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ORIGINAL ARTICLE / ÖZGÜN MAKALE

The role of radiological and clinical findings in determining lobectomy decision in patients with undiagnosed resectable lung lesions

Tanısız rezektabl akciğer lezyonlarında lobektomi kararının belirlenmesinde radyolojik ve klinik bulguların rolü

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ABSTRACT

Background: The aim of this study was to evaluate the role of radiological and clinical findings in determining lobectomy decision in undiagnosed resectable lung lesions.

Methods: Between January 2014 and April 2023, a total of 135 patients (114 males, 21 females; mean age: 60.8±11.5 years; range, 17 to 84 years) who underwent lobectomy or wedge resection based on clinical and radiological data were retrospectively analyzed. Patients with undiagnosed lung lesions, whose diagnosis could not be confirmed through transthoracic fine needle aspiration biopsy or bronchoscopic endobronchial ultrasound, were included in the study. Clinical data including age, sex, smoking status, history of extrapulmonary cancer, family history of lung cancer, and presence of chronic obstructive pulmonary disease/idiopathic pulmonary fibrosis were noted. Radiological data including lesion size, margin characteristics, internal structure of the lesion, relationship of the lesion with surrounding tissues, and nuclear imaging results were also recorded.

Results: Malignant lesions were detected in 74 patients, while benign lesions were detected in 61 patients. Comparing benign and malignant lesions, age, lesion size, lesion localization, presence of pleural retraction, and moderate-to-high maximum standardized uptake value (SUV_{max}) on positron emission tomography-computed tomography were found to be correlated with malignancy.

Conclusion: The accurate assessment of lung lesions and prompt identification of possible malignancy are of paramount importance for implementing appropriate treatment strategies.

Keywords: Clinical findings, lobectomy, lung lesions, radiological findings.

ÖZ

Amaç: Bu çalışmada, tanısız rezektabl akciğer lezyonlarında lobektomi kararının belirlenmesinde radyolojik ve klinik bulguların rolü değerlendirildi.

Çalışma planı: Çalışma Ocak 2014 - Nisan 2023 tarihleri arasında klinik ve radyolojik verilere göre lobektomi veya kama rezeksiyonu uygulanan toplam 135 hasta (114 erkek, 21 kadın; ort. yaş: 60.8±11.5 yıl; dağılım, 17-84 yıl) retrospektif olarak incelendi. Tanısız akciğer lezyonu olan, transtorasik ince iğne aspirasyon biyopsisi veya bronkoskopik endobronşial ultrasonografi yöntemi ile tanı konulamayan hastalar çalışmaya dahil edildi. Yaş, cinsiyet, sigara kullanımı, ekstrapulmoner kanser öyküsü, ailede akciğer kanseri öyküsü ve kronik obstrüktif akciğer hastalığı/idiyopatik pulmoner fibrozis varlığı dahil olmak üzere klinik veriler kaydedildi. Lezyonun boyutu, kenar özellikleri, lezyonun iç yapısı, lezyonun çevre dokular ile olan ilişkisi ve nükleer inceleme sonuçları dahil olmak üzere radyolojik veriler de kaydedildi.

Bulgular: Hastaların 74'ünde malign lezyon, 61'inde benign lezyon tespit edildi. Benign ve malign lezyonların karşılaştırılmasında yaş, lezyonun boyutu, lezyonun yerleşim yeri, plevral çekinti varlığı, pozitron emisyon tomografisi ve bilgisayarlı tomografide orta ila yüksek standardize edilmiş maksimum tutulum (SUV_{max}) düzeyleri malignite ile ilişkili bulundu.

Sonuç: Akciğer lezyonlarının doğru bir şekilde değerlendirilmesi ve olası malignitelerin hızlı bir şekilde tespiti, doğru tedavi stratejilerinin uygulaması açısından büyük önem arz etmektedir.

Anahtar sözcükler: Klinik bulgular, lobektomi, akciğer lezyonları, radyolojik bulgular.

