

## Factors affecting the interval from diagnosis to treatment in patients with lung cancer

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### ABSTRACT

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**Aims and background.** We aimed to investigate the factors affecting the interval from the beginning of the symptoms until diagnosis and treatment in patients with lung cancer.

**Methods.** Records of 119 lung cancer patients diagnosed in our pulmonary diseases clinic between 2004 and 2006 were evaluated retrospectively. Demographic data, histopathological tumor type, TNM stage, ECOG performance status, presence of endobronchial lesions, and radiological localization of the tumor were determined. Intervals from the first symptom to contacting a doctor, to diagnosis and to treatment were calculated. The interval from first admission to a clinic and referral to a chest physician was also calculated.

**Results.** Of 119 patients, 74% were diagnosed as non-small cell and 26% were as small cell lung cancer. Forty-eight percent of the patients were at stage 3B and 36% were at stage 4. ECOG performance status was 0 in 6%, 1 in 52%, 2 in 36%, 3 in 3%, and 4 in 2%. Endobronchial lesions were observed in 50% of the patients, and the lesions had a central radiological localization in 59%. Fifty-four percent of the patients presented to a chest physician first. Patients who first presented to an internal medicine clinic were referred to our pulmonary disease clinic significantly later than those who presented to other clinics ( $P = 0.005$ ). The median period from the beginning of the symptoms until contacting a doctor was 35 days (range, 1-387), until diagnosis was 49 days (range, 12-396), and until beginning the treatment was 57 (range, 9-397) days. The presence of endobronchial lesions, radiological localization, TNM stage and ECOG performance status were not found to be related to the intervals from the first symptom to presentation to a doctor, to diagnosis or to the beginning of the treatment.

**Conclusions.** Lung cancer patients consult a doctor after a relatively long symptomatic period. Patient delays may be shortened by increasing the awareness of patients about lung cancer symptoms. Diagnostic procedures should be performed more rapidly to shorten doctor delays.

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### Introduction

Lung cancer is one of the most common cancers around the world as a consequence of increasing trends in smoking<sup>1</sup>: 12.8% of cancer cases and 17.8% cancer deaths are attributed to lung cancer<sup>2</sup>. In a previous study evaluating the incidence of lung cancer in Turkey, it was found to be 41.7 per 100,000 in men and 4.8 per 100,000 in women<sup>3</sup>.

Despite improvements in diagnostic and therapeutic procedures, the prognosis of lung cancer patients is poor. Only about 20% of patients are candidates for radical surgery and cure<sup>4</sup>. Five-year survival rates of surgery in patients with early stage lung cancer is approximately 75-80%. However, early treatment of unresectable locally advanced non-small cell lung cancer does not influence the prognosis<sup>5,6</sup>.

**Key words:** delays in diagnosis, lung cancer prognosis.

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As prevention of the population at risk for lung cancer is one of the primary goals, various screening trials have been carried out, but no decrease in mortality has been reported<sup>7,8</sup>. Patients with lung cancer are subject to different kinds of delays in terms of diagnosis and treatment<sup>9</sup>. This may result from the factors related to the patient and health care systems. The diagnostic delay from the very first symptom to the final diagnosis has been reported to be between 3 and 7 months<sup>10,11</sup>.

The objective of our study was to evaluate the interval from the first symptom to admission, diagnosis and treatment and also the factors impacting these intervals.

## Material and methods

The Turkish Healthcare System has been organized as a three-step pattern, and every citizen can easily reach the care system. Patients have the right to choose their doctor, as well as admission to a specific clinical branch they would like by passing from an initial visit to a general practitioner. Patients can change their doctor and medical service whenever they want on demand. The concerned doctor may refer his patient to another doctor or medical service whenever necessary.

Available records of lung cancer patients, who had been followed in our clinic between January 2004 and December 2006, were evaluated retrospectively, and 119 patients were included in the study. Demographic data, histopathological tumor type, tumor stage according to tumor, node, metastasis (TNM) classification, performance status as defined by the Eastern Cooperative Oncology Group (ECOG), the presence of endobronchial lesions, and radiological localization of the tumor were determined. Information was obtained as regards to a family history of lung cancer. The first symptoms related to lung cancer were investigated and grouped in five categories: cough, dyspnea, hemoptysis, chest pain and others. At the same time, the date of the first symptoms and dates of admission, diagnosis and treatment were also recorded. Intervals from the first symptom to contact to a doctor, to diagnosis and to treatment were calculated. The interval from admission to our clinic and the beginning of treatment was evaluated separately. The interval from the first presentation to a clinic and referral to a chest physician was also calculated.

