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Prospective evaluation of patients with small cell lung cancer: A single center study

Küçük hücreli akciğer kanseri tanısı alan hastalarımızın prospektif incelemesi: Tek merkezli çalışma

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Abstract

Aim: Small cell lung cancer (SCLC) is the most aggressive form of lung cancer. No major treatment advances have occurred for SCLC over the past 30 years, unlike non-small cell lung cancer (NSCLC). We aimed to prospectively examine demographic, clinical, radiological properties, its association with cigarette smoking, delays in diagnosis, treatment responses, toxicities, prognostic factors, and survivals.

Methods: Patients diagnosed with small cell lung cancer during 4 years in Ondokuz Mayıs University, Department of Chest Diseases were included in our prospective cohort study. The demographic characteristics of the patients, symptoms, performance status, laboratory, radiologic, bronchoscopy findings, staging procedures, periods from the initiation of the symptoms to the admission of the patients to our department and definitive diagnosis, chemotherapy responses and toxicities were recorded. Follow-ups were performed in our clinic. Dates of deaths of patients who died outside our hospital were followed up from the records of census directorate. Patients that we lost to follow up, with missing data, or those who did not give consent for participation in the study were excluded.

Results: The study group consisted of 88 patients (82 males, 6 females). The mean age was 61.16 years. The main symptoms on admission were cough (77%), fatigue (62%), dyspnea (60%). Among all, 39% of patients had limited disease whereas the remaining 61% were extensive. The median delay between the occurrence of first symptom and the patient's presentation to our clinic was 30 days and the median delay before diagnosis was 10 days. Seventy-seven patients were given cisplatin/carboplatin-etoposide as the first line and irinotecan as second line chemotherapy. Overall median survival was 355 (30.8) days, 416 (47) days in limited stage and 296 (48) days in the extensive stage (P=0.003). Six-month cumulative survival was 76%, and 12-month cumulative survival was 44%. Univariate analysis showed that increased LDH levels, performance score >1, extensive stage and weight loss were poor prognostic factors (P=0.042, 0.001, 0.003, 0.022). In multivariate analysis, serum LDH levels, performance score >1 and extensive disease were independent poor prognostic factors.

Conclusion: The ratio of our female patients is still much lower than the world average. Time from the admission of our patients to diagnosis was shorter than most of the developed countries. However, treatment response rates and survival periods were within lower limits of world reports. Stage, PS, LDH can be used as independent prognostic factors.

Keywords: Small cell lung cancer, Chemotherapy, Prognosis, Survival

Öz

Amaç: Küçük hücreli akciğer kanseri en saldırgan akciğer kanseri türüdür. Küçük hücreli dışı akciğer kanserinin aksine son 30 yılda tedavide kaydadeğer bir ilerleme gösterilememiştir. Biz bu çalışmada SCLC hastalarının demografik, klinik, radyolojik özelliklerini, sigara ile ilişkisini, tedavi gecikmelerini, tedavi yanıtları, toksisiteleri, prognoza etki eden faktörleri ve yaşam sürelerini incelemeyi amaçladık.

Yöntemler: Samsun Ondokuz Mayıs Üniversitesi Tıp Fakültesi Göğüs Hastaıklarında 4 yıllık sürede küçük hücreli akciğer kanseri tanısı alan hastalar prospektif kohort çalışmamıza dahil edildi. Hastaların demografik özellikleri, semptomları, performans durumları, laboratuvar, radyolojik, bronkskopik bulguları, evreleme tetkikleri, semptom başlangıcından bölümümüze müracat, müracattan tanıya kadar geçen süreler, kemoterapi yanıt ve toksisiteleri kaydedildi. Takipler bölümümüzde yapıldı. Hastanemiz dışında vefat eden hastaların ölüm tarihleri nüfus müdürlüğünden alındı. Takipten çıkan, eksik verisi olan veya onam vermeyen hastalar çalışmadan çıkarıldı.