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Lung cancer, the most commonly diagnosed cancer type worldwide, is the leading cause of cancer-related deaths in men and the third most common cause in women after breast and colorectal cancer.[1,2] In early-stage disease, lung cancer has a high long-term survival rate with surgical treatment, reaching up to 75%. Therefore, the accurate assessment of lung lesions is crucial for tailoring appropriate treatment strategies.

Despite the existence of numerous treatment options for lung cancer today, the consensus among authorities is that the most optimal curative treatment option remains early-stage anatomical surgical resection and systematic lymph node dissection.[3,4] In resectable undiagnosed lung lesions, clinical and radiological findings play a pivotal role in determining the appropriate treatment approach for the disease. Certain clinical and radiological risk factors have been identified to make the approach to the lesion as accurate as possible. These risk factors can be classified into two main headings: those pertaining to the patient and those related to the radiological characteristics of the lesion as evidenced by imaging modalities. Patient-related risk factors include age, sex, smoking and/or exposure to other carcinogens, family history of lung cancer, history of extrathoracic malignancy, and chronic pulmonary inflammatory diseases such as chronic obstructive pulmonary disease (COPD) or idiopathic pulmonary fibrosis (IPF).[5] On the other hand, lesion-related risk factors include lesion diameter, localization in the upper lobes, spiculated contours, attenuation of the lesion, increase in lesion size or attenuation on follow-up imaging, and high metabolic activity on functional imaging results.[6]

In the present study, we aimed to evaluate the role of radiological and clinical findings in lobectomy decision in patients with undiagnosed resectable lung lesions.

PATIENTS AND METHODS

This single-center, retrospective study was conducted at Karadeniz Technical University Faculty of Medicine, Department of Thoracic Surgery between January 2014 and June 2023. A total of 135 patients (114 males, 21 females; mean age: 60.8±11.5 years; range, 17 to 84 years) with undiagnosed lung lesions who underwent lobectomy or wedge resection according to clinical and radiological data were included. Data including age, sex, comorbidities, radiological findings, preoperative diagnosis, surgery, pathology results and survival of the patients were obtained from the hospital information management system and patient files. Patients who received a preoperative diagnosis and those who did not receive a preoperative diagnosis but underwent surgical intervention other than lobectomy or wedge resection were excluded from the study.

Using the digital records and patient files, the following data were obtained: age, sex, smoking history, family history of cancer, comorbidities (presence of COPD, IPF), history of cancer, presenting symptoms, computed tomography (CT) findings (lesion margin characteristics, size of the lesion, presence of calcifications, lesion side, lobular localizations, central/peripheral localization, solid/subsolid state, presence of pleural retraction), maximum standardized uptake value (SUV_{max}) of the lesion on positron emission tomography-computed tomography (PET-CT), SUV_{max} value in lymph nodes, whether transthoracic fine needle aspiration (TTNA) biopsy or flexible bronchoscopy was performed before the procedure, intraoperative frozen-section analysis, histopathological type of the lesion, and pathological Tumor, Node, Metastasis (TNM) stage. Lesions were staged according to the 8th Edition of the TNM Staging System.[7]

The classification based on lesion size was as follows:

- Lesion size <2 cm
- 2 cm ≤ lesion size ≤3 cm
- 3 cm < lesion size

The classification according to the PET-CT SUV_{max} values of the lesion was as follows:

- PET SUV_{max} value of the lesion <5
- 5≤ PET SUV_{max} value of the lesion ≤10
- PET SUV_{max} value of the lesion >10

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). The conformity of the data to normal distribution was assessed by Kolmogorov-Smirnov test. Descriptive data were presented in mean ± standard deviation (SD) for normally distributed variables and median and interquartile range (IQR) for non-normally distributed variables. Categorical data were presented in number and frequency. The Student t-test was used to compare normally distributed variables between two groups, while the Mann-Whitney U test was used for non-normally distributed variables. Categorical data were compared using the chi-square test. A p value of <0.05 was considered statistically significant.

