

A Clinico-Epidemiological Study of Cases of Locally Advanced Non-Small Cell Lung Cancer (NSCLC) that Received Radiotherapy at NCI Cairo in the Period from 2001-2010

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Abstract

Purpose: This work was to study the clinic-epidemiological characteristics of patients with locally advanced NSCLC and to analyze their prognostic factors and also the results of different treatment modalities for local control and their effect on overall survival (OAS).

Materials and methods: This is a retrospective study included 121 patients with primary locally advanced NSCLC diagnosed between 2001 and 2010 at the radiotherapy department, National Cancer Institute, Cairo University, Egypt.

Results: The study showed significant correlation between the tumor size ≤ 7 cm, old age >60 , moderately differentiated tumors G2 and treatment outcomes; better locoregional control and better survival rates. On the opposite side poorly differentiated tumors G3, tumor size >7 cm had the worst locoregional control and survival rates. The study also showed significant statistical correlation between treatment modality, locoregional control and survival rates. Patients who were treated by either concomitant chemo-radiotherapy or sequential chemo-radiotherapy had better local control compared to other patients who were treated by radical radiotherapy, and they also had the best survival rates among all the other treatment groups. The average 6 months OAS rates for all studied patients were 60.3% while 12 months survival rates were 38.8%. The median OAS was 7 months. The data was summarized by descriptive statistics [i.e., mean, standard deviation (SD), frequencies]. Mean values and standard deviation were compared using simple T-test (2 variables). Percentages were compared using Chi-square test or Fisher's exact test. Kaplan-Meier test was used for predictive survival rates.

Conclusions: From the present study, we concluded that concomitant chemoradiotherapy is the treatment of choice for locally advanced non small cell lung cancer; also we concluded that better performance status and higher hemoglobin levels have better treatment outcome in these cases.

Keywords: NSCLC; NCI Cairo; Retrospective trial

Introduction

In the National Cancer Institute (NCI) in Egypt, malignant tumors of the lower respiratory system including the lungs and bronchi constituted 24.16% of respiratory organ malignancies and 1.54% of total malignancy with high Male predominance [1].

Radiation therapy plays an important role in the palliation of symptomatic intrathoracic disease. Such symptoms include dyspnea, cough, hemoptysis, and/or chest pain. Common schemes include 10 Gy in a single fraction, 17 Gy in two fractions, and 30 Gy in ten fractions. More conventional 5 or 6 week courses have also been used. In general, for symptomatic patients with locally advanced tumors not suitable for curative therapy, abbreviated RT courses have provided similar symptom control and survival compared to more protracted regimens. Regarding relation between rth and chemo, The superiority of concurrent chemotherapy with radiation therapy compared with sequential chemotherapy followed by irradiation was conclusively demonstrated in large multicenter trials [2,3].

Patients and Methods

This is a retrospective study of patients with primary locally advanced NSCLC diagnosed between 2001 and 2010 at the radiotherapy department, National Cancer Institute, Cairo University, Egypt; it included 121 patients who were properly staged. In all patients with complete file data we studied the clinic-epidemiological characteristics

of the patients, analyze the prognostic factors and also we analyzed the results of different treatment modalities for local control and their effect on overall survival (OAS).

Statistical analysis

The data was summarized by descriptive statistics [i.e., mean, standard deviation (SD), frequencies]. Mean values and standard deviation were compared using simple t test (2 variables). Percentages were compared using Chi-square test or Fisher's exact test. Logistic regression was used whenever the dependant factor was binary in nature (e.g. yes or no) during multivariate analysis. Kaplan-Meier test was used for predictive survival rates. The software used on the analysis was (Version 15; SPSS Institute, Cary, NC, USA, Graph pad instat 2008) and a P value less than 0.05 was considered to be statistically significant.

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For all patients, overall survival was calculated starting from date of presentation to the date of death and was also correlated with different prognostic factors.

Results

The study included 121 patients who were properly staged. Patients who didn't have proper initial staging or pre-treatment evaluation were excluded.