Bulgular: Çalışma grubu 88 hastadan oluşuyordu. Bu hastaların 82'si erkek, 6'sı kadındı. Ortalama yaş 61,16 idi. Başvuru anındaki esas semptomlar öksürük (%77), yorgunluk (%62), dispne (%60) olarak tespit edildi. Tanı anında hastaların %39'u sınırlı hastalık iken %61'i yaygın evrede idi. İlk semptomdan kliniğimize başvurana kadar geçen sure ortalama 30 gün, tanı konulmasına kadar geçen süre ise 10 gündü. 77 hastaya birinci basamak tedavi olarak cisplatin/carboplatin-etoposide, ikinci basamak tedavi olarak da irinotecan uygulandı. Genel ortalama yaşam süresi 355 (30,8) gün olup sınırlı hastalıkta 416 (47) gün, yaygın hastalıkta 29 (48) gün olarak bulundu (P=0,003). 6 aylık kümülatif survival %76 iken, 12 aylık kümulatif survival %44 idi. Tek değişkenli analalizlerde LDH seviyeleri artışı, performans skoru (PS) >1, yaygın hastalık ve kilo kaybı kötü prognostik faktörlerdi (P=0,042, 0,001, 0,003, 0,022). Çok değişkenli analizlerde ise serum LDH seviyeleri, performans skoru >1 ve yaygın hastalık bağımsız kötü prognostik faktörler olarak belirlendi.

Sonuç: Kadın hasta oranımız halen dünya ortalaması altında. Hastaların kabulünden tanı konulana kadar geçen süre çoğu gelişmiş ülkeden daha kısa olmasına rağmen tedaviye yanıt oranları ve yaşam süreleri dünyada bildirilenlerin alt sınırındaydı. Evre, PS, LDH bağımsız prognostik faktor olarak kullanılabilir.

Anahtar kelimeler: Küçük hücreli akciğer kanseri, Kemoterapi, Prognoz, Yaşam süresi

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Introduction

Lung cancer is the most prevalent and preventable cancer type. Small cell lung cancer (SCLC) is the most aggressive form among all types associated with smoking [1].

SCLC accounts for 15% of all new lung cancers [2]. Small cell lung cancer (SCLC) is distinguished from non-small cell lung cancer by its rapid doubling time, high growth fraction, central localization, and the early development of widespread metastases. It has different histological, clinical and treatment features among lung cancers. Although the cancer is initially highly responsive to chemotherapy and radiotherapy, most patients will relapse with broadly resistant disease within a few months to a year from initial therapy. Consequently, most patients (60-70%) will have extensive stage disease at the time of diagnosis. The 5-year survival rate remains low at <7% overall, and most patients survive for only 1 year or less after diagnosis. [3] In contrast to NSCLC where significant improvements are observed with targeted agents and immunotherapies, no major treatment advances have occurred for SCLC over the past 30 years. [4] The major treatment of SCLC is still systemic chemotherapy or chemotherapy combined with radiotherapy.

In this study, we aimed to prospectively examine demographic, clinic, radiological properties of our patients diagnosed with SCLC, its association with cigarette smoking, delays in diagnosis, treatment results, side effects, prognostic factors, and survival.

Materials and methods

Patients who were diagnosed with small cell lung cancer were followed up for a period of 4 years in Ondokuz Mayıs University Faculty of Medicine, Department of Chest Diseases. The patients that we lost to follow up or have missing data, those not giving consent for inclusion into the study were excluded. This is a prospective, single center, cohort study that was approved by Ondokuz Mayıs University Ethics Committee (OMU KAEK, 2007/48)

After obtaining the histories of the patients, their physical examinations were performed. Age, gender, smoking status, weight loss, and other symptoms were recorded. Performances of the patients were determined in accordance with "European Cooperative Oncology Group (ECOG)" criteria [5]. Periods starting from the initiation of the symptoms until admission to our department and getting diagnosed were recorded. In the first admission, laboratory examinations (complete blood count, urea, lactate dehydrogenase (LDH), serum glutamate oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), alkaline phosphatase (ALP), serum albumin were performed. Chest radiography and thoracic Computed Tomography (CT) were obtained from patients. For staging, Magnetic Resonance Imaging of the brain, upper abdomen CT and bone scintigraphy or Positron Emission Tomography (PET/CT) were performed. Bronchoscopy findings, and if present, other methods of diagnosis were recorded. Histopathological assessment was performed in the pathology department of our hospital, in accordance with histological and cytological criteria of SCLC. Staging was performed according to Veterans' Affairs Lung Study Group (VALG) classification [6].

