 4).

4. Discussion

The survival and recurrence of NSCLC tumors after surgery depend on various factors, including demographic characteristics, environmental, race, molecular factors, and tumor characteristics. Although many studies have examined predictors of survival in patients with NSCLC after surgery,[34–40] the number of studies that have examined the effect of the number of NLNs removed during surgery on OS and RFS is very limited.[33,41,42] The role of the number of NLNs removed on survival and tumor recurrence after surgery in patients with NSCLC is still unclear. Knowing the effect of the number of negative nodes removed on postoperative outcomes can significantly help the staging and management of patient treatment, improve survival, and reduce tumor recurrence after surgery.

According to our knowledge, no study has investigated the effect of the number of NLNs removed on survival and recurrence rates in Iranian patients with NSCLC. In this study, we investigated the effect of the number of NLNs on OS, RFS, and recurrence after surgery in 1002 patients with NSCLC with a median age of 66 years. According to the results of our study, more than half of the patients had a history of smoking. In terms of the primary location of the tumor, nearly two-thirds of the patients were peripheral tumors and adenoma-carcinoma. Most of the patients were diagnosed in stages II/III, and almost one-third of the patients had tumor metastasis. The 5-year survival rate of patients was 36%, and the survival rate was different based on various factors, including the number of NLNS removed. The OS, recurrence, and RFS in patients with >20 NLNs were significantly higher than in patients with <20 NLNs. The OS rate in patients whose number of removed NLNs was <10, 10 to 19, 20 to 30, and 30 was 14%, 25%, 33%, and 43%, respectively. The rate of tumor recurrence in patients with a number of removed NLNs < 20 was significantly higher than a number of removed NLNs > 20. The lowest recurrence rate was observed in patients with the number of removed NLNs > 30.

Multivariate Cox analysis showed that, after adjusting for other variables, a higher number of removed NLNs was significantly associated with an increased survival rate. In addition, age < 65 years, comorbidity, tumor size > 3, advanced tumor stage, presence of metastasis, LNR > 0.3, total lobectomy, tumor location (central vs peripheral), and advanced pathological stage of the tumor are significantly associated with decreased survival of patients with NSCLC, while adjuvant chemotherapy was significantly associated with improved survival of patients after surgery which these results were in line with the results of studies conducted in this field.[33,41,42]

In a retrospective study, Wang et al,[33] by evaluating the prognostic impact of the presence of lymph node metastasis and the number of NLN removed on OS and disease-free survival (DFS) in 482 patients with N1 and N2 patients with NSCLC showed that OS and DFS were significantly associated with both the ratio of metastatic lymph nodes and the number of NLN. They showed that the survival rate for patients with the number of NLNs > 30, 10 to 30, and <10 was 38%, 25%, and 17%, respectively, which was in line with the results of our study. They reported that NLN is a strong prognostic factor for OS and DFS of patients with NSCLC stage II/IIIa and can be used as a useful classification scheme for treatment management of patients with NSCLC. They reported that NLN is a strong prognostic factor for OS and DFS of patients with NSCLC and can be used as a useful classification scheme for the treatment management of patients with NSCLC. In our study, unlike their study, in addition to stage II/IIIa, patients with advanced stages were also examined, and the results were confirmed for patients with advanced tumor stages as well. In another study in 2020, Zhou et al[41] evaluated the relationship between the number of NLNs and survival in patients with NSCLC; they showed that the number of NLNs was an independent prognostic factor of OS in patients with NSCLC. They showed that the postoperative survival rate of patients increases with the increase in the number of NLN removed during the surgery, which confirmed the results of our study.

In another study in 2023, Yang et al,[42] evaluated the correlation between the number of NLN and the prognosis of patients with stages I–IIIa SCLC who underwent lobectomy in

Table 2

Univariate analysis of factors predicting patient survival.

