

Does Tumor Localization of Operated NSCLC Have an Effect on Relapse and Survival?

Çağlayan Geredeli

Okmeydanı Eğitim ve Araştırma Hastanesi, Tıbbi Onkoloji Kliniği, İstanbul

ABSTRACT

Objective: Our aim was to investigate the effect of tumor localization on relapse and survival in early stage lung cancer.

Material and Methods: In this multicentered, retrospective study, 182 early stage non small cell lung cancer patients were included between the years of 2012-2015. The localizations of the primary tumor were determined as right upper lobe, right middle lobe, right lower lobe, left upper lobe, left middle lobe and left lower lobe. Overall survival and relapse-free survival rates were compared according to the lobes.

Results: In total 182 patients were included. The median age was 61 years. Median follow up time was 24.8 months. Of the patients, 38 (20.9%) were stage 1, 82 (45.1%) were stage 2 and 62 (34.1%) were stage 3A. According to tumor localization, 23 (12.6%) were right lower lobe tumors, 13 (7.1%) were right middle lobe tumors, 61 (33.5%) were right upper lobe tumors, 27 (14.8%) were left lower lobe tumors, 58 (31.9%) were left upper lobe tumors. No significant effect was detected on relapse-free survival ($p=0.862$) and overall survival in terms of tumor localization. ($p=0.750$).

Conclusion: In patients with early stage NSCLC, there was no significant difference in relapse-free survival and overall survival in terms of tumor localization.

Keywords: early stage, lung cancer, tumor location

ÖZ

Opere Küçük Hücre Dışı Akciğer Kanseri Tumor Lokalizasyonunun Relaps ve Sağkalım Üzerine Etkisi Varmıdır?

Amaç: Akciğer heterojen bir organdır bu yüzden erken evre akciğer kanserinde tumor lokalizasyonunun nükse ve sağkalıma etkisini araştırmak istedik.

Gereç ve Yöntem: Çalışmaya retrospektif multisentrik olarak 2012-2015 tarihleri arasında 182 erken evre küçük hücre dışı akciğer kanserli hasta alındı. Primer tumorün sağ üst lob, sağ orta lob, sağ alt lob, sol üst lob ve sol alt loblardaki lokalizasyonları tespit edildi. Loblara göre relapsız sağkalım ve genel sağkalım oranları karşılaştırıldı.

Bulgular: Toplam 182 hasta alındı. Median yaş 61 idi. Median takip süresi 24.8 ay idi. 38 (%20,9) evre 1, 82 (%45,1) evre 2, 62 (%34,1) evre 3A hasta vardı. Tumor lokalizasyonuna bakıldığında sağ alt lob 23 (%12,6), sağ orta lob 13 (%7,1), sağ üst lob 61 (%33,5), sol alt lob 27 (%14,8), sol üst lob 58 (%31,9) tumor vardı. Tumor lokalizasyonu relapsız sağ kalım ($p=0,862$) ve genel sağ kalım ($p=0,750$) açısından anlamlı bir farklılık göstermedi.

Sonuç: Erken evre küçük hücre dışı akciğer kanserli hastalarda tumor lokalizasyonu relapsız sağkalım ve genel sağkalım açısından herhangi bir anlamlı farklılık göstermedi

Anahtar kelimeler: erken evre, akciğer kanseri, tumor lokalizasyonu

INTRODUCTION

Lung cancer ranks first in cancer-related deaths both in the world and in Turkey⁽¹⁾. Despite standard multimodal therapies, the disease has an aggressive course. Various adjuvant chemotherapies and goal-oriented therapies are used in order to prevent aggressiveness of the disease, to delay relapse in operated patients and to prolong overall survival in metastatic patients

(2-4). Conventional staging systems are used in order to make these treatments more effective and not to administer the unnecessary treatment to the patients who do not need treatment⁽⁵⁾. Despite the treatments in line with the staging systems, the aggressive course of the disease continues. For these reasons, the researchers began to search for various prognostic and predictive properties as they believed that other factors apart from the stage could affect the direction

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Yazışma adresi: Uzm. Dr. Çağlayan Geredeli, Okmeydanı Eğitim ve Araştırma Hastanesi, Tıbbi Onkoloji Kliniği, İstanbul - Türkiye

e-posta: caglayange@hotmail.com

and variety of treatment. It was considered whether the tumor localization in lung could be one of these prognostic factors, but different results were attained (6-13). We also investigated whether or not tumor localization in operated NSCLC patients had a prognostic effect on relapse and survival.

