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RESEARCH ARTICLE / ÖZGÜN ARAŞTIRMA

Phenotypic Features of Emphysema in Patients with Lung Cancer and COPD Coexistence

Akciğer Kanseri ve Kronik Obstrüktif Akciğer Hastalığı Birlikteliği Olan Hastalarda Amfizemin Fenotipik Özellikleri

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ABSTRACT

Objective: In this study, we examined the relationship between the phenotypic features of emphysema in the coexistence of lung cancer and chronic obstructive pulmonary disease (COPD).

Material and Methods: Patients who were diagnosed with lung cancer and had concurrent COPD in a pulmonology department of a training and research hospital between January 1, 2016, and December 31, 2018, were retrospectively evaluated.

Results: A total of 248 patients were evaluated. In our study, no correlation was found between the phenotype and severity of emphysema and lung cancer, and also no relation was found between histological type and localization of the tumor. However, there was a significant difference between the visual emphysema phenotypes and body mass index (BMI) (p=0.003) and forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) (p=0.003), centrilobular emphysema (CLE) severity and BMI (p<0.001), FEV_1 (p=0.004), FEV_1/FVC (p<0.001), and paraseptal emphysema, and BMI (p=0.003). Furthermore, there was a significant difference between COPD stages and BMI (p=0.007), FEV_1 (p<0.001), FEV_1/FVC (p<0.001), and surgery rate (p=0.001). A significant correlation was observed between lung cancer and localization of tumor (p<0.001), histological type (p=0.018), and surgery rate (p<0.001).

Conclusion: No correlation was found between the visual type and severity of emphysema associated with parenchymal damage, as revealed by the quantitative evaluation of computed tomography, and the histological type and location of lung cancer. Although a significant rate of CLE was observed in 72.2% of our patient population, it could not be statistically documented due to the absence of our control group. The fact we could not find any study in the literature examining the relationship between the severity of visual emphysema phenotypes and lung cancer. Hence, this subject requires further studies with a larger number of patients and a control group.

Keywords: Chronic obstructive pulmonary disease, computed tomography, emphysema, lung cancer.

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ÖZ

Amaç: Çalışmada, akciğer kanseri ve kronik obstrüktif akciğer hastalığı (KOAH) birlikteliğinde amfizemin fenotipik özellikleriyle ilişkisi incelendi.

Gereç ve Yöntemler: Bu çalışmada, 01 Ocak 2016 ve 31 Aralık 2018 tarihleri arasında akciğer kanseri tanısı almış, aynı zamanda KOAH tanısı da bulunan hastalar retrospektif olarak değerlendirildi.

Bulgular: Çalışmada 248 hasta değerlendirildi. Amfizemin fenotipi ve şiddeti ile tümörün histolojik tip ve lokalizasyonu arasında ilişki bulunmadı. Ancak vizüel amfizem fenotipleri ile beden kitle indeksi (BKİ) (p=0,003) ve birinci saniyedeki zorlu ekspiratuvar volüm (FEV_1)/zorlu vital kapasite (FVC) (p=0,003), sentrilobüler amfizem şiddeti ile BKİ (p<0,001), FEV_1 (p=0,004), FEV_1/FVC (p<0,001) ve paraseptal amfizem ile BKİ (p=0,003) arasında anlamlı ilişki saptandı. Ayrıca KOAH evreleri ve BKİ (p=0,007), FEV_1 (p<0,001), FEV_1/FVC (p<0,001), cerrahi oranı (p<0,001) arasında da anlamlı ilişki tespit edildi. Akciğer kanseri ile tümör lokalizasyonu (p<0,001), histolojik tip (p=0,018) ve cerrahi oranı (p<0,001) arasında da anlamlı ilişki gözlendi.

Sonuç: Parankim hasarıyla giden amfizemin bilgisayarlı tomografinin kantitatif değerlendirilmesiyle ortaya konulan vizüel tip ve ciddiyeti ile akciğer kanserinin histolojik tip ve lokalizasyonu arasında herhangi bir ilişki saptanmadı. Hasta popülasyonunun %72,2'sinde izlenen sentrilobüler amfizem anlamlı bir oran olsa da kontrol grubunun yokluğu nedeniyle istatistiksel değerlendirme yapılmadı. Literatüre bakıldığında da vizüel amfizem fenotiplerinin şiddeti ile akciğer kanseri arasındaki ilişkiyi inceleyen herhangi bir çalışma bulunmadı. İleride daha fazla hasta sayısı ile kontrol grubu içeren çalışmalara gereksinim bulunmaktadır.