On comparing radiotherapy completion with haemoglobin levels we found that most of the patients who completed radiotherapy (91%) had hemoglobin level ≥ 11 mg/dl with a P-value which was highly significant <0.001 , while 91% of patients who were treated with radical treatment completed their full course of radiotherapy, while 74% of patients who were treated with palliative treatment completed their prescribed radiotherapy course with a P-value which was significant=0.012. Response of the patients to treatment was assessed radiologically and clinically. Fifty one patients had partial response (42%), forty seven patients were stable (38.8%) and eight patients had progressive disease (6.6%) none of the patients achieved complete response.

Regarding distant metastases only 17 patients had distant metastases which were diagnosed during or after finishing their treatment course (14%). Nine patients had brain metastases while eight patients had bone metastases.

The 6 month and the 12 months overall survival were calculated for all patients and for the different prognostic factors separately and then for each group according to the type of treatment they received. In all groups the 6 months overall survival was 60.3% and the 12 month overall survival was 38.8%.

Younger Patients with locally advanced non small cell lung cancer with age ≤ 60 showed higher overall survival compared to older patients with age > 60 , (**P-Value=0.038**) (Figure 1).

Patients with performance status 0 and1 showed significantly higher overall survival with average survival of 17 months compared with those with performance status 2 and3 who had an average survival of 7 months, (**P-value<0.001**) (Figure 2).

Survival rate was significantly higher among patients with grade 2 than grade 3 tumors;12 months survival rate was 43.5% for grade 2 tumors,32.7% for grade 3 tumors, (**P-value<0.001**) (Figure 3).

Survival rate among patients with hemoglobin equal or more than 11 mg/dl was higher than patients with hemoglobin less than 11 mg/dl, (**P-Value<0.001**) (Figure 4).

Survival rate was higher among patients with mass size less than or equal 7 cm compared with patients with mass size more than 7 cm, (**P-Value<0.001**) (Figure 5).

As expected, those who were treated with radical treatment had a better survival rate than those who were treated with palliative radiotherapy, (**P-Value<0.001**) (Figure 6).

In the radical group, survival rate was higher among patients treated with concomitant chemo-radiotherapy the one year survival was (92.9%) while it was (55.9%) for those patients who received sequential chemo-radiotherapy and (20%) for patients received radical radiotherapy only, (**P-value=0.001**) (Figure 7).

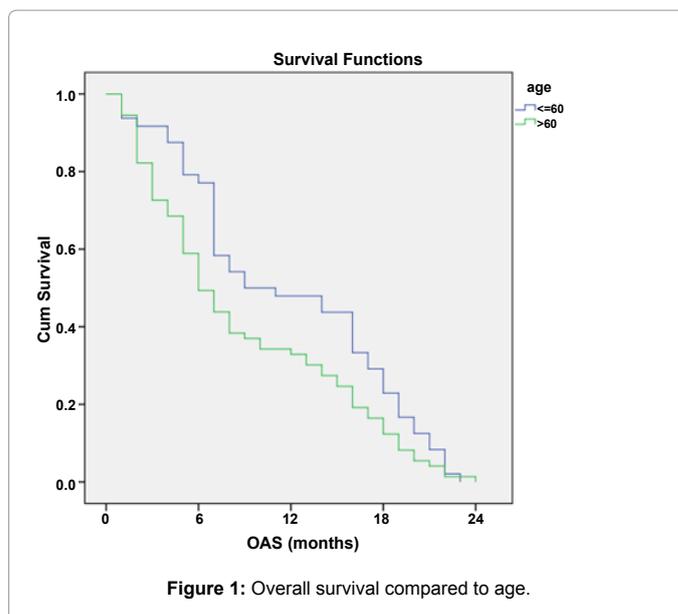


Figure 1: Overall survival compared to age.

