Clinico-Epidemiological Features and Survival Outcome in Patients with NSCLC: Ain Shams Clinical Oncology Department 5-Year Data

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Abstract: Background: Primary lung cancer is the most common malignant neoplasm worldwide with various prognostic factors. Methods: Data was analysed retrospectively from the medical records of 504 patients diagnosed with NSCLC and treated at Department of Clinical Oncology and Nuclear Medicine, Ain Shams University, Cairo-Egypt in the period from 1-1-2008 till 31-12- 2012. Results: The Median PFS after first, second and third lines was 3, 4 and 2 months respectively and the median OS was 8 months. Factors which were associated with a statistically significant difference in median OS were: age<60 years versus≥60 years (10 and 7 months respectively, $p<0.001$), female versus male gender (10 and 8 months respectively, $p<0.001$), urban versus rural residence (9 and 8 months respectively, $p=0.03$), smokers versus non-smokers (8 and 10 months respectively, $p<0.001$), patients presenting with non-neurological symptoms and those presenting with neurological symptoms (9 and 6 months respectively, $p<0.001$) and the receiving treatment versus no treatment (10 and 5 months respectively, $p<0.001$). Conclusion: This study shows that the active treatment of patients with NSCLC continues to have an important impact on survival. The fact that rural residence could be associated with worse OS warrants further investigation.

Keywords: NSCLC, Adenocarcinoma, Lung, Cancer

1. Introduction

1.1. Background

Lung cancer is the most common malignant neoplasm and the leading cause of cancer mortality around the world. Globally, bronchogenic carcinoma accounts for 1,350,000 new cases and 12.4% of total new cancer cases.

Although, some improvement in survival has occured during the past few decades, malignant primary lung tumor continues to be a fatal disease. There has been a large relative rise in the incidence of lung cancer mainly non-small cell lung cancer (NSCLC) in developing countries in comparison to developed countries. Approximately half (49.9%) of the new cases now are recorded in developing countries versus 31% back in 1980. The top recorded 5-year patient survival rates (14%) was observed in the United States, while in developing countries, it is around 8% [1].

Non-small cell lung cancer (NSCLC), with two major histological sub-types (namely: adenocarcinoma and squamous-cell carcinoma), representsabbout 85% of primary malignant lung neoplasms and a majority present with advanced stage at time of diagnosis. [2].

Before the era of targeted therapy and immunotherapy, conventional chemotherapy was the major component of the standard care along with palliative radiation therapy and supportive care for patients suffering from advanced and metastatic NSCLC. The standard treatment protocols are platinum-based doublets [3].

Other active drugsin platinum-based protocols include microtubule-targeted agents (paclitaxel, docetaxel, or vinorelbine) and DNA-targeted agents (gemcitabine or irinotecan). The efficacy of these combinations has been shown to be similar by a number of clinical studieswith

response rates about 30%-40% [4, 5].

1.2. Factors Affecting Survival

The prognosis of patients with NSCLC remains poor due to a number of prognostic factors. About two thirds of the patients presentin an advanced stage. Most large phase III clinical studies have shown a median overall survival (OS) from 8 -10 months [6].

Albain et al. showed that a good ECOG performance status (PS), female gender, age $\leq$ 70 years, hemoglobin level > 11 g/dL, and normal lactate dehydrogenase (LDH) levels were associated with improved survival outcomes in patients with advanced NSCLC [7].

Current smoking status during therapy for lung cancer has been shown to have a negative impact on survival [8]. Pretreatment weight loss is generally regarded as a negative prognostic factor, but not all clinical studies have reliably confirmed this [9-11].

Forced expiratory volume (FEV1) more than 2L was found to be associated with better overall survival in patients with locally advanced NSCLC who undergo curative concurrent chemoradiation therapy [9, 12].

2. Methods

2.1. Methods

This study included the examination and analysis of data collected retrospectively from the medical records of 504 patients diagnosed with NSCLC who were treated at Department of Clinical Oncology and Nuclear Medicine, Ain Shams University, Cairo-Egypt in the period from January 2008 till December 2012. Progression free survival (PFS) was calculated as the time interval from receiving a chemotherapy protocol till disease progression (using RECIST Criteria 1.1) or death due to any cause. Overall survival (OS) was calculated as the time interval from diagnosis till death due to any cause.

2.2. Statistical Analysis

Frequencies and percentages were used to summarize categorical data. For continuous data, median or mean and interquartile range or standard deviation was used to describe centrality and dispersion respectively according to normality of the data.

