

Trends in lung cancer incidence within the last 10 years: An Eastern Anatolian single center experience

Son 10 yıldaki akciğer kanseri insidansındaki eğilimler: Doğu Anadolu'da tek merkez deneyimi

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Abstract

Aim: Lung cancer is the most common cause of cancer-related deaths among men and women, and mortality and morbidity rates vary according to different histological groups. Therefore, histological type determination is extremely important. The purpose of the study is to investigate the histological subtypes of lung cancer cases within the last 10 years in one of the biggest centers of the Eastern Anatolian Region, considering the changes made in the 2015 updates in lung tumors by World Health Organization (WHO), and investigate the relationship between these histological sub-types and distribution according to year, gender and age.

Methods: In this cross-sectional study, patients who were referred for lung biopsy between January 2010 and December 2019 and diagnosed with lung carcinoma were retrospectively analyzed.

Results: Our study shows that the frequency of lung cancer, along with histological subtypes, has increased throughout the years. The most common lung cancer type, regardless of gender, is Squamous Cell Carcinoma (SCC), followed by Small Cell Lung Carcinoma (SCLC) and Adenocarcinoma. Adenocarcinoma and SHC were the most common subtypes among females and males, respectively. A significant relationship was observed between gender and histological type ($P<0.001$).

Conclusion: The data from our study suggest that the incidence of lung cancer increased throughout the years, similar to the data from our country and other developing countries around the world. In terms of subtypes, among developing countries, Adenocarcinoma rate increased while SCC rate decreased. In our study, the most common histological types increased at a similar rate. Adenocarcinoma was the most common lung cancer among females, similar to other developing countries. The most common lung cancer overall remained the same: SCC. This was considered an indication of the unchanged smoking habits of males.

Keywords: Lung cancer, Histopathology, Incidence

Öz

Amaç: Akciğer kanseri kadın ve erkeklerde kansere bağlı ölümlerin en sık nedeni olup farklı histolojik gruplara göre mortalite ve morbidite oranı değişkenlik göstermektedir. Bu nedenle histolojik tip tayini son derece önemlidir. Çalışmamızın amacı, 2015 Dünya Sağlık Örgütü (DSÖ) Akciğer tümörlerinin güncellenmesinde yapılan değişiklikleri temel alarak Doğu Anadolu Bölgesindeki en büyük merkezlerden birisinde son 10 yılda akciğer kanseri tanısı almış vakaların histolojik alt tiplerini ve aynı zamanda bu histolojik alt tiplerin yıl, cinsiyet ve yaş dağılımı arasındaki ilişkisini incelemektir.

Yöntemler: Kesitsel tipteki bu çalışmada, Ocak 2010-Aralık 2019 yılları arasında merkezimizde akciğer biyopsi materyali olarak gönderilmiş ve akciğer karsinomu tanılı olgular retrospektif olarak incelenmiştir.

Bulgular: Çalışmamızda akciğer kanseri sıklığı yıllara göre artmış olup histolojik tipler benzer oranda artmıştır. En fazla görülen akciğer kanseri tipi kadın ve erkeklerin toplamında sırasıyla Skuamöz Hücreli Karsinom (SHK), Küçük Hücreli Akciğer Karsinomu (KHAK) ve Adenokarsinomdur. Kadınlarda en fazla adenokarsinom, erkeklerde ise SHK görülmüş olup istatistiksel olarak cinsiyet ile histolojik tip arasında anlamlı bir ilişki izlenmiştir ($P<0,001$).

Sonuç: Çalışmamızda ülkemizdeki ve gelişmekte olan ülkelerdeki veriler ile benzer şekilde akciğer kanseri sıklığında yıllara göre bir artış izlenmiştir. Gelişmiş ülkelerde adenokarsinom sıklığı artarken SHK sıklığı azalmıştır. Çalışmamızda ise en fazla görülen histolojik tipler benzer oranda artmıştır. Bunun yanı sıra gelişmiş ülkelerle benzer şekilde kadınlarda en fazla görülen akciğer kanseri tipi adenokarsinom olarak bulunmuştur. Tüm popülasyonda ise en sık görülen akciğer kanser tipi değişmemiş olup halen SHK dur. Bu durum erkeklerde sigara içme alışkanlığındaki değişikliklerin olmaması ile ilişkilendirilebilir.

