INTRODUCTION

Lung cancer is one of the primary reasons behind deaths caused by cancer all around the world. Small cell lung cancer (SCLC) comprises 15 to 25% of all lung cancer cases. SCLC is centrally located for most cases. Among the most common complaints are cough, dyspnea, hemoptysis and pain. Symptoms manifest themselves related to an intrathoracic disease or distant metastases. SCLC has a rapid and destructively progressive course. It is considered a systemic disease since it metastasize to distant organs at the early stage. SCLC often metastasize to brain, bones, liver, adrenal and to the opposite lung (1).

More than 50% of cases with lung cancer are diagnosed after the age of 65 while 30% of them follow the suit around the age of 70. The prevalence of accompanying diseases, various geriatric troubles and nutritional disorders are major problems for cases with lung cancer diagnosed at an advanced age. The current primary therapy options for SCLC include chemotherapy (CT) and radiotherapy (RT). SCLC has a poor prognosis in the long run even though it is responsive to CT (2). Various studies have been carried out in an effort to gain insight into factors with an impact on prognosis for SCLC. It is reported that the stage, the Eastern Cooperative Oncology Group performance score (ECOG PS), laboratory parameters and treatments applied in pursuit were evaluated. 3-month survival rate of patients was 75.9%, 50.2% for 6-month, 21.4% for 1 year, and 5.5% for 2 years during follow up. ECOG PS and stage were found statistically significant risk factors in model created to determine overall survival.

Conclusion: Performance score at the time of diagnosis, stage and presence of liver metastasis are identified as prognostic factors for SCLC and of these factors are quite valuable to predict the clinical outcome.

Key words: SCLC; prognostic factors; survival

Factors Affecting Survival in Small Cell Lung Cancer

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ABSTRACT

Objective: Small cell lung cancer (SCLC) constitutes about 15-25% of lung cancers with high mortality rate. Herein we observed the effect of parameters at the time of diagnosis to survival of cases with SCLC.

Methods: We evaluated 65 patients who were followed up in our oncology department retrospectively.

Results: Tumor location and stage at the time of diagnosis, smoking history, accompanying comorbidities, ECOG PS, laboratory parameters and treatments applied in pursuit were evaluated. 3-month survival rate of patients was 75.9%, 50.2% for 6-month, 21.4% for 1 year, and 5.5% for 2 years during follow up. ECOG PS and stage were found statistically significant risk factors in model created to determine overall survival.

Conclusion: Performance score at the time of diagnosis, stage and presence of liver metastasis are identified as prognostic factors for SCLC and of these factors are quite valuable to predict the clinical outcome.

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INTRODUCTION

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Conclusion: Performance score at the time of diagnosis, stage and presence of liver metastasis are identified as prognostic factors for SCLC and of these factors are quite valuable to predict the clinical outcome.

Key words: SCLC; prognostic factors; survival
of normal distribution, and through Mann Whitney U test when they did not. Inter-group rates of the categorical variables were tested via Chi-Square Analysis. Survival rates were tested through Kaplan Meier Survival analysis. Risk factors were defined by Cox regression analysis through test Forward method. Statistical significance level (alpha) was considered as p<0.05.

**RESULTS**

The study included a total of 65 cases including 64 men and 1 woman with an average diagnostic age of 62.4±9.8 years. 93.8% of the cases were smokers. Number of Cigarettes packs/year average of cases was 52.0±25.4. Among comorbid diseases were Essential Hypertension (EH) (15.4%), Diabetes Mellitus (12.3%), Chronic Obstructive Pulmonary Disease (7.7%), Coronary Artery Disease (3.1%) and others (6.2%). ECOG PS scores of the cases at the time of diagnosis were 6.2%- 0, 30.8%- 1, 32.3% - 2, 23.1% - 3,

7.7% - 4. Cases were diagnosed through bronchoscopy (72.3%), Transthoracic biopsy (75.0%) and with a 2nd line therapy were cases of metastasis. The percentage of liver metastasis. (Table 2) was statistically high to a significant extent (p=0.006 p<0.001). There was a statistically significant difference for metastatic site percentages (p<0.001). Cases of exitus had a high percentage of liver metastasis. (Table 2).