Chemotherapy was administered to patients who were diagnosed during the limited stage, and simultaneous thoracic Radiotherapy (RT) was administered to patients with favorable general conditions. Only chemotherapy was administered to patients who were in the extensive stage. Platinum-based (cisplatin or carboplatin) and etoposide protocol was administered as first-line, and irinotecan or topotecan was administered as second-line chemotherapy. Chemotherapy toxicities were recorded in accordance with "Common Terminology Criteria for Adverse Events (CTCAE)" criteria. Chemotherapy responses were assessed with "Response Evaluation Criteria in Solid Tumors (RECIST)" [7] criteria.

At the end of the treatment, prophylactic cranial RT was administered to patients having full response. After the treatment, follow-ups were performed in our clinic. Dates of deaths of patients who died outside our hospital were followed up from the records of census directorate.

Statistical analysis

Data were presented as frequency in categorical variables, mean (standard deviation, SD) for normally distributed continuous variables and as median (25-75%) for those that do not comply with normal distribution. Survival times were given as median (SD).

In the comparison of continuous variables, "student t test" was used for variables complying with normal distribution, and "Mann-Whitney U" test was used for those that do not comply. In the comparison of categorical variables, chi-square and Fisher exact test were used. Kaplan Meier survival analysis and Log Rank analysis were used in the comparison of groups with respect to survival time. Impact of independent variables on survival was assessed with Cox regression analysis. Level of statistical relevance was $P<0.05$.

Results

A total of 493 patients were diagnosed with lung cancer in our clinic. The number of patients diagnosed with SCLC and NSCLS were 97 (19.67%), and 388 (78.7%), respectively. Other 8 (4.15%) patients were diagnosed with carcinoid tumor, lymphoma, and sarcoma.

Nine out of 97 SCLC patients were lost to follow up. Remaining 88 patients were included in this study. Six (6.8%) were female, 82 (93.2%) were male (M/F=14.7/1). The overall mean age was 61.16 (10.7) years (61.5 (10.3) years in males and 55.3 (14.9) years in females). There was no significant difference between the mean ages of males and females (p>0.05). The age groups that had the highest incidence of cancer in both genders was over the age of 65 years.

All patients except 2 non-smoker women were smokers. One was subjected to passive smoking for 25 years due to her husband. Fifty-one (58%) of the patients smoked more than 40 package/years. Fifty-nine (67%) were still smoking.

Main symptoms of the patients were examined (Table 1). Cough was the most frequent symptom in 24 (27.3%) patients. Shortness of breath ranked number two in 22 (25%) patients.

We detected paraneoplastic syndromes in 14 (15.9 %) patients, "Syndrome of inappropriate antidiuretic hormone secretion" (SIADH) in 9 (10.2%) patients, hypercalcemia in 4 (4.5%) patients, and gynecomastia in 1 (1.1%) patient.

Median time from the initiation of complaints of the patients to their admission to our department was 30 days (15–60 days), median time from admission to diagnosis was 10 days (7-16 days) (Table 2).

Chest radiography results of our patients are given in Table 3. None were normal. The most frequent abnormality was the hilar enlargement in 72 patients (81.8%).

Bronchoscopy was performed to all patients except 1, who refused the procedure. Sixty-nine patients (78.4 %) were diagnosed by bronchoscopy, thirteen patients (14.7 %) by CT guided transthoracic biopsy, two patients (2.3 %) by thoracoscopy, mediastinoscopy and lymph node biopsy each. Bronchoscopic findings of the patients are presented in Table 4.

Performance status of the patients were as follows: 28 (31.8%) ECOG 0, 19 (21.6%) ECOG 1, 26 (29.5%) ECOG 2, 12 (13.6%) ECOG 3 and 3 (3.4%) ECOG 4. Two ECOG 4 patients died before the initiation of chemotherapy. The remaining patient who was in the limited stage despite being ECOG 4 fully responded to chemotherapy. The patient who rejected prophylactic cranial RT died 6 months later due to brain metastasis and progression in the primary mass.

Majority of the patients were in the extensive stage 53 (60.2%), 35 (39.7%) patients were in the limited stage. Locations of metastasis detected during extensive stage are given in Table 5 in detail.

