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Research Article

Mass Localization Relationship with Nodal Metastases in Right Lung Located Non-Small Cell Lung Cancer

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Abstract

Objectives: Surgical treatment of non-small cell lung cancer (NSCLC) is the most effective treatment for operable cases. Correct staging is extremely important in both prognosis and treatment selection. Lymph node invasion at the time of diagnosis is seen in 28-38% of NSCLC cases. The aim of our study is whether there is a relationship between the localization of the mass and the mediastinal lymph node region in the right lung non-small cell lung cancer.

Methods: 235 patients with a mass in the right lung were included in the study. One patient who could not reach his data and 23 patients who had only mediastinoscopy were excluded from the study.

Results: The location of the positive lymph node and the location of the mass were evaluated. Upper paratracheal lymph node were observed in upper lobe tumors, subcarinal area metastases were observed in lower lobe and santal tumors. In the analysis, upper paratracheal (2N), lower paratracheal (4N) and interlobar (11N) lymph nodes for upper lobe tumors; subcarinal (7N) lymph node for lower lobe tumors; interlobar (11N) lymph node for central lesions were found to be statistically significant in terms of lobe-specific metastatic lymph involvement.In the study, preoperative evaluation of metastatic mediastinal lymph nodes with PET-CT was found to be statistically significant for mediastinal lymph nodes except for station 8. High sensitivity (76.7%-96.6%) and low specificity values (18%-75%) were determined in the evaluation of metastatic lymph nodes.

Conclusion: Because of PET-CT alone is not sufficient in medistinal staging, invasive evaluation is very important for correct staging. In the results of our study, upper paratracheal lymph node were observed in upper lobe tumors, subcarinal area metastases were observed in lower lobe and santal tumors. In the light of this information, lobe-specific lymph node dissection will not performed in right lung masses. But in complete mediastinal lymph node dissection, lobe-specific lymph nodes for metastasis should especially be considered.

Keywords: Non-small cell lung cancer, right lung location, nodal metastasis, pet-ct

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Cancer is one of the most important health problems in the world. Lung cancer is responsible for 17.8% of cancer-related deaths and 12.8% of all cancer cases.[1,2] Since lung cancer is usually diagnosed after intrathoracic dissemination or the development of metastatic disease, chance of healing may be provided after surgical treatment.[3] The incidence rate reported for advanced disease in Turkey is higher than United States of America and Europe (86.7%).

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[4] Surgical treatment of non-small cell lung cancer (NSCLC) is the most effective treatment for operable cases. Correct staging is extremely important in both prognosis and treatment selection. The TNM Classification of Malignant Tumors Staging System is used in the long-term treatment of NSCLC and distant organ metastasis, and involvement of mediastinal lymph nodes is very important in treatment selection.[5] Spread of the tumor, mediastinal spread and involvement of mediastinal lymph nodes after primary tumor diagnosis are important in evaluating tumor stage and operability.[6] Lymph node invasion at the time of diagnosis is seen in 28-38% of NSCLC cases.[7] Among noninvasive staging tools, thoracic computed tomography (CT) has been replaced by positron emission tomography integrated computed tomography (PET/CT) to determine the mediastinal lymph node status, and there are many studies reporting the superiority of PET/CT.[8,9] PET imaging using radiolabeled F-18-2-fluorodeoxy-D-glucose (FDG) has been used as a screening method for noninvasive staging of many cancers, including lung cancer.[10] The aim of our study is whether there is a relationship between the localization of the mass and the mediastinal lymph node region in the right lung non-small cell lung cancer.

Methods

Ethics committee approval for our study was obtained from the local ethics committee. The patients who were operated for non-small cell lung cancer in a tertiary health center, were evaluated retrospectively. 235 patients with a mass in the right lung were included in the study. One patient who could not reach his data and 24 patients who had only mediastinoscopy were excluded from the study. In preoperative evaluation, according to tumor location and thorax computed tomography, cases are divided into 4 groups as upper lobe tumors, lower lobe tumors, middle lobe tumors and central tumors.