Anahtar kelimeler: Akciğer kanseri, amfizem, bilgisayarlı tomografi, kronik obstrüktif akciğer hastalığı.

INTRODUCTION

Lung cancer and chronic obstructive pulmonary disease (COPD) are the most common lung diseases. Lung cancer is the first type of cancer among men and is also the most common cause of cancer-related death worldwide.[1,2] COPD, on the other hand, causes progressive and devastating lung dysfunction and ranks fifth among the causes of death among all diseases.[3,4] COPD is a phenotypically complex disease with incomplete reversal due to tissue damage, in which small airway disease and emphysema may occur together or separately.[4]

Many meta-analyses have shown a strong relationship between airway obstruction and emphysema and lung cancer.[5,6] Although smoking is a common risk factor for both diseases, COPD poses a risk for lung cancer independent of smoking.[7] This situation can be explained by the fact that events such as inflammation, extracellular matrix proteolysis, telomere shortening, oxidative stress, and genetic predisposition, which are thought to play an active role in the pathophysiology of COPD, also it is important in the pathophysiology of lung cancer.[3]

According to the dominant pathological change, COPD is divided into two important phenotypes: Emphysema dominant type and chronic bronchitis dominant type.[3] If emphysema is the dominant type, it is visually classified as centrilobular emphysema (CLE), panlobular emphysema, and paraseptal emphysema (PSE), and its distinction is made by computed tomography (CT).[8] CT is the best method used in the non-invasive diagnosis of emphysema.[9] CT examination shows the distribution of emphysema but cannot give us information about the severity of the disease. The quantitative evaluation of CT provides an idea about both its severity and its lobar distribution.[10]

In our study, to understand the relationship between emphysema and lung cancer, we aimed to see the relationship between visual emphysema type and severity and lung cancer type and localization using the quantitative evaluation of CT images in patients followed up with the diagnosis of lung cancer and COPD.

MATERIAL AND METHODS

Patients with lung cancer and COPD and followed up in Izmir Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital between January 01, 2016, and December 31, 2018, were evaluated retrospectively. Age, gender, smoking history, body mass index (BMI), pulmonary function test (PFT) parameters, and thorax CT images of the patients were recorded.

Spirometry was performed with the Spire ZAN 100 device. Postbronchodilator forced expiratory volume in 1 second/forced vital capacity (FEV_1/FVC) values below 0.7 were evaluated as COPD according to Global Initiative for Chronic Obstructive Lung Disease.[11] COPD was graded as FEV_1% ≥0.8 mild, 0.5 ≤FEV_1% <0.8 moderate, 0.3 ≤FEV_1% <0.5 severe, and FEV_1% <0.3 very severe.

In our hospital, 64 detectors 126 slice Hitachi CT devices are used in CT scans. The degree and type of emphysema were classified as centrilobular (subclassified as trace, mild, moderate, confluent, and advanced destructive emphysema), panlobular, and paraseptal (subclassified as mild or substantial) by the radiologist according to the Fleischner Society guidelines.[8]

Localization, histological type, and stage of the tumor were recorded. Patients were staged according to the 8th staging system of lung cancer recommended by the International Association for the Study of Lung Cancer.

All of the patients included in the study were over the age of 40, the diagnosis of COPD was made at least 6 months before the diagnosis of lung cancer, all of them had thoracic CT and PFT at the time of diagnosis.

Patients with diseases such as asthma, lung fibrosis, tuberculosis, and bronchiectasis were not included in the study.

Our study was approved by the ethical committee with the decision dated December 14, 2018 and numbered T.39 K.N:9.

Statistical Analysis

Categorical data were described using observed frequencies and percentages, and continuous variables were summarized by their means and standard deviations (or medians and interquartile ranges when distribution is skewed). Statistical analyses were performed with IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, N.Y., USA). All tests were two-sided and the significance level was set to 5%.

The normality assumption of parametric tests for numerical variables was checked with Shapiro-Wilk test. Age, BMI, FEV_1, and FEV_1/FEVC numerical variables were compared between levels of categorical variables with interdependent sample t-test and analysis of variance (ANOVA) according to the presence of two or more levels or, alternatively Mann-Whitney U-test and Kruskal-Wallis test was used. Tukey's honestly significant difference *post hoc* test was used after checking the assumption of homogeneity of variances with Levene's test in ANOVA. Dunn's test was applied as *post hoc* with Bonferroni correction for pairwise comparison in Kruskal-Wallis. Associations between two categorical variable were investigated with Chi-square test or Fisher Exact test (in some situations P-values estimated by Monte Carlo sampling).

