ORIGINAL ARTICLE

Prognostic factors in elderly patients with advanced non-small cell lung cancer treated with first-line cisplatin-based chemotherapy: A retrospective analysis of single institution

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Summary

Purpose: *Non-small cell lung cancer (NSCLC) makes up 80-85% of all lung cancers cases. Lung cancer in older individuals is frequently undertreated. Patients eligible for cisplatin-based chemotherapy should be selected carefully. The aim of this retrospective single-center study was to evaluate prognostic factors for overall survival (OS) in elderly (≥65 years) patients with advanced NSCLC who received first-line cisplatin-based chemotherapy.*

Methods: *We retrospectively reviewed 110 elderly patients with locally advanced or metastatic NSCLC who had been administered cisplatin-based first-line chemotherapy between December 2004 and November 2011.*

Seventeen potential prognostic variables were chosen for analysis. Univariate and multivariate analyses were conducted to identify prognostic factors associated with OS.

Results: *Among the 17 variables of univariate analysis, 4 were identified to have prognostic significance for OS: comorbidities (p<0.001), Eastern Cooperative Oncology Group (ECOG) performance status (PS) (p=0.02), first-line chemotherapy cycles (p<0.001) and serum albumin level (p=0.04). Multivariate analysis showed that only ECOG PS (p=0.01) was independent prognostic factor for OS.*

Conclusion: *PS was important prognostic factor in elderly patients with advanced NSCLC. The findings of this study may facilitate pretreatment prediction of OS and therefore can be used for selecting the most appropriate treatment for elderly patients.*

Key words: advanced lung cancer, cisplatin-based chemotherapy, elderly patients, prognostic factors, survival

Introduction

Lung cancer is the most common cause of cancer-related deaths worldwide [1]. NSCLC represents 80-85% of all lung cancers cases. At the time of diagnosis, two-thirds of lung cancer patients have advanced disease. The median survival time for advanced disease is 5.8-12.6 months and the overall 5-year survival rate in this patient population is less than 10% [2,3]. Data from the Surveillance, Epidemiology, and End Results (SEER) Program data in the United States show that the median age at diagnosis in NSCLC patients is 69 years [4]. Aging causes changes in organ function and drug pharmacokinetics. Thus, in older individuals lung cancer is frequently undertreated. For this reason, lung cancer in elderly patients is a progressively widespread problem faced by the oncologist [5,6].

The Elderly Lung Cancer Vinorelbine Italian Study Group (ELVIS) showed that systemic chemotherapy resulted in significant survival benefits when compared with best supportive care [7]. Despite the fact that platinum-based doublets are considered the standard therapy for patients with advanced NSCLC, no elderly-specific platinum based prospective phase III study has been explored. Nonetheless, retrospective subgroup analyses of several phase III trials for elderly patients have been carried out [8-11]. These studies indicated that progression-free survival (PFS) and OS, and also response rate were not significantly superior between age groups. Grade 3-4 toxicities in elderly patients were higher in some studies [9, 10], whereas this was not confirmed in others [8,11]. Therefore, the best treatment for elderly patients remains to be defined.

Very different prognostic factors have been iden-

tified in several studies concerning survival in patients with advanced NSCLC [12-14]; however, only very few studies are dealing with elderly patients [15-18]. Determining the prognostic factors of survival in advanced NSCLC patients treated with first-line cisplatin-based chemotherapy can possibly help in the decision-making process for individual patients.

The aim of this retrospective study was to analyse prognostic factors possibly related with OS in elderly patients with advanced NSCLC treated with first-line cisplatin-based chemotherapy.

Methods

Patient population

We retrospectively reviewed 110 locally advanced or metastatic NSCLC patients older than 65 years of age, who were treated with first-line cisplatin-based chemotherapy from December 2004 to November 2011 at the Department of Medical Oncology, Dicle University. Patient data were retrieved from their medical records.

Patients who had received prior treatment were excluded.