Variable	Five-year survival rate (%)	HR dead (95% CI)	*P* value
Age (year)			.048
<65	37.3	Ref	
≥65	35.3	1.06 (1.001–1.12)	
Sex			.28
Female	34.9	Ref	
Male	38.02	1.09 (0.95–1.25)	
Marital status			.81
Unmarried	36.2	Ref	
Married	36	1.01 (0.65–1.36)	
Education			.41
<Diploma	35.02	Ref	
≥Diploma	36.5	0.96 (0.80–2.11)	
BMI (kg/m^2)			.58
<25	35.8	Ref	
≥25	36.2	0.98 (0.70–3.7)	
Family history of lung cancer			.54
No	35.3	Ref	
Yes	36.5	0.97 (0.60–4.11)	
Smoking status			.58
No	35.8	Ref	
Yes	36.7	1.03 (0.5–7.1)	
Comorbidity			.041
No	39.8	Ref	
Yes	35.5	1.13 (1.01–1.26)	
Type of pulmonary lobectomy			
Lobe	38.5	Ref	–
Total	33.2	1.16 (1.01–1.32)	.035
Other	38.9	0.95 (0.7–3.02)	.29
Tumor location			
Peripheral	36.9	Ref	.036
Central	33.7	1.32 (1.01–1.63)	
Tumor type			.037
Adenoma–carcinoma	37.5	Ref	
Squamous cell carcinoma	32.1	1.2 (1.02–1.41)	
Positive lymph node count			.006
<5	38.4	Ref	
≥5	30.2	1.31 (1.05–1.65)	
T-stage tumor			
T1	44.5	Ref	–
T2	35.5	1.3 (1.01–1.61)	.001
T3	18.4	2.38 (1.2–3.59)	.001
T4	8.8	6.11 (3.1–9.09)	.001
Tumor size (cm)			.004
≤3	50.4	Ref	
>3	25.1	2.11 (1.3–2.91)	
Metastasis			
No	60.2	Ref	.001
Yes	12.5	4.3 (2.6–6.1)	
Lymph node ratio (%)			.001
≤0.3	37.2	Ref	
>0.3	20.2	2.21 (1.22–3.3)	
Pathological stage			
IIa	58.1	Ref	–
IIb	55.2	1.2 (0.9–3.08)	.55
IIIa	18.7	3.2 (1.19–5.2)	.001
Adjuvant chemotherapy			.009
No	18.1	–	
Yes	39.4	0.67 (0.52–0.83)	

BMI = body mass index, CI = confidence interval, HR = hazard ratio.

3 groups with the number of NLNs removed <3, 3 to 7, and >7, showed; a higher number of resected NLNs was significantly associated with improved postoperative survival in stages I–IIIa SCLC patients who underwent lobectomy, which confirmed the results of our study. Ludwig et al,[23] showed that the number of removed NLNs during surgery in patients with NSCLC can be associated with improved survival of patients after surgery and reduced tumor recurrence. The correlation between increasing the number of removed NLNs during surgery with increased survival rate and decreased tumor recurrence has been reported in a number of other cancers such as gastric, breast, and esophageal cancer.[19,43,44]

Takamori et al,[45] by evaluating the effect of the number of removed NLNs on the survival of patients after surgery in 1584 patients with SCLC showed that the removal of a higher number of NLNs during surgery was associated with