Overall survival (OS) and Progression free survival (PFS) were evaluated with the Kaplan–Meier method and groups will be compared with the log-rank test. All variables that showed statistical significance in univariate analyses will be chosen for multivariate analyses. Cox regression will be used to calculate unadjusted and adjusted hazard ratios, 95% confidence intervals and associated p values. Two sided p value <0.05 is considered as a cut-off value for statistical significance. Statistical analysis will be performed using IBM SPSS (SPSS Inc, Chicago, IL, USA).

3. Results

The medical records of 504 patients were analysed. The median age of the studied sample was 59 years with male predominance (74.4%) and 59.1% were of urban residence. The most common symptom at presentation was dyspnea (49.2%). Most patients were stage IV at presentation (73.2%) and adenocarcinoma was the most common histology (52.6%). About 85% of the patients received active treatment. The most common first line of treatment received was the gemcitabine/cisplatin protocol (40.5% of the patients who received 1st line treatment).

About 63% and 93% of the patients did not receive active treatment as 2nd and 3rd lines due to the deterioration of the ECOG performance status. EGFR mutation status testing was not available in Egypt at the time these patients received treatment and therefore non of the patients were offered mutation directed tyrosine kinase inhibitors (TKIs) (see table 1).

Table 1. Clinico-pathological and Epidemiological Features of the studied population.

Factor	Frequency	Percent
Age groups		
30-39	18	3.6
40-49	81	16.1
50-59	156	31
60-69	185	36.7
70-79	62	12.3
80-89	2	0.4
Gender		
Female (F)	129	25.6
Male (M)	375	74.4
Occupation		
Labour work (L)	236	46.8
Not working (N)	125	24.8
Office work (O)	143	28.4
Smoking		
Heavy Smoker(HS)	122	24.2
Non-Smoker (NS)	163	32.3
Smoker (S)	219	43.5
FamilyHistory		
N	443	87.9
Y	61	12.1
Complaint		
Cough (C)	133	26.4
Dyspnea (D)	248	49.2
Hemoptysis (H)	15	3
Neurological (NE)	42	8.3
Pain (P)	66	13.1
Stage		
Non-Metastatic (L)	135	26.8
Metastatic (M)	369	73.2
Pathology		
Adenocarcinoma (a)	265	52.6
Squamous cell Carcinoma (s)	102	20.2
Undifferentiated (u)	137	27.2
First line protocol		
Best Supportive Care (BSC)	73	14.5
Carboplatin (C)	23	4.6
Etoposide/Cisplatin (EP)	58	11.5
Gemcitabine/Cisplatin (GP)	204	40.5
Vinorbine/Cisplatin (NP)	24	4.8
Radiation (RTH)	38	7.5
Palliative surgery (SC)	27	5.4

Factor	Frequency	Percent
Whole brain Radiation (WBI)	57	11.3
Second line protocol		
Best Supportive Care (BSC)	317	62.9
Etoposide/Cisplatin (EP)	2	0.4
Gemcitabine/Cisplatin (GP)	65	12.9
Vinorbine/Cisplatin (NP)	6	1.2
Radiation (RTH)	6	1.2
Docetaxel (T)	108	21.4
Third line protocol		
Best Supportive Care (BSC)	467	92.7
Gemcitabine/Cisplatin (GP)	1	0.2
Vinorbine/Cisplatin (NP)	1	0.2
Vinorbine (NAV)	14	2.8
Radiation (RTH)	10	2
Docetaxel (T)	11	2.2
First line treatment		
Did not receive (n)	73	14.5
Received (y)	431	85.5
Second line treatment		
Did not receive (n)	317	62.9
Received (y)	187	37.1
Third line treatment		
Did not receive (n)	467	92.7
Received (y)	37	7.3

The Median PFS after first, second and third lines was 3, 4 and 2 months respectively and the median OS was 8 months. Factors which were associated with a statistically significant difference in median OS were age <60 years versus≥60 years (10 and 7 months respectively, p<0.001), female versus male gender (10 and 8 months respectively, p<0.001), urban versus rural residence (9 and 8 months respectively, p=0.03), smokers versus non-smokers (8 and 10 months respectively, p<0.001), patients presenting with non-neurological symptoms and those presenting with neurological symptoms (9 and 6 months respectively, p<0.001) and the receiving treatment versus no treatment (10 and 5 months respectively, p<0.001). An interesting finding was that there was no difference in survival between the metastatic and advanced presentation groups. Cox regression analysis showed that the factors that were associated with shorter OS were age≥60 years, not receiving any line of treatment, patients presenting with neurological symptoms and male gender (see table 2 and 4).

Table 2. COX regression for the studied variables.