RESULTS

The records of 248 patients diagnosed COPD and also lung cancer diagnosis in our clinic between January 01, 2016, and December 31, 2018, were evaluated retrospectively.

The mean age of the patients was 64.1 (±8.4) years, 95.2% of the patients were male. The median BMI was 24.4 kg/m2 (21.2–27.3), only one (0.4%) of the patients had never smoked. The mean FEV_1 of the patients was 54.6% (±16). Table 1 shows the demographic and clinical characteristics of the patients.

In our study, no correlation was found between visual emphysema phenotypes and age, gender, FEV_1, COPD and lung cancer stage, tumor localization, and histological type (p=0.124, p=0.062, p=0.077, p=0.487, p=0.301, p=0.055, and p=0.732, respectively), a significant correlation was observed between BMI and FEV_1/FVC and emphysema phenotypes. In the coexistence of CLE and PSE, BMI was found to be low, while it was higher in the group without emphysema (p=0.003). FEV_1/FVC was significantly lower in CLE group compared to the PSE group and the group without emphysema (p=0.003) (Table 2).

A significant correlation was observed with BMI, FEV_1, and FEV_1/FVC according to the grade of CLE. As with other parameters, no correlation was found with LC histological types. It was observed that BMI, FEV_1, and FEV_1/FVC decreased as the CLE grade increased (respectively p<0.001, p=0.004, and p<0.001). An inversely proportional relationship was found between PSE grade and only BMI (p=0.003). The relevant data about CLE and PSE are discussed in Tables 3 and 4.

When evaluated according to COPD stages without considering visual emphysema, a strong inverse correlation was found between BMI, FEV_1, FEV_1/FVC, and the number of operable patients (p=0.007, p<0.001, p<0.001, and p=0.001, respectively).

Table 1: Clinical characteristics of patients

Characteristic	Study sample (n=248)	
	n	%
COPD severity		
Mild	14	5.6
Moderate	130	52.4
Severe	91	36.7
Extremely severe	13	5.3
Lung cancer stage		
Stage 1	29	11.7
Stage 2	40	16.1
Stage 3	102	41.1
Stage 4	77	31.1
Visual emphysema		
None	47	18.9
Centrilobular	80	32.3
Paraseptal	22	8.9
Centrilobular/paraseptal	99	39.9
Centrilobular emphysema		
None	69	27.8
Mild	70	28.2
Moderate	43	17.3
Confluent	40	16.2
Advance	26	10.5
Paraseptal emphysema		
None	127	51.2
Mild	102	41.1
Moderate		–
Confluent	19	7.7
Advance		–
Frequent exacerbation		
Yes	1	0.4
No	247	99.6
Tumor location		
Central region	79	31.9
Periphery	169	68.1
Histologic profile		
Adenocarcinoma	76	30.7
Squamous cell carcinoma	133	53.6
Small cell carcinoma	15	6.0
Other	24	9.7
Treatment		
Surgery	60	24.2
Non-surgery	188	75.8

COPD: Chronic obstructive pulmonary disease.