Table 1: Symptoms of small cell lung cancer patients

Symptoms	Number	%
Cough	24	27.3
Shortness of breath	22	25.0
Extra-thoracic pain	13	14.8
Hemoptysis	9	10.2
Chest pain	8	9.1
Swelling of the head and neck	3	3.4
Fatigue, weakness	3	3.4
Hoarseness	2	2.3
Loss of appetite-weight loss	2	2.3
Numbness, tingling	2	2.3
Total	88	100.0

Table 2: Time from the first symptoms of the patient to diagnose

	Time (day) Mean	Median	Min-Max
Symptom - admission	53 (66)	30 (15-60)	1-365
Admission - diagnosis	13.6 (11.1)	10 (7-16)	2-60
Symptom-diagnosis	67 (69)	39.5 (27-71)	8-38

Table 3: Distribution of chest radiography findings of SCLC patients

Abnormal findings	Number*	%
Hilar enlargement	72	81.8
Consolidation	21	23.9
Atelectasis	20	22.7
Pleural effusion	18	20
Enlargement in mediastinum	15	17
Peripheral nodule or mass	13	14.8
Normal	0	0

(*) More than one finding is present in some of the cases

Table 4: Bronchoscopic findings of SCLC patients

Findings		Number*	%
Vocal cord paralysis		9	10
Trachea	External Pressure	5	5.7
	Infiltrated	7	8
Carina	Blunt	15	17
	Infiltrated	8	9.1
Bronchus	Endobronchial lesion	35	39.8
	External pressure	54	61.4
	Infiltrated	39	44.3
Normal		11	12.6

(*) More than one finding is present in some of the cases

Table 5: Locations of metastasis detected during the extensive stage

Location of metastasis (*)	Number	%
Liver	26	31
Bone	23	27.4
Brain	16	19
Adrenal	9	10.7
Abdomen (liver except for adrenal)	5	6
Opposite lung	1	1.2

(*) More than one metastatic involvement might be present in a patient

While rate of weight loss was 72.5% in extensive stage, it was 39.4% in limited stage. A significant difference was present between the two stages in terms of weight loss [(x^2=7.8, sd=1, P<0.01), (OR=4.1, %95 GA 1.6<OR<10.3)] and survival (P=0.022).

Survival times were similar when compared according to laboratory parameters such as hemoglobin, white blood cell, thrombocyte counts, urea, SGOT, SGPT, ALP and serum albumin. Serum LDH level significantly impacted survival. Median LDH level was 424.5 (332-516) U/L in the limited stage, and 491 (385.7–696.5) U/L in the extensive stage (P=0.044).

Eleven (12.5%) out of 88 patients could not receive chemotherapy. Five died during the initial period after diagnosis. Six patients refused treatment. Seventy-seven (87.5%) patients received platinum-based treatment, thirty-three (42.9%) of which were in limited, and 44 (57.1%) of which were in extensive stage. Twelve patients (15.6%) died after 1-2 cycles. Thirteen patients (16.9%) received 3-4 cycles, and 52 patients (67.5%) received 5-6 cycles of "first line" chemotherapy. Neutropenic fever developed in 16 of the patients (20.8%). One patient died due to pancytopenia and neutropenic fever, 1 patient died due to pneumocystis carinii pneumonia and gastric perforation. Twelve patients (15.6%) developed Grade 1 nephrotoxicity; 1 patient (1.3%) had Grade 2 hepatotoxicity. None of the patients had advanced nephro- or hepatotoxicity. Six patients had stable, 30 patients had partial and 13 patients had complete response. 19 patients had (27.9%) progression. 9 patients who were lost to follow-up were not included in this assessment.

Progression occurred in the primary lesion of the thorax (32.5%) most. The second progression location was brain metastasis (11.7%). Sixteen patients who were found to have progressed after 3 months were administered the same protocol for a second time. Three developed stable disease, 2 had partial response and 6 had progression. Four patients died following chemotherapy and the other patient died 3 weeks later.

A total of 41 patients (53.2%) received RT, 22 of which (28.6%) received RT for curative purposes and 19 (24.7%), for palliative purposes. Palliative RT was applied mostly to the brain (%18.2).

