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Factors affecting delay in diagnosis and treatment of lung cancer

Akciğer kanserinde tanı ve tedavi gecikme faktörleri

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Abstract

Aim: Lung cancer (LC) is one of the most prominant causes of mortality in the world. Delays in diagnosis and treatment gravely affect the prognosis of the disease. Our aim is to investigate the factors that affect delay in diagnosis and treatment in patients with LC.

Methods: In this retrospective cohort study, LC patients who were diagnosed in the pulmonary diseases clinic between January 2010 and August 2011 were retrospectively evaluated from patient files. The sociodemographic characteristics of the patients (age, gender, occupation and educational level), symptom type, presence of other malignancies, radiological location of the lesion, diagnostic method, histological type, presence of endobronchial lesion, stage of LC, length of times between admission, diagnosis and treatment were noted.

Results: One hundred seven (87.7%) patients were male and 15 patients (12.3%) were female. Eighty-nine patients (73%) were under the age of 70 years. Ninety-eight patients were diagnosed with non-small cell (NSCLC) and 24 patients, with small cell lung cancer (SCLC). The mean duration from symptom onset to admission to the hospital (SA), from symptom onset to pathological diagnosis (SP), from symptom onset to initiating treatment (ST), from admission to the hospital until pathological diagnosis (AP), from admission to the hospital until initiating treatment (AT) were 30, 60, 75,5, 14, 33 days, respectively. There were statistically significant differences between SP, AP, AT periods (P=0.017, P=0.011 and P=0.006 respectively) with regards to education levels, and between SA, SP, ST, and from symptom onset to performing an initial radiological examination (SR) periods in terms of social security institution (P<0.05 for all). AT time of patients with SCLC was shorter than that of patients with NSCLC.

Conclusion: Early diagnosis of LC is particularly important. Therefore, determination of factors affecting the delay in diagnosis and treatment of LC, probable causes, and solutions should be investigated.

Keywords: Lung cancer, Delays, Diagnosis, Treatment

Öz

Amaç: Akciğer kanseri dünya çapında en önemli mortalite nedenlerinden biridir. Tanı ve tedavi gecikmesi hastalığın prognozunu etkileyen en önemli faktörlerdendir. Amacımız; akciğer kanseri tanısı almış hastalarda tanı ve tedavi gecikmesini etkileyen faktörleri araştırmaktır.

Yöntemler: Ocak 2010 – Ağustos 2011 tarihleri arasında göğüs hastalıkları kliniğinde tanı konulan akciğer kanserli hastaların dosyaları retrospektif olarak incelendi. Hastaların sosyodemografik özellikleri (yaş, cinsiyet, meslek ve eğitim düzeyi), semptom tipi, başka malignite varlığı, lezyonun radyolojik lokalizasyonu, tanı yöntemi, histolojik tip, endobronşiyal lezyon varlığı, akciğer kanseri evresi, başvuru, tanı ve tedavi arasındaki sürelerin uzunluğu kaydedildi. Çalışma, retrospektif kohort çalışmasıdır.

Bulgular: Olguların 107’ si (%87,7) erkek ve 15’ i (%12,3) kadındı. 89 olgu (%73) 70 yaş altındaydı. 98 olgu küçük hücre dışı akciğer kanseri (KHDAK) iken 24 olgu küçük hücreli akciğer kanseri (KHAK) idi. Semptomlarının başlangıcından hastaneye başvurusuna (SB), semptomların başlangıcından patolojik tanıya (SP), tedavi başlangıcına (ST), başvurudan patolojik tanıya (BP), başvurudan tedavi başlangıcına (BT) kadar geçen ortalama süre sırayla 30, 60, 75,5, 14, 33 gün olarak bulundu. Öğrenim düzeyi ile SP, BP, BT süreleri (sırasıyla P=0,017, P=0,011 ve P=0,006); sosyal güvence ile SB, SP, ST, SR süreleri arasında istatistiksel olarak anlamlı farklılık saptandı (P<0,05 tümü için). KHAK’ de BT süresi KHDAK’ ye göre daha kısa olduğu saptandı

Sonuç: Akciğer kanserinde erken tanı konulması oldukça önemlidir. Bu nedenle tanı ve tedaviyi geciktirecek faktörlerin saptanması, olası nedenlerinin ve çözümlerinin araştırılması gerekmektedir.

Anahtar kelimeler: Akciğer kanseri, Gecikmeler, Tanı, Tedavi

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Introduction

Lung Cancer (LC) is a major cause of cancer-related morbidity and mortality and is responsible for an estimated 1.6 million new diagnoses and more than 1.4 million (13%) annual cancer deaths [1,2]. It is the third most common cancer, and the most frequent when considering both genders. The number of LC deaths has increased substantially due to increased prevalence of smoking and environmental pollution in industrialised countries within the last century [3].

