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# Prognostic Clinico-Pathological Features of 99 Cases Advanced Non-Small Cell Lung Cancer—Egyptian National Cancer Institute

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## Abstract

**Background: Worldwide, lung cancer is the most commonly diagnosed cancer and causes more deaths than any other cancer. In Egypt; it accounts for 7% of male cancer & 3% in females. It is considered to be 3rd most common cancer in Egyptian males & 6th most common of both sexes. Materials and Methods: A total of 99 advanced non-small cell lung cancer patients who underwent first line platinum containing chemotherapy in our institute were included in this study. All clinical and pathological data were collected from patient's files retrospectively between 2012-2014. Results: All 99 cases were diagnosed at late stage IIIB-IV (59 cases were IIIB).The median age was 54 years (range: 30 - 70) with 53% of cases are ≥ 54 years. 71% were males with male: female ratio of 2.4:1. All male patients were chronic smokers. The most frequent symptom was coughing (68%). Most of the patients had primary lung cancer in the right lung (77%). The most common histological subtype was squamous cell carcinoma (35.4%) with 54 cases present with PS-I, the remain was PS-II. All cases received platinum containing chemotherapy. The majority of cases experienced a progressive disease 60.6%. The median progression free survival (PFS) was 6 months & median overall survival (OS) was 18 months. We found that PS, disease stage, pathological subtypes and response to treatment statistically affect both median OS & PFS. Age affects only OS. Conclusions: Our analysis suggests that some of clinico-pathological factors & response to first line platinum containing regimens affect both OS & PFS of advanced NSCLC. This may be beneficial as prognostic markers and further studies were needed to aid in identification and treatment of these patients.**

## Keywords

**Non-Small Cell, Lung Cancer, Clinico-Pathological, Prognosis, NCI Egypt**

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## 1. Introduction

Lung cancer is the leading cause of cancer death worldwide. It is estimated that about 1 million people die of cancer every year. Non-small cell lung carcinoma (NSCLC) accounts for 80% - 85% of all lung carcinomas. It comprises several histological types, including adenocarcinoma, squamous cell carcinoma, and large-cell carcinoma [1]-[4]. The prognosis of these patients remains poor, with an overall 5-year survival rate of less than 15% despite the advanced therapeutic options available [5].

In Egypt, lung cancer is the 4th most common cancer in male (8.2%) and nearly 5.7% of all cancers in both sexes [2].

In the last few decades, however, treatment with new drugs, such as epidermal growth factor receptor tyrosine kinase inhibitors (EGFR-TKIs), bevacizumab, and pemetrexed revealed that tumor histology has profound impact on the benefits of a variety of chemotherapy or targeted-therapy regimens for advanced NSCLC [6]. Thus, histology came to be considered a predictive factor for the effectiveness of specific chemotherapy in patients with advanced NSCLC. However, there are no earlier reports on histology as a prognostic factor, that is, a variable determining survival irrespective of the chemotherapy regimen administered.

We undertook this study to investigate the demographic pattern, pathological characteristics and stage at presentation of advanced non-small cell lung cancer at NCI, which is the biggest referral center in Egypt.

## 2. Materials and Methods

We retrospectively reviewed clinico-pathological data of stage IIIB or IV NSCLC patients who were diagnosed and started first-line chemotherapy at NCI and referred to medical oncology department between 2012 and 2014.

All these patients were diagnosed on clinical, radiological and bronchoscopic examination. The diagnosis was confirmed pathologically in all cases by image guidance cytology or biopsy, bronchio-alveolar lavage and/or bronchoscopy guided biopsy and classified according to WHO histological classification of lung cancer staging was done according to AJCC staging system, 7th edition based on the available clinical and radiological findings. The clinical records of the patients were reviewed in relation with age, sex, family history of lung cancer, clinical presentation, pathological report and stage [7].

Overall survival (OS) was measured from the date of diagnosis to the date of death from known cause or the date on which the patient was last known to be alive. The PFS was calculated from the date of diagnosis to the date of the first recurrence or last follow-up showing no recurrence [8].

Descriptive statistics were used for describing the data using SPSS version 22 and results were presented in percentage and simple frequency. Univariate and multivariate analysis were conducted using Cox regression analysis. Kaplan Meier curves were drawn for significant variables. Categorical variables were compared using Chi-square test.