Table 2: Characteristics of visual emphysema

Characteristics	None (n=47)		Centrilobular (n=80)		Paraseptal (n=22)		Centrilobular/ Paraseptal (n=99)		p
	n	%	n	%	n	%	n	%	
Age, years, mean (SD)	64.6	8.8	65.5	9.1	61.0	8.2	63.5	7.4	0.124
Sex									0.062
Male	41	87.2	78	97.5	21	95.5	96	97.0	
Female	6	12.8	2	2.5	1	4.5	3	3.0	
BMI, kg/m^2, median	25.7		24.7		24.4		23.5[a]		**0.003**
(25th–75th percentile)	(23.9–29.4)		(21.4–28.4)		(20.2–26.8)		(20.8–26.0)		
FEV_1, mean (SD)	56.3 (13.9)		51.0 (17.1)		59.0 (16.5)		55.3 (15.5)		0.077
FEV_1/FVC, median	68.0		64.0[a]		70.0[b]		65.0		**0.003**
(25th–75th percentile)	(63.0–72.0)		(52.0–69.0)		(64.0–74.0)		(58.0–70.0)		
COPD severity									
Mild	2	4.3	4	5.0	1	4.5	7	7.1	0.478
Moderate	28	59.6	35	43.8	14	63.6	53	53.5	
Severe	17	36.1	34	42.5	6	27.3	34	34.3	
Extremely severe	0	0.0	7	8.7	1	4.6	5	5.1	
Lung cancer stage									0.301
Stage 1	7	14.9	9	11.3	3	13.6	10	10.1	
Stage 2	13	27.7	13	16.3	2	9.1	12	12.1	
Stage 3	18	38.3	35	43.7	10	45.5	39	39.4	
Stage 4	9	19.1	23	28.7	7	31.8	38	38.4	
Tumor location									0.055
Central region	13	27.7	20	25.0	12	54.5	34	34.3	
Peripheric	34	72.3	60	75.0	10	45.5	65	65.7	
Histologic profile									0.732
Adenocarcinoma	12	25.5	30	37.5	5	22.7	29	29.3	
Squamous cell carcinoma	28	59.6	39	48.8	14	63.6	52	52.5	
Small cell carcinoma	1	2.1	5	6.2	1	4.6	8	8.1	
Other	6	12.8	6	7.5	2	9.1	10	10.1	
Treatment									0.177
Surgery	17	36.2	16	20.0	4	18.2	23	23.2	
Non-surgery	30	63.8	84	80.0	18	81.8	76	76.8	

[a]: Significant difference with none group, p<0.05, [b]: Significant difference with centrilobuler group, p<0.05. BMI: Body mass index, FEV_1: Forced expiratory volume in 1 second, FVC: Forced vital capacity, COPD: Chronic obstructive pulmonary disease.

Lung cancer patients were followed up in our clinic, 76 (30.7%) patients were diagnosed with adenocarcinoma, 133 (53.6%) of them were squamous cell carcinoma, 15 (6.0%) patients were small cell carcinoma, and 24 (9.7%) of them were other types of lung cancer (neuroendocrine carcinoma, large cell carcinoma, carcinoid, and adenosquamous). The lesion was located peripherally in 169 (68.1%) of the patients. One hundred and seventy-nine (72.2%) patients were stage 3 and 4. Sixty (24.2%) patients were operated.

In our study, a significant correlation was observed between lung cancer stage and tumor localization, histological type, and surgical treatment (p=0.001, p=0.018, p<0.001) (Table 5). Centrally located tumors were predominantly (46.1%) detected in stage 3. Histology and stages of the lung cancer are explained in Table 5. Squamous cell lung cancer and small cell lung cancer tended to be located centrally (p=0.001). Patients who underwent surgical treatment were also predominantly in the tumor group with peripheral localization (30.2%) (p=0.001).

DISCUSSION

COPD is a heterogeneous disease and is an independent risk factor for lung cancer.[5,10] Components of chronic bronchitis and emphysema

Table 3: Characteristics of centrilobular emphysema

Characteristics	None (n=69)		Mild (n=70)		Moderate (n=43)		Confluent (n=40)		Advance (n=26)		p
	n	%	n	%	n	%	n	%	n	%	
Age, years, mean (SD)	63.5	8.7	63.7	9.0	64.1	7.3	64.7	7.9	66.2	8.4	0.655
Sex											0.151
Male	62	89.9	68	97.1	42	97.7	38	95.0	26	100	
Female	7	10.1	2	2.9	1	2.3	2	5.0	0	0.0	
BMI, kg/m^2, median	25.3		25.2		24.4		21.8[a,b]		20.5[a,b]		**<0.001**
(25th–75th percentile)	(21.8–27.9)		(23.1–28.2)		(20.8–26.6)		(20.4–25.0)		(19.0–24.2)		
FEV_1, mean (SD)	57.2 (14.7)		53.3 (16.9)		60.1 (15.5)		51.5 (16.0)		46.7[a,c] (13.7)		**0.004**
FEV_1/FVC, median	68.0		66.0		66.0		60.5[a,b]		54.0[a,b,c]		**<0.001**
(25th–75th percentile)	(63.5–72.0)		(62.0–72.0)		(58.0–72.0)		(49.0–67.5)		(46.0–64.0)		
COPD severity											0.073
Mild	3	4.4	3	4.4	4	9.3	3	7.5	1	3.8	
Moderate	42	60.9	37	52.9	26	60.5	15	37.5	10	38.5	
Severe	23	33.3	24	34.3	13	30.2	20	50.0	11	42.3	
Extremely severe	1	1.4	6	8.6	0	0.0	2	5.0	4	15.4	
Lung cancer stage											0.539
Stage 1	10	14.5	4	5.7	6	14.0	6	15.0	3	11.5	
Stage 2	15	21.7	10	14.3	7	16.3	5	12.5	3	11.5	
Stage 3	28	40.6	27	38.6	20	46.5	15	37.5	12	46.2	
Stage 4	16	23.2	29	41.4	10	23.2	14	35.0	8	30.8	
Tumor location											0.126
Central region	25	36.2	26	37.1	7	16.3	11	27.5	10	38.5	
Peripheric	44	63.8	44	62.9	36	83.7	29	72.5	16	61.5	
Histologic profile											0.170
Adenocarcinoma	17	24.6	17	24.2	14	32.5	16	40.0	12	46.2	
Squamous cell carcinoma	42	60.9	37	52.9	25	58.1	18	45.0	11	42.3	
Small cell carcinoma	2	2.9	9	12.9	2	4.7	1	2.5	1	3.8	
Other	8	11.6	7	10.0	2	4.7	5	12.5	2	7.7	
Treatment											0.228
Surgery	21	30.4	13	18.6	14	32.6	7	17.5	5	19.2	
Non-surgery	48	69.6	57	81.4	29	67.4	33	82.5	21	80.8	