Treatment

Patients were divided into 3 groups. The first group (GC) was administered gemcitabine 1000 mg/m^2, days 1 and 8 and cisplatin 75 mg/m^2, day 1. The second group (DC) received 75 mg/m^2 docetaxel and cisplatin 75 mg/m^2, both on day 1. The third group (PC) received 175 mg/m^2 paclitaxel and 75 mg/m^2 cisplatin, both on day 1. Courses were repeated every 3 weeks

Factors analysed

Seventeen potential prognostic variables were chosen on the basis of previously published clinical trials. The variables were divided into two categories: gender (male or female), ECOG PS (0-1, 2-3), histology (squamous cell carcinoma or nonsquamous cell carcinoma), stage (locally advanced or metastatic), comorbidities (0-1 or ≥2), weight loss ≥5% within the previous 3 months (present or absent), haemoptysis (present or absent), smoking history (present or absent), first-line chemotherapy cycles (1-3 or ≥4), site of metastases (presence vs. absence in the liver or brain), and laboratory parameters (<median or ≥ median) at the time of first-line chemotherapy administration.

Statistical analyses

All of the analyses were performed using the SPSS statistical software program package (SPSS, version 11.0 for windows). The differences of the clinical characteristics between the two groups were analyzed by chi-square test and Student's t-test. Overall survival was calculated from the start of the first cycle of chemotherapy to the date of death from any cause or the date of the last follow-up. Overall survival was estimated using the Kaplan-Meier method. The Cox proportional hazards regression model was used to determine statistically significant variables related to survival. Differences were assumed to be significant when p value was less than 0.05.

Results

Patient characteristics

The median patient age was 70 years (range 65-83) with 97 patients (88.2%) being males and 13 (11.8%) females. The number of patients with a PS score 0-1 was 60 (54.5%). Fifty-five patients (50.0%) were diagnosed with metastatic NSCLC and 55 (50.0%) had locally advance disease. Squamous cell carcinoma was the most common histologic type (40.0% of the patients). Seventeen patients (15.9%) received second-line chemotherapy. The median OS was 13.9 months (range 12.1-15.8). The patient baseline characteristics are listed in Table 1.

Prognostic factor analysis

The results of univariate analysis are summarized in Table 2. Among the 17 variables assessed in univariate analysis, 4 were identified to have prognostic significance: comorbidities (p<0.001), PS (p=0.02), first-line chemotherapy cycles (p<0.001) and serum albumin level (p=0.04).

Multivariate analysis included the 4 significant factors in univariate analysis. The results of multivariate analysis are shown in Table 3. Cox proportional hazard model showed that only PS was independent prognostic factor for survival (p=0.01; Figure 1), while comorbidities showed a strong trend for statistical significance.

Discussion

Despite the fact that platinum-based doublets are considered standard therapy for patients with advanced NSCLC, the optimal treatment in elderly patients remains to be defined. Elderly patients eligible for cisplatin-based chemotherapy should be selected carefully.

Poor PS is usually accepted as negative prognostic factor for survival in all cancer patients [19-21]. Although the importance of this factor was also confirmed in advanced NSCLC patients [22], there are only few studies about the impact of PS on OS in elderly patients with advanced NSCLC. In some studies PS was found to be an independent prognostic factor of OS survival [18,23], while Kefeli et al. [15] reported no significant effect on OS in multivariate analysis. In our study PS proved independent prognostic factor for OS.

The importance of comorbidities for OS in elderly patients with advanced NSCLC is still a subject of controversy [24-27]. The trials by Gridelli et al. [24] and Frasci et al. [25] showed that comorbidity was associated with statistically inferior OS. Contrary to this, Maione