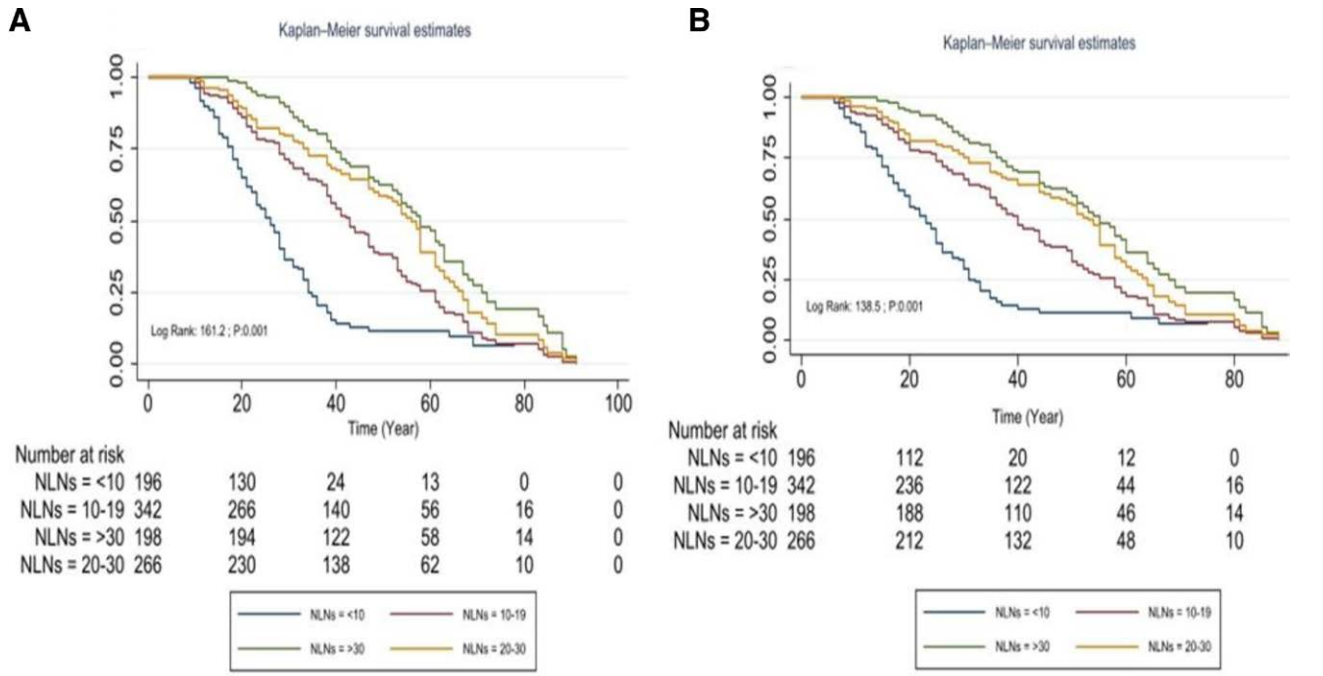

Figure 2. Patients' OS (graph A) and RFS rate (graph B) based on the number of NLNs removed. NLN = negative lymph node, OS = overall survival, RFS = recurrence-free survival.

improved survival of patients with SCLC after surgery. Becker et al,[46] proved that, in patients with NSCLC, more extensive removal of NLNs during surgery (>16) was significantly associated with improved survival of patients after surgery and reduced tumor recurrence. Osarogiagbon et al,[47] reported that the number of NLNs removed during surgery may increase mortality and decrease the survival of patients with NSCLC. They revealed that lymph node assessment is not as effective as it should be in patients with surgically removed NSCLC who have no evidence of cancer spread to the lymph nodes. This increases the likelihood of underestimating the risk of long-term mortality and missing out on identifying patients who may benefit from additional therapy after surgery. This highlights a significant issue in quality of care that needs to be addressed.

Our study had limitations and strengths that should be noted. The most significant limitation of our study was the retrospective design and the extraction of data from the patient's medical record, which hindered the measurement of several crucial cancer-related factors and markers. Furthermore, because of the reliance on reviewing patient medical records, there were missing or unknown variables, including tumor characteristics, which could have impacted the accuracy of the outcome estimates. In addition, this study was conducted on a specific population with specific characteristics, and the generalization of its results to other populations should be cautious. A prospective study design can help to estimate the results more accurately. Our study's most important strength was implementing a thorough multicenter research project on the Iranian population. This study had a large sample size and aimed to explore the impact of the number of removed NLNs on the survival and recurrence rate of patients with NSCLC while adjusting for other variables.

In conclusion, our study showed that the number of removed NLNs ≥ 30 was associated with an increased OS rate and decreased recurrence rate in patients with NSCLC after surgery. The increase in the number of NLNs removed during surgery was also associated with increased OS and RFS rates. Thus, paying attention to the number of NLNs removed during surgery can be a key factor in improving the survival prediction of patients with NSCLC.

Author contributions

Conceptualization: Mansour Bahardoust, Danyal Yarahmadi, Fatemeh Daneshfar, Meisam Haghmoradi, Babak Goodarzy, Adnan Tizmaghz.
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Software: Behnaz Niroomand, Shabnam Rashidi, Babak Goodarzy, Adnan Tizmaghz.
Validation: Fatemeh Daneshfar.

Table 3

Comparison of demographic and tumor characteristics based on the number of NLNs removed.

