

# Clinical Features and Outcomes of Small-Cell Lung Cancer Cases from Northern Turkey

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## Abstract

**Objective:** To evaluate the clinical features and outcomes of small-cell lung cancer (SCLC) cases that were diagnosed in our clinic.

**Design:** Retrospective epidemiologic study.

**Setting:** Department of pulmonary disease at a tertiary teaching hospital.

**Patients or participants:** One hundred and fifty five patients with a pathological diagnosis of SCLC between January 1988 and December 1997.

**Interventions:** None

**Measurements and results:** One hundred and fifty five patients diagnosed to have SCLC comprised the study group. The group included 141 male and 14 female patients aged 32 to 85 years with a mean age of  $58 \pm 8.1$  years. 96.8% of male and 30% of female patients were current smokers. The most frequent presenting symptoms were cough, dyspnea, and chest pain, 28%, 23.2%, and 19.2%, respectively. The most common radiologic finding was a central mass ( $\geq 4$ cm in diameter) with hilar and/or mediastinal lymphadenopathy. The diagnosis was

established by histopathologic examination of the biopsy specimens obtained by various means, in which bronchoscopy was the sole means of diagnosis in 90.7% of the patients. Staging procedures were performed in all patients resulting as: 40 (25.8%) patients in limited stage (LS) and 115 (74.2%) patients in extensive stage (ES). Metastasis was most frequently to the bones (42.9%) followed by the liver (27.6%) and the brain (12.3%). Sequential chemoradiotherapy (radiotherapy after completion of chemotherapy) was administered to LS and only chemotherapy to ES patients. The response rates including both complete and partial responses that could be evaluated for 73 patients were 80%, 41.5%, and 52% for LS, ES, and overall patients, respectively. Median survival (for 73 patients) was 311 days, 163 days, and 201 days for LS, ES, and overall patients, respectively.

**Conclusions:** Although demographic and clinical features of the patients were nearly the same with that of the previous series, except higher ES disease in our study, the median survival values and the response rates including both complete and partial responses for both LS and ES disease were lower than the previous series.

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**Key words:** Small-cell lung cancer, staging, median survival, response rate

**Abbreviations:** SCLC = small-cell lung cancer, LS = limited stage, ES = extensive stage

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## Introduction

Primary carcinoma of the lung is a major health problem with a generally grim prognosis. Lung cancer accounts for 32% of all cancer deaths in men and for 25% of deaths in women and it is the leading killer cancer. Small-cell lung cancer (SCLC) makes up about 20% of all the lung cancer cases. (1,2)

Although many studies related to lung cancer were carried out in western countries as well as in our country, unfortunately there was not such a study in our region, that is the Black Sea region. Thus, we retrospectively designed the present study to evaluate the clinical features and outcomes of SCLC cases that were diagnosed in our clinic, Ondokuz Mayıs University Department of Pulmonary Medicine between January 1988 and December 1997.

## Materials and Methods

**Eligibility criteria:** Histologically and/or cytologically documented SCLC in our clinic between January 1988 and December 1997.

The files and records of the patients seen in our clinic were carefully reviewed to identify eligible patients and all the data including;

**a) Demographic characteristics:** Age, gender, marital status, smoking status, occupation, birth and living place,

**b) History:** Chief complaint, symptoms, past and family histories,

**c) Physical examination findings,**

**d) Laboratory values:** Complete blood count (CBC), whole blood chemistry, urinalysis, electrocardiography (ECG), echocardiography,

**e) Radiologic findings:** Chest x-ray, abdominal ultrasonographic scans and thoracic computed tomography (CT) scans,

**f) Diagnostic procedures:** Bronchoscopy including both forceps biopsy and transbronchial procedures, percutaneous (CT or USG guided) transthoracic procedures, sputum cytology, thoracentesis and pleural biopsies, lymph node biopsies, surgical routes,

**g) Staging procedures:** Thoracic, abdominal and cranial CT scans, bone scintigraphy, bone marrow biopsies, magnetic resonance imaging of the thorax,

**h) Treatment modalities:** Chemotherapy and radiotherapy (both palliative and curative) protocols,

**i) Response:** Complete response, partial response, stable disease and progressive disease,

**j) Survival,**  
were evaluated.

The definitions we used for staging and response are: (3)

**Limited stage (LS):** Defined as no detectable disease

outside the hemithorax, with or without ipsilateral, mediastinal, hilar, or supraclavicular lymph nodes.

**Extensive stage (ES):** Defined as any disease occurring beyond the sites listed for limited stage.

**Complete response (CR):** The disappearance of all known disease, determined by two observations not less than four weeks apart.

**Partial response (PR):** 50% or more decrease in total tumor load of the lesions that have been measured to determine the effect of the therapy by two observations not less than four weeks apart.

**Stable disease (SD) (no change):** Neither a 50% decrease in total tumor size can be established nor a 25% increase in the size of one or more measurable lesions has been demonstrated.