RESULTS

Transthoracic fine needle aspiration (TTNA) biopsy or endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) could not be performed in 84 patients (62.2%). Of these patients, the location of the lesion was not suitable for the procedure in 50 cases (59.52%), while 34 (25.18%) patients declined the procedure. Fifty-one (37.77%) patients underwent TTNA/EBUS-TBNA, but no diagnosis could be made. Intraoperative frozen-sections were studied in 73 patients (54.07%), while they could not be studied in 62 patients (45.92%). In 62 patients, frozen-section could not be performed in 41 patients as the lesion was located centrally, in eight patients because the lesion size was small and could not be palpated, and in 13 patients because the pulmonary reserves were limited and the lesion was smaller than 2 cm and no additional procedure was planned. Lobectomy was performed in 75 patients (55.5%), while wedge resection was performed in 60 patients (44.5%). In 13 cases, although the pathology result was malignant after wedge resection, no completion lobectomy was performed. Since the patients had limited pulmonary reserves and severe comorbidities, only wedge resection was performed and no additional procedure was performed. In 14 patients, lobectomy was performed although the lesions were benign, considering that the lobes would not function effectively due to the irreversible damage caused by the lesions in the existing lobes and lobe destruction. Pathological examination revealed that 61 (45.18%) lesions were benign and 74 (54.81%) lesions were malignant. In benign lesions, necrotizing granulomatous lesions were the most common diagnosis with a percentage of 36.06%, while in malignant lesions, adenocarcinoma ranked first with a percentage of 39.18%. Upon examination of the pathological stages of malignant lesions, 24 (40.67%) were found to be Stage I, 22 (37.28%) were Stage II, and 13 (22.03%) were Stage III.

Table 1. Demographic data of patients (n=135)

Data	n	%	Mean±SD
Age (year)			60.8±11.5
Sex			
Female	24	17.7	
Male	114	82.3	
Presence of COPD/IPF			
Yes	35	25.9	
No	100	74.1	
Smoking			
Yes	96	71.1	
No	39	29.9	
History of cancer			
Yes	37	27.4	
No	98	72.6	
Family history of cancer			
Yes	23	17	
No	112	83	
Complaint			
Yes	75	55.6	
Cough	46	34.2	
Back pain	16	11.8	
Shortness of breath	13	9.6	
No	60	44.4	

SD: Standard deviation; COPD: Chronic obstructive pulmonary disease; IPF: Idiopathic pulmonary fibrosis.

Table 2. Radiological data of the lesions (n=135)

Data	n	%
Margin characteristics of the lesion		
Smooth	40	26.6
Lobulated	22	16.3
Spicular	73	54.1
Presence of calcification		
Yes	33	24.4
No	102	75.6
Side		
Right	76	56.3
Left	59	43.7
Lobular localization		
Superior	77	57
Inferior	49	36.3
Middle	9	6.7
Localization		
Central	41	30.3
Peripheral	94	69.7
Nodule type		
Solid	112	83
Subsolid	23	17
Pleural retraction		
Yes	91	67.4
No	44	32.6
PET-CT SUV_{max} values		
0-4.99	45	33.3
5-10	46	34.1
10	44	32.6
PET-CT lymph node involvement		
Positive	36	26.7
Negative	99	73.3

PET-CT: Positron emission tomography-computed tomography; SUV_{max}: Maximum standardized uptake value.

Table 3. Significant patient and lesion parameters according to lesion size

	Size						
	<2 cm (n=25)		2 cm - 3 cm (n=47)		>3 cm (n=63)		
Parameters	n	%	n	%	n	%	*p*
Localization							<0.001
Peripheral	25	100.0	41	87.2	28	44.4	
Central	0	0.0	6	12.8	35	55.6	
Solid	15	60.0	35	74.5	62	98.4	<0.001
Pleural retraction	11	44.0	23	48.9	47	74.6	0.005
PET-CT SUV value							
0-4.99	19	76.0	17	36.2	9	14.3	<0.001
5-10	6	24.0	21	47.7	19	30.1	
>10	0	0.0	9	19.1	35	55.6	<0.001
PET-CT lymph involvement	1	4.0	7	14.9	28	44.4	0.015
Malignant diagnosis	6	24.0	26	55.3	42	66.6	<0.001
Lobectomy	1	4.0	22	46.8	52	82.5	<0.001

PET-CT: Positron emission tomography-computed tomography; SUV: Standardized uptake value.