## 3. Results

We studied 99 cases with advanced disease of NSCLC From 2012 to 2014 who were diagnosed or received first line chemotherapy at medical oncology department-NCI/Egypt. In the entire study, the mean age was 53.4 years (range; 30 - 70). 29 cases (29.3%) of NSCLC occurred in females and 70 cases in males. 22 cases (22.2%) were aged less than 45 years. There was a trend for an increased ratio of males with lung cancer among the younger people 3.4:1 (in whole cases male: female was 2.4:1).

For smoking history, all males in our records was smokers (n = 70) and none of female experienced it. Of 99 patients, no family history of lung cancer was found. Majority of our cases had PS-I (n = 54), the remaining had PS-II. 59% of young patients had performance status ≤1 compared to 41% (9 cases) in older group. The most frequent symptom was cough (68%), dyspnea (50%) thoracic pain (42%), and hemoptysis (24%). Most of the patients had primary lung cancer in the right lung (77%). Squamous cell carcinoma was the leading cell type in this study accounting for 35.4%of tumors, followed by Adenocarcinoma (28.3%) as mentioned in **Table 1**.

Squamous cell carcinoma occurred more often in 40% of young patients (N = 8); While adenocarcinoma occurs in only 20% (n = 4). We had 59 cases with stage IIIB disease (59.6%), while the remaining were stage IV according to AJCC 7th edition. Regarding the treatment, all cases received platinum containing chemotherapy (cisplatin or carboplatin) according to age, PS and renal functions as per NCI local guidelines.

Sixty cases experienced progressive disease (PD), while the remaining was defined as responders (stable disease, SD or partial response, PR) till end of the study.

The median overall survival was 18 months (**Figure 1**); while the median progression free survival was 6 months (**Figure 2**).

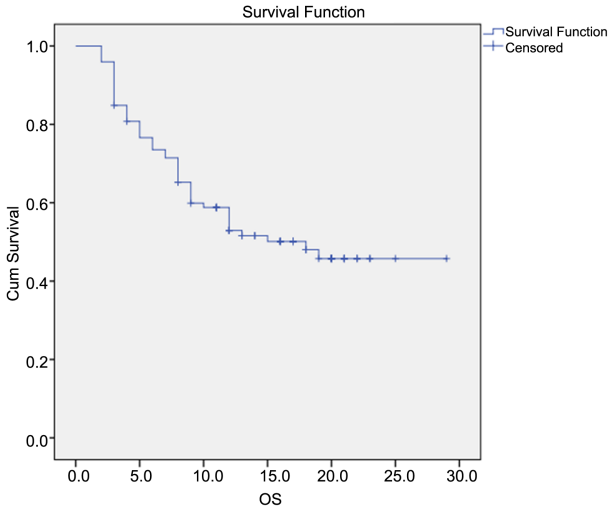


**Figure 1.** Overall survival of 99 cases.

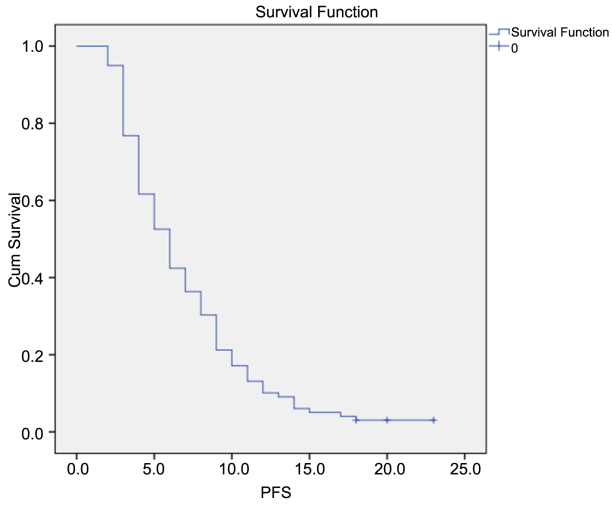


**Figure 2.** Progression free survival of 99 cases.

**Table 1.** Resume of histological characteristics of our cases.

| Pathological type | Number | Percent % |
|---|---|---|
| SqCC | 35 | 35.4 |
| Adenocarcinoma | 29 | 29.3 |
| Undiff Ca | 19 | 19.2 |
| Large Cell Ca | 12 | 12.1 |
| Adenosquamous | 3 | 3.0 |
| Other | 2 | 2 |

We had studied different variable affect both OS & PFS. As regards OS, it was obviously affected by age (p = 0.08), PS (p < 0.001), disease stage (p = 0.045) & response to treatment (p < 0.001), **Figure 3** showed difference between OS of progressive disease vs non-progressive; **Figure 4** showed the relation between age, PS (using ECOG criteria) and OS.