Twenty-five patients were administered second line chemotherapy due to relapse or resistance to treatment; from these, 3 patients had stable disease, 2 had partial disease and 9 had progression. Five patients died after the first cycle; 3 patients died during the early period following the second cycle. One patient had to discontinue treatment due to acute abdomen. Two patients (2.6%) developed neutropenic fever due to second line chemotherapy, 3 patients developed (3.9%) grade 1 nephrotoxicity, 5 patients had (6.5%) grade 1, 1 patient (1.3%) had grade 2 hepatotoxicity. Median survival period of patients who received "second line" chemotherapy due to progression was 106 (34) days. Chemotherapy responses in accordance with stage were assessed, and statistically significant differences were

found between the stages (P=0.034). Response rates to platinum-based and etoposide in the limited and extensive stage were evaluated (Table 6).

Table 6: Response rates to platinum-based and etoposide due to stages

Response	Limited	Extensive
Stable	1(3.2%)	5(13.5%)
Partial	14(45.2%)	16(43.2%)
Complete	10(32.3%)	3(8.1%)
Progression	6(19.4%)	13(35.1%)
Total	31	37

When all patients were evaluated, median survival was 355 (30.8) days, 6-month cumulative survival was 76%, and 12-month cumulative survival was 44% (Figure 1).

Median survival was 416 (47.2) days in the limited stage and 296 (48.4) days in the extensive stage (P=0.003) (Figure 1). As a result of multivariate analyses, stage was concluded to be an independent prognostic factor [OR=2.1, (95% C.I. 1.1 – 3.8), P=0.019] (Figure 2).

In univariate analyses, ECOG 0 and 1 patients were compared with ECOG 2, 3 and 4 patients according to PS. Median survival time was 364 (25.4) days in ECOG 0 and 1 patients, and 134 (76) days in other patients (P=0.001). PS was an independent prognostic factor based on multivariate analyses [OR=2.8, (95% C.I. 1.4 – 5.3), P=0.004].

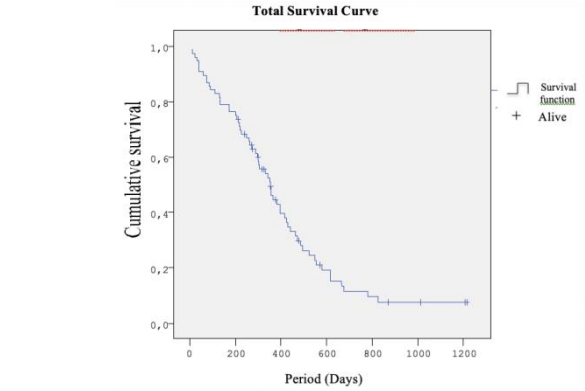

Figure 1: Overall median survival

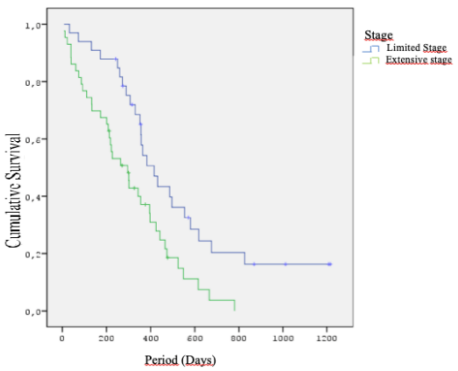

Figure 2: Survival curve in patients with small cell lung cancer according to stages

Discussion

SCLC is still at the top of the list of lung cancer related deaths among both genders in many countries of the world. Our male/female patient ratio is higher than other centers from Turkey, and much higher than other European countries and USA [8-10].

When we consider the fact that most of our patients came from rural areas, we can say that women smoke less than men and they might have developed less cancer. In the reports of big cities like Ankara, İstanbul and İzmir, female ratios are higher than ours. Though we do not have smoking ratios, smoking might be more common in women living in big cities.

The risk increases with increasing package/years ratio [11]. In a study performed in California with 4782 SCLC patients, only 2.5% of the patients were non-smokers [12] In a study of Mayo Clinic performed on 5628 patients with lung cancer, only 16 out of 635 SCLC patients (2.5%) had never smoked [13]. In our patient group, smoking ratio was 97.7%. All the men were smokers, only 2 women had never smoked. These findings support the fact that smoking is quite effective in etiology, and it especially reminds us that although significantly fatal, SCLC is almost completely preventable by not smoking.

