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Advanced Non-Small Cell Lung Cancer: Retrospective Study of Prognostic Factors

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Abstract

Objective: The objective of the study is to investigate and improve our understanding of the impact of several potential prognostic factors on overall survival (OS) in patients with advanced non-small cell lung cancer (NSCLC).

Methods: Records of patients with advanced NSCLC (stage IIIB, IV) received first-line chemotherapy were reviewed. Age, gender, Eastern Cooperative Oncology Group performance status (ECOGPS), stage, histologic type, smoking status, leucocytic count, type of chemotherapy, albumin and hemoglobin level were evaluated for their prognostic significance in multivariate analysis.

Results: A total of 140 patients with advanced NSCLC treated with first-line chemotherapy were identified. The median age was 54 (range from 35-83) years. The majority of patients were male (72%), had stage IIIB (67%) and were in PS 0or1 (75.7%). Forty-six percent had adenocarcinoma. Most patients were smokers (85%) and received platinum-based chemotherapy (78.6%).1-year OS was 39.3% with median survival time of 10 months (95% CI: 7.95-12).ECOGPS of 2(P=0.04), squamous histology (P=0.03), elevated leucocytic count (P=0.02),low hemoglobin level(P=0.02), smoking (P=0.03), low albumin level (P=0.05) and stage IV (P=0.01)were found to be independent prognostic factors for poor survival in multivariate analysis. While age (P=0.23), sex (P=1) and type of chemotherapy whether platinum-based or not (P=0.8) were insignificant factors for survival.

Conclusion: From this study, we concluded that prognostic factors as smoking, ECOG PS of 2, squamous histology, stage IV, high leucocytic count, low hemoglobin level, low albumin level are found to have a significant impact on the survival while, gender, age, and type of chemotherapy are not. However, these results and additional information regarding prognostic factors in patients with advanced NSCLC in prospective studies should be validated.

Keywords: Lung cancer; Non-small cell lung cancer (NSCLC); Overall survival (OS); Prognostic factors

Introduction

Lung cancer is one of the most commonly diagnosed cancers and is the leading cause of death from cancer in the United States and Europe [1,2]. Lung cancer is divided into two major classes: 1) Non- small cell lung cancer (NSCLC), accounts for 85% and 2) Small cell lung cancer (SCLC), accounts for 15% [3]. Based on histology NSCLC is classified into squamous cell cancer (SCC)(29%), adenocarcinoma (32%) and rest have other subtypes [4]. Unfortunately, about 56% of patients with lung cancer at the time of diagnosis have advanced disease [5]. The outcome of patients with advanced NSCLC generally is poor, a large meta-analysis demonstrated a 2-month increase in median survival after platinum-based therapy and an absolute 10% improvement in the 1-year survival rate compared with best supportive care [6].

Prognostic factors can contribute to clinical decision making help to individualize treatment in advanced stages of NSCLC. In a review of the literature published between 1990 and 2001, Brundage et al. [7] criticized the great variations in the published literature. There are variations in study populations, in the type of statistical analysis and the type of treatment.

The aim of our study is to investigate and improve our understanding of the impact of several potential prognostic factors on overall survival (OS) in patients with advanced NSCLC.

Patients and Methods

Records of all patients with advanced NSCLC (stage IIIB, IV) attended to Clinical Oncology and Nuclear Medicine Department between 2004-2013 were reviewed. Patients who never received any chemotherapy were excluded. Demographic and clinical data included: age, gender, histologic tumor type, stage of disease, smoking status, ECOG performance status (PS), type of chemotherapy received were collected. Also, laboratory investigations including hemoglobin level, leucocytic count, and albumin level were obtained from medical records. Recorded data of subjective, objective responses and date of death or last follow-up were reviewed.

Overall survival (OS) was defined as the period between date of diagnosis and date of death or last follow-up.

Age, gender, PS, stage, histologic type, smoking status, leucocytic count, type of chemotherapy, albumin and hemoglobin level were evaluated for their prognostic significance in multivariate analysis.

Statistical Methods

The data were coded and entered into a computer using SPSS version 15.0. Kaplan-Meier test was used to estimate overall survival. Multivariate analysis for prognostic factors which affect survival was determined using Mann-Whitney test where in $P<0.05$ was considered to indicate statistical significance.

Results

A total of 140 patients with advanced NSCLC treated with first-line chemotherapy were identified. Patient's characteristics are summarized in Table 1. The median age was 54 (range from 35-83) years. The majority of patients were male (72%), had stage IIIB (67%) and were in PS O or1 (75.7%). Forty-six percent had adenocarcinoma. Most patients were smokers (85%) and received platinum-based chemotherapy (78.6%). 1-year OS was 39.3% with median survival time of 10 months (95% CI: 7.95-12%) (Figure 1).