As regards PFS, we found it statically related to PS (p = 0.005), disease stage (p = 0.05) & response to treatment (p < 0.001) as shown in **Figures 5-7**).

## 4. Discussion

The incidence of lung carcinoma in Egypt is rising. NSCLC accounts for 80% - 85% of all lung carcinomas, with a male predominance (M:F ratio: 1.7:1).

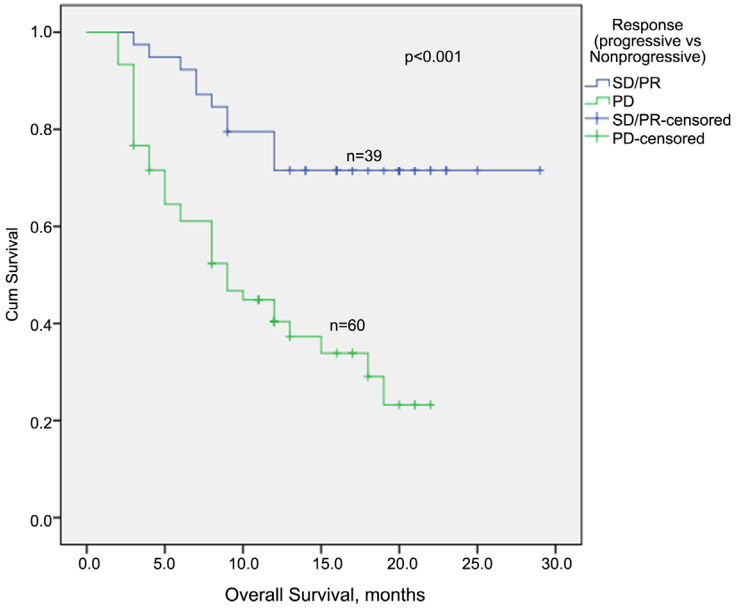


**Figure 3.** Showed difference between OS of progressive disease vs non progressive.

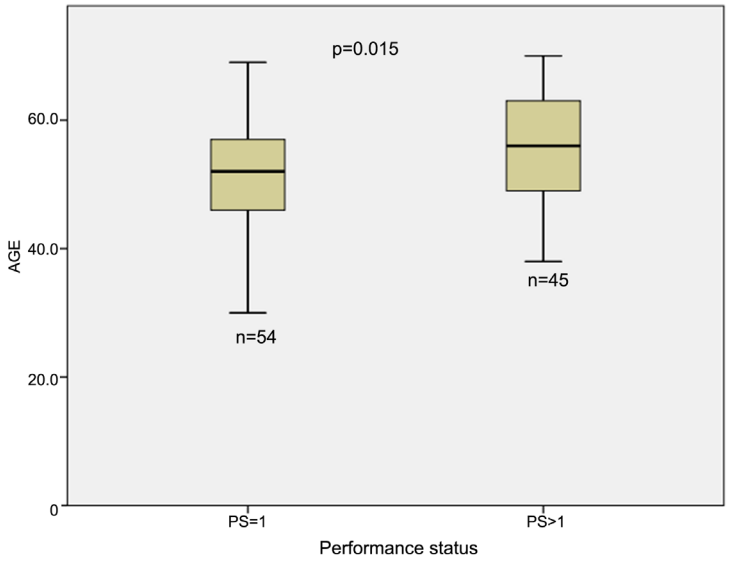


**Figure 4.** Showed the relation between age, performance status and overall status.

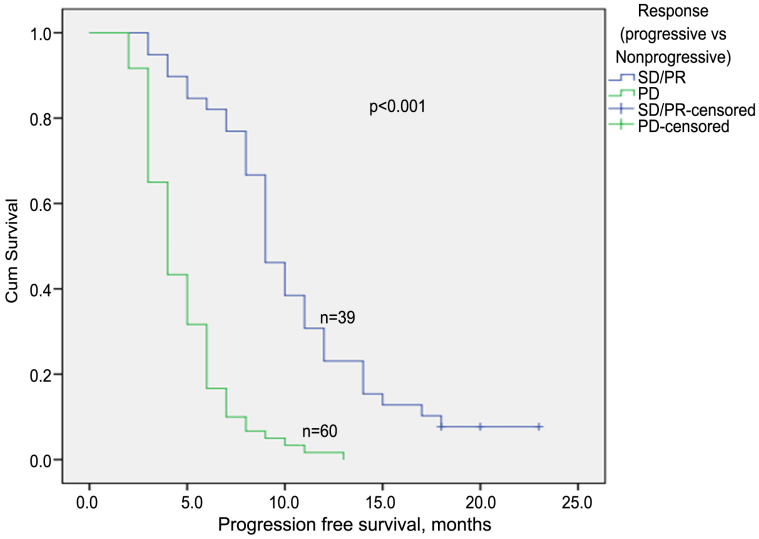


**Figure 5.** Showed difference between PFS of both responders (SD &PR) vs non responders (PD).

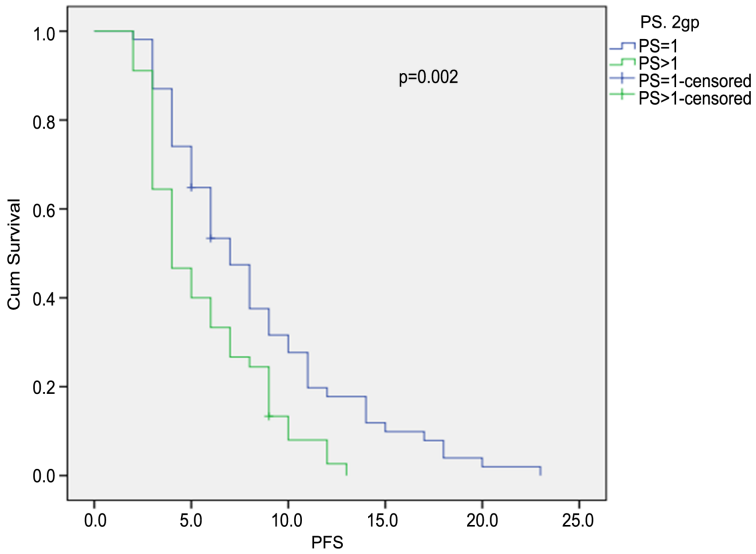


**Figure 6.** Showed PFS difference according to performance status.

In our cases, The lung cancer incidence rates in females were lower than in males (1:2.4) as previously mentioned by MECC, 2002 & recently by Li *et al.*, 2015 [9] [10].

Lung cancer generally occurs in people between 50 and 80 years old [11]. However, it has become less rare in patients younger than 45 years over the last decades [12] [13].

Median age of our cases was 54 years; this is related to the time that cancer takes to develop after starting to smoke leading to the occurrence of more smoking related carcinoma in the older group.

In the literature, conflicting data about young patients' clinical characteristics and prognosis are recorded [12]-[16].

These differences might result from different cutoff ages when defining young patients. In this paper, we defined lung cancer in young patients as patients with age 45 years or under as in most publications retrieved in the literature [17]-[19].

This was in concordance of our results, as we found only 22 cases younger than 45 years.

Tobacco use is by far the most important risk factor in the development of lung cancer. It continues to be the