Delay in diagnosis and treatment is a widespread problem in patients with lung and non-lung cancers. Many determinants play a role in diagnostic delay. They can be divided into delays in the patients' first seeking health care and delays within the health care system. Patient delay involves several factors, related to the patient's perception of symptoms, educational level, age, and perceived risk [4]. Diagnostic and treatment waiting times experienced by LC patients are the product of the disequilibrium between a healthcare system's supply and demand of diagnostic and treatment services, inefficient coordination between healthcare professionals, lack of defined diagnostic practice standards and an absence of system performance auditing mechanisms. Some trials show that treatment delays increase the risk of poor clinical outcomes and are associated with poorer patient experiences in subsequent cancer care [5,6]. Prolonged time between thorough radiological examination and biopsy has been reported to result in an increase in tumor size and stage [7]. Some authors showed that longer time to treatment was a significant negative prognostic factor in patients with stage III LC and in those with stage III LC undergoing surgical resection [8,9]. Early recognition of lung cancer symptoms combined with early medical help–seeking behavior can have the potential to increase survival and decrease mortality from LC [10-12]. To prevent this situation, suspected cases should be referred to centers where further examinations and treatment can be performed as soon as possible, and necessary procedures should be expeditiously performed.

The aim of the study was to investigate the factors that can affect the periods from onset of symptoms to diagnosis and the initiation of treatment.

Materials and methods

Totally, 122 (107 male and 15 female) patients who were admitted to the department of pulmonary diseases between January 2010 and August 2011 were included. Numerous factors causing a delay in diagnosis and treatment were investigated in patients who were diagnosed histologically with LC. The medical records of patients were reviewed retrospectively, and data were obtained and processed from the chest disease informed consent forms, which had been signed by each patient during admission to the hospital. This retrospective cohort study was conducted according to the Ethical Principles for Medical Research Involving Human Subjects (Declaration of Helsinki). The trial was approved by Research Ethics Committee and performed in accordance with accepted ethical standards (Ankara Ataturk Chest Diseases and Chest Surgery Training and Research Hospital Clinical Research Ethics Committee, date: April 9th, 2012).

The common characteristics of the patients who were included in the study were as follows:

- Histopathologically diagnosed with lung cancer
- Underwent clinical staging after necessary tests were performed [13]
- Received and completed treatment, or did not approve of the treatment

Patients who were diagnosed with LC based on clinical or radiological assessments were excluded.

The medical records of the patients were reviewed, and necessary data were obtained by filling the study forms. The sociodemographic characteristics of the patients (age, gender, occupation and educational status), place of residence, smoking habit, social security, symptom type, presence of other malignancies, family history of LC, radiological location and size of the lesion, diagnostic method, histological type of the lesion, presence of endobronchial lesion, stage of LC, performance status, time from symptom onset to admission to the hospital (SA), time from symptom onset to pathological diagnosis (SP), time from symptom onset to initiating treatment (ST), time from symptom onset to performing an initial radiological examination (SR), time from admission to the hospital to performing an initial radiological examination (AR), time from admission to the hospital to pathological diagnosis (AP) and time from admission to the hospital to initiating treatment (AT) were retrospectively obtained (Figure 1), and their relationships with each other were evaluated.

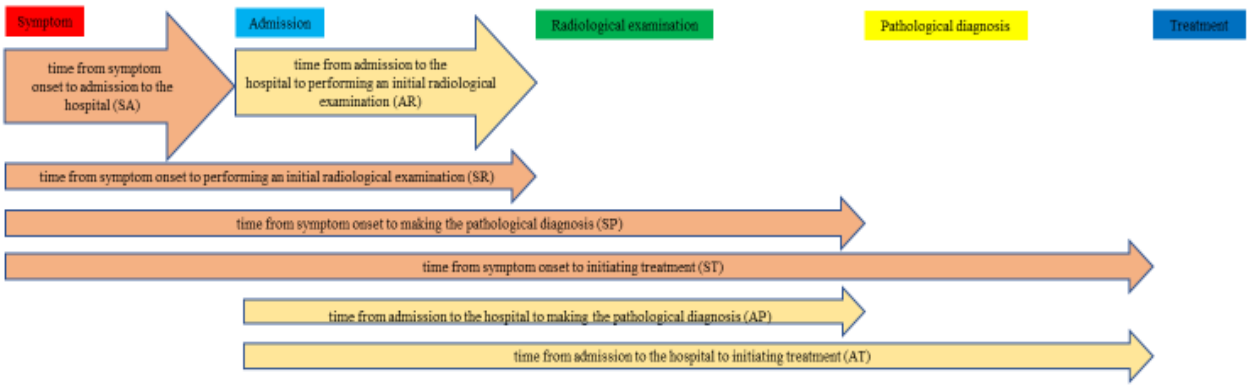

Figure 1: Timeline of symptom, admission, radiological examination, diagnosis and treatment