The most frequent symptom was cough followed by shortness of breath, extrathoracic pain and hemoptysis, which are consistent with the literature [14].

Many studies report that diagnosis and treatment delays might negatively affect the tumor stage and prognosis [15]. Our results show that time from the admission of the patients to our clinic to diagnosis is shorter than many studies carried out throughout the world [16] and in our country [17-19]. When we consider the above-mentioned data, delays in world occur in places where primary care implementations are mandatory. Data on hand reveals this drawback of primary care implementations, and points to the fact that physicians must be more careful when they are examining their patients to not cause delays.

Most of SCLC disease is centrally located and hilar enlargement is the major radiologic anomaly [20]. Therefore, the rate of bronchoscopic diagnosis is higher than that in literature. [21].

Cohen et al [22] suggested for the first time that some laboratory values during the admission of SCLC patients might be prognostic factors with their studies in 1981 and found out that albumin and hemoglobin values were especially related to survival. Some studies found that low levels of hemoglobin, thrombocyte, increase in white cell, and neutrophil count were effective on survival [23,24]. However, they were ineffective in some other studies [25]. In our study, increase in white cell and neutrophil count, low levels of hemoglobin, and thrombocyte were ineffective on survival, contrary to some other studies [23,25]. Serum LDH level is the most studied parameter among laboratory values and the one which affects survival. In most studies, LDH value above the normal limit is indicative of poor prognosis. [23-26]. There are rare studies stating that it has no effect on survival [27,28]. In our study, LDH increase was an independent prognostic factor.

In a study by Rawson et al. [29] PS, stage, Na, ALP, SGOT and LDH were important prognostic factors. Among the laboratory tests that we evaluated, hemoglobin, white blood cell, thrombocyte counts, urea, SGOT, SGPT, ALP and serum albumin were not effective on survival.

There are many studies demonstrating that weight loss is a prognostic factor that affects survival [23,30]. In our study, weight loss was effective on survival only in univariate analyses. In the study by Arınç et al. [31], age (under and over the age 60 years), weight loss, gender, Hb, thrombocyte and albumin values, pleural effusion, having a mass with a size over or under 4 cm, liver and brain metastasis were ineffective on survival; stage, PS and SVCS were independent prognostic factors.

When we consider all our patients (limited and extensive stages), 19% had complete and 44% of the patients had partial response to chemotherapy, 8% had stable disease. Progression developed at a ratio of 27.9%. While our general response rate in limited stage was 77.5%, and complete response rate was 32.3%, these values were 51.3% and 8.12% in the extensive stage, respectively. The reason for our lower complete response rates compared to references might be related to living conditions, general conditions, and nutrition problems of our patients. Indeed, in Canada, lung cancer risk was inversely proportional with income, education, and social class in both sexes [32].

Death ratio due to chemotherapy complications in SCLC is below 5% [33]. Eight of our patients died right after chemotherapy (6 patients after the first and 2 patients after 2 cycles). However, these patients had multiple metastases during diagnosis and 3 of them were ECOG 3. It is difficult to say whether the reasons of their death were due to primary disease or chemotherapy complications. Since all these patients received chemotherapy, ethically, carrying out controlled studies seems impossible. Though chemotherapy must be administered in SCLC irrespective of performance score, we should also keep in mind the fact that these patients might prematurely die following chemotherapy.

Since 1970, disease stage and performance status of the patients have traditionally been used to predict survival periods of patients with SCLC. The prognostic factor that is supported by studies is performance status [23,25,34]. In our study, median survival was longer in the limited stage. Performance status of the patients were also effective on survival in line with references [25,34]. Stage and PS were independent prognostic factors.

Limitations

Our limitations include small sample size, short study period, and the fact that evaluation of laboratory and clinical parameters simultaneously may have caused complexity.