Table 4. Significant patient and lesion parameters between malignant and benign groups

	Malignant (n=74)			Benign (n=61)			
Parameters	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			64.3±9.4			56.7±12.4	<0.001
Localization							0.005
Peripheral	44	59.5		50	82.0		
Central	30	40.5		11	18.0		
Pleural retraction	51	68.9		30	49.2		0.020
PET-CT SUV value							<0.001
0-4.99	12	16.2		33	54.1		
5-10	26	35.1		20	32.8		
>10	36	48.7		8	13.1		
Lobectomy	61	82.4		14	22.9		<0.001

SD: Standard deviation; PET-CT: Positron emission tomography-computed tomography; SUV: Standardized uptake value.

Demographic data of the 135 patients included in the study are presented in Table 1, while the radiological characteristics of the detected lesions and PET-CT findings are provided in Table 2. In this study, lesions were classified according to size as <2 cm, 2 cm-3 cm, and >3 cm. The demographic characteristics of patients and the radiological features of the lesions were compared based on lesion sizes. Parameters found to be significant are presented in Table 3. Following pathological examinations, lesions were classified as malignant and benign, and the demographic data of patients and the radiological characteristics of the lesions were compared. Parameters with significant differences between the groups are presented in Table 4.

DISCUSSION

Despite being known for many years and being the subject of numerous studies, lung cancer continues to be a significant public health issue. The accurate evaluation of lung lesions is crucial for assessing appropriate treatment strategies. Surgery is the most optimal treatment method proven by current data to offer a chance of cure in lung cancer. Therefore, it becomes inevitable to explore surgical treatment methods as much as possible.[8] In this context, clinical and radiological findings have a pivotal role in determining the correct treatment approach for undiagnosed lung lesions.

This study underscores five key points associated with malignancy in lung lesions. Age is the first factor to consider. Our study results showed a significant correlation between advanced age and malignant lesions. Patients aged 60 years and older were more likely to have a malignant lesion. The second factor is the presence of pleural retraction. Pleural retraction in the lesion was identified as a factor indicative of malignant lesions. The third factor is lesion size. In the present study, as lesion size increased, the probability of malignancy increased, and an increase in the solid component of lesion was observed with increasing size. The fourth factor is central localization. A significant correlation was found between central localization of the lesion and malignant character. It was also found that the size of the lesions and SUV_{max} values increased, as the localization of the lesion moved from peripheral to central. Therefore, lesions with central localization were found to be more likely to be malignant. Finally, a significant correlation was found between malignant lesions and moderate-to-high SUV_{max} values on PET-CT. As the size of the lesions and the amount of solid component increased, SUV_{max} values also increased.

Malignant lesions were diagnosed in 54.41% of the patients included in the present study. The mean age of patients with malignant lesions was 64.3±9.4 years, while that of patients with benign lesions was 56.7±12.4 years. Consistent with previous studies, there was a statistically significant relationship between advanced age and malignancy risk. Siegel et al.[9] showed a strong correlation between advanced age and malignancy, which is consistent with our findings. However, studies investigating the relationship between age and the follow-up of pulmonary nodules and malignancy are limited. In our opinion, there is a strong correlation between the increasing carcinogenic exposure over time, the prolonged duration of smoking, and the weakening of the body's immune system with advanced age and the increased likelihood of malignant lesions.