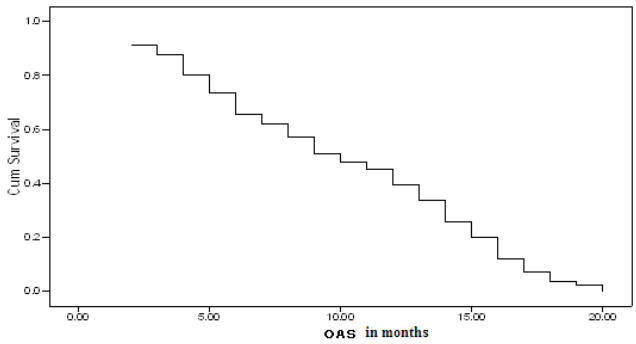

Figure 1: Overall survival of all studied patients in months.

ECOGPS of 2 (P=0.04), squamous histology (P=0.03), elevated leucocytic count (P=0.02), low hemoglobin level (P=0.02), smoking (P=0.03), low albumin level (P=0.05) and stage IV (P=0.01) were found to be independent prognostic factors for poor survival in multivariate analysis. While age (P=0.23), sex (P=1) and type of chemotherapy whether platinum-based or not (P=0.8) were insignificant factors for survival.

Discussion

One advantage of this study is a uniform patients population as regard stage, diagnosis and treatment as most patients (78.6%) received platinum-based chemotherapy but its weakness is due to a retrospective nature. 1-year OS rate was 39.3% comparable to that reported in previous studies [6,8]. Although 2-drugs regimens are better than single agent, 3-drugs regimens are not better in terms of improving OS compared with 2-drugs combinations [9]. Current research has shifted to targeted systemic therapy that selectively targets cancer cells so reducing toxicity [10]. Targeted agents as erlotinib and bevacizumab have successes in enhancing survival [8,11].

Patients with poorer PS, stage IV disease, high leucocytic count, low albumin level, anemia, squamous histology, smoking had significantly worse overall survival.

Character	No	%
Age		
Median (range)	54 (35-83)years	
≤ 60 years	88	62.9
> 60years	52	37.1
Gender		
Male	101	72.1
Female	39	27.9
ECOG PS		
0-1	106	75.7
2	34	24.3
Histology		
Adenocarcinoma	65	46.4
Squamous cell carcinoma	35	25
Others	40	28.6
Smoking status		
Smokers	119	85
Non-smokers	21	15
Stage		
IIIB	94	67.1
IV	46	32.9
Hemoglobin level		
<10g/dl	50	35.7
≥ 10g/dl	90	64.3
Leucocytic count		
≤ 10.5 × 109/L	92	65.7
>10.5 × 109/L	48	34.3
Type of chemotherapy		
Platinum-based	110	78.6
Non platinum-based	30	21.4
Albumin level		
< 3.5 g/dl	47	33.6
≥ 3.5 g/dl	93	66.4

Table 1: Patients characteristics.

It is accepted generally that PS and stage are associated with poorer outcomes [7]. Low serum albumin is associated with ongoing systemic

inflammation [12]. Systemic inflammation has been found to predict poor outcome in patients with different cancers including lung cancer [13]. Smoking has been described as a prognostic factor in lung cancer [14-17]. Experimental studies have shown that nicotine inhibits apoptosis induced by gemcitabine, cisplatin and paclitaxel [18].

The prognostic significance of complete blood count findings has been reported less consistently [19-22]. None of the previous studies observed that both the pretreatment leucocytic count and hemoglobin level were of independent prognostic value but our results highlight the prognostic importance of both values in OS. Anemia may reflect cachexia associated with cancer, especially metastatic cancer.

Worse survival in patients with high leucocytic count may reflect either a greater burden of tumor cells within the bone marrow or a possible concomitant subclinical infection or the effect of a yet un described chemokine or cytokine secreted by the tumor into the circulation [23].

No significant differences in OS were found based on platinum therapy in multivariate analysis, indicating that the effect of prognostic factors on OS was more profound than the benefit from platinum-based therapy. Age and sex did not significantly affect OS, comparable to that observed by others [23-25]. While Jafri et al. [26] reported that younger age (<60 years) had significant impact on OS, one explanation could be that patients diagnosed at a young age may have a more biologically aggressive disease so more metastatic sites and worse outcome. Female gender had good prognosis in a study conducted by Henschke et al. [27]. However, there is a continuous need to identify specific and sensitive biomarkers that may predict prognosis in NSCLC as the Notch signaling pathway [28].

Conclusion

From this study, we concluded that prognostic factors as smoking, ECOG PS of 2, squamous histology, stage IV, high leucocytic count, low hemoglobin level, and low albumin level were found to have a significant impact on the survival, while, gender, age, and type of chemotherapy were not. However, these results and additional information regarding prognostic factors in patients with advanced NSCLC in prospective studies should be validated.

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