Table 1. Patient, disease and chemotherapy characteristics

Characteristics	Patients, N (%)
Sex	
Male	97 (88.2)
Female	13 (11.8)
Age (years), median (range)	70 (65-83)
Comorbidities	
0 or 1	94 (85.5)
≥2	16 (14.5)
Performance status	
0-1	60 (54.5)
2-3	32 (29.1)
Unknown	18 (16.4)
Smoking history	
Current or former	81 (73.7)
Never	15 (13.6)
Unknown	14 (12.7)
Weight loss	
Yes	23 (20.9)
No	77 (71.0)
Unknown	10 (9.1)
Haemoptysis	
Yes	25 (22.7)
No	78 (70.9)
Unknown	7 (6.4)
Stage	
III	55 (50.0)
IV	55 (50.0)
Histology	
Squamous cell carcinoma	44 (40.0)
Nonsquamous cell carcinoma	24 (21.8)
Unknown	42 (38.2)
Chemotherapy regimen	
GC	36 (32.7)
DC	45 (40.9)
PC	29 (26.4)
Chemotherapy cycles	
1-3	45 (40.9)
≥4	65 (59.1)
Second-line chemotherapy	17 (15.5)
Metastatic sites	
Liver	12 (10.9)
Brain	10 (9.1)
Laboratory parameters, median	
Hemoglobin, g/l	12.4
WBC	8555
ALT, U/l	19
Albumin, g/dl	3.3
Alkaline phosphatase, U/l	89
LDH, U/l	237

GC: gemcitabine plus cisplatin, DC: docetaxel plus cisplatin, PC: paclitaxel plus cisplatin

Table 2. Univariate analysis of overall survival time by categorical variable

Variables	Log-rank	Degrees of freedom	p-value
Sex	0.04	1	0.83
Comorbidities	18.5	1	<0.001
Stage	1.4	1	0.22
Smoking history	0.5	1	0.47
Performance status	5.3	1	0.02
Histology	0.1	1	0.69
Weight loss	1.8	1	0.17
Haemoptysis	0.01	1	0.97
First-line chemotherapy cycles	16.2	1	<0.001
Second-line chemotherapy	0.6	1	0.40
Metastatic sites			
Liver	0.03	1	0.85
Brain	2.3	1	0.12
Laboratory parameters, median			
Hemoglobin	0.4	1	0.50
WBC	0.01	1	0.90
ALT	0.5	1	0.47
Albumin	3.9	1	0.04
Alkaline phosphatase	0.5	1	0.46
LDH	2.8	1	0.09

Table 3. Multivariate analysis of overall survival

Prognostic factors	OR	95% CI	p-value
Comorbidities	2.69	0.98-7.36	0.053
Performance status	4.91	1.46-16.4	0.01
First-line chemotherapy cycles	0.11	0.14-1.12	0.08
Albumin	0.56	0.22-1.42	0.22

Figure 1. Patient overall survival according to performance status (PS).

et al. [26] and Feliu et al. [27] did not observe any prognostic value of comorbidities. In our elderly patients with advanced NSCLC, OS was strongly influenced by comorbidities in univariate analysis, but not in multivariate analysis (OR=2.69, 95% CI 0.98-7.36, p=0.053).
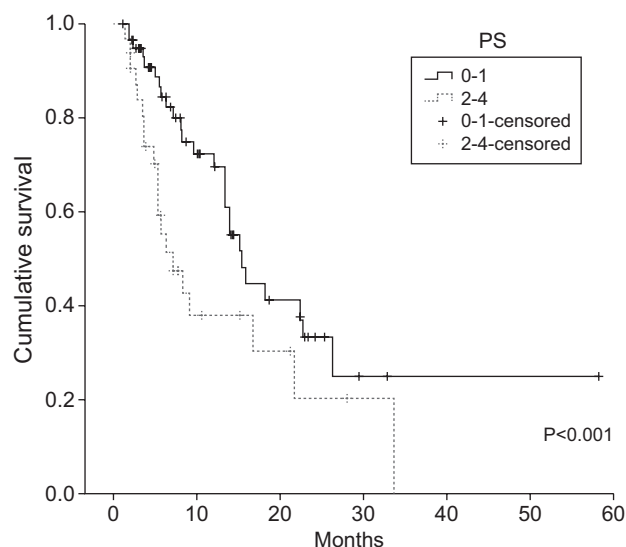
    The present study has some limitations. Firstly, it was retrospective in nature; secondly, molecular characteristics of the tumor were not evaluated; and thirdly, the number of the patients included was rather small.

    In conclusion, PS was identified as significant

prognostic factor for OS in elderly patients with advanced NSCLC who were administered first-line palliative cisplatin-based chemotherapy. The results of this study may facilitate the pretreatment prediction of OS survival and therefore could help select the mot appropriate chemotherapy regimen or any other therapeutic approach in elderly patients with advanced NSCLC.

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