Preoperative Evaluation

In perorpative evaluation, thorax computed tomography was performed for all patients. Cranial MRI and positron emission tomography were performed to evaluate the distant metastases and mediastinal lymph nodes of the patients. Mediastinal lymph nodes which had SUVMax: 2.5 and higher were accepted as positive in PET-CT. Cardiology consultation was requested for patients at cardiac risk or 65 years of age or older. It was evaluated with ECG and ECO in the preoperative period. Advanced breathing tests were requested for patients with a respiratory capacity of 40% or less. While Transthoracic IIBx was performed for patients with peripheral tumors for peroperative diagnosis, all patients were evaluated by fiberoptic bronchoscopy. Mediastinal staging was determined in accordance with ESTS and ATS guidelines. EBUS and mediastinoscopy were used in preoperative mediastinal staging. Systemic lymph node dissection was performed with at least 3 stations intraoperatively.

Postoperative Follow-up

Histopathological staging was determined according to the 8. IASCL TNM classification. Tumor histopathologies were divided into adenocarcinoma, squamous cell carcinoma and other (large cell and adenosquamous cell carcinoma). In postoperative period, the patients were followed for the first 2 years by thoracic computed tomography at 3 months intervals. And the patients were followed up every 6 months between 2-5 years and once a year after 5 years with oncology.

Statistical Analysis

Chi-square Test or Fisher's Exact Test were used to determined the relationship between demographic and clinical data of the patients and descriptive statistics and categorical data. Student T Test and Mann Whitney U Analysis were used for continuous variables. P value of <0.05 was considered significant in the study. SPSS program (Version 22, SPSS Inc., Chicago, IL, USA) was used for calculations.

Results

23 female patients (10.9%) and 188 male patients (89.1%) were included in the study. The mean age was 58.69±9.61 (range 26-87) years. 73.5% of the patients were 65 years and younger and 26.5% were over 65 years old. While 46 patients were diagnosed by fiberoptic bronchoscopy (21.8%) and 62 patients (29.4%) by transthoracic biopsy, 103 patients (48.8%) were diagnosed by intraoperative frozen. There were 49 patients (23.2%) with a mass in the lower lobe, 97 patients (46%) in the upper lobe, 50 patients (23.7) with a central mass and 15 patients (7.1%) with a mass in the middle lobe. While lobectomy was performed in 186 patients (88.2%), pneumonectomy was performed in 25 patients (11.8%). The mean tumor diameter was 4.54±2.56 cm (range 1-20). When looking at tumor T stage, there were 67 patients (31.8%) with T1, 83 patients (39.3%) with T2, 33 patients (15.6%) with T3, and 28 patients (13.3%) with T4. There were 135 (64%) patients with pN0, 39 (18.5%) patients with pN1, and 37 (17.5%) patients with pN2. While 104 patients (49.3%) had squamous cell carcinoma, 93 patients (44.1%) had adenocarcinoma and 14 patients (6.6%) had large cell and adeosquamous cell carcinoma. 46 patients (21.8%) were stage I, 100 patients (47.4%) stage II, 65 patients (30.8%) stage III. The mean SUVMAX value was 11.8. In Table 1, the location

Table 1. Mass location with positive lymph node

Variables	Upper Lobe * n (%)	Lower Lobe ** n (%)	Middle Lobe *** n (%)	Central**** n (%)	p
Pathological LN					
2	4 (4.1)	0	0	0	0.029*
					0.267**
					0.576***
					0.260****
4	14 (17.3)	4 (9.5)	0	3 (7)	0.038*
					0.601**
					0.190***
					0.260****
7	0	8 (19.5)	1 (8.3)	5 (11.4)	0.001*
					0.002**
					0.955***
					0.327****
8	0	4 (11.4)	0	4 (12.5)	0.016*
					0.117**
					0.358***
					0.077****
9	2 (4.1)	1 (3.4)	2 (20)	2 (7.7)	0.427*
					0.484**
					0.056***
					0.708****
10	10 (11.6)	6 (14.3)	0	8 (17.8)	0.612*
					0.773**
					0.167***
					0.270****
11	12 (15.8)	13 (33.3)	1 (8.3)	14 (38.9)	0.015*
					0.143**
					0.175***
					0.023****

of the positive lymph node and the location of the mass were evaluated. Upper paratracheal lymph node were observed in upper lobe tumors, subcarinal area metastases were observed in lower lobe and santal tumors. In the analysis, upper paratracheal (2N), lower paratracheal (4N) and interlobar (11N) lymph nodes for upper lobe tumors; subcarinal (7N) lymph node for lower lobe tumors; interlobar (11N) lymph node for central lesions were found to be statistically significant in terms of lobe-specific metastatic lymph involvement.