### Table 2: Factors affecting mortality

<table>
<thead>
<tr>
<th>Alive</th>
<th>Exitus</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic information</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis Avg.±SD</td>
<td>59.2±9.3</td>
<td>63.1±9.9</td>
</tr>
<tr>
<td>Gender n (%)</td>
<td>Male</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Female</td>
<td>0 (0.0)</td>
<td>1 (1.9)</td>
</tr>
<tr>
<td>Smoking (Pack/year) Avg.±SD</td>
<td>48.4±31.2</td>
<td>52.9±24.2</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>N/A</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td>DM</td>
<td>0 (0.0)</td>
<td>8 (15.1)</td>
</tr>
<tr>
<td>HT</td>
<td>3 (25.0)</td>
<td>7 (13.2)</td>
</tr>
<tr>
<td>COPD</td>
<td>0 (0.0)</td>
<td>5 (9.4)</td>
</tr>
<tr>
<td>CAD</td>
<td>0 (0.0)</td>
<td>2 (3.8)</td>
</tr>
<tr>
<td>Other</td>
<td>2 (16.7)</td>
<td>2 (3.8)</td>
</tr>
<tr>
<td>RT</td>
<td>9 (75.0)</td>
<td>28 (52.8)</td>
</tr>
<tr>
<td>At diagnosis</td>
<td>ECOG PS Avg.±SD</td>
<td>1.3±1.1</td>
</tr>
<tr>
<td>n (%)</td>
<td>0</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>1</td>
<td>7 (58.3)</td>
<td>13 (24.5)</td>
</tr>
<tr>
<td>2</td>
<td>2 (16.7)</td>
<td>19 (35.8)</td>
</tr>
<tr>
<td>3</td>
<td>0 (0.0)</td>
<td>15 (28.3)</td>
</tr>
<tr>
<td>4</td>
<td>1 (8.3)</td>
<td>4 (7.5)</td>
</tr>
<tr>
<td>Method of diagnosis</td>
<td>Bronchoscopy</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Transthoracic biopsy</td>
<td>0 (0.0)</td>
<td>8 (15.1)</td>
</tr>
<tr>
<td>Metastatic sites</td>
<td>Limited</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Extensive</td>
<td>19 (29.2)</td>
<td>46 (80.8)</td>
</tr>
<tr>
<td>Right</td>
<td>38 (58.5)</td>
<td>27 (41.5)</td>
</tr>
<tr>
<td>Left</td>
<td>22 (33.8)</td>
<td>21 (33.8)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>Yes</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td>Metastatic sites</td>
<td>N/A</td>
<td>10 (83.3)</td>
</tr>
<tr>
<td>Liver</td>
<td>1 (8.3)</td>
<td>7 (13.2)</td>
</tr>
<tr>
<td>Bone</td>
<td>0 (0.0)</td>
<td>20 (37.7)</td>
</tr>
<tr>
<td>Other (Indicate)</td>
<td>0 (0.0)</td>
<td>9 (17.0)</td>
</tr>
<tr>
<td>Metastatic sites</td>
<td>N/A</td>
<td>10 (83.3)</td>
</tr>
<tr>
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<td>1 (8.3)</td>
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</tr>
<tr>
<td>Bone</td>
<td>0 (0.0)</td>
<td>20 (37.7)</td>
</tr>
<tr>
<td>Other (Indicate)</td>
<td>0 (0.0)</td>
<td>9 (17.0)</td>
</tr>
<tr>
<td>At diagnosis</td>
<td>VCSS</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>VCSS Biochemical tests Avg.±SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDH</td>
<td>319.4±187.6</td>
<td>274.3±984.3</td>
</tr>
<tr>
<td>Na</td>
<td>135.4±3.8</td>
<td>136.3±3.9</td>
</tr>
<tr>
<td>AST</td>
<td>22.6±4.6</td>
<td>40.4±43.1</td>
</tr>
<tr>
<td>ALT</td>
<td>20.8±8.2</td>
<td>34.6±37.4</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.7±0.4</td>
<td>3.6±0.6</td>
</tr>
<tr>
<td>Ca</td>
<td>9.1±0.5</td>
<td>9.1±0.8</td>
</tr>
<tr>
<td>CT</td>
<td>12 (100)</td>
<td>34 (64.2)</td>
</tr>
<tr>
<td>RT</td>
<td>9 (75.0)</td>
<td>28 (52.8)</td>
</tr>
<tr>
<td>1st Line CT</td>
<td>No CT</td>
<td>9 (75.0)</td>
</tr>
<tr>
<td>Carbolplatin + Etoposide</td>
<td>11 (91.7)</td>
<td>31 (58.5)</td>
</tr>
<tr>
<td>CT cure count Avg.±SD</td>
<td>4.3±1.8</td>
<td>3.1±2.8</td>
</tr>
<tr>
<td>2nd Line CT</td>
<td>No CT</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Average length of follow-up Avg.±SD</td>
<td>11.3±16.0</td>
<td>6.0±6.1</td>
</tr>
</tbody>
</table>

46 of cases were administered with CT for the follow-up period while 19 of them were not. 37 of the cases were administered with carboplatin+etoposide while 4 of them were administered with carboplatin+etoposide. 15 of the cases were administered with 2nd line therapy. All of those without a 1st line therapy and with a 2nd line therapy were cases of exitus (Table 2).

**ECOG PS average for the followed cases of exitus at the time of diagnosis, and percentages of the extensive stage were statistically high to a significant extent (p<0.006 p<0.001).** There was a statistically significant difference for metastatic site percentages (p<0.001). Cases of exitus had a high percentage of liver metastasis. (Table 2)
ECOG PS and stage were found to be statistically significant risk factors for the model established in an effort to identify the general survival among age, gender, cigarette pack/year, ECOG PS, stage, localization, pleural effusion, VCSS and comorbidity at the time were diagnosed (Figure 1).