Conclusions

We would like to emphasize that the ratio of our female patients is still much lower than the world data; SCLC is causally related to smoking, and the time from the admission of our patients to diagnosis is shorter when compared with the data obtained in our country and many western countries. However, treatment response rates and survival periods are within but closer to lower limits. Contrary to widespread belief, side effects of second line chemotherapy are tolerable. Weight loss, stage, PS, LDH can be used as prognostic factors, and we also would like to emphasize strongly that development of novel medications are necessary in the treatment of SCLC with future studies.

References

1. Ettinger DS, Aisner J. Changing face of small-cell lung cancer: real and artifact. J Clin Oncol. 2006; 24:4526–7. doi: 10.1200/JCO.2006.07.3841.
2. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin. 2012;62(1):10-29. doi: 10.3322/caac.20138.
3. Byers LA, Rudin CM. Small cell lung cancer: where do we go from here? Cancer.2015;121:664-72. doi: 10.1002/cncr.29098.
4. Oronsky B, Reid TR, Oronsky A, Carter CA. What's New in SCLC? A Review. Neoplasia. 2017;19(10):842–7. doi: 10.1016/j.neo.2017.07.007.
5. WHO, Handbook for reporting results of cancer treatment, in WHO Offset publication No.48. 1979; 745.Geneva.
6. Zelen M. Keynote address on biostatistics and data retrieval. Cancer Chemother Rep 3. 1973;4 (2):31-42.
7. Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Dancey J, Arbuck S, et al. New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). European Journal Of Cancer. 2009;45:228–47. doi: 10.1016/j.ejca.2008.10.026.
8. Bozkurt B, Selçuk T, Fırat P, Kalyoncu AF, Artvinli M. 1972–2002 döneminde Hacettepe Üniversitesi Tıp Fakültesi Hastanesi'nde akciğer kanseri tanısı konulan hastaların histolojik ve epidemiyolojik değerlendirmesi. Toraks Dergisi. 2004;5(3):143-8.
9. Ferlay J, Autier P, Boniol M, , Heanue M, Colombet M, Boyle P. Estimates of the cancer incidence and mortality in Europe in 2006. Annals of Oncology. 2007;18(3):581-92. doi: 10.1093/annonc/mdl498.
10. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T et al. Cancer statistics, 2008. CA Cancer J Clin. 2008;58:71. doi: 10.3322/CA.2007.0010.
11. Bernhardt EB, Jalal SI. Small cell lung cancer Cancer Treat Res. 2016;170:301-22. doi: 10.1007/978-3-319-40389-2_14.
12. OU SH, Ziogas A, Zell JA. Prognostic factors for survival in extensive stage small cell lung cancer (ED-SCLC): the importance of smoking history, socioeconomic and marital statuses, and ethnicity. J Thorac Oncol. 2009 Jan;4(1):37-43. doi: 10.1097/JTO.0b013e31819140fb.
13. Yang P, Allen M, Aubry M, Wampfler J, Marks RS, Edell ES, et al. Clinical Features of 5,628 Primary Lung Cancer Patients. Chest. 2005;128:452-62. doi: 10.1378/chest.128.1.452
14. Wang S, Zimmermann S, Parikh K, Mansfield AS, Adjei AA. Current Diagnosis and Management of Small-Cell Lung Cancer Mayo Clin Proc. 2019 Aug;94(8):1599-1622. doi: 10.1016/j.mayocp.2019.01.034.
15. Salomaa ER, Sällinen S, Hiekkanen H, Lippo K. Delays in the diagnosis of lung cancer. CHEST 2005;128: 2282-88. doi: 10.1378/chest.128.4.2282.
16. Koyi H, Hillerdal G, Branden E. Patient's and doctor's delays in the diagnosis of chest tumors. Lung Cancer. 2002;35:53-7. doi: 10.1016/s0169-5002(01)00293-8.
17. Erbaycu AE, Özsöz A, Çakan A. Akciğer kanserinde tanı gecikmesine hastanın ve hekimin etkisi. Solunum Hastalıkları. 2005;16:161-65.
18. Özlü T, Bülbül Y, Öztuna F, Çan G. Akciğer kanseri tanısını ne kadar sürede koyabiliyoruz? Tüberküloz ve toraks dergisi. 2002;50:288-91.