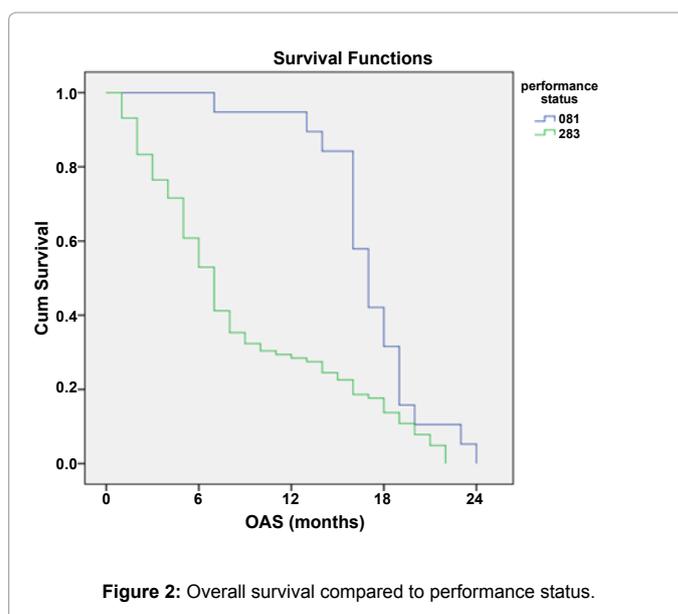


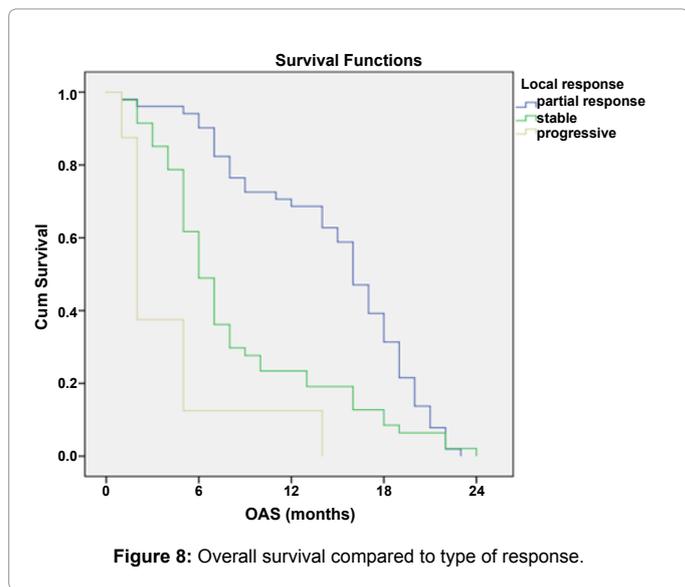
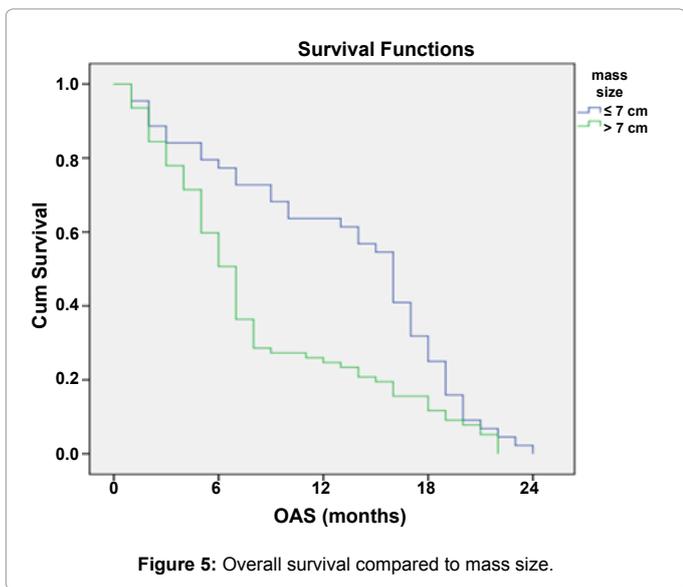
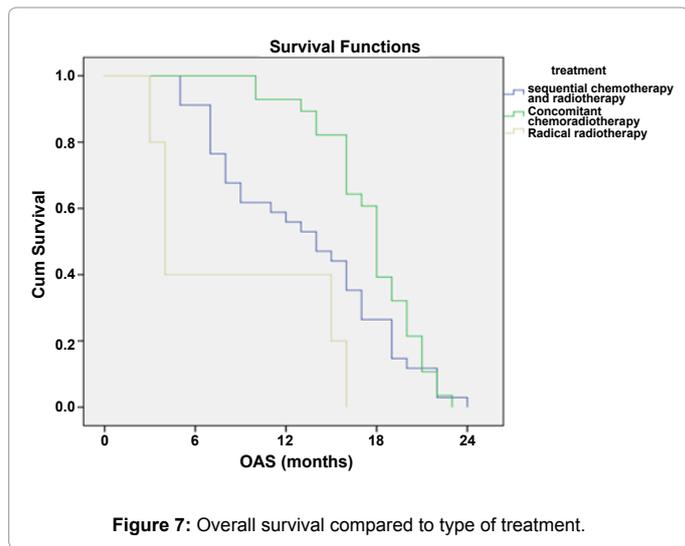