**Progressive disease (PD):** 25% or more increase in the size of one or more measurable lesions or emergence of new lesions.

**k) Statistical analysis:** A computer program (SPSS) was used for all statistical analyses. Survival was calculated from the day of diagnosis using the method of Kaplan and Meier.

## Results

**The study group:** Over the 10-year study period, one hundred and fifty five patients were diagnosed to have small-cell lung cancer (SCLC) comprised the study group.

**Age:** Within the study group, 74 (47.7%) were 56-65 years old, 33 (21.3%) were 46-55 years, 26 (16.7%) were 66-75 years, 16 (10.3%) were 36-45 years, 3 (1.93%) were <35 years, and 3 (1.93%) were 76-85 years old (figure 1). The mean age was 58±8.1 years.

**Gender:** The group included 141 male and 14 female patients with male to female ratio (M/F) of 10/1 (figure 1).

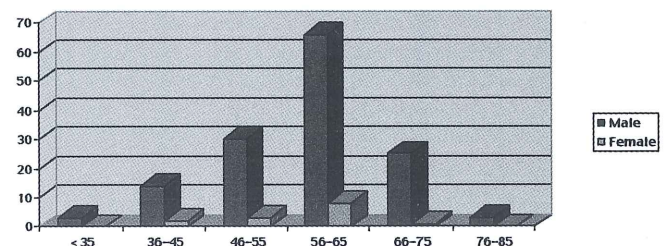


Fig. 1. Age and gender of the SCLC cases

**Occupation:** The occupations were diverse, with the largest sub-groups consisting of 44 (28.3%) farmers and 25 (16.1%) factory workers.

**Risk factors:** Data regarding the habitual use of tobacco available on 137 patients, revealed that 96.8% of males and 30% of females were current smokers, and median cumulative cigarette consumption was 35 pack-years. In addition, two females were passive smokers. There was no history of other risk factors for SCLC including asbestos.

**Past history:** In 3 (1.93%) patients the SCLC was diagnosed as a second primary cancer. All of the three patients have been diagnosed as epidermoid carcinoma of the larynx and treated, and also followed-up for 5, 6, and 10 years, respectively.

**Family history:** 13 (8.3%) patients who were all current smokers had also a cancer history in their first-degree relatives.

**Chief complaints:** The most frequent ones were cough, progressive dyspnea, and chest pain, with 28%, 23.2%, and 19.2%, respectively (Table 1).

| Chief Complaints       | no. of patients (%) |
|------------------------|---------------------|
| Cough ± sputum         | 44 (23.8)           |
| Dyspnea                | 36 (23.1)           |
| Chest pain             | 30 (19.2)           |
| Extrathoracic pain     | 16 (10.3)           |
| Fatigue                | 8 (5.1)             |
| Hoarseness             | 8 (5.1)             |
| Anorexia + weight loss | 7 (4.5)             |
| Hemoptysis             | 6 (3.8)             |

**Clinical findings:** Physical examination revealed superior vena cava syndrome in 12 (7.7%) patients. Neither Pancoast syndrome nor Cushing syndrome was not diagnosed in the group.

**Laboratory findings:** CBC and whole blood chemistry values were evaluated and the abnormal ones were noted as follows; mean hemoglobin level was 12.3 gr/dl (N: 13-18 gr/dl), mean sedimentation rate was 61.33 mmhr (N: <20 mmhr), mean LDH level was 736.7 U/L (N: 95-500 U/L).

**Radiologic findings:** Both chest x-ray and thoracic CT findings were evaluated for 125 patients. A hilar mass with mediastinal widening was the most common ab-

normality on chest x-ray. Thoracic CT scans mostly revealed a centrally located solid mass ( $\geq 4$  cm in diameter) of irregular borders and ipsilateral hilar and/or mediastinal lymphadenopathies. Cavitation was detected in only one patient and also there was neither chest wall invasion by the tumor nor solitary pulmonary nodules.

**Diagnostic procedures:** The detailed documentation of diagnostic procedures were shown in Table 2. Fiberoptic bronchoscopy was the most effective procedure for diagnosis that reached the diagnosis in 141 (90.7%) patients. Thoracotomy was needed in only 3 (1.9%) patients in order to make a diagnosis. There was only one postmortem diagnosis.

| Procedure                                 | no. of patients (%) |
|---|---------------------|
| Fiberoptic bronchoscopy                   | 141 (90.7)          |
| Transthoracic biopsy (CT guided)          | 4 (2.5)             |
| Thoracotomy                               | 3 (1.9)             |
| Sputum cytology                           | 2 (1.3)             |
| Video assisted thoroscopic surgery (VATS) | 1 (0.7)             |
| Pleural biopsy                            | 1 (0.7)             |
| Liver biopsy                              | 1 (0.7)             |
| Excisional lymph node biopsy              | 1 (0.7)             |
| Postmortem biopsy                         | 1 (0.7)             |