19. Yılmaz A, Aybatlı A. Akciğer kanseri tanı ve tedavisinde gecikmeler. Toraks Dergisi. 2005;6(1):68-72.
20. Webb RW, Higgins CB, ed. Lung cancer and bronchopulmonary neoplasms. In:Thoracic imaging Pulmonary and cardiovascular radiology. Lippincott Williams and Wilkins: Philadelphia. 2005;3:75-9.
21. Rivera MP, Mehta AC; American College of Chest Physicians. Initial diagnosis of lung cancer: ACCP evidence-based clinical practice guidelines (2nd edition) Chest. 2007 Sep;132(3 Suppl):131S-148S. doi: 10.1378/chest.07-1357.
22. Cohen MH, Makuch R, Johnston-Early A, Ihde DC, Bunn PA Jr, Fossieck BE Jr et al. Laboratory parameters as an alternative to performance status in prognostic stratification of patients with small cell lung cancer. Cancer Treat Rep. 1981;65:187-95.
23. Bremnes M, Sundstrom S, Aasebø U, Kaasa S, Hatlevoll R, Aamdal S. The value of prognostic factors in small cell lung cancer: results from a randomised multicenter study with minimum 5 year follow-up. Lung Cancer. 2003;39:303–13. doi: 10.1016/s0169-5002(02)00508-1.
24. Quoix E, A Purohit, M Faller-Beau M, Moreau L, Oster JP, Pauli G. Comparative prognostic value of lactate dehydrogenase and neuron-specific enolase in small-cell lung cancer patients treated with platinum-based chemotherapy. Lung Cancer. 2000;30:127–34. doi: 10.1016/s0169-5002(00)00131-8.
25. Paesmans M, Sculier JP, Lecomte J, Thiriaux J, Libert P, Sergysels R,et al. Prognostic factors for patients with small cell lung carcinoma: analysis of a series of 763 patients included in 4 consecutive prospective trials with a minimum follow-up of 5 years. Cancer 2000;89:523–33. doi: 10.1002/1097-0142(20000801)89:3<523:aid-cncr7>3.0.co;2-6.
26. Deng T, Zhang J, Meng Y, Zhou Y, Li W. Higher pretreatment lactate dehydrogenase concentration predicts worse overall survival in patients with lung cancer. Medicine Baltimore). 2018 Sep;97(38):e12524. doi: 10.1097/MD.0000000000012524.
27. Osterlind K, Hansen HH, Hansen M, Dombernowsky P, Andersen PK. Long-term disease-free survival in small-cell carcinoma of the lung: a study of clinical determinants. J Clin Oncol. 1986;4:1307–13. doi: 10.1200/JCO.1986.4.9.1307.
28. Li J, Dai CH, Chen P, Wu JN, Bao QL, Qiu H, et al. Survival and prognostic factors in small cell lung cancer. J Med Oncol. 2010 Mar,27(1):73-81. doi: 10.1007/s12032-009-9174-3.
29. Rawson N, Peto J, An overview of prognostic factors in small cell lung cancer. A report from the Subcommittee for the Management of Lung Cancer of the United Kingdom Coordinating Committee on Cancer Research. Br J Cancer. 1990;61(4):597-604. doi: 10.1038/bjc.1990.133.
30. Tamura M, Ueoka H, Kiura K, Tabata M, Shibayama T, Miyatake K et al. Prognostic factors of small-cell lung cancer in Okayama Lung Cancer Study Group Trials. Acta Med Okayama. 1998;52(2):105–11. doi: 10.18926/AMO/31310.
31. Arınç S, Gönlügür U, Devran O, Erdal N, Ece F, Ertugrul M et al. Prognostic factors in patients with small cell lung carcinoma. Med Oncol. Apr 2010. doi: 10.1007/s12032-009-9198-8.
32. Mao Y, Hu J, Ugnat AM, Semenciw R, Fincham S. Socioeconomic status and lung cancer risk in Canada. Int J Epidemiol. 2001;30:809–817. doi: 10.1093/ije/30.4.809.
33. Jackman DM, Johnson BE. Small cell lung cancer. Lancet. 2005;366:1385-96. doi: 10.1016/S0140-6736(05)67569-1.
34. Buccheri G, Ferrigno D. Prognostic factors in lung cancer: tables and comments. Eur Respir J. 1994;7(7):1350–64. doi: 10.1183/09031936.94.07071350.

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