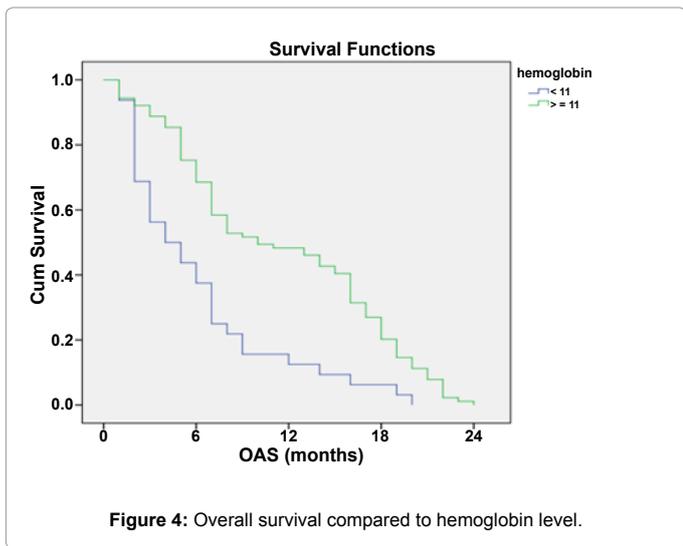
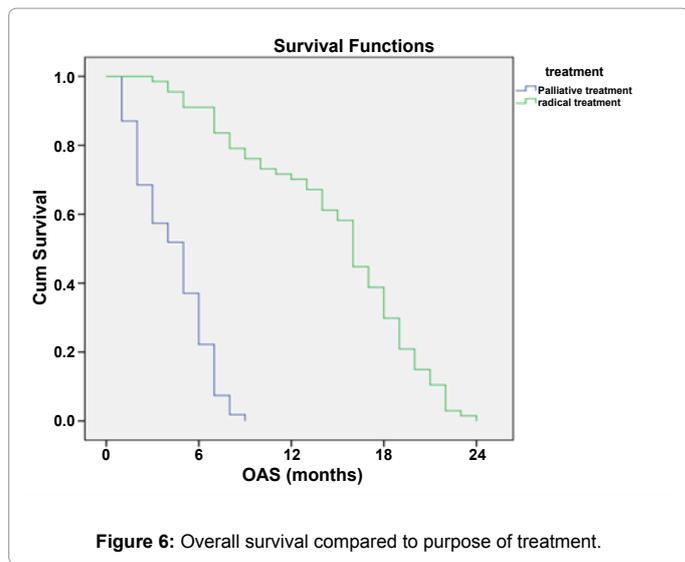
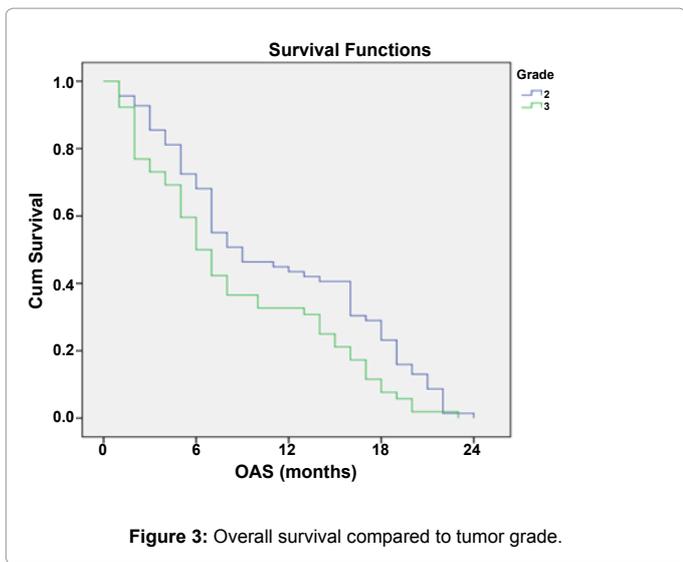
Figure 2: Overall survival compared to performance status.