[a]: Significant difference with none group, p<0.05, [b]: Significant difference with mild group, p<0.05, [c]: Significant difference with moderate group, p<0.05. BMI: Body mass index, FEV_1: Forced expiratory volume in 1 second, FVC: Forced vital capacity, COPD: Chronic obstructive pulmonary disease.

may be completely separate or may be together to some extent. This condition is expressed as chronic bronchitis dominant or emphysema dominant. Similarly, lung cancer is a heterogeneous disease consisting of different histological subtypes. In the etiology of both, there are many common causes such as smoking habits, environmental exposure, genetics, and previous diseases. In this study, we wanted to examine the relationship between different histological types in lung cancer and the phenotypic type and severity of emphysema.

Lung cancer patients followed up in our hospital were retrospectively evaluated. Two hundred and forty-eight patients with concurrent COPD were included in the study. Two hundred and forty-seven (99.6%) patients had a history of smoking. This reminded us again of the importance of smoking in the etiology of both lung cancer and COPD.

Only 18.9% of our patients with lung cancer and COPD coexistence did not have emphysema. About 39.9% of the patients had PSE and CLE together and 32.3% of them had only CLE. Although CLE was observed in most of the patients (72.2%), there can be a relationship between CLE and lung cancer, but because we did not have a control group that we could not statistically state this result. Mouronte-Roibás et al.[12] found emphysema in 82.2% of the patients with lung cancer, similar to our study, in their study consisting of patients diagnosed with lung cancer with concurrent COPD and a con-

Table 4: Characteristics of paraseptal emphysema

Characteristics	None (n=127)		Mild (n=102)		Confluent (n=19)		p
	n	%	n	%	n	%	
Age, years, mean (SD)	65.1	9	63	7.7	63.1	7.1	0.146
Sex							0.419
Male	119	93.7	98	96.1	19	100.0	
Female	8	6.3	4	3.9	0	0.0	
BMI, kg/m^2, median (25^{th}–75^{th} percentile)	25.0 (21.8–28.4)		23.8[a] (20.8–26.4)		22.6[a] (20.1–25.5)		**0.003**
FEV_1, mean (SD)	53 (16.2)		56.1 (15.8)		57.3 (15.1)		0.249
FEV_1/FVC, median (25th–75th percentile)	65.0 (55.0–70.0)		65.0 (59.0–72.0)		66.0 (55.0–70.0)		0.524
COPD severity							0.457
Mild	6	4.7	6	5.9	2	10.5	
Moderate	63	49.6	55	53.9	12	63.2	
Severe	51	40.2	37	36.3	3	15.8	
Extremely severe	7	5.5	4	3.9	2	10.5	
Lung cancer stage							0.406
Stage 1	16	12.6	11	10.8	2	10.5	
Stage 2	26	20.5	12	11.8	2	10.5	
Stage 3	53	41.7	41	40.2	8	42.2	
Stage 4	32	25.2	38	37.2	7	36.8	
Tumor location							
Central region	33	26.0	40	39.2	6	31.6	0.102
Peripheric	94	74.0	62	60.8	13	68.4	
Histologic profile							0.922
Adenocarcinoma	42	33.1	28	27.4	6	31.6	
Squamous cell carcinoma	67	52.8	57	55.9	9	47.4	
Small cell carcinoma	6	4.7	7	6.9	2	10.5	
Other	12	9.4	10	9.8	2	10.5	
Treatment							0.789
Surgery	33	26.0	23	22.5	4	21.1	
Non-surgery	94	74.0	79	77.5	15	78.9	