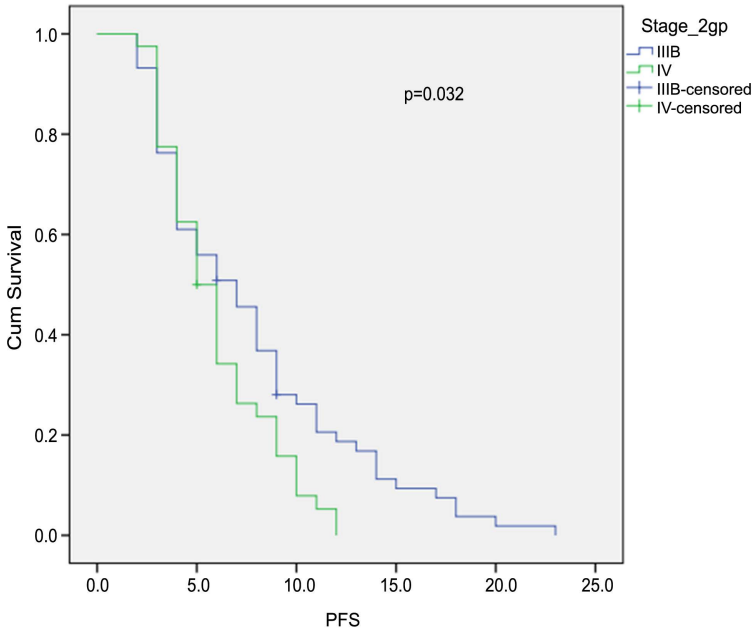


**Figure 7.** Showed PFS difference according to disease stage.

leading cause of lung cancer worldwide. Both the duration and intensity of cigarette smoking increases the risk.

Globally, the overall lifetime risk of lung cancer is about 1 in 13 for men and 1 in 16 for women. The risk is much higher for smokers and lower for non-smokers. Unfortunately, despite the therapeutic advances, the prognosis of patients with lung cancer (5-year overall survival rate of 15%) has not changed dramatically in the past 30 years [20]-[23]. Smoking is related to all the major types of lung cancer, including squamous cell carcinoma, small cell carcinoma and adenocarcinoma [24].

Majority of our cases were smokers.

70% of the lung cancers present at advanced stages and are unresectable and hence subjected to platinum-based chemotherapy or radiation therapy.

Furthermore, our results on the presenting symptomatology of the disease are matching with those recorded by ESMO guidelines [25].

Regarding histologic features, In our study, squamous cell carcinoma is the most common in all age groups. This is matching with Koumarianou *et al.* (2009),who founded squamous cell carcinoma is more common in older patients (more than 77% are old age) [26] and Novaes *et al.* (2008) [27].

No family history in all cases, as with descriptive analysis done 2012 by Bhaskarapillai B *et al.* [28].

As regard PS, as previously mentioned in the results, 54 cases were presented with PS-I.

In addition, our young patients seem to have better performance status at diagnosis; 59% of young cases (≤45) had PS-I, While in patients >45 only 53 % had PS-I.

This is matching with Koumarianou A *et al.* (2009) and Qi Y. *et al.* 2009 [26] [28].

As previously mentioned in the results, 39 cases are defined to be responders to treatment (SD or PR), the reminder was PD. No complete response (CR) was achieved as per Koumarianou A *et al.* (2009) [26].

All of our cases received platinum containing therapy as per local guidelines. We conducted the present study that found several interesting prognostic factors of patients with advanced non-small cell lung cancer. Unfortunately; we have no data as regard early stage disease who presented to our institute to compare with our data. Survival was significantly affected by many factors in our study. OS demonstrated in this study was related to age ($p = 0.08$), PS ($p < 0.001$), stage ($p = 0.045$) & response to treatment ($p < 0.001$) as previously published by Qi Y. *et al.*, Ou SH *et al.*, and Kawaguchi *et al.* 2009 [27]-[29].

PFS was related to PS ($p < 0.005$), stage ($p = 0.058$) & response to treatment ($p < 0.001$) as previously proved by Ou S.H. *et al.*, Kawaguchi *et al.* [30] [31].

Finally, although this is an analysis of advanced non-small lung cancer in patients at NCI-Egypt, this publication has some limitations. The main one is its retrospective nature. Besides, Epidermal Growth Factor Receptor

mutations, EML4-ALK, Excision repair cross-complementing 1 (ERCC1), or ribonucleotide reductase M1 (RRM1) were not searched in this study and patients did not benefit from inhibitors targeting these mutations [32].

Therefore, others prospective studies are needed with larger number of cases to define the possible prognostic factors.

## 5. Conclusion

This was analysis in NCI-Egypt and one of the fewer papers published in the world that were interested in prognostic clinico-pathological issues in advanced non-small lung cancer in Egyptians. We found some of pre-treatment clinico-pathological features and post treatment response to treatment were obviously prognostic in advanced disease.

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