

Delays in the diagnosis and treatment of non-small-cell lung cancer

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ABSTRACT

Aims. To investigate patterns of delays among patients with non-small-cell lung cancer and to identify reasons for the delays.

Methods. This prospective study included 101 patients with non-small-cell lung carcinoma. Clinical files of the patients were analyzed and a questionnaire was created to obtain data. Several time intervals and delays were determined for each patient. The reasons for the delays were also evaluated.

Results. The mean time was 59.9 days for the application interval, 40.3 days for the referral interval, 16.4 days for the diagnostic interval, and 24.7 days for the treatment interval. The application interval was longer than 30 days (patient's delay) in 48 patients (48.5%). There was a doctor delay in 54 (53.5%) patients, a referral delay in 47 (46.5%) patients, a diagnostic delay in 37 (36.6%) patients, and a treatment delay in 57 (56.4%) patients. The mean total time was 119.6 days. Sixty-two patients (62.6%) had a total delay. The most common reason for patient's delay was neglect of symptoms by patients. A low index of suspicion for lung cancer was the most common cause for referral delay. The low performance of diagnostic tests was the frequent reason for diagnostic delay.

Conclusions. Patient's and doctor's delays were a common problem among patients with non-small-cell lung cancer. The rate of doctor's delay was higher than that of patient's delay. Several efforts such as education of the physicians and people about lung cancer should be made to reduce these delays.

Introduction

Lung cancer is a rapidly increasing problem in developing countries. It is the most common neoplasm in Turkey. The annual age-standardized incidence rate was 61.6/100,000 in males and 5.1/100,000 in females in 1993-1994¹. The prognosis of lung cancer is still very poor, with an overall 5-year survival rate of about 15%². Lung cancer is the most common cause of cancer mortality in both males and females and is the cause of 12.8% of cancer cases and 17.8% of cancer deaths worldwide³. Only less than 20% of patients with lung cancer present at operable stages⁴. It has been accepted that the survival and cure rates are higher in cancer patients diagnosed in the earlier stages⁵.

It is easy to presume that delays result in a larger cancer and a reduction in survival time. Diagnostic and treatment delays continue to remain very common problems among patients with lung cancer. Such delays have been noted in both developing and developed countries^{4,6-9}. Many reports have shown that delays may affect tumor stage and survival rate^{10,11}. Reducing delays may increase the proportion of early stage cancers and improve survival¹⁰. Several groups such as The British Thoracic Society, The Swedish Lung Cancer Study Group and The Canadian Study Group have made recommendations on the waiting times in diagnosis and treatment pathways¹²⁻¹⁴. The objectives of the present study were twofold: (i) to investigate patterns of de-

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lays among patients with non-small-cell lung cancer and compare them with recommendations of study groups, (ii) to identify reasons for these delays.

Methods

The present study was conducted at the Sureyyapasa Chest Diseases and Thoracic Surgery Training and Investigation Hospital. We investigated all the patients with lung cancer diagnosed in two pulmonology clinics between January 2009 and May 2009. Patients who had tumor pathology other than non-small-cell lung carcinoma, those with metastatic lung cancer from other organ cancers, those who did not respond to the questionnaire, and those who did not remember some dates in their disease course were excluded from the study. The study included 101 patients who had the inclusion criteria. Consent was obtained from each patient after full explanation of the purpose and nature of the study.

Clinical files of the patients were analyzed and a questionnaire was created to obtain data by interview with the patients. For each patient, the following information was gathered based on these data: sex, age, educational level, smoking habit, comorbidity, symptoms, diagnostic methods, tumor histology, clinical TNM stage, treatment modality, date of initial symptoms, date of first doctor visit, date of admission to our hospital, date of diagnosis, and date of initiation of the treatment.

The following time intervals and delays were determined for each patient: the patient's *application interval* was defined as the time elapsed from the onset of symptoms to the first doctor's visit. It was calculated in 99 patients who had symptoms. An application interval that exceeded 30 days was considered indicative of a *patient's delay*⁶. The *referral interval* was defined as the time from the first doctor's visit to admission to our hospital for the further investigation, and an interval that exceeded 14 days was considered indicative of a *referral delay*. The diagnosis interval was regarded as the time elapsed from admission to our hospital to the pathological diagnosis. A diagnosis interval that exceeded 14 days was considered as indicative of a *delayed diagnosis*. The *treatment interval* was the time elapsed from the diagnosis to treatment, and an interval that exceeded 14 days was considered as indicative of a *delayed treatment*. *Doctor's interval* was defined as the time elapsed the first doctor's visit to treatment, and an interval that exceeded 6 weeks was considered as indicative of a *doctor's delay*. The *total interval* was the time elapsed from the onset of symptoms to treatment, and if it exceeded 72 days it was considered indicative of a *total delay*^{12,14}. It was calculated in 99 patients who had symptoms. Figure 1 demonstrates the time intervals and delays used in the study.