[a]: Significant difference with none group, p<0.05. BMI: Body mass index, FEV_1: Forced expiratory volume in 1 second, FVC: Forced vital capacity, COPD: Chronic obstructive pulmonary disease.

trol group consisting of patients diagnosed with COPD only, and they also found that 71.2% of patients had CLE. They found a statistically significant relationship between lung cancer and CLE compared to the control group. The absence of a control group is the limiting factor of our study, and we think that we will obtain more meaningful results by forming a control group in the future.

The BMI of our patients with lung cancer without visual emphysema was significantly higher than the other groups (p=0.003). In particular, we found that BMI was the lowest in patients with CLE and PSE. When we examined the studies of Wang et al.,[1] in contrast to our study, BMI was found to be lower in lung cancer arm without COPD (p<0.001). Interestingly, in another study by Wang, the BMI value of patients with LC was significantly higher than patients without lung cancer (p<0.001), while no difference was found between the emphysema dominated group and the non-emphysema-dominant group in terms of BMI (p=0.348).[3]

When we evaluated the visual emphysema phenotypes separately as CLE and PSE, we found an inversely proportional relationship between CLE grade and BMI, FEV_1, and FEV_1/FVC, but we also found a similar relationship between PSE grade and BMI alone. As the degree of CLE increased, the percentage of adenocarcinoma increased (none-24.6%, advance-46.2%), the percent-

Table 5: Characteristics of lung cancer stages

Characteristics	Stage 1 (n=29)		Stage 2 (n=40)		Stage 3 (n=102)		Stage 4 (n=77)		p
	n	%	n	%	n	%	n	%	
Age, years, mean (SD)	67.1	6.8	62	8.3	64.2	9	64	7.9	0.091
Sex									0.986
Male	28	96.6	38	95.0	97	95.1	73	94.8	
Female	1	3.4	2	5.0	5	4.9	4	5.2	
BMI, kg/m^2, median (25th–75th percentile)	24.4 (21.6–26.8)		24.9 (22.3–28)		24.6 (21.3–27.7)		23.1 (20.9–26.2)		0.282
FEV_1, median (25th–75th percentile)	56.0 (46.0–66.0)		58.0 (46.0–71.0)		55.5 (41.0–65.0)		49.0 (39.0–64.0)		0.154
FEV_1/FVC, median (25th–75th percentile)	67.0 (60.0–71.0)		67.0 (60.5–70.0)		66.0 (55.0–72.0)		64.0 (56.0–70.0)		0.752
Tumor location									**<0.001**
Central region	0	0.0	4	10.0	47	46.1	28	36.4	
Peripheric	29	100.0	36	90.0	55	53.9	49	63.6	
Histologic profile									**0.018***
Adenocarcinoma	11	37.9	16	40.0	29	28.4	20	26.0	
Squamous cell carcinoma	17	58.6	21	52.5	61	59.8	34	44.1	
Small cell carcinoma	0	0.0	1	2.5	3	2.9	11	14.3	
Other	1	3.5	2	5.0	9	8.9	12	15.6	
Treatment									**<0.001**
Surgery	11	37.9	27	67.5	22	21.6	0	0.0	
Non-surgery	18	62.1	13	32.5	80	78.4	77	100.0	

*: Based on Monte Carlo sampling. BMI: Body mass index, FEV_1: Forced expiratory volume in 1 second, FVC: Forced vital capacity.

age of squamous cell carcinoma decreased inversely (none-60.9%, advance-42.3%), the rates were close to each other in the PSE group, except for small cell carcinoma. In small cell carcinoma, we observed that as the severity of PSE increased, the percentage also increased (none-4.7%, confluent-10.5%). We could not detect any relationship between lung cancer and CLE and PSE, We thought that we could not reach any significant result due to the small number of patients. When we searched the literature, we could not find an article investigating the relationship between the severity of CLE and PSE and lung cancer.