Anahtar kelimeler: Akciğer Kanseri, Histopatoloji, İnsidans

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Introduction

Lung cancer is the most common cause of cancer-related deaths among men and women, and mortality and morbidity rates vary according to different histological groups. In 2019, there were 228,150 new cases only in the United States of America [1]. Lung cancers are clinically separated into two main groups as Small Cell Lung Carcinoma (SCLC) and Non-small Cell Lung Carcinoma (NSCLC) based on differences in treatment. SCLC cases constitute 13% while NSCLC constitutes 83% of the cases; however, histological sub-type of 3% of the lung cancer cases is unknown [1, 2].

SCLC is treated by chemo-radiotherapy instead of surgery, because the tumor is usually at an advanced stage at the time of diagnosis. On the other hand, NSCLC generally has a chance for surgical operation [3]. Due to the differences in treatment, detection of histological type is crucial for lung neoplasia. WHO reclassified lung neoplasia in terms of their pathologies in 2015 and made many changes to the 2004 classification. Epithelial malignancy is the most common one among lung malignancies and they are mainly categorized as follows based on the new classification (Table 1).

Table 1: WHO 2015 lung cancer classification [4]

Adenocarcinoma	Sarcomatoid carcinoma (SC)
Squamous Cell Carcinoma (SCC)	Pleomorphic carcinoma
Neuroendocrine Carcinoma	Fusiform Cell carcinoma
Small Cell Carcinoma (SCLC)	Giant Cell carcinoma
Large Cell Neuroendocrine Carcinoma (LCNC)	Carcinosarcoma
Large Cell Carcinoma (LCC)	Pulmonary blastoma
Adenosquamous Carcinoma (ASC)	Unclassified and Other carcinomas
	Lymphoepithelioma-like Carcinoma
	NUT carcinoma

There are various main categories other than epithelial neoplasia that are less frequent, namely, Mesenchymal Neoplasia, Lymphohistiocytic Tumors, Ectopic Tumors, and Metastatic Tumors [4]. The purpose of the study is to investigate the histological subtypes of lung cancer within the last 10 years in the Medical Pathology Department of one of the biggest centers of Eastern Anatolian Region, considering the changes made with the 2015 updates, and investigate the relationship between these histological sub-types and distribution according to year, gender and age.

Materials and methods

The study involved 1242 lung carcinoma cases that were referred to our center for lung biopsy between January 2010-December 2019. Based on 2015 WHO classification, two pathologists evaluated paraffin blocks, hematoxylin-eosin (H&E) and immunohistochemical slides of each case, and their pathology reports. The cases were divided according to their histological subtypes. The relationship between gender, age, year, and these sub-categories was investigated. Clinical information such as the gender and age of patients, and year of the cases were obtained from the hospital registry. The cases that missed any of the clinical information were excluded from the study. The study was ethically approved by the local ethics committee by the decision numbered B.30.2.ATA.0.01.00/46.

Statistical analysis

Statistical analysis was performed using IBM SPSS20. The data was presented as mean, standard deviation, median, minimum, maximum, percentage, and number. Normality of continuous variables was evaluated by the Shapiro Wilk-W test

when sample size was <50 and the Kolmogorov Smirnov test when sample size >50. Independent Samples t-test was used for comparison of normally distributed independent groups, whereas Mann Whitney U-test was utilized for comparing the non-normally distributed data. Pearson's chi-square test, Chi-square Yates test and Fisher's Exact test were used if the expected value in a 2x2 comparison between categorical values was >5, between 3-5 and <3, respectively. The coherence of the clinical golden standard and newly developed diagnosis test is evaluated by calculating Cohen's Kappa coefficient. A *P*-value <0.05 was considered statistically significant.

Results

The mean age of 1242 cases was 67 years, among which 1085 (87.4%) were males, and 157 (12.6%) were females. The male to female ratio was approximately 10/1. The mean age of the males and females were 65 and 69 years, respectively. There was no significant difference between females and males in terms of age (*P*=0.21).