In the study, preoperative evaluation of metastatic mediastinal lymph nodes with PET-CT was found to be statistically significant for mediastinal lymph nodes except for station 8. High sensitivity (76.7% - 96.6%) and low specificity values (18% - 75%) were determined in the evaluation of metastatic lymph nodes. (Table 2) The relationship between PET-CT involvement and mass is shown in table 3.

Table 2. Preoperative evaluation of metastatic mediastinal lymph nodes with PET-CT

Variables	Sensitivity	Specificity	p
PET-CT, LN			
2	88.9	50	0.017
4	92	24.4	0.004
7	96.1	18	0.002
8	94.6	25	0.105
9	94.6	50	0.009
10	96.6	21.4	<0.001
11	76.7	75	0.018

Discussion

Internationally, lung cancer remains the leading cause of cancer-related death in men and women.[11] According to the level of economic development, there is no difference in cancer deaths among men, but in industrialized coun-

Table 3. Mass relation with PET-CT involvements

Variables	Upper Lobe * n (%)	Lower Lobe ** n (%)	Middle Lobe *** n (%)	Central**** n (%)
PET-CT LN, Positive				
2	4 (8.2)	15 (15.5)	6 (12)	0
4	5 (10)	29 (29.9)	15 (30)	2 (13.3)
7	17 (34.7)	18 (18.6)	17 (34)	5 (33.3)
8	3 (6.1)	1 (1)	1 (2)	0 (0)
9	1 (2)	1 (1)	0 0	0 (0)
10	29 (59.2)	51 (52.6)	23 (46)	8 (53.3)
11	1 (2)	2 (2.1)	2 (4)	0 (0)

tries it has a higher rate of lung cancer deaths among women compared to developing countries.[12] Lung cancer is divided into two main groups as small cell lung cancer and non-small cell lung cancer. This grouping was determined in stages using histopathological features and immunohistochemical markers. Adenocarcinoma is the most common histological subtype of lung cancer in men and women. [13] Before the 1990s, squamous cell lung carcinoma was the most common histological subtype, especially among men. Since then the incidence of adenocarcinoma is increasing in the USA, Canada, many European countries and Japan compared to squamous cell carcinomas.[14] Women have higher rates of adenocarcinoma than squamous and small cell lung cancer.[15] In our study group, while 104 patients (49.3%) had squamous cell carcinoma, 93 patients (44.1%) had adenocarcinoma and 14 patients (6.6%) had large cell and adeosquamous cell carcinoma. The results differed from the literature. In our study group, there were 23 female patients (10.9%) and 188 male patients (89.1%). The mean age was 58.69±9.61 (range 26-87) years. 73.5% of the patients were 65 years and younger and 26.5% were over 65 years old. And our results were compatible with the literature.[16,17]

Surgical options for evaluation of mediastinal lymph nodes (LNs) in non-small cell lung cancer (NSCLC) include LN sampling, complete ipsilateral mediastinal LN dissection (MLND), and ultraradical bilateral MLND via median sternotomy.[18] Ipsilateral MLND does not improve survival compared to sampling in patients with early-stage NSCLC,[19] but microinasion ensures correct staging and adjuvant planning. Ipsilateral MLND does not increase mortality or morbidity, and lymph node dissection is recommended in patients with resectable NSCLC.[19] However, recent advances in lung cancer screening and imaging opportunities enable earlier diagnosis of NSCLC. In the early stages, adapting MLND to patient and tumor led to selective LN dissection (SLND) based on the lobe specificity of lymphatic spread. SLND has been advocated in some articles, especially for patients with advanced age, no significant LN metastasis, and/or respiratory dysfunction.[20] Shimada et al. suggested avoiding resection of the LN in the subcarinal region in upper lobe tumors or the LN in the upper mediastinum in lower lobe tumors.[20] In the study of Yoshimasu et al., SLND was suggested based on intraoperative histological examination of three mediastinal LN levels, primarily defined as sentinel LN mapping. [21] While in the study of Kudo et al., it was detected that tumor location may contribute to determining the optimal management strategy and predicting the prognosis correctly,[22] the results of the study of Saeteng et al. were inconsistent with these data.[23]