As the COPD stage progressed, BMI, FEV_1, FEV_1/FVC, and the number of patients who could be treated surgically decreased incompatible with the literature. Although similar studies are numerous, Huber et al.[13] studies have shown a decrease in BMI and FEV_1 with an increase in a stage in COPD.

In our study, squamous and small cell lung cancer tended to be predominantly centrally located, in accordance with our knowledge. In their study, Hajmanoochehri et al.[14] found also that squamous cell lung cancer and small cell lung cancer were mostly located in the central and adenocarcinoma lung cancer was located peripherally (p<0.001).

In conclusion, We could not find any correlation between visual emphysema phenotype and severity with lung cancer histological type and location. In the future, we aim to reschedule the study by increasing the number of patients and creating a control group, which are the two limiting factors of our study.

Disclosures

Ethics Committee Approval: The study was approved by The University of Health Sciences Dr. Suat Seren Chest Diseases and Surgery Training and Research Hospital Ethics Committee (date: 14.12.2018, number: T.39 K.N:9).

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REFERENCES

1. Wang W, Dou S, Dong W, Xie M, Cui L, Zheng C, et al. Impact of COPD on prognosis of lung cancer: From a perspective on disease heterogeneity. Int J Chron Obstruct Pulmon Dis 2018;13:3767–76.

2. Schabath MB, Cote ML. Cancer progress and priorities: Lung cancer. Cancer Epidemiol Biomarkers Prev 2019;28:1563–79.
3. Wang W, Xie M, Dou S, Cui L, Zheng C, Xiao W. The link between chronic obstructive pulmonary disease phenotypes and histological subtypes of lung cancer: A case-control study. Int J Chron Obstruct Pulmon Dis 2018;13:1167–75.
4. El-Zein RA, Young RP, Hopkins RJ, Etzel CJ. Genetic predisposition to chronic obstructive pulmonary disease and/or lung cancer: Important considerations when evaluating risk. Cancer Prev Res (Phila) 2012;5:522–7.
5. González J, Henschke CI, Yankelevitz DF, Seijo LM, Reeves AP, Yip R, et al. Emphysema phenotypes and lung cancer risk. PLoS One 2019;14:e0219187.
6. Carr LL, Jacobson S, Lynch DA, Foreman MG, Flenaugh EL, Hersh CP, et al. Features of COPD as predictors of lung cancer. Chest 2018;153:1326–35.
7. Schwartz AG, Lusk CM, Wenzlaff AS, Watza D, Pandolfi S, Mantha L, et al. Risk of lung cancer associated with COPD phenotype based on quantitative ımage analysis. Cancer Epidemiol Biomarkers Prev 2016;25:1341–7.
8. Lynch DA, Austin JH, Hogg JC, Grenier PA, Kauczor HU, Bankier AA, et al. CT-Definable subtypes of chronic obstructive pulmonary disease: A statement of the fleischner society. Radiology 2015;277:192–205.
9. Tubío-Pérez RA, Torres-Durán M, Pérez-Ríos M, Fernández-Villar A, Ruano-Raviña A. Lung emphysema and lung cancer: What do we know about it? Ann Transl Med 2020;8:1471.
10. Park J, Hobbs BD, Crapo JD, Make BJ, Regan EA, Humphries S, et al. Subtyping COPD by using visual and quantitative CT imaging features. Chest 2020;157:47–60.
11. Vogelmeier C, Agusti A, Anzueto A, Barnes P, Bourbeau J, Criner G, et al. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary Disease 2021 Report. Available at: http:// goldcopd. org. Accessed Dec 12, 2020.
12. Mouronte-Roibás C, Fernández-Villar A, Ruano-Raviña A, Ramos-Hernández C, Tilve-Gómez A, Rodríguez-Fernández P, et al. Influence of the type of emphysema in the relationship between COPD and lung cancer. Int J Chron Obstruct Pulmon Dis 2018;13:3563–70.
13. Huber MB, Kurz C, Kirsch F, Schwarzkopf L, Schramm A, Leidl R. The relationship between body mass index and health-related quality of life in COPD: Real-world evidence based on claims and survey data. Respir Res 2020;21:291.
14. Hajmanoochehri F, Mohammadi N, Zohal MA, Sodagar A, Ebtehaj M. Epidemiological and clinicopathological characteristics of lung cancer in a teaching hospital in Iran. Asian Pac J Cancer Prev 2014;15:2495–500.