Pleural retraction is caused by thickening of the interlobular septa of the lung. Thickening of the septa is caused by tumor enlargement, inflammatory cells, or lymphatic obstruction due to fibrosis. It is known that the presence of pleural retraction is an important indicator for malignancy.[10,11] First described by Simon[12] in association with carcinomatous lesions, this finding was later reported in 75% of patients with bronchoalveolar cell carcinoma. In a larger study, Hill[13] confirmed the association of pleural retraction with malignancy. The CT appearance and significance of this sign were examined by Zwirewich et al.[14] In thin-section CT scans, pleural retractions were observed in 27% of benign nodules and 58% of malignant nodules. Pleural retraction was observed in 79% of patients with alveolar carcinoma and 62% of patients with squamous cell carcinoma.[15] In the present study, lesions in malignant and benign patients were compared in terms of the presence of pleural retraction. It was found that 51 of 74 patients with malignant lesions (68.9%) and 30 of 61 patients with benign lesions (49.2%) had this finding. Consistent with the literature, pleural retraction was identified as a significant predictor of malignant lesions.

In the present study, centrally localized lesions had a higher rate of malignancy compared to peripherally localized lesions and were found to have higher moderate-to-high SUV_{max} values. Additionally, centrally localized lesions were found to be larger in size compared to peripherally localized ones. In the present study, 41 lesions were centrally localized and 94 were peripherally localized. While 35 of the centrally localized lesions were >3 cm in size, 66 of the peripherally localized lesions were ≤3 cm in size. As lesion size increases, the probability of malignancy and moderate-to-high SUV_{max} values also increase. The sensitivity and specificity of PET-CT also increase as lesion size increases. Several studies have shown that the sensitivity of PET-CT significantly decreases in subcentimetric nodules.[16,17] In a study by Nomori et al.,[18] the sensitivity was 0% in lesions with a size <1 cm. This finding also suggests that the increasing malignancy rate of centrally localized lesions detected in the present study may be associated with larger lesion sizes.

The relationship between nodule size and the risk of malignancy has been demonstrated in many studies. According to literature data, the prevalence of malignancy of nodules detected in lung cancer screenings was 0 to 1% for nodules <5 mm in diameter, 6 to 28% for nodules 5-10 mm in diameter, 33 to 64% for nodules 11-20 mm in diameter, and 64 to 82% for nodules >20 mm in diameter.[19] Guidelines for nodule management also highlight that the primary variable determining the course of action is nodule size.[9,10,19,20] In the present study, malignant lesions were detected in six out of 25 patients (24%) with lesions smaller than 20 mm, in 26 out of 47 patients (55.3%) with lesions sized 20-30 mm, and in 42 out of 63 patients (66.6%) with lesions larger than 30 mm. Consistent with the literature, malignancy risk increased with increasing lesion size. The larger size of the lesion in malignant cases can be attributed to the increased rate of mitosis and a shorter half-life of cells with malignant potential.

Furthermore, PET-CT imaging is recognized for its enhanced capability in detecting malignant lesions and facilitating more precise staging, particularly in cases of malignancy. In most screening studies, the diagnostically invasive technique of TTNA biopsy is used to investigate nodules for diagnostic purposes; however, this technique requires considerable expertise, is rarely used for biopsies of small and deep-seated lesions, and has low sensitivity for benign lesions. The PET-CT is a non-invasive technique and previous studies have demonstrated that it has an average sensitivity of 96% and a specificity of 73.5% in characterizing solitary pulmonary nodules (SPNs). Gugiatti et al.[21] compared PET-CT with TTNA and surgical biopsies for SPNs and demonstrated that PET-CT had a lower cost and reduces inappropriate invasive diagnostic procedures and their complications. While evaluating the SUV_{max} values of lesions on PET-CT in patients included in our study, moderate or high SUV_{max} values were detected in 45.9% of benign lesions and 83.8% of malignant lesions. When the two groups were compared in terms of SUV_{max} values, malignant lesions had higher SUV_{max} values. Malignant cells have high glucose consumption due to their rapid catabolism. Fluorodeoxyglucose (FDG) competes with glucose and is, therefore, retained more in malignant cells. This is why the SUV_{max} value of the malignant group is higher.