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences 20.00 (SPSS) software. The Mann–Whitney U test was used to compare delay times and affecting factors, and the Kruskal–Wallis multiple comparison test was performed when there was a difference in delay times between the groups. A *P*-value of <0.05 was considered statistically significant in both tests.

Results

Totally, 107 (87.7%) patients were male and 15 (12.3%) were female. Ninety-eight (80.3%) patients had non-small cell lung cancer (NSCLC): 30 (30.7%) had stage I–III and 68 (69.3%) had stage IV cancer. Twenty-four (19.7%) patients had small cell lung cancer (SCLC); 9 (37.5%) had limited stage (I-III) cancer, and 15 (62.5%) had extensive stage (IV) cancer. The performance status in 89.4% of the patients was Eastern Cooperative Oncology Group (ECOG) 1 and 2. Gender, smoking habit, histological types, cancer stage and performance status of the patients are presented in Table 1. The distribution of patients by place of residence was as follows: 72 lived in rural areas whereas 50 lived in the city center. The distribution of patients according to education level, occupational group and social security is presented in Table 2.

Chronological data of the patients was shown in Table 3. In this table, minimum, maximum, and mean values of delay times are presented.

No significant relationship was found between delay times and age, gender, occupation, and place of residence. There was no significant difference between the groups in terms of educational status and time of SA. Periods of AP and AT were longer only in the literate group.

Significant differences were detected between educational status and delay times in terms of SP, AP, AT. It was found that high school and college graduates contacted the hospital earlier than the other educational status groups, while the literate group received a diagnosis and treatment later than patients with other educational statuses (*P*=0.017, *P*=0.011 and *P*=0.006, respectively) (Table 4).

There was a significant difference between the social security groups in terms of SA, SP, ST, SR. It was found that patients with a pension fund had the shortest SA, SP, ST and SR times, whereas patients with a health card for the uninsured had the longest period of time (*P*<0.05 for all) (Table 5).

When the first complaints of patients admitted to the hospital were interpreted, those with hemoptysis were found to apply to the hospital earlier than those with chest pain (*P*=0.001).

There was no significant difference between the groups in terms of smoking history, chronic lung disease, family history of lung cancer, other malignancies, radiological tumor location, lobular location of the lesions, tumor diameter, presence of an endobronchial lesion, lung cancer stage and ECOG performance status.

The mean AT time was shorter in patients with SCLC (mean: 27 days) than in those with NSCLC (mean, 34 days) (*P*=0.027).

Table 1: Characteristics of the patients

	n	%
Age		
Under 70 years	89	73
70 years and over	33	27
Smoking habit		
Yes	105	86
No	17	14
Histological type		
NSCLC	98	80.3
Stage I–III	30	30.7
Stage IV	68	69.3
SCLC	24	19.7
Limited stage	9	37.5
Extensive stage	15	62.5
Place of Residence		
Rural	72	59
Urban	50	41

NSCLC: non-small cell lung cancer, SCLC: small cell lung cancer

Table 2: Distribution by educational level, occupational group, and social security

	Number	%
Educational Level		
Illiterate	11	9
Literate	21	17.2
Primary school graduate	69	56.5
Secondary school graduate	6	5
High school + University graduate	15	12.3
Occupational Group		
Farmer	36	30.3
Artisan	26	21.3
Housewife	14	11.4
Worker	24	19.7
Officer	12	9.8
Driver	10	8.2
Social Security		
SSI	57	46.7
SSOASE	24	19.7
Pension fund	19	15.6
Health Card for Uninsured People in Turkey	22	18

SSI: Social Security Institution, SSOASE: Social Security Organization for Artisans and the Self-Employed

Table 3: Chronological data

Delay time (days)	Minimum	Maximum	Mean	SD
Symptom-Admission (SA)	0	365	30	69.8
Symptom-Pathological Diagnosis (SP)	1	382	60	73.0
Symptom-Treatment (ST)	18	394	75.5	65.7
Symptom-Radiological examination (SR)	0	365	30	70.3
Admission-Radiological examination (AR)	0	60	0	8.3
Admission-Pathological Diagnosis (AP)	0	228	14	24.6
Admission-Treatment (AT)	2	242	33	29.7
Pathological Diagnosis-Treatment (PT)	0	132	14	16.7