Statistical analyses were done with SPSS 14.0. Family histories of lung cancer, radiological localization of the tumor, presence of endobronchial lesions, and tumor stage were evaluated with the *t* test. The first symptom related to lung cancer, first admission clinic, performance status and the relationship of the intervals were analyzed with the Kruskal Wallis test.

## Results

One hundred and nineteen patients, 109 (92%) men and 10 (8%) women were evaluated. Mean age of the

population was  $62.77 \pm 10.25$ . Twenty six (22%) of the patients had a family history of lung cancer.

Histopathological tumor type was non-small cell lung cancer in 88 (74%) and small cell lung cancer in 31 (26%). According to the TNM classification, 6 (5%) of the patients were stage IB, 1 (1%) was stage IIA, 5 (4%) were stage IIB, 7 (6%) were stage IIIA, 57 (48%) were stage II-IB, and 43 (36%) were stage IV. ECOG performance status of the patients was 0 in 7 (6%), 1 in 63 (52%), 2 in 43 (36%), 3 in 4 (3%), and 4 in 2 (2%).

Endobronchial lesions were observed in 59 (50%) of the patients by fiberoptic bronchoscopy. Seventy (59%) of the lesions were localized radiologically in the central region. Lesions were diagnosed by pleural biopsy in 3 (3%), by liver biopsy in 2 (2%), and by lymph node biopsy in 2 (2%) of the patients.

Among the first symptoms related to lung cancer, cough was the most frequent. No significant relationship between symptom type and the intervals to admission to a doctor or beginning treatment was observed (Table 1). More than half of the patients presented to a chest physician first (54%). Patients who first presented to an internal medicine specialist were referred to our pulmonary disease clinic significantly later than those who presented to other clinics ( $P = 0.005$ ).

The median number of days from the beginning of symptoms to contacting a doctor was 35 (range, 1-387), to the diagnosis was 49 (range, 12-396), and to the beginning of treatment was 57 (range, 9-397). The median of days from admission to our clinic to the beginning of treatment was 14 (range, 3-55) (Table 2). There was not a statistically significant relationship between age, gender, TNM classification, ECOG performance status, presence of endobronchial lesions, radiological localization of the lesion, family history of lung cancer and the intervals from the first symptom to admission, diagnosis or beginning the treatment.

## Discussion

Most patients with lung cancer are diagnosed in an advanced stage. As screening is not currently recom-

**Table 1 - Frequency of first symptoms related with lung cancer and intervals from symptoms to admission and treatment**

First symptom	Frequency No. (%)	Mean interval from symptom to admission (days)	Mean interval from symptom to treatment (days)
Cough	38 (31.9)	62.52	76.00
Dyspnea	25 (21)	69.56	85.08
Hemoptysis	13 (10.9)	73.84	93.23
Chest pain	24 (20.2)	70.62	87.60
Others	19 (16.0)	52.42	73.05
Total	119 (100)	65.28	82.37

**Table 2 - Intervals from symptom onset to contacting a doctor, to admission to our clinic, to diagnosis, to treatment and the interval from admission to our clinic to the beginning of the treatment**

Interval	Minimum-maximum (days)	Median (days)	Mean (days)
First symptom to contacting a doctor	1-387	35	65.3 ± 67.4
Referral from other clinics to our clinic	0-220	2	7.1 ± 21.2
Symptom onset to diagnosis	12-396	49	76.7 ± 66.7
Symptom onset to treatment	9-397	57	82.4 ± 67.3
Admission to our clinic to beginning of treatment	3-55	14	18.7 ± 11.8

mended, efforts to improve lung cancer survival have concentrated on detecting patients with resectable tumors. Doubling time of lung tumors ranges from 4 to 56 weeks, and tumor growth is exponential, which can be a negative factor for a patient's prognosis if the diagnosis is delayed<sup>4</sup>. It has been recommended that the interval between a patient's first presentation to a general practitioner and the operation should not be more than 6 to 8 weeks<sup>12</sup>. The recommendations of the Swedish Lung Cancer Study Group suggest that 80% of all patient diagnostic tests should be completed within 4 weeks of referral to a specialist and treatment should be started within 6 weeks<sup>13</sup>.