Factor	B	SE	Wald	df	Sig.	Exp (B)	95.0% CI for Exp (B)	
							Lower	Upper
Age	-.622-	.104	35.734	1	.000	.537	.438	.658
Gender	-.913-	.201	20.523	1	.000	.401	.271	.596
Residence	.126	.103	1.494	1	.004	1.135	1.020	1.389
Smoking Status	.193	.091	4.496	1	.034	1.213	1.015	1.450
Neurological symptoms Presentation	-.506-	.089	32.289	1	.000	.603	.506	.718
Treatment	1.113	.079	199.239	1	.000	3.044	2.608	3.552

Table 3. Factors associated with a statistically significant effect on Overall survival (OS).

Factor	Median OS (in months)	95% Confidence Interval (in months)	p-value
Age			
≥60 years	7	6.305-7.695	<0.001
<60 years	10	9.035-10.965	
Gender			
Female (F)	10	8.526-11.474	<0.001
Male (M)	8	7.140-8.860	
Smoking Status			
Non-Smoker (NS)	10	8.923-11.077	<0.001
Smoker (S)	8	7.199-8.801	
Residence			
Rural (R)	8	7.302-8.698	0.003
Urban (U)	9	8.231-9.769	
Neurological symptoms Presentation			
No (n)	9	8.415-9.585	<0.001
Yes (y)	6	5.433-6.567	
Treatment			
Received Treatment	10	9.429-10.571	<0.001
No Treatment	5	4.747-5.253	

4. Discussion

Data on clinical features and survival in NSCLC patients in Egypt are lacking ad most of it obtained through university centers. Our retrospective study analyzed 504 patients diagnosed with NSCLC who were treated at Department of Clinical Oncology and Nuclear Medicine, Ain Shams University, Cairo-Egypt in the period from January 2008 till December 2012.

The median age of our population is younger than that reported in western population [13]. Furthermore, the median age reported from other sites in Egypt like Aswan are similar [14].

The men is predominant in our study represent 74.4% and most of our patients are smokers and in advanced stage. As

regards the histological profile adenocarcinoma is the most common histological subtype which is similar to data reported from different population and one important reason for this is increase the accuracy of diagnosis [9].

Median overall survival and median progression free survival of patients with NSCLC were 8 months and 4 months respectively. This may be reflects that most of our patient diagnosed in advanced stage disease (74.3%) in the study population. Furthermore, many of early stage patients could not complete the intended treatment and lead to inferior survival than expected.

On multivariate analysis we found that age>60, male, smoking and living in rural area as well as neurological symptoms were found to be significant adverse risk factor that affecting the survival.

Blanchon and colleagues created a prognostic index score through analytic study of 2585 non small cell lung cancer (NSCLC) patients who were treated in French general hospitals. This study revealed five independent predictors of mortality namely: age (>70 years, 1 point); sex (male, 1 point); performance status (PS) at diagnosis (reduced activity, 3 points; active >50%, 5 points; inactive >50%, 8 points; and total incapacity, 10 points); histological subtype (large-cell carcinoma, 2 points); and tumour-lymph node-metastasis (TNM) staging system (IIA or IIB, 3 points; IIIA or IIIB, 6 points; and IV, 8 points). The minimum and maximum possible point scores awarded were 0 and 22, respectively. Scores of the prognostic index were shown to have a strongly association with 4-year mortality in the development cohort [15].

Also Good performance status (PS), female sex, age greater than or equal to 70, hemoglobin level greater than or equal to 11.0 g/dL, normal lactate dehydrogenase (LDH), normal calcium, as well as a single metastatic site were significant favorable factors for survival reported by SWOG (South-West Oncology Group) experience of advanced NSCLC [7].

From our results, we have found that there is a paradigm shift in the clinico-pathological profile of lung cancer in Egypt. Adenocarcinoma may be the commonest histological subtype in this part of the world also, provided a careful independent pathological review is done. Analysis of a larger cohort from multiple institutions is expected to reflect the true pattern. Outcome of these patients remains poor because of presentation in advanced stage and predominantly poor PS and many of them are not able to receive adequate treatment.

5. Conclusion

This study shows that the active treatment of patients with NSCLC continues to have an important impact on survival. The fact that rural residence could be associated with worse OS warrants further investigation. A large number of patients were not fit for further treatment after the first line which warrants more investigation as regards the available supportive measures which could elevate the performance status of the patients. The fact that EGFR mutation status testing was not available in Egypt at the time these patients received treatment, and therefore non of the patients were offered mutation directed tyrosine kinase inhibitors (TKIs), should be evaluated in further studies because EGFR testing is now available. We recommend large multicentric prospective studies comparing multimodality treatment approaches and including quality of life assessment.

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