

Prognostic factors for the survival of 66 cases with extensive stage-small cell lung cancer

Heng Cao¹, Yonggui Hong¹ (Co-first author), Shouran Zhao¹, Nengchao Wang¹,
Fuyou Zhou¹, Xiaodong Xie² (✉)

¹ Department of Oncology, The Fourth Affiliated Hospital of Henan University of Science and Technology, Anyang 455000, China

² Department of Oncology, The General Hospital of Shenyang Military, Shenyang 110840, China

Abstract

Objective The objective of this retrospective study was to investigate the prognostic factors associated with survival among patients with extensive stage-small cell lung cancer (ES-SCLC).

Methods Clinical data from 66 patients with ES-SCLC diagnosed via histopathology or cytology between July 2005 and July 2009 at Anyang Tumor Hospital (China) were analyzed. Univariate and multivariate Kaplan-Meier, log-rank, and Cox proportional hazard regression analyses were conducted.

Results The 12-, 24-, and 36-month survival rates among patients with ES-SCLC were 40.9%, 13.6%, and 6.1%, respectively. The median survival time (MST) was 10 months. Univariate analyses indicated that weight loss, efficacy of first-line chemotherapy, total number of chemotherapy cycles, treatment method, and serum sodium levels significantly influenced survival among patients with ES-SCLC. Multivariate analyses suggested that the efficacy of first-line chemotherapy, total number of chemotherapy cycles, and serum sodium levels were independent prognostic factors associated with survival.

Conclusion The efficacy of first-line chemotherapy, total number of chemotherapy cycles, and serum sodium levels are important prognostic factors for patients with ES-SCLC.

Key words: extensive stage-small cell lung cancer (ES-SCLC); survival rate; prognosis

Received: 21 June 2015
Revised: 6 July 2015
Accepted: 25 August 2015

Based on the estimated GLOBOCAN 2011 statistics, lung cancer is the most common cancer worldwide, the leading cause of cancer death among men, and the second-leading cause of cancer among women [1]. Small cell lung cancer (SCLC) accounts for approximately 15%–18% of all lung cancers and is associated with smoking [2–3]. According to the Veterans Administration Lung Study Group staging system, SCLC can be divided into limited stage (LS) and extensive stage (ES) disease [4]. LS-SCLC involves a primary tumor contained within a single hemithorax and/or mediastinal nodes, along with ipsilateral supraclavicular disease. ES-SCLC refers to disease located beyond the LS areas that cannot be confined to a single radiotherapy portal, and includes widely metastatic disease.

SCLC is an aggressive malignancy with a tendency toward early, distant metastasis. Patients with LS-SCLC are treated with radiation, whereas those with ES-SCLC are

treated with chemotherapy plus radiation; the survival rates of these patients are 10% and 2%, respectively. The median survival times of patients with SCLC range from 12 to 20 months [5]. The present retrospective study analyzed prognostic factors associated with survival in 66 patients with ES-SCLC to provide a theoretical basis for clinical treatment.

Materials and methods

Clinical data

We retrospectively reviewed the clinical data of 66 patients admitted to the United States Veterans Hospital who were diagnosed with ES-SCLC from July 2005 to July 2009 at Anyang Tumor Hospital, China. The diagnostic criteria included a malignant pleural effusion or pericardial effusion, distant metastasis, significant compression of the superior vena cava, and/or vocal cord paralysis. For all

patients, baseline medical examinations included a bone scan, lung computed tomography (CT), brain magnetic resonance imaging, cervical lymph node examination, abdominal ultrasound, and adrenal ultrasound or CT.

Therapy method and measures

All patients received first-line chemotherapy, and a subset also received radiotherapy. Radiotherapy was administered to patients with chest lesions, mediastinal and supraclavicular lymph node involvement, or whole-brain or bone metastases. Chemotherapy regimens included etoposide plus cisplatin or carboplatin, irinotecan plus cisplatin, or epirubicin plus etoposide and cisplatin. The tumor response to treatment was categorized as a complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD) based on the Response

Evaluation Criteria in Solid Tumors Guidelines.

This study evaluated the following clinical prognostic indicators: gender, age, smoking, Karnofsky Performance Status (KPS), chemotherapy cycles, and number of first-line therapies; other evaluated parameters included the baseline levels of hemoglobin, platelets, and serum sodium, as well as weight loss.

Statistical analysis

The study data were assessed using a log-rank statistical analysis. Univariate and multivariate Cox regression models were used to identify the risk factors. The SPSS 17.0 statistical software package (SPSS, Inc., USA) was used for the statistical analyses. A *P* value < 0.05 was considered statistically significant.