MATERIAL and METHODS

The study was designed as a retrospective study. The files of 182 patients with non small cell lung cancer admitted to Medical Oncology clinic of Konya Necmettin Erbakan University, Meram Medical Faculty and Medical Oncology clinic of Istanbul Okmeydanı Education and Research Hospital between 2012-2015 were examined. Parameters such as age, gender, histological subtype, operation type, smoking status, comorbidity, tumor localization, tumor stage were recorded from the patient files. Relapse free survival (RFS) was recorded as the time that passed from the date of diagnosis to the emergence of relapse in operated patients. In addition, from the patients' files the last visit date and date of death were recorded. The survival times of the patients were determined.

SPSS 15.0 for Windows program was used for statistical analysis. Of descriptive statistics; number and percentage were used for categorical variables, mean, standard deviation, minimum, maximum were used for numerical variables. Genotype frequencies were assessed with the Hardy-Weinberg equation. Because the numerical variables did not fulfill the normal distribution condition, the comparisons of more than two independent groups were carried out with Kruskal Wallis test, and the comparisons of two independent groups were performed with Mann-Whitney U test. A comparison of odds ratios in independent groups was done with Chi Square analysis. Monte Carlo simulation was applied when the conditions were not met. Statistical significance level of alpha was accepted as $p < 0.05$.

RESULTS

In total 182 patients were included in the study. The median age was 61 (36-80). Of the patients, 163 (89.6) were male and 19 (10.4%) were female. Of the patients 144 (79.1%) were smokers and 38 (20.9%) were not smokers. The follow up time was 24.8

months (± 22.9 months). In the course of follow up, 68 (37.4%) patients had relapse. Twenty nine (15.9%) patients died.

When the stages of 182 patients in total were evaluated, 38 (20.9%) patients were stage 1, 82 (45.1%) patients were stage 2 and 62 (34.1%) patients were stage 3A (Table 1).

According to tumor localization, 23 (12.6%) were right lower lobe tumors, 13 (7.1%) were right middle lobe tumors, 61 (33.5%) were right upper lobe tumors, 27 (14.8%) were left lower lobe tumors and 58 (31.9%) were left upper lobe tumors (Table 1).

According to the operation type, there were 6 (3.3%) wedge resection, 1 (0.5%) segmentectomy, 89 (48.9%) lobectomy and 32 (17.6%) pneumonectomy. Fifty four (29.7%) patients were not operated (Table 1).

The distribution of the histologic subtype of tumor indicated that of the patients, 92 (50.5%) had squamous cell carcinoma, 50 (27.5%) had adenocarcinoma, 6 (3.3%) had adenosquamous cell cancer, 7 (3.8%) had large cell carcinoma, 1 (0.5%) had neuroendocrine carcinoma and 26 (14.3%) had undefined subtype (Table 1).

Table 1. Characteristics of the patients.

Characteristics	Mean \pm SD (Range)	n	%	
Age	61 \pm 9,4 (36-80)			
Gender, Male (%)		163	89,6	
Tumor Localization	Right lower lobe	23	12,6	
	Right middle lobe	13	7,1	
	Right upper lobe	61	33,5	
	Left lower lobe	27	14,8	
Smoking	Left upper lobe	58	31,9	
	Wedge resection	144	79,1	
	Segmentectomy	6	3,3	
	Lobectomy	1	0,5	
Operation type	Pneumoectomy	89	48,9	
	Not operated	32	17,6	
	Postoperative stage	Stage I	54	29,7
		Stage II	38	20,9
Stage IIIa		82	45,1	
Compatible with NSCLC		62	34,1	
Postoperative pathological diagnosis	Adenocancer	26	14,3	
	Squamous cell cancer	50	27,5	
	Adenosquamous	92	50,5	
	Large cell	6	3,3	
	Neuroendocrine	7	3,8	
		1	0,5	

Table 2. Statistical analysis of tumor localization.