In the present study, the critical role of clinical and radiological data in the evaluation and treatment planning processes of undiagnosed lung lesions were examined. The results obtained provide important information for the accurate and effective management of pulmonary lesions.

The increasing use of CT scans has led to a significant rise in the incidental detection of pulmonary nodules. Pulmonary nodule management guidelines and pulmonary nodule malignancy risk scoring systems have been developed to evaluate these nodules for malignancy and ensure proper management. The main pulmonary malignancy risk prediction models are the Brock University, Mayo Clinic, and Herder pulmonary nodule malignancy risk prediction models. Among the parameters included in these models, age and nodule size were found to be risk factors associated with malignancy in accordance with the literature, while smoking history, family history of lung cancer, history of extrapulmonary malignancy, nodule localization, nodule attenuation characteristics, and presence of spiculation in the nodule were not statistically associated with malignancy. This suggests the need for optimization of the models or the development of a new model tailored to our population.

The results of the present study have helped us develop a better understanding of the probability of malignancy in pulmonary lesions. Based on the data from this study and insights from the literature, we have developed an algorithm in our clinic to assess the probability of malignancy in undiagnosed pulmonary lesions. The patients were classified according to the

Table 5. The algorithm we created to evaluate the possibility of malignancy of undiagnosed pulmonary lesions

Clinical characteristics of patients and radiological characteristics of lesions				Score
Age	<60	≥60		
Score	1	2		
Size	1-2 cm	2-3 cm	>3 cm	
Score	1	2	3	
Localization	Peripheral	Central		
Score	1	2		
Presence of pleural retraction	No	Yes		
Score	1	2		
PET-CT SUV_{max} value of lesions	1-4.99	5-10	>10	
Score	1	2	3	
Total score				

PET-CT: Positron emission tomography-computed tomography; SUV_{max}: Maximum standardized uptake value.

clinical and radiological characteristics of the lesion and a scoring system was developed based on age, lesion size, attenuation, localization, and PET-CT SUV_{max} value. Points were assigned as follows: age <60 years= 1 point, age ≤60 years= 2 points; lesion size 1-2 cm= 1 point, 2-3 cm= 2 points, and >3 cm= 3 points; absence of pleural retraction= 1 point, presence of pleural retraction= 2 points; peripheral lesion localization= 1 point, central lesion localization= 2 points; PET-CT SUV_{max} value 1-5= 1 point, 5-10= 2 points, and >10= 3 points. These parameters are shown in Table 5. Accordingly, patients were followed if the total score was <6, preoperative diagnostic procedures were performed and surgery was planned accordingly if the score was between 6 and 10, and surgery was performed directly if the score was between 10 and 12.

Nonetheless, the limitations to our study include the fact that it was a single-center, retrospective study and was performed with a limited number of patients. In future studies, the addition of criteria such as tumor markers, follow-up time of the lesion, presence of a second tumor and family history will make the studies more meaningful in determining the prognosis. In addition, our results may guide the development of new applications that may contribute to the treatment planning of undiagnosed lung lesions.

In conclusion, clinical and radiologic data should be evaluated together in the assessment and treatment planning of pulmonary lesions. This can help patients achieve the most optimal treatment outcomes and is an important step in optimizing treatment strategies. Future research should continue in this direction to further enhance our understanding of pulmonary lesions and improve their treatment.

Ethics Committee Approval: The study protocol was approved by the Karadeniz Technical University Faculty of Medicine Scientific Research Ethics Committee (date: 21.09.2023, no: 2023/178). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Concept, design, literature search, writing manuscript: B.O.G., O.T., S.K., A.T.; Supervision: B.O.G., O.T., S.K., C.T.; Resources, materials, data collection and/or processing: B.O.G., O.T., S.K., A.T., A.A.; Analysis and/or interpretation: B.O.G., O.T., A.T., C.T.; Critical review: B.O.G., O.T., S.K., A.T., C.T.

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