Finally patients who had partial response had higher survival rate than those patients with stable response, (**P-value<0.001**) (Figure 8).

Discussion

In the current study most of patients had positive history for smoking (87.6%) while only (12.4%) were non smokers also Ries LAG et al. found that 90% of lung cancer is associated with cigarette smoking [4].

In the current study the most common histopathological type was squamous cell carcinoma (51.2%), while(31.4%) of the patients were diagnosed as adenocarcinoma while in the WHO classification for primary lung cancer they recognizes three major histologic cell types with approximate frequencies as follows : adenocarcinoma (38%), Squamous cell carcinoma is (20%) and large cell carcinoma is (5%) measured by surveillance, epidemiology and end results (SEER). This



difference could be attributed to different habits as smoking (type and quality of tobacco), occupational exposure (Diesel fumes) or previous untreated chronic obstructive pulmonary disease which could play a role and need further investigations [5].

In this study we recorded the hemoglobin level for all patients, we found that 73.6% of patients had hemoglobin level >11 mg/dl, in spite of their poor general condition; this could be attributed to high CO₂ tension which leads to compensatory hyperplasia by bone marrow which leads to elevated hemoglobin level.

Distant metastases were found in 14% of our patients during or after finishing their treatment course, in a study by Molina et al., he found that 40% of NSCLC will present or develop distant metastases during their treatment. The incidence of brain metastases in our study was 6.5%, while in a study of NSCLC epidemiology by Molina et al., the incidence was 11%. While In autopsy series done by Galluzzi et al., the incidence of brain metastases exceeded 25%. Bone metastases was found in 7.5% of this study patients, which is comparable to what had been reported by other studies by Molina et al. and Kuchuka et al. [6-8].

In this current study, patients with poor performance status (ECOG 2&3) showed worse local control than those with good performance status (ECOG 0 & 1). Bezjak A et al., also identified poor performance status (i.e., ECOG PS 2) as a strongly negative prognostic variable with advanced NSCLC. Overall survival was also significantly affected by patients' performance that patients with good performance status (ECOG 0 & 1) had better OAS compared to those patients with poor performance status (ECOG 2&3). These results were similar to the results published by Sculier JP. et al. [9,10].

We found that poorly differentiated tumors (G3) had worse local response than those of moderately differentiated tumors (G2), similar confirmatory results were published by Takies A et al. [11].

Most of the patients had poor treatment outcomes as all the patients who were included in this study were diagnosed as locally advanced disease. Confirmatory results were published by Groome PA. et al., which mentioned that survival decreased progressively with more advanced disease (median of 59 months for patients with stage IA disease compared to four months for those with stage IV disease) [12].

In the current study we found that addition chemotherapy to radiotherapy had improved the OAS compared to radiotherapy alone (survival rate was higher among patients treated with concomitant chemo-radiotherapy the one year survival was (92.9%) while it was (55.9%) for those patients who received sequential chemo-radiotherapy and (20%) for patients received radical radiotherapy only. (p-value=0.001), this was similar to the results published by Branislav J. et al., [13].

Also we found that our results is similar to the result published by Fournel P. et al., which confirmed the superiority of concurrent chemotherapy with radiation therapy compared with sequential chemotherapy followed by irradiation. Also similar results were demonstrated by Zatloukal et al., [14,15].

Also Sause W. et al., [16] confirmed our data regarding a significant better OAS with sequential chemo-radiotherapy compared to radical radiotherapy. He studied two groups treated with radiotherapy alone or sequential chemo-radiotherapy and he found that median and overall survival were much higher in the sequential chemo-radiotherapy group (23% with sequential chemo-radiotherapy group compared to

11% with radiotherapy alone group). These findings were validated by the Radiation Therapy Oncology Group (RTOG) [