		n	Tumor localization					p
			Right lower lobe	Right middle lobe	Right upper lobe	left lower lobe	Left upper lobe	
Age			57,2±10,7	64,1±6,6	61,3±9,3	60,5±10,7	59,2±8,3	0,111
Gender	Man	n (%)	26 (86,7)	13 (81,3)	65 (94,2)	24 (82,8)	54 (85,7)	0,265
	Women	n (%)	4 (13,3)	3 (18,8)	4 (5,8)	5 (17,2)	9 (14,3)	
Smoking		n (%)	24 (82,8)	10 (66,7)	54 (79,4)	22 (75,9)	49 (77,8)	0,789
Operation	Wedge Resection	n (%)	0 (0,0)	0 (0,0)	3 (6,3)	1 (4,2)	2 (4,3)	0,199
	Segmentectomy	n (%)	0 (0,0)	0 (0,0)	0 (0,0)	1 (4,2)	0 (0,0)	
	Lobectomy	n (%)	13 (61,9)	4 (40,0)	30 (62,5)	14 (58,3)	28 (59,6)	
	Pneumonectomy	n (%)	2 (9,5)	4 (40,0)	6 (12,5)	5 (20,8)	14 (29,8)	
	Unoperated	n (%)	6 (28,6)	2 (20,0)	9 (18,8)	3 (12,5)	3 (6,4)	
Postop Stage	Stage I	n (%)	3 (12,5)	2 (18,2)	10 (17,2)	8 (30,8)	16 (28,1)	0,288
	Stage II	n (%)	12 (50,0)	4 (36,4)	25 (43,1)	11 (42,3)	30 (52,6)	
	Stage IIIa	n (%)	9 (37,5)	5 (45,5)	23 (39,7)	7 (26,9)	11 (19,3)	
Histopathology	Adenocarcinoma	n (%)	3 (11,1)	0 (0,0)	1 (1,5)	0 (0,0)	4 (6,6)	0,232
	Squamous cell carcinoma	n (%)	0 (0,0)	1 (7,7)	3 (4,5)	0 (0,0)	3 (4,9)	
	Adenosquamous carcinoma	n (%)	0 (0,0)	0 (0,0)	0 (0,0)	1 (3,4)	0 (0,0)	
	Large cell carcinoma	n (%)	10 (43,5)	3 (27,3)	25 (43,1)	11 (44,0)	20 (34,5)	
	Neuroendocrine carcinoma	n (%)	0 (0,0)	0 (0,0)	3 (6,3)	1 (4,2)	2 (4,3)	
Median follow-up			28,0±28,2	19,9±19,5	25,7±26,0	22,5±19,0	24,7±18,8	0,481
Recurrenc		n (%)	10 (43,5)	3 (27,3)	25 (43,1)	11 (44,0)	20 (34,5)	0,758
RFS			24,5±27,0	22,8±20,0	23,7±26,7	20,6±18,9	21,6±17,7	0,782

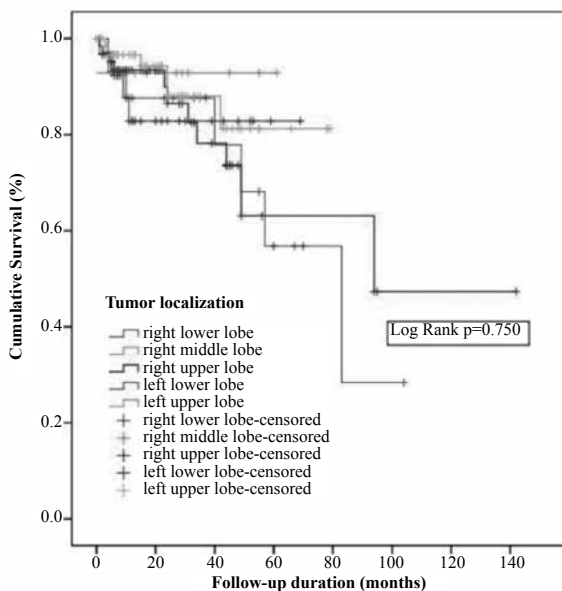


Figure 1. The overall survival graph of tumor localization.