Evaluation of the frequency of lung cancer throughout the years revealed that the highest and lowest number of diagnoses were made in 2019 and 2010. The number of new diagnoses stayed the same between 2010 and 2014. It escalated in 2015 and increased gradually thereafter (Table 2) (Figure 1).

Table 2: Lung cancer distribution by years

Year	n	%
2010	72	5.8
2011	78	6.28
2012	72	5.8
2013	86	6.92
2014	82	6.6
2015	128	10.31
2016	138	11.11
2017	171	13.77
2018	181	14.57
2019	234	18.84
TOTAL	1242	100

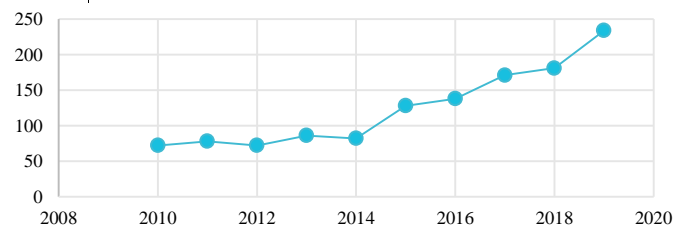


Figure 1: Lung cancer distribution by years

The percentages of the cases in terms of their classification were as follows: 578 cases were SCC (46.5%), 250 were SCLC (20.1%), 221 were adenocarcinoma (17.8%), 66 were Non-classified Carcinoma (NOS) (5.3%), 56 were Metastases (4.5%), 24 were LCNC (1.9%), 17 were Lymphoma (1.4%), 9 were Malign Mesenchymal Neoplasia (MMN) (0.7%), 7 were ASC (0.7%), 7 were LCC (0.7%), 7 were SK (0.7%). According to the pathological diagnosis, the most common one in the group was SCC, followed by SCLC and adenocarcinoma (Table 3). There was a significant relationship between gender and histological type (*P*<0.001). Adenocarcinoma was most common in women, while SCC was most common in men. Evaluation of the most frequent pathological diagnoses revealed that 45 out of 157 lung cancer cases in females were adenocarcinoma (28.6%), 43 were SCC (27.3%) and 31 were SCLC (19.7%). In males, 535 of 1085 lung cancer cases were SCC (49.3%), 219 were SCLC (20.1%), and 176 were (16.2%) adenocarcinoma.

When the distribution of pathological diagnoses was evaluated, it was observed that all pathological diagnoses had increased, but there was no significant relationship between the distribution by years and pathological diagnosis ($P=0.06$) (Table 4). Similarly, no significant relationship was observed between the distribution by years and gender ($P=0.13$) (Figures 2 and 3).

Table 3: The relationship between the three most common histological types and gender

	Adenocarcinoma	SCC	SCLC	P-value
Male	176	535	219	<0.001
Female	45	43	31	

SCC: Squamous Cell Carcinoma, SCLC: Small Cell Carcinoma

Table 4: Pathological diagnosis distribution by years

Year	Adeno carcinoma	SCC	MMN	Metastasis	ASC	LCNC	SCLC	SC	LCC	Lymphoma	NOS
2010	8	38	0	3	0	1	16	1	3	2	0
2011	13	40	0	6	0	4	12	1	1	1	0
2012	8	35	0	3	0	1	22	1	1	1	0
2013	9	43	0	3	2	2	26	0	0	0	1
2014	16	37	1	0	0	3	22	0	0	3	0
2015	15	72	3	3	0	2	23	0	0	3	7
2016	22	64	1	6	0	2	32	2	0	0	9
2017	28	77	1	11	0	2	25	0	0	3	24
2018	42	74	1	12	0	2	31	1	0	0	18
2019	60	98	2	9	5	5	41	1	2	4	7

SCC: Squamous Cell Carcinoma, ASC: Adenosquamous Carcinoma, LCC: Large Cell Carcinoma, SC: Sarcomatoid carcinoma, LCNC: Large Cell Neuroendocrine Carcinoma, SCLC: Small Cell Carcinoma NOS: Non-Classified Carcinoma, MMN: Malign Mesenchymal Neoplasia