SD: Standard deviation

Table 4: Relationship between educational status and delay times

Educational Status	SP (days)	AP (days)	AT (days)
Illiterate	51.0	10.50	27.0
Literate	77.0	22.0	55.0
Primary school graduate	64.0	14.0	32.5
Secondary school graduate	44.0	11.0	30.0
High school + University graduate	36.0	10.0	34.0

Mean time SP: From symptom onset to the pathological diagnosis, AP: From admission to the hospital to the pathological diagnosis, AT: From admission to the hospital to initiating treatment

Table 5: Relationship between social security type and delay times

Social Security	SA (days)	SP (days)	ST (days)	SR (days)
SSI	37.5	67.0	82.0	45.0
SSOASE	30.0	40.0	63.0	30.0
Pension fund	20.0	35.5	50.0	20.0
Health Card for Uninsured People in Turkey	45.0	70.5	95.0	52.0

SSI: Social Security Institution, SSOASE: Social Security Organization for Artisans and the Self-Employed, mean time SA: From symptom onset to admission to the hospital, SP: From symptom onset to the pathological diagnosis, ST: From symptom onset to initiating treatment, SR: From symptom onset to performing an initial radiological examination

Discussion

Lung cancer is the leading type of cancer in the world that causes the most deaths among both men and women. Primary treatment for patients with early stage NSCLC is surgery. In cases with advanced stage of LC and where surgery cannot be performed, radiotherapy and/or chemotherapy are options of treatment [1]. It is a widely accepted principle that cancer patients should be diagnosed as early as possible. Delays in diagnosis and treatment are common in cancer patients [14]. Some studies have reported that delays in diagnosis and treatment may affect tumor stage and prognosis, whereas other

studies have reported no significant association between these delays and tumor progression and prognosis [15].

The aim of our study was to investigate whether sociodemographic characteristics, past medical and family history of patients and tumor characteristics affect time to admission, diagnosis, and treatment.

Most recommendations of recent American College of Chest Physicians LC guidelines emphasize a maximum delay of 7–14 days between visits with a general practitioner and specialist [16]. Fernandes et al. [17] reported that the mean time until the multidisciplinary committee made a final LC diagnostic decision was 20.6 (13.1) days. In our study, this time was 14 (24.6) days and shorter.

In total, in our study, 107 (87.7%) patients were male and 15 (12.3%) were female. In a similar study conducted in our hospital in 2007 [18], the number of women was low (12.1–18 %). In another study, 58.7% of patients were male [19]. The reason for this is that the smoking habit in Turkey is less common among women. Furthermore, there was also the predominance of men in another study population [4] and this is consistent with the epidemiology of lung cancer.

In the distribution of groups by occupation, farmers (30.3%) ranked first; in terms of social security type, social security institution (SSI) (46.7%) ranked first and health card for uninsured people (18%) ranked third. We found no significant relationship between delay times and occupation. In similar study in China, it was found that there was an increased risk of developing lung cancer with decreasing income [20].

In our study, we found that 105 patients (86%) had a smoking history. This rate was reported as 75.6% in the study by Fernandez et al. [17], 84.6 % in the study by Özdemir et al. [18], and 91.5% in the study by Akpınar et al [21]. Tobacco consumption is the main risk factor for LC and has been increasing in recent years.

It was determined that the patients who graduated high school and university (12.7%) admitted to a doctor earlier than the other groups and that the literate group was the only group that was diagnosed and received treatment at a longer period after admission. The knowledge and awareness of patients were associated increasing educational level. It was found that patients with a lower education level had a higher risk of developing lung cancer.

As for diagnostic methods used in our study, fibreoptic bronchoscopy (FOB) ranked first with 65 cases and transthoracic fine needle aspiration biopsy ranked second with 37 cases. Similar results were obtained in the studies of Chandra et al. [13] and Fernandez et al. [20]. We reported that 98 (80.3%) patients had NSCLC in this study. However, we found more patients with stage 4-LC in our study compared to Acharya et al. [22].

The mean time of SA was 30 days in our study. Similar results were obtained in two other studies reported from Turkey, which reported 42.5 days and 35 days for this time [21,23]. A study in the literature reported 76 days for SA [24]. In a study conducted in Cuba, similar results were obtained with 24.3 days [4]. Time of SA mostly depends on patient-related factors (symptoms, educational level, age etc) but it may be less due to environmental factors (place of residence, transfer to health centers). So, this period is very variable.