	Number of NLNs resected				
	<10	10–19	19–30	>30	
Variable	(*n*: 196)	(*n*: 341)	(*n*: 267)	(*n*: 198)	*P* value
Age (year)					.45
<65	81 (41.3%)	137 (40.2%)	105 (39.3%)	76 (38.4%)	
≥65	115 (58.7%)	204 (59.8%)	162 (60.7%)	122 (61.6%)	
Sex					.077
Male	112 (57.1%)	208 (61%)	179 (67%)	114 (57.6%)	
Female	84 (42.9%)	133 (39%)	88 (33%)	84 (42.4%)	
Education					.22
<Diploma	147 (75%)	243 (71.3%)	202 (75.7%)	140 (70.7%)	
≥Diploma	49 (25%)	98 (28.7%)	65 (24.3%)	58 (29.3%)	
BMI (kg/m^2)	24.8 ± 1.9	24.6 ± 1.7	24.1 ± 1.7	24.2 ± 1.8	.001
Family history of lung cancer (yes)	65 (33.2%)	111 (32.6%)	96 (36%)	82 (41.4%)	.19
Smoking status (yes)	101 (51.5%)	175 (51.3%)	146 (54.7%)	99 (50%)	.38
Comorbidity (yes)	169 (86.2%)	298 (87.4%)	225 (84.3%)	169 (85.4%)	.14
Tumor location					.15
Peripheral	135 (68.9%)	229 (67.2%)	174 (65.2%)	140 (70.7%)	
Central	61 (31.1%)	112 (32.8%)	93 (34.8%)	58 (29.3%)	
Tumor type					.087
Adenoma–carcinoma	136 (69.4%)	235 (68.9%)	173 (64.8%)	108 (54.5%)	
Squamous cell carcinoma	60 (30.6%)	106 (31.1%)	94 (35.2%)	90 (45.5%)	
Positive lymph node count					.41
<5	141 (71.9%)	249 (73%)	182 (68.2%)	139 (70.2%)	
≥5	55 (28.1%)	92 (27%)	85 (31.8%)	59 (29.8%)	
T-stage tumor					.077
≤T2	139 (70.9%)	251 (73.6%)	178 (66.7%)	114 (57.6%)	
>T2	57 (29.1%)	90 (26.4%)	89 (33.3%)	84 (42.4%)	
Tumor size (cm)					.082
≤3	96 (50%)	201 (58.9%)	162 (60.6%)	85 (42.9%)	
>3	96 (50%)	140 (41.1%)	105 (39.4%)	113 (57.1%)	
Metastasis (yes)	45 (22.9%)	98 (28.7%)	96 (36%)	69 (34.8%)	.015
Lymph node ratio (%)					.021
≤0.3	186 (94.9%)	310 (90.9%)	234 (87.6%)	165 (83.3%)	
>0.3	10 (5.1%)	31 (9.1%)	33 (12.4%)	33 (16.7%)	
Pathological stage					.11
II	47 (24%)	70 (20.5%)	49 (18.4%)	36 (18.2%)	
III	149 (76%)	271 (79.5%)	218 (81.6%)	162 (81.8%)	
Adjuvant chemotherapy (yes)	127 (64.8%)	223 (65.4%)	179 (67%)	132 (66.7%)	.51
Recurrence rate (yes)	187 (90.8%)	311 (91.2%)	192 (71.9%)	121 (61.1%)	.001

BMI = body mass index, NLN = non-small-cell lung cancer.

Table 4

Predictors of survival in patients with NSCLC based on Cox multivariate analysis.

Variable	HR	95% CI	*P* value
NLNs (≥20 vs <20)	0.59	0.41–0.8	.001
Age (≥65 vs <65)	1.08	1.02–1.14	.035
Comorbidity (yes vs no)	1.21	1.03–1.42	.006
Type of pulmonary lobectomy (total vs lobe)	1.45	1.1–1.81	.001
Tumor location (central vs peripheral)	1.22	1.02–1.43	.041
Tumor type (squamous cell carcinoma vs adenoma–carcinoma)	1.3	1.0.9–1.5	.028
T-stage tumor (>II vs <II)	3.8	1.81–5.82	.001
Tumor size (>3 vs ≤3)	2.18	1.2–3.2	.006
Metastasis (yes vs no)	4.1	2.1–6.11	.001
Lymph node ratio (>0.3 vs ≤0.3)	1.98	1.18–2.69	.001
Pathological stage (III vs II)	2.7	1.5–3.9	.001
Adjuvant chemotherapy (yes vs no)	0.69	0.49–0.9	.001

CI = confidence interval, HR = hazard ratio, NLN = non-small-cell lung cancer, NSCLC = non-small-cell lung cancer.

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