Table 1 Univariate analysis of 66 patients with ES-SCLC

Characteristics	n	Survival rate (%)			MST (month)	95% CI	P
		1-year	2-year	3-year			
Gender							0.088
Male	50	36.0	8.0	4.0	9.0	7.0–11.0	
Female	16	56.3	31.3	12.5	13.0	6.3–19.7	
Age (years)							0.566
≤ 65	47	38.3	12.8	6.4	10.0	8.1–11.9	
> 65	19	47.4	15.8	5.3	11.6	4.5–18.7	
Smoking							0.077
Yes	42	38.1	7.1	2.4	10.0	6.8–13.2	
No	24	45.8	25.0	12.5	11.0	6.2–15.8	
Hemoglobin							0.196
Normal	55	40.0	10.9	1.8	10.0	7.9–12.1	
Lower	11	45.5	27.3	27.3	11.6	2.4–20.8	
Platelet							0.686
Normal	49	44.9	12.2	6.1	11.0	8.8–13.2	
High	17	29.4	17.6	5.9	9.0	6.3–11.7	
Weight loss (%)							0.006
< 5	19	57.9	31.6	15.8	14.0	9.2–18.8	
≥ 5	47	34.0	6.4	2.1	9.0	7.4–10.6	
KPS score							0.631
≥ 80	35	45.7	20.0	5.7	11.0	7.5–14.5	
< 80	31	35.5	6.5	6.5	10.0	6.7–13.3	
Efficacy of first-line CT							0.001
CR	12	75.0	33.3	25.0	15.0	11.6–18.4	
PR	36	36.1	13.9	2.8	10.0	8.3–11.7	
SD	5	28.6	0.0	0.0	5.0	3.7–6.3	
PD	8	27.3	0.0	0.0	8.0	5.9–10.1	
Chemotherapy cycles							< 0.001
< 4	16	6.3	0.0	0.0	6.0	4.7–7.3	
≥ 4	50	52.0	18.0	8.0	12.0	9.6–14.4	
Treatment method							0.033
Chemotherapy	42	35.7	11.9	2.4	8.0	6.1–9.9	
Chemotherapy + radiotherapy	24	50.0	16.7	12.5	11.6	7.6–15.6	
Serum sodium							< 0.001
Normal	42	57.1	21.4	9.5	13.0	10.0–16.0	
Lower	24	12.5	0.0	0.0	7.0	5.1–8.9	

MST: median survival time; KPS: Karnofsky performance status

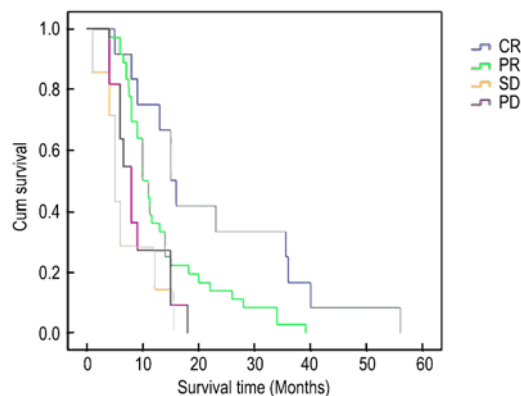


Fig. 1 Survival curves for patients with ES-SCLC who were treated with first-line chemotherapy

Results

The patients' characteristics were summarized in Table 1 and Fig. 1. The 1-, 2-, and 3-year overall survival (OS) rates were 40.9%, 13.6%, and 6.1%, respectively. The median OS was 10 months. Univariate analyses revealed that weight loss, efficacy of the first-line therapy, number of chemotherapy cycles, treatment method, and serum sodium level were adverse prognostic factors among the 66 patients with diagnosed ES-SCLC in this study.

According to the multivariate analysis (Table 2), the efficacy of first-line therapy with respect to CR (hazard ratio (HR) = 0.284, 95% confidence interval (CI) = 0.103–0.779; $P = 0.015$), < 4 chemotherapy cycles (HR = 2.052, 95% CI = 1.017–4.141; $P = 0.045$), and lower serum sodium level (HR = 2.363, 95% CI = 1.271–4.393; $P = 0.007$)

were independent prognostic factors for OS in the 66 patients with ES-SCLC.

Discussion

In the past 30 years, the incidence of ES-SCLC has increased and now accounts for 75% of SCLC cases. Only 2% of patients with ES-SCLC survive beyond 5 years, and the median OS among these patients is 10 months [4, 6]. In most patients with ES-SCLC, the disease will eventually progress, leading to a cancer-related death. Therefore, a great deal of evidence-based medicine is required to formulate individualized clinical treatments.

Studies have suggested that various factors influence the treatment results, disease progression, and long-term survival in patients with SCLC. Among the 66 patients with ES-SCLC in the present study, the 12-, 24-, and 36-month OS rates were 40.9%, 13.6%, and 6.1%, respectively. The MST of these patients was 10 months. Univariate analyses revealed that gender was not a prognostic factor for ES-SCLC ($P = 0.088$), although a trend was associated with this factor. Notably, the MSTs among men and women were 9 and 13 months, respectively, although this might have been affected by the small sample size. In a previous study, female sex was a strong prognostic factor among patients with smoking-related SCLC [7]. However, in our study, smoking was not a prognostic factor; among patients with ES-SCLC, the MSTs associated with smoking and non-smoking were 10 and 11 months, respectively ($P = 0.077$). The univariate analyses revealed that age ($P = 0.566$), the hemoglobin level ($P = 0.196$), platelet level ($P = 0.196$), and KPS ($P = 0.631$) did not correlated with OS in the present study. Earlier studies [7–9], how-