In our study, the time of AR varied from 0 to 60 days. In the literature, this duration was 20 days [18]. This duration in our study was shorter than that reported in other studies. It was considered that in Turkey, the patients could easily apply to tertiary healthcare institutions, so time was not wasted.

The mean time of ST and AP in our study were 75.5 days and 14 days, respectively. In similar studies, ST times were 112, 138, 154, 185, 122 and 160 days [14,15,18,20,21,24]. In a study in Spain including 415 patients, the delay between the first symptoms and the beginning of treatment was 124 days [25]. The time reported in our study is shorter that reported in other studies. AP period was also shorter than other studies [14,18,21,24]. These show the ease of access to health centers and the speed of healthcare services in our country compared to other countries.

We observed that the mean time of AT was 33 days and the mean time of PT was 14 days. AT period is shorter in our study and Turkey [14,18,21,24] and PT period is similar to another study conducted in Turkey [18] and shorter than other studies [20,24,26]. These data show that our country is better than developed countries regarding diagnosis and treatment of LC. Kim et al. [27] reported that the median treatment interval was 51 days (interval 49-53 days). Although the PT interval in our study is longer compared to other studies, we had patients were diagnosed and began treatment on the same day. Gomez et al. [28] found that the median diagnosis-to-treatment interval was 27 days and intervals <35 days were associated with improved survival for patients with localized disease and those with distant metastatic diseases surviving ⩾1 year.

In our study, the time of SP was 60 days, whereas it was 143 days in the study by Chandra et al. [20]; prolonged interval until the diagnosis was attributed to the poor performance status of the patients. In 2014, Fernandez's study found that total delay (from onset of symptoms to confirmation of diagnosis) was 67.4 days [4]. The similarity between the results of our study and results of this study, even in more technologically advanced countries, suggest that poor organization and management of health services, not just material shortages, play an important role in diagnostic delay. Chest/shoulder pain was the only first symptom associated with a shorter median SP for lung cancer and for early-stage lung cancer, the median SP for any symptom was 141 days compared with 87 days for late-stage lung cancer in the study of Walter et al [29]. However, in our study, there was no significant relationship between the mean SP time, first symptom and stages of LC.

No significant relationship was found between delay times and age, gender, occupation, and place of residence. In a similar study conducted in our hospital, there was no relationship between delay times and age, occupation, and social security status, but in terms of place of residence, people who lived in towns were found to have prolonged time in getting a diagnosis and treatment than those living in villages [21]. This result was attributed to the small number of patients included in the study groups.

There was no significant difference between the groups in terms of educational level and time of SA. Times of AP and AT were longer only in the illiterate group. Matching results were also found in the study by Özdemir et al [18]. It was

attributed to the fact that patients in the well-educated group acted more consciously after they realised the seriousness of the situation. Remarkably, in our study, delay times were shorter in the illiterate group only. This difference was attributed to the small number of patients in the group.

In our study, we found that the time of AT was shorter in patients with SCLC (mean, 27 days) than patients with NSCLC (mean, 34 days). In the study conducted by El Quazzani et al. [22], this time was shorter in patients with SCLC [24]. These results were associated with the fact that the prognosis of patients with SCLC is worse than that of patients with other types of cancer and treatment is immediately initiated, as response to chemotherapy is good. In another study, the delay in specialist visit was shorter in SCLC may be because of the acute presenting symptoms.

Comparable results were found in the study of Akpınar et al. [21]. Gender, place of residence, presence of other malignancies and presence of chronic pulmonary disease did not affect the time from the onset of first complaints to referral to a doctor as well as the time of ST. In a study, patients at elevated risk of developing cancer had greater levels of comorbidities affecting respiratory function, such as COPD. Therefore, symptoms become difficult to distinguish, and potential lung cancer symptoms can be confused with existing respiratory conditions [30].

There was no relationship between delay times and the presence of an endobronchial lesion, radiological location of tumor, tumor stage, and performance status in the study of Yaman et al. [23], akin to our study. Although Evans et al. [19] found that the PT interval was shorter for patients with early stage disease (stage I), they suggested that they were given priority for treatment over patients with stage II or III disease.

Limitations

It was a small study conducted at a single center, which limits the generalizability of the results. We did not analyze the size of the tumor and record the comorbidities of patients. Since our study was retrospective, some time periods could not be determined. There were insufficient data in the medical records of patients about the causes of shorter or longer delay times. We did not examine whether the presented data was associated with survival.

Conclusions

Delay in the diagnosis and treatment of lung cancer is an important and widespread problem. There is a need for studies that reveal the magnitude and possible causes of diagnosis and treatment delays in our country. Studies about this subject should be conducted to identify the magnitude and causes, as well as results and solutions to the problem.

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