In light of this information, one of our aims in the study was to analyze the lymphatic propagation mode of NSCLC according to the location of the tumor as described by the systematic MLND. When looking at the studies on this subject in the literature, Riquet et al. found that pN0 status was more common in upper lobe masses on the right side, pN1 was more common in lower lobe masses, and the frequency of pN2 was found to be similar in all lobes. However, in this group, N2 disease was found in the inferior mediastinum in 5% of upper lobe masses and in the superior mediastinum in 10% of lower lobe masses.[24] In the study of Fang et al., it was reported that 4R (80.8%) metastasis had the highest rate in right upper lobe lesions. Also, station 7 involvement also occurred at a relatively high rate (21.8%) and lymph nodes at station 8 (1.3%) and station 9 (2.6%) were less likely to be involved than other stations. The highest metastasis rate in middle lobe lesions was observed in the subcarinal region, station 7 (82.9%), station 4R (51.4%), station 3 (35.7%), and station 2R (37.1%). Only 1 patient (2.9%) had positive lymph nodes in the lower region. In the right lung lower lobe lesions, station 7 (86.0%) was also the most common area, followed by station 4R (43.0%), station 2R (14.0%) and station 3 (34.9%).[25] In our study group, upper paratracheal lymph node were observed in upper lobe tumors, subcarinal area metastases were observed in lower

lobe and santal tumors. In the analysis, upper paratracheal (2N), lower paratracheal (4N) and interlobar (11N) lymph nodes for upper lobe tumors; subcarinal (7N) lymph node for lower lobe tumors; interlobar (11N) lymph node for central lesions were found to be statistically significant in terms of lobe-specific metastatic lymph involvement. When our results were evaluated, the involved lymph node areas were compatible with the literature, however, we consider that obtaining different data in terms of significance in the statistical analysis was due to the fact that the study group was not homogeneous. In the light of this information, we consider that lobe-specific lymph node dissection is not appropriate in right lung masses, but lobe-specific lymph nodes should be taken into consideration in the evaluation of metastasis in a complete mediastinal lymph node dissection.

Although 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) is not diagnostic in the preoperative evaluation of patients with lung cancer, it has been increased daily practice in recent years. Useful and complementary information has been provided to clinicians in terms of functional characteristics of lesions, preoperative staging of the disease and treatment planning.[26,27] Considering the publications in the literature regarding the preoperative evaluation of mediastinal lymph nodes with PET/CT, in the study of Yang et al., it was reported that PET/CT improves sensitivity, specificity, accuracy, positive predictive value and negative predictive value in the evaluation of locoregional lymph nodes in non-small cell lung cancer compared to advanced CT, and a better nodal staging has positive effects on diagnosis and treatment. [28] In the study of Billé et al., it was stated that PET-CT provided high specificity, but low sensitivity, and accuracy in intrathoracic nodal staging of NSCLC patients, therefore it was necessary for surgical staging.[29] In the study, preoperative evaluation of metastatic mediastinal lymph nodes with PET-CT was found to be statistically significant for mediastinal lymph nodes except for station 8. High sensitivity (76.7%-96.6%) and low specificity values (18%-75%) were determined in the evaluation of metastatic lymph nodes.

Therefore, we consider that PET-CT alone would not be sufficient for the preoperative evaluation of metastatic lymph nodes, and invasive mediastinal staging was absolutely necessary in appropriate patients.

Limitation

The main limitation of the study that it was retrospective, the number of patients was insufficient, and it was performed by more than one surgeon.

Conclusion

PET-CT is very important in the evaluation of mediastinal metastases in the preoperative period. Particularly, the evaluation of these lymph nodes due to high sensitivity should be paid attention. Because of PET-CT alone is not sufficient in medistinal staging, invasive evaluation is very important for correct staging. In the results of our study, upper paratracheal lymph node were observed in upper lobe tumors, subcarinal area metastases were observed in lower lobe and santal tumors. In the light of this information, lobe-specific lymph node dissection will not performed in right lung masses. But in complete mediastinal lymph node dissection, lobe-specific lymph nodes for metastasis should especially be considered.

Disclosures

Ethics Committee Approval: E1-20-817 (Ankara City Hospital, No.1 Ethics Committee).

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Conflict of Interest: None declared.

Authorship Contributions: Concept – E.C.; Design – E.C.; Supervision – E.C.; Materials – O.O.Y.; Data collection &/or processing – E.C.; Analysis and/or interpretation – E.C.; Literature search – A.G.; Writing – A.G.; Critical review – O.O.Y.

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