Lung cancer is the primary cause of cancer-related deaths worldwide [6]. In the last decade, lung cancer incidence has significantly decreased in industrialized countries. Particularly, the decrease in males' smoking habits reduced lung cancer. Inversely, cultural change in industrialized countries increased the number of smoking females, causing an increase in lung cancer prevalence. The scenario for developing countries is slightly different. The difference is more distinct for females. In industrialized countries, lung cancer is more common in females compared to other countries [7]. In the United States of America and the United Kingdom, incidence and mortality rates of lung cancer have been decreasing since the 1990s. In a study dated 2014, which was conducted on 452,714 lung cancer cases between 1977-2010 in the USA, Lewis et al. [8] stated that lung cancer rate per 100,000 people had decreased after it peaked at the beginning of the 1990s. They particularly emphasized the decrease in the lung cancer rate among males. They underlined the fact that the decrease in SCC was more distinct and they linked this to the decrease in smoking, while also stating that adenocarcinoma had increased among females. On the other hand, the rate of lung cancer did not fluctuate in developing countries, particularly in Brazil, Russia, India, China, and South Africa since the rate of smoking in males and females was still high. According to GLOBOCAN 2012 data, in China, the rate of lung cancer was 21% among all cancers and the rate of lung-cancer related deaths was 27%. Consequently, it is the most common malignancy and the cause of cancer-related mortality [9].

In our study, it is seen that the rate of lung cancer has increased, like the data from other developing countries, and the greatest number of new diagnoses was observed in 2019. The number of cases stayed the same between 2010-2015. The number escalated in 2015 and increased gradually thereafter. The rate increased for both genders, and no significant relationship was observed between the gender of the patient and the increase in lung cancer.

Lung carcinomas are a heterogeneous tumor group with more than 50 subtypes [10]. To be able to benefit from the treatment most efficiently, histological identification and biomarker information should be obtained correctly. Thus, the identification of histological sub-types gains more importance for diagnosis and treatment [11]. Consequently, the WHO prepared a clearer classification of lung neoplasia to enable pathologists and clinicians to speak the same language. Lung cancers have been divided into two main groups for years: SCLC and NSCLC. The most common NSCLCs are adenocarcinoma, SCC and LCC. According to the WHO 2015 classification, SCC and adenocarcinoma have different subtypes, and a more detailed classification of the histological subtype is used in resection materials [11].

The frequency of adenocarcinoma increases gradually, and it is the most common lung cancer in developed countries [12]. Adenocarcinoma constitutes more than 40% of all lung cancers, and 60% of NSCLC. More than 70% of the surgically operated cases are adenocarcinoma [8, 11]. SCC constitutes 20% of lung cancers and its incidence in the developed countries has decreased in recent years. It is strong related to smoking [13]. Survival rate is higher for SCCs than adenocarcinomas. LCC,

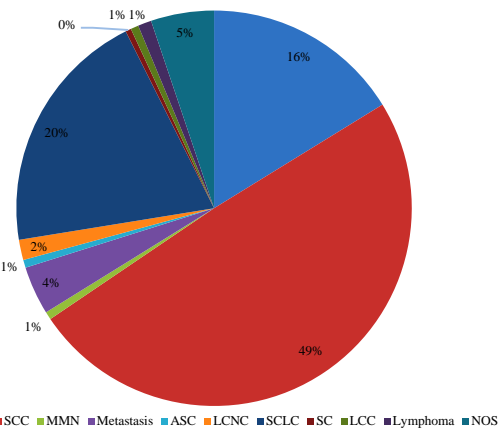


Figure 2: Distribution of pathological diagnoses in men (SCC: Squamous Cell Carcinoma, ASC: Adenosquamous Carcinoma, LCC: Large Cell Carcinoma, SC: Sarcomatoid carcinoma, LCNC: Large Cell Neuroendocrine Carcinoma, SCLC: Small Cell Carcinoma NOS: Non-Classified Carcinoma, MMN: Malign Mesenchymal Neoplasia)