There was no statistical significance when the tumor localization was compared with age ($p=0.111$), gender ($p=0.265$), smoking status ($p=0.789$), the operation type ($p=0.199$), the stage of the tumor

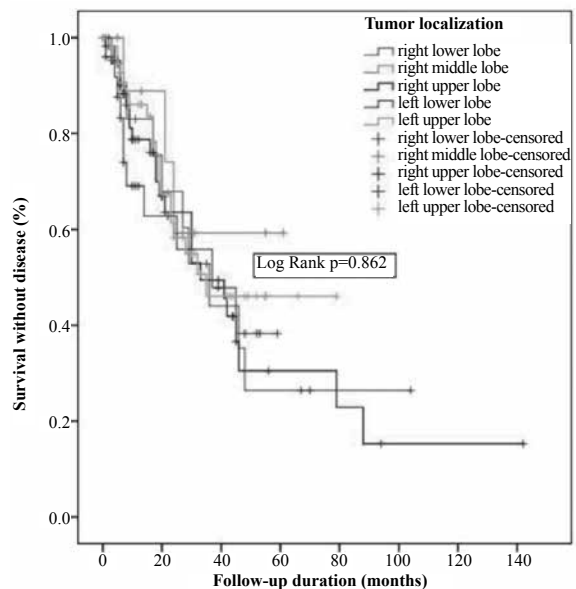


Figure 2. The relapse-free survival graph of tumor location.

($p=0.789$) (Table 2), the histologic subtype of the tumor ($p=0.232$), overall survival ($p=0.750$) (Figure 1), relapse-free survival ($p=0.862$) (Figure 2) (Table 2).

Stage 1, stage 2 and stage 3A in NSCLC patients was not statistically significant in terms of tumor localization ($p=0.288$) (Table 2).

DISCUSSION

NSCLG has an aggressive course despite the standard multimodal therapies. Various adjuvant chemotherapies and goal-oriented therapies are used in order to prevent aggressiveness of the disease, to delay relapse in operated patients and to prolong overall survival in metastatic patients⁽²⁻⁴⁾. Conventional staging systems are used in order to make these treatments more effective and not to administer the unnecessary treatment to the patients who do not need treatment⁽⁵⁾. Despite the treatments in line with the staging systems, the aggressive course of the disease continues. For these reasons, the researchers began to search for various prognostic and predictive properties as they believed that other factors apart from the stage could affect the direction and variety of treatment. It was considered whether the tumor localization in lung could be one of these prognostic factors, but different results were attained. Whitson et al.⁽⁶⁾ stated that tumor localization was not a prognostic factor in the operated T1 and T2 NSCLC patients. Also, Puri et al.⁽⁷⁾ demonstrated that the tumor localization was not a predictive marker in the operated stage 1 and 2 NSCLC patients. However, Iwasaki et al.⁽⁸⁾ found that survival was shorter in the operated NSCLC patients with left lower lobe tumor. Rocha et al.⁽⁹⁾ detected that postoperative stage progressed in the early stage operated NSCLC patients with left lower lobe tumor. Ou SE et al.⁽¹⁰⁾ found that when the tumors were larger than 4 cm in diameter, the operated stage 1b NSCLC patients with the middle and lower lobe tumors had higher operative mortality. In our study, we found that tumor localization did not contribute to both relapse-free survival and overall survival in stage I and stage II NSCLC patients. Our results were similar to the result of Whitson' and Puri's studies. Kudo et al.⁽¹¹⁾ found that the survival of left lower lobe tumors was worse if the lymph nodes were positive. Again, Inoue et al.⁽¹²⁾ found that the survival of upper lobe tumors in operated N2-positive stage 3A tumors was better than that of lower and middle lobe tumors. However, to the contrary of Inoue, Ichinose et al.⁽¹³⁾ found that the survival was better in left lower lobe tumors in the patients with N2-positive

stage 3A tumors. In the study by Hayakawa et al.⁽¹⁴⁾ conducted on the patients who received definitive radiotherapy without being operated, the survival of the upper lobe tumors was observed to be better than the lower lobe tumors. In our study, no statistically significant difference was found in both of relapse-free survival and overall survival in stage 3A patients in terms of tumor localization. In the light of the above mentioned studies, the survival of the left lower lobe tumors was found to be shorter, however; there was no significant correlation between tumor localization and survival in our study.

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