**Staging:** All patients underwent staging procedures that include thoracic, abdominal and cranial CTs, bone scintigraphy, and if the mentioned procedures were negative for metastasis unilateral bone marrow biopsy was made. As a result of the staging procedures it was seen that 40 (25.8%) patients were in limited stage and 115 (74.2%) patients were in extensive stage (Table 3). Bone was the most common metastatic site (42.9% of patients) that was followed by the liver (27.6% of patients) and the brain (12.3% of patients).

| Stage           | no. of patients (%) |
|-----------------|---------------------|
| Limited stage   | 40 (25.8)           |
| Extensive stage | 115 (74.2)          |
| Total           | 155 (100)           |

**Treatment modalities:** A sequential chemoradiotherapy for limited stage and only chemotherapy for extensive stage patients were planned. Sequential chemoradiotherapy comprised of administration of 6 courses of chemotherapy every 21 days and curative radiotherapy of 50-55 cGy 6 weeks after completion of chemotherapy.

Each course of chemotherapy lasted 3 days and included administration of etoposide, 100 mg/m<sup>2</sup>/day, and cisplatin, 100 mg/m<sup>2</sup>, only during the first day. For ES patients the same chemotherapy protocol was applied and also radiotherapy was administered for cranial metastasis.

**Response rates:** Evaluation of response could be done for 73 patients. The complete response was 35%, 15.1%, and 20.5% for LS, ES, and overall patients, respectively and partial response was 45%, 26.4%, and 31.5% for LS, ES, and overall patients, respectively. The response rates including both complete and partial response were 80%, 41.5%, and 52% for LS, ES, and overall patients, respectively (Table 4).

**Survival:** Survival that could be evaluated for 73 patients was calculated from the day of diagnosis using the method of Kaplan and Meier. The median survival was 311 days, 163 days, and 201 days for LS, ES, and overall patients, respectively.

## Discussion

The mean age of our patients was 58±8.1 years which is similar to the previous series in the literature (1,2). Only 3 patients (1.93%) were younger than 35 years which is approximately the same with the previous studies in the literature (1,2).

The present study has revealed that mainly the males were affected with a male to female ratio of 10/1 which was higher than the previous studies in western countries, but was consistent with that of the developing countries, that either lack regulations or are far less strict in regulating nicotine and tar content of cigarettes and also in which the average tar yield is higher than western countries (2,4).

The role of smoking as the most important cause of lung cancer is undeniable and has been implicated as the main cause of almost 90% of the deaths from lung cancer.

Like all the other lung cancers, SCLC is linked to environmental factors. The strongest association is with cigarette smoking and up to 98% of the patients have a history of smoking (1,2,5). Our study also underlined this fact impressively that 96.8% of males and 30% of females were current smokers with median cumulative cigarette consumption of 35 pack-years.

In our study, the most common chief complaints were cough, dyspnea and chest pain, in decreasing order, and the most frequent radiologic abnormality was an irregularly bordered hilar mass with mediastinal widening. Fiberoptic bronchoscopy was the sole means of diagnosis in about 90% of the patients which were all consistent with the classical knowledge about SCLC.(1,5)

As a result of the staging procedures, it was seen that 40 patients (25.8%) were in LS, whereas 115 patients (74.2%) were in ES, in which the bones, the liver and the brain were the most commonly involved organs. The values for ES were higher than the previous series (5,6). Approximately 60-70% of the patients were in ES which might be due to a delay in presentation of the patients to our clinic.

In the literature (5-13), it is well known that the median survival for untreated patients is 4 to 6 months for LS SCLC and 5 to 9 weeks for ES SCLC patients. Combination chemotherapy or chemoradiotherapy for LS produces expected overall and complete response rates of 80 to 90% and 50%, respectively. For ES, expected overall and complete response rates are 60 to 80% and 15 to 20%, respectively. The response rates for both of LS and ES were lower in our study than the values mentioned above although we applied standart treatment protocols (Table 4). Also the median survival values that were 311 days, 163 days, and 201 days for LS, ES, and overall patients, respectively are lower than the previous series (5-13).

In conclusion, although demographic and clinical features of our SCLC patients were nearly the same with the

| Modalities (for 73 patients) |                                     |                                       |                             |
|------------------------------|-------------------------------------|---------------------------------------|-----------------------------|
| Response                     | Limited Stage<br>no.of patients (%) | Extensive Stage<br>no.of patients (%) | Total<br>no.of patients (%) |
| Complete response            | 7 (35)                              | 8 (15.1)                              | 15 (20.5)                   |
| Partial response             | 9 (45)                              | 14 (26.4)                             | 23 (31.5)                   |
| Stable disease               | 1 (5)                               | 6 (11.3)                              | 7 (9.5)                     |
| Progressive                  | 3 (15)                              | 25 (47.2)                             | 28 (38.5)                   |
| TOTAL                        | 20 (100)                            | 53 (100)                              | 73 (100)                    |

literature, except higher rate of ES disease in our study, the response rates including both partial and complete response for both of LS and ES disease and also the median survival values were lower than the previous series.

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