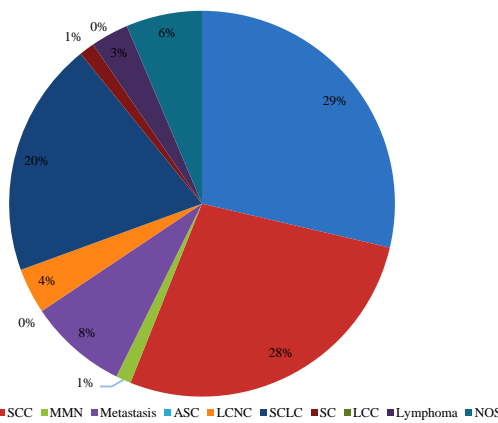


Figure 3: Distribution of pathological diagnoses in women (SCC: Squamous Cell Carcinoma, ASC: Adenosquamous Carcinoma, LCC: Large Cell Carcinoma, SC: Sarcomatoid carcinoma, LCNC: Large Cell Neuroendocrine Carcinoma, SCLC: Small Cell Carcinoma NOS: Non-Classified Carcinoma, MMN: Malign Mesenchymal Neoplasia)

Discussion

The incidence of lung cancer increases in the 6th and 7th decades, and it is most observed between 40-70 years of age. It is more common among males compared to females, the ratio of males to females being 9/1 [5]. In this study, this ratio was 10/1. The mean age of all cases was 67, which were both similar to the literature data.

used for NSCLC, does not specifically differentiate from, or carry the morphological and immunochemical features of adenocarcinoma, SCC, and neuroendocrine carcinoma. The frequency of the LCC is exceptionally low [14]. ASC is a rare lung carcinoma that constitutes 0.4-4% of all lung carcinomas. In 1978, the Japanese Lung Cancer Society reported that to be able to diagnose ASC, components of SCC and adenocarcinoma have to constitute 20% of each tumor [15]. In the last WHO classification, it is required for each component to form 10% of the tumor [16]. Pleomorphic, fusiform cell and giant cell carcinomas constitute less than 3% of lung cancers [11]. SCLC, which is an aggressive malignancy with common metastases, constitutes 10% of all lung cancers. In most cases, recurrence and metastases are observed within the first 2 years and survival rate is less than 10% [8].

Before the 1990s SCC was the most common histological sub-type, especially among males. Later, adenocarcinoma took the lead in the USA, Canada, most of the European countries and in Japan [7]. Among females, adenocarcinoma rates are higher compared to SCC and SCLC rates and its rate increases parallel to the increase in lung cancer incidence [17]. Similarly, in our study, adenocarcinoma was the most common subtype in females.

The frequency of the histological types reported by the studies in our country is different than those from developed countries but comparable to those conducted in developing countries. Goksel et al. [5] reported the SCC, SCLC and adenocarcinoma rates as 45.4%, 20.5% and 20.2%, respectively. Bircan et al. [18] reported the SCC, SCLC, adenocarcinoma and non-classified NCSLC rates as 37.9%, 14.9%, 12.6%, 26.4%, respectively. Yurdakul et al. [19] reported 77.7% of the cases as NCSLC, 15.5% as SCLC and 6.8% as non-classified malign epithelial tumors. In our study, the data were comparable with studies from our country and other developing countries: SCC was the most common subtype, followed by SCLC and adenocarcinoma. Histological diagnoses were significantly different among females and males: Adenocarcinoma was most common among females, whereas SCC was most common among males. Further evaluation revealed that 45 of 157 lung cancer cases in females were adenocarcinoma (28.6%), 43 were SCC (27.3%) and 31 were SCLC (19.7%). In males, 535 of 1085 lung cancer cases were SCC (49.3%), 219 were SCLC (20.1%), and 176 were (16.2%) adenocarcinoma.

Limitations

Since the mortality rate due to lung cancer is high in our region, data such as lifestyle, habit, exposure, and diet of the patients could not be evaluated adequately. Our unit has a significant role in reflecting the data from the region since it is a tertiary center serving most of the Eastern Anatolian Region. We believe that a comprehensive study that presents the epidemiological data is essential and should be conducted in the future.

Conclusion

Our data were similar to studies from our country and other developing countries, as it showed that the frequency of lung cancer increased by years. In developed countries, adenocarcinoma frequency increased, while SCC frequency decreased. The most common histological subtype in our study

increased at a similar rate. Besides, like developed countries, adenocarcinoma was found to be the most frequent lung cancer type among females. In this population, the most common lung cancer type remained the same, SCC. We presume that this finding is in accordance with the continued smoking habit of males.

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