Estimated median survival times of ECOG PS groups proved a statistically significant difference (p<0.001) (Table 4).

Table 4: Estimated median survival times of ECOG PS groups

<table>
<thead>
<tr>
<th>ECOG PS</th>
<th>Median</th>
<th>SEM</th>
<th>95% CI</th>
<th>Log-Rank p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>13</td>
<td>0.8</td>
<td>11.4</td>
<td>14.6</td>
</tr>
<tr>
<td>1</td>
<td>10</td>
<td>1.9</td>
<td>6.3</td>
<td>13.7</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>2.0</td>
<td>3.0</td>
<td>11.0</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>1.2</td>
<td>0.0</td>
<td>4.3</td>
</tr>
<tr>
<td>4</td>
<td>0</td>
<td>.</td>
<td>.</td>
<td>.</td>
</tr>
</tbody>
</table>

3-month survival percentages of the cases for follow-up were 75.9% while 6-month, 1-year and 2-year percentages were 50.2%, 21.4%, and 5.5% respectively. Estimated median survival time was 7 months (Figure 2, Table 5). Estimated median survival time for the extensive stage was 1.2 months while the median value for the limited stage was 11.6 months. Estimated median survival times of the groups proved a statistically significant difference (p<0.001) (Figure 3, Table 6).

Table 5: Overall survival

<table>
<thead>
<tr>
<th>Overall survival</th>
<th>Estimated overall survival time (month) median±SEM (m%95 CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival</td>
<td>7.0±1.0 (5-9)</td>
</tr>
<tr>
<td>3 months</td>
<td>75.9%</td>
</tr>
<tr>
<td>6 months</td>
<td>50.2%</td>
</tr>
<tr>
<td>1 year</td>
<td>21.4%</td>
</tr>
<tr>
<td>2 year</td>
<td>5.3%</td>
</tr>
</tbody>
</table>

DISCUSSION

SCLC is a type of cancer with a highly aggressive course and a low long-term survival rate (5). It is argued that some laboratory parameters at the time of diagnosis can be put into use as prognostic factors for SCLC patients (6). Advanced age, comorbidities that surface with age, and decreased physiological reserve point to a poor prognosis. At the time of diagnosis, about 2/3 of patients are at the extensive stage (7). Retrospectively carried out with 18153 SCLC cases, a study revealed that the median survival time was 6 months for all the patients, 1 year for patients at the limited stage, and 4 months for those at the extensive stage (8).

Mean age of the patients in our study was 62.4±9.8 years while the most common comorbidity was HT. Majority of the patients was at the extensive stage (29.2% at the limited stage, and 70.8% at the extensive stage). Patients at the extensive stage lived for a shorter period of time (Median time: 1.2 months). Median survival time for the patients at the limited stage was 11.6 months. Estimated median survival time for all the patients accounted for 7 months. 78.5% of exitus cases were...
within the first 6 months following the inception of therapy is univariate and multivariate analyses (16). Further, they identified no significant difference when it came to a multivariate analysis. The stage was a prognostic factor for survival; however, the analysis was limited to the female gender. Among prognostic factors for the limited stage was good PS, normal serum CEA, and VEGF level. In addition, Prophylactic Cranial Irradiation (PCI) and the number of metastatic lesions were reported to be independent prognostic factors for patients at limited and extensive stages. Female gender was defined as a good prognostic factor to survive. Among prognostic factors for the limited stage were good PS, normal serum CEA, and VEGF level and PCI. Among prognostic factors for extensive stage were good PS, a metastatic site, normal serum CEA, and VEGF level (17).

Clinical stage at the time of diagnosis is one of the key prognostic factors. Limited stage seemed a better prognosis than the extensive stage. Increasing number of metastasis at the stage worsens the prognosis (12). Chen et al. argue that after restoring other known factors, low PS does not estimate the poor survival, and PS should not be the sole factor for therapy decisions (11). Clark et al. pointed out that a good performance score, female gender, and limited stage are good prognostic factors (13). In addition, Foster et al. revealed that hyponatremia is an independent determinant of mortality (30-32% (19)). Among the metastatic sites in our study were liver for 30.8%, bone for 15.4%, brain for 12.3%, and others for 10.8% of the cases. Bonemetaestases point to a poor prognosis for lung cancer patients. Mortality rate increases for majority of patients with a bone metastasis or a complication induced by bone involvement (19). Cases of exitus had an extremely high percentage of liver metastasis in our study.

In conclusion, our study could not prove through laboratory tests that LDH, Na, AST, ALT, and Ca scores are independent prognostic factors. Age, pleural fluid and VCSS were not found to be prognostic factors. Performance score, stage and liver metastasis were identified as significant factors which define the prognosis. Knowing about some prognostic factors at the time of diagnosis is extremely important to estimate clinical results for this type of cancer. In addition, gaining insight into the specific administration of therapy, response to treatment, and some predictive factors to know about toxicity are highly important for patient selection and post-therapy response expectations.

Patient's Consent: Written informed consent was not obtained due to the retrospective nature of the study.

Financial Aid: None.

Conflict of Interests: None.

REFERENCES