The results of our study demonstrated a median delay of 57 days from the first symptom to treatment. Salomaa *et al.*<sup>4</sup> determined this interval to be 112 days in a Swedish study, the mean time of the diagnostic procedures of lung cancer was reported to be 7 months, of which 5.5 months was due to a delay related with doctors. Annakkaya *et al.*<sup>14</sup> reported a median interval from symptom to treatment of 90 days. Our results showed a shorter delay time for this interval. This may be due to a fairly small capacity of our hospital and our pulmonary diseases clinic, with 2 or 3 lung cancer patients seen a week. Also, the Turkish Health Care System contributes to this symptom-to-treatment interval being shorter, as a first visit to a general practitioner is not necessary and delays resulting from this procedure are therefore eliminated.

The symptom-to-diagnosis interval has also been reported to have a wide range. It may be affected by many factors including the attitudes of the patient and the doctor, the biology of the tumor, and the structure of the health care system. Porta *et al.*<sup>10</sup> demonstrated a mean symptom-to-diagnosis interval of 3.07 months and a weak relationship between symptom-to-diagnosis interval and tumor stage at diagnosis except for breast cancer. They also reported that the symptom-to-diagnosis interval was not a significant predictor of survival. In our study, we found a shorter mean symptom-to-diagnosis

interval of 76.7 ± 66.7 days (median, 49). González *et al.*<sup>15</sup> found this period to be 85.7 ± 87 days, whereas Pita-Fernández *et al.*<sup>16</sup> reported a median symptom-to-diagnosis interval of 2.1 months. The relatively shorter duration in our study may be attributed to the predominance of patients in an advanced stage (stage IIIB and IV) in our study population. This theory is also supported by other studies and explained by the diagnostic procedures in advanced disease that can be performed faster without the need for several investigations which usually have to be done in limited disease<sup>4,9,13</sup>. A relation between tumor stage and delay in diagnosis was also observed in the study of Myrdal *et al.*<sup>13</sup>, suggesting that a short delay time was observed in mainly patients with advanced disease. This was explained by the impact of severity of signs and symptoms on the rapidity of the medical decision process. Prognosis was reported to be less affected by diagnostic delay in stage I-II disease. There are also studies opposing this theory<sup>9,11</sup>.

A long treatment delay was reported not to be associated with a worse prognosis in advanced stage, whereas it was an important factor in limited disease<sup>4</sup>. Also, surgically treated patients had a longer hospital delay time with respect to others, which might be due to various time-consuming procedures that had to be done before surgery<sup>9</sup>. Survival was another parameter found not to be affected by the interval of symptom to diagnosis<sup>4,16</sup>. In our study, we did not evaluate the survival or prognoses of the lung cancer patients because data were lacking, and it was a limitation of the study.

Performance status of the patients, presence of endobronchial lesions and radiological localization were not found to be related with the intervals of symptoms to admission, diagnosis and treatment. Moreover, it was determined that family history of lung cancer did not affect these intervals, although, it is thought to be related with early admission.

González *et al.*<sup>15</sup> reported the first symptoms related with lung cancer as cough (10.6%), hemoptysis (19.5%), chest pain (26.5%) and shortness of breath (9.7%). The first visits were to primary care in 72%, emergency service in 22%, and pulmonologist in 6%<sup>16</sup>. In our study, cough was the most frequent symptom, although it was not related to the symptom-to-admission interval. First visits were to a chest physician in 54%, an internal medicine specialist in 34%, and others in 12%. We determined a difference in the intervals of referral of the patients to a chest physician, which reached statistical significance for internal medicine. This may be due to other diagnostic procedures performed in internal medicine clinics. It could be speculated that delays in diagnosis increase with an increasing number of doctors involved in the process.

The period from the beginning of the first symptom to contacting a doctor could be called "hospital admission time", and extending this time beyond 30 days could be defined as "patient delay"<sup>11</sup>. Patient delay may result from

late onset of symptoms, awareness of lung cancer symptoms, and not recognizing symptoms related to lung cancer by attributing them to other comorbid diseases. Low educational level and the older age of our study population might have contributed a lack of perception of lung cancer symptoms, resulting in a long patient delay. The period between admission of the patient and the beginning of treatment can be called "doctor delay"<sup>17</sup>. Doctor delay could be improved by shortening the time spent waiting for an appointment, for the pathology laboratory, for the consultative council and for drug supply.

## Conclusions

Lung cancer patients consult a doctor after a long symptomatic period, and referral to a chest physician also generally takes a long time. Patient delays may be shortened by increasing patient awareness about lung cancer symptoms, especially in groups at risk, whereas it is important to quicken diagnostic procedures in order to shorten doctor delays.

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