Table 2 Multivariate analysis of survival in 66 patients with ES-SCLC

Characteristics	Degree of freedom	Regression coefficient	Standard error	HR (95% CI)	Wald	<i>P</i>
Weight loss (%)						
< 5	1	0.069	0.348	1.071 (0.542–2.118)	0.039	0.844
≥ 5				1.00		
Efficacy of first-line CT	3				9.322	0.025
CR		–1.260	0.515	0.284 (0.103–0.779)	5.972	0.015
PR		–0.511	0.369	0.600 (0.291–1.236)	1.918	0.166
SD		0.384	0.514	1.468 (0.536–4.020)	0.557	0.455
PD				1.00		
Chemotherapy cycles						
< 4	1	0.719	0.358	2.052 (1.017–4.141)	4.024	0.045
≥ 4				1.00		
Treatment method						
Chemotherapy	1	–0.451	0.300	0.637 (0.354–1.147)	2.261	0.133
Chemotherapy + radiotherapy				1.00		
Serum sodium						
Normal				1.00		
Lower	1	0.860	0.316	2.363 (1.271–4.393)	7.379	0.007

ever, reported that an age ≤ 65 years, KPS < 80 , anemia, and elevated platelet level were prognostic factors for OS. The results of this study are consistent with those of a study conducted by Wu^[10], which suggested that among cases of ES-SCLS, anemia treatment might be the only influential factor. In the present study, univariate analyses indicated that weight loss ($P = 0.006$), efficacy of first-line chemotherapy ($P = 0.001$), total number of chemotherapy cycles ($P = 0.001$), treatment method ($P = 0.033$), and serum sodium levels ($P < 0.001$) had significant influences on the survival of patients with ES-SCLC.

The multivariate analyses in the present study suggested that the efficacy of first-line chemotherapy on CR (HR = 0.284, 95% CI = 0.103–0.779; $P = 0.015$), < 4 chemotherapy cycles (HR = 2.052, 95% CI = 1.017–4.141; $P = 0.045$), and a lower serum sodium level (HR = 2.363, 95% CI = 1.271–4.393; $P = 0.007$) were independent prognostic factors of survival.

This retrospective study was conducted at a single center and involved a small sample size. Accordingly, larger prospectively designed, multi-center studies will be required to further address the prognostic factors for survival among patients with ES-SCLC. In this study, we observed that a normal serum sodium level, efficacy of first-line treatment with respect to CR, and ≥ 4 treatment cycles were associated with longer survival. Simultaneously, patients should be given nutritional support and active treatments to improve immunity. This study of patients with ES-SCLS might provide a basis for treatment decisions, improving patients' quality of life, and prolonging survival.

Conflicts of interest

The authors indicated no potential conflicts of interest.

References

1. Jemal A, Bray F, Center MM, *et al.* Global cancer statistics. *CA Cancer J Clin*, 2011, 61: 69–90.
2. Khuder SA. Effect of cigarette smoking on major histological types of lung cancer: a meta-analysis. *Lung Cancer*, 2001, 31: 139–148.
3. Govindan R, Page N, Morgensztern D, *et al.* Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. *J Clin Oncol*, 2006, 24: 4539–4544.
4. Neal JW, Gubens MA, Wakelee HA. Current management of small cell lung cancer. *Clin Chest Med*, 2011, 32: 853–863.
5. Chua YJ, Steer C, Yip D. Recent advances in management of small-cell lung cancer. *Cancer Treat Rev*, 2004, 30: 521–543.
6. Jett JR, Schild SE, Kesler KA, *et al.* Treatment of small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest*, 2013, 143(5 Suppl):e400S–e419S.
7. Wheatley-Price P, Ma C, Ashcroft LF, *et al.* The strength of female sex as a prognostic factor in small-cell lung cancer: a pooled analysis of chemotherapy trials from the Manchester Lung Group and Medical Research Council Clinical Trials Unit. *Ann Oncol*, 2010, 21: 232–237.
8. Li J, Dai CH, Chen P, *et al.* Survival and prognostic factors in small cell lung cancer. *Med Oncol*, 2010, 27: 73–81.
9. Ren ZH, Zhang CH, Li M, *et al.* The clinical observation of combined chemotherapy of irinotecan and cisplatin in the treatment of relapsed advanced small cell lung cancer. *Chinese-German J Clin Oncol*, 2008, 7: 506–508.
10. Wu C, Li F, Jiao SC. Prognostic Factors for Survival of Patients with Extensive Stage Small Cell Lung Cancer—a Retrospective Single Institution Analysis. *Asian Pac J Cancer Prev*, 2012, 13: 4959–4962.

DOI 10.1007/s10330-015-0110-z

Cite this article as: Cao H, Hong YG, Zhao SR, *et al.* Prognostic factors for the survival of 66 cases with extensive stage small cell lung cancer. *Oncol Transl Med*, 2016, 2: 12–15.