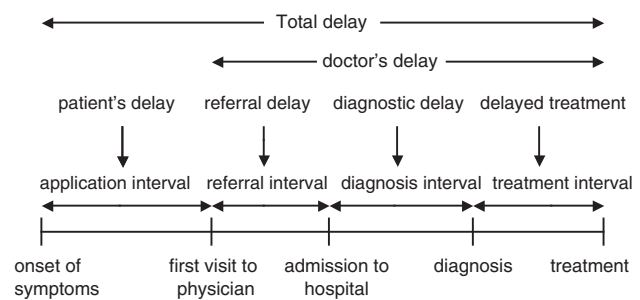


Figure 1 - Components of the time from onset of symptoms to treatment and delays.

Results

The study included 101 patients with non-small-cell lung carcinoma, consisting of 91 (90.1%) males and 10 (9.9%) females with a mean age of 60.6 years (range, 28-84 years). Characteristics of the study population are presented in Table 1.

Table 2 presents the values of the intervals. The mean duration was 59.9 days for the application interval, 40.3 days for the referral interval, 16.4 days for the diagnosis interval, and 24.7 days for the treatment interval. The mean total duration was 119.6 days.

Distribution of the patients in the intervals with respect to delay criteria is given in Table 3.

The application interval was shorter than 30 days in 51 patients (51.5%) and longer than 30 days in 48 patients (48.5%). According to these results, 48.5% of the patients had patient's delays. Fifty-four (53.5%) patients had doctor's delays. The referral interval was longer than 14 days in 47 patients (46.5%), diagnostic workups took more than 14 days in 37 patients (36.6%), and waiting for treatment more than 14 days in 57 patients (56.4%). The number of delays identified in 101 patients was 189 in 4 different steps (application, referral, diagnosis, and treatment) during the disease course between the first symptom and treatment.

Reasons for delays are summarized in Table 4. The most common reason for patient's delay was ignoring the symptoms by the patient. Of the 47 patients with a referral delay, lung cancer was not suspected in 40 patients (76.9%) at the time of their first visit. Five patients (9.6%) had delays in chest X-ray examinations. Forty-three (42.6%) patients were examined by two different doctors during the referral interval and 27 (26.7%) by 3, 19 (18.8%) by 1, and 12 (11.9%) 4 or more. A total of 101 patients made 309 doctor's visits during this period. We identified 41 reasons in 37 patients having a diagnostic delay. The most common reason for a diagnostic delay was low performance in diagnostic methods, followed by factors associated with the patient. Our healthcare system, staging procedures, limited availability of radiotherapy facilities and factors associated with patients were the frequent reasons of treatment delays.

Table 1 - Characteristics of the study population

Characteristic	No. cases	%
Sex		
Male	91	90.1
Female	10	9.9
Mean age, yr (range)	60.6 (24-84)	
Education level		
No formal education	13	12.9
Primary school	66	65.3
High school	17	16.8
University	5	5
Smoking habits		
Nonsmoker	8	8
Smoker	66	65.3
Exsmoker	27	26.7
Presenting symptom		
No symptom	2	2
Symptom	99	98
Cough	69	69.7
Weight loss	61	61.6
Dyspnea	48	48.5
Chest pain	46	46.5
Hemoptysis	34	34.3
Other	49	49.5
Diagnostic method		
Bronchoscopy	56	55.5
Transthoracic FNA	29	28.7
Thoracentesis	1	1
Lymph node aspiration	1	1
Sputum cytology	1	1
Mediastinoscopy	5	5
Thoracoscopy	1	1
Thoracotomy	7	6.8
Tumor histology		
Squamous carcinoma	42	41.6
Adenocarcinoma	12	11.9
Non-small-cell carcinoma	47	46.5
Stage		
IA	5	5
IB	13	12.8
IIB	3	3
IIIA	20	19.8
IIIB	20	19.8
IV	40	39.6

FNA, fine needle aspiration.

Table 2 - Values associated with several intervals (days)

Interval	No.	Mean	SD	Median	95% CI
Application	99	59.9	103	25	39.6-80.2
Referral	101	40.3	72.1	13	26.1-54.6
Diagnosis	101	16.4	13.7	13	13.7-19.1
Treatment	101	24.7	18.3	21	20.8-28.6
Doctor's	101	71.7	55.7	56	59.8-83.6
Total	99	119.6	74.6	98	103.7-135.5

Table 3 - Distribution of patients in the intervals with respect to delay criteria

Intervals	No. cases	%
Application interval (days)	99	
≤30	51	51.5
>30	48	48.5
Referral interval (wk)	101	
≤2	54	53.5
>2	47	46.5
Diagnosis interval (wk)	101	
≤2	64	63.4
>2	37	36.6
Treatment interval (wk)	101	
≤2	44	43.6
>2	57	56.4
Doctor's delay (wk)	101	
≤6	47	46.5
>6	54	53.5
Total delay (days)	99	
≤72	37	37.4
>72	62	62.6

Table 4 - Possible reasons for delays

Reason	No. cases	%
Patient's delays (n = 48)		
Neglect of symptoms	18	37.5
Socio-cultural factors	11	22.9
Economic factors	11	22.9
Distance to health center	1	2.1
Delays in health care system	1	2.1
Other	6	12.5
Total	48	100
Referral delays (n = 47)		
Low index of suspicion for lung cancer	40	76.9
Delays in chest X-ray examination	5	9.6
Delays in health care system	5	9.6
Reasons associated with patient	2	3.9
Total	52	100
Diagnostic delays (n = 37)		
Low performance of diagnostic methods	22	53.7
Factors associated with patient	7	17.1
Low index of suspicion for lung cancer	6	14.6
Delays in the laboratory system	4	9.7
Delays in health care system	2	4.9
Total	41	100
Treatment delays (n = 57)		
Delays in health care system	18	30.5
Staging procedures	11	18.6
Limited availability of RT facilities	10	17
Factors associated with patient	10	17
Consultations	6	10.1
Unknown	4	6.8
Total	59	100

Discussion

Delays are a common problem among patients with lung cancer in Turkey and the other countries^{4,6-9,11-15}. It is generally accepted that cancer should be detected as early as possible because survival and cure rates are higher in patients diagnosed in the earlier stages of dis-

ease^{11,15}. Many reports have shown that delays affected tumor stage and prognosis^{5,11,15}. A previous study showed that 20% of the patients awaiting radiotherapy with a curative intent became incurable while they were on the waiting list¹⁶. Patients with cancer and their families have anxieties. Delayed presentation of cancer also has a significant economic impact, since it is far less ex-

pensive to treat patients with early stage disease. If the delay time becomes shorter, it may increase the ratio of patients with early stage cancers, thereby improving survival¹⁰. Rapid diagnosis and assessment in patients with cancer are important to minimize patient anxiety¹². The British Thoracic Society and the other study groups have made recommendations to respiratory physicians and other health care professionals for reducing delays in the diagnosis and treatment of lung cancer¹²⁻¹⁴.

The present study was undertaken to measure delays in patients with non-small-cell lung cancer, to evaluate whether the length of the delays was acceptable according to the study groups' recommendations, and to identify the possible reasons for delays. The study indicated that there were several delays between the onset of symptoms and beginning of treatment in our patients. The delays can be described as total delay, patient's delay, referral delay, diagnostic delay, and treatment delay. The median total time in this study of 98 days compares favorably with reported median total time of 112 days in the USA¹⁵ and 4.6 months and 189 days in Sweden^{13,17}, but less favorably with median total time of 71.5 days in Turkey¹⁸.

In our study, the median application interval was 25 days. A previous report presented a longer median application interval than ours (i.e., 30 days)¹⁸. Our median application interval was long compared with a median application interval of 14 days in the USA¹⁵ and 21 days in Sweden¹⁷. Different application intervals in series may result from demographic characteristics of the patients. It is known that the length of this interval may be associated with several factors in patients with pulmonary tuberculosis. Age, sex, educational level, economic status and initial symptom may affect the application interval¹⁹. In the present study, the mean and median durations between the first appointment with a doctor and beginning of treatment were 71.7 and 56 days, respectively. A previous report noted that the mean time between the first appointment with a doctor and beginning of treatment was 97.2 days⁶. In another study, the median time between the first appointment with a doctor and beginning of treatment was 73 days¹⁵. We found that the mean and median durations were 40.3 and 13 days for referral interval, 16.4 and 13 days for diagnosis interval, and 24.7 and 21 days for treatment interval, respectively. A previous study reported a longer mean referral and diagnostic interval but shorter mean treatment interval than our study⁶. In a study from Spain, it was noted that the treatment interval was longer than ours²⁰. Our results indicated that referral interval was longer than both diagnosis and treatment intervals.

Several study groups have made recommendations on the times for waiting in the diagnosis and the treatment pathways of lung cancer¹²⁻¹⁴. According to Turkish and Brazilian studies^{6,21}, an application interval exceed-

ing 30 days is considered as a patient delay. The British Thoracic Society (BTS)¹² recommends that all patients should be seen for an initial evaluation by a pulmonary physician within 1 week of referral from their primary care physician. Diagnostic tests should be performed within 2 weeks of the decision. The Swedish Lung Cancer Study Group¹³ recommends that in 80% of all patients, diagnostic tests should be completed within 4 weeks of consultation by a specialist and treatment should be started within 2 weeks thereafter. In Canadian recommendations¹⁴, a maximum 4-week elapse could be accepted between the first visit to a general practitioner and diagnosis, and the waiting time for surgery should not exceed 2 weeks. It was noted that the rates of delay were 37.9% for patient's delay, 73.9% for doctor's delay, 60.1% for institutional delay, 36.4% for diagnosis delay, 69.6% for treatment delay, and 71.2% for total delay in their series⁶. Salomaa *et al.*¹⁵ reported that about half of their patients fulfilled the criteria of the BTS recommendations. Sixty-six percent of their patients fulfilled the diagnostic delay criteria, and 49% fulfilled treatment delay criteria of the Swedish Lung Cancer Study Group. Only 26% could have the Canadian recommendation of a 4-week limit. In the present study, 48 patients (48.5%) had patient's delay. The rates of delay were 53.5% for doctor's delay, 46.5% for referral delay, 36.6% for diagnosis delay, 56.4% for treatment, and 62.6% for total delay. The present study shows that the rates of doctor's delay were higher than those of patient's delay. Also, the rate of treatment delay was higher than rates of diagnosis and referral delay in our study.

Many reasons for delays have been identified in previous reports. There are two main factors associated with patient's delay. The first is information for the public about the symptoms of lung cancer and risks of smoking. The other important factor is access to health services or a doctor¹⁷. Demographic characteristics of the patients such as age, sex, educational level and economic status may affect the length of the application interval¹⁹. According to study of Bjerager *et al.*²², symptoms not related to the lungs, chest X-ray without suspicion of cancer, comorbidity, long waiting times for diagnostic investigations, and lack of explicit follow-up appointments are important reasons for delays in patients with lung cancer. The attitudes of primary care physicians and their relations with respiratory physicians can affect the length of delays⁴. Pre-hospital delays are largely dependent on the severity of symptoms, level of patient education and complex socioeconomic factors. Waiting for diagnostic investigations, the need for multiple additional investigations, waiting for staging procedures, and assessment of comorbidity are the main reasons for delays²³. Organizational problems in the health care and laboratory systems are the other reasons for doctor's delays¹⁸. Long waiting lists for radiotherapy and surgery can result in treatment delays^{16,20}. In the present study, the most common reason for a pa-

patient's delay was neglect of symptoms by the patient. A low index of suspicion for lung cancer was the most common cause for referral delay. The most common reason for a diagnostic delay was low performance of diagnostic methods, followed by factors associated with patients. Our healthcare system, staging procedures, limited availability of radiotherapy facilities and factors associated with patients were the frequent reasons of treatment delays.

In conclusion, the present study suggests that our patients with lung cancer had several delays from onset of symptoms to the commencement of treatment. According to our data, doctor delay was more significant than patient delay. Several efforts should be made to reduce these delays. Education of physicians and the public about symptoms of lung cancer, reductions in healthcare system and laboratory delays, together with improvements in economic status and socio-cultural factors are the most important factors likely to reduce delays in diagnosis and treatment among cancer patients.

References

1. Fidaner C, Eser SY, Parkin DM: Incidence in Izmir in 1993-1994: First results from Izmir Cancer Registry. *Eur J Cancer*, 37: 83-92, 2001.
2. American Cancer Society: Cancer facts and figures 2006. American Cancer Society, Atlanta, 2006.
3. Parkin GM, Pisani P, Ferlay J: Global cancer statistics. *CA Cancer J Clin*, 49: 33-64, 1999.
4. Gonzalez JM, de Castro FJ, Barrieco M, Cordovilla R, Fernández JL, Gómez FP, Moreno de Vega B, Ramos J, Serrano AR: Delays in the diagnosis of lung cancer. *Arch Bronconeumol*, 39: 437-441, 2003.
5. Robinson E, Mohilever J, Zidan J, Sapir D: Delay in diagnosis of cancer. Possible effects on the stage of diseases and survival. *Cancer*, 54: 1454-1460, 1984.
6. Yilmaz A, Damadoglu E, Salturk C, Okur E, Tuncer LY, Halezeroglu S: Delays in the diagnosis and treatment of primary lung cancer: Are longer delays associated with advanced pathological stage? *Upsala J Med Sci*, 113: 287-296, 2008.
7. Chandra S, Mohan A, Guleria R, Singh V, Yadav P: Delays during the diagnostic evaluation and treatment of lung cancer. *Asian Pac J Cancer Prev*, 10: 453-456, 2009.
8. Sood J, Wong C, Bevan R, Veala A, Sivakumaran P: Delays in the assessment and management of primary lung cancers in South Auckland. *N Z Med J*, 122: 42-50, 2009.
9. Billings JS, Wells FC: Delays in the diagnosis and surgical treatment of lung cancer. *Thorax*, 51: 903-906, 1996.
10. Neal RD, Allgar VL, Ali N, Leese B, Heywood P, Proctor G, Evans J: Stage, survival and delays in lung, colorectal, prostate and ovarian cancer: comparison between diagnostic routes. *Br J General Pract*, 57: 212-219, 2007.
11. Christensen ED, Harvald T, Jendresen M, Aggestrup S, Petersen G: The impact of delayed diagnosis of lung cancer on the stage at the time of operation. *Eur J Cardiothorac Surg*, 12: 880-884, 1997.
12. British Thoracic Society: BTS recommendations to respiratory physicians for organizing the care of patients with lung cancer: The Lung Cancer Working Party of the British Thoracic Society Standards of Care Committee. *Thorax*, 53 (suppl 1): 1-8, 1998.
13. Myrdal G, Lambe M, Hillerdal G, Lamberg K, Agustsson TH, Stahle E: Effect of delays on prognosis in patients with non-small cell lung cancer. *Thorax*, 59: 45-49, 2004.
14. Simunovic M, Gagliardi A, McCready D, Coates A, Levine M, DePetrillo D: A snapshot of waiting times for cancer surgery provided by surgeons affiliated with regional cancer centers in Ontario. *Can Med Assoc J*, 165: 421-425, 2001.
15. Salomaa ER, Sallinen S, Hiekkanen H, Liippo K: Delays in the diagnosis and treatment of lung cancer. *Chest*, 128: 2282-2288, 2005.
16. O'Rourke N, Edwards R: Lung cancer treatment waiting times and tumour growth. *Clin Oncol*, 12: 141-144, 2000.
17. Koyi H, Hillerdal G, Branden E: Patient's and doctor's delays in the diagnosis of chest tumors. *Lung Cancer*, 35: 53-57, 2002.
18. Özlü T, Bülbül Y, Öztuna F, Çan G: Time course from first symptom to the treatment of lung cancer in the Eastern Black Sea Region of Turkey. *Med Princ Pract*, 13: 211-214, 2004.
19. Güneylioglu D, Yilmaz A, Bilgin S, Bayram U, Akkaya E: Factors affecting delays in diagnosis and treatment of pulmonary tuberculosis in a tertiary care hospital in Istanbul, Turkey. *Med Sci Monit*, 10: CR62-67, 2004.
20. Aragonese FG, Moreno N, Leon P, Fontan EG, Folque E, The Bronchogenic Carcinoma Cooperative Group of the Spanish Society of Pneumology and Thoracic Surgery (GC-CB-S): Influence of delays on survival in the surgical treatment of bronchogenic carcinoma. *Lung Cancer*, 36: 59-63, 2002.
21. Silva PPA, Pereira JR, Ikari FK, Minamoto H: Cancer de pulmão e retardo diagnostico: analise de 300 cases. *Rev Ass Med Brasil*, 38: 145-149, 1992.
22. Bjerager M, Palshof T, Dahl R, Vedsted P, Olesen F: Delay in diagnosis of lung cancer in general practice. *Br J Gen Pract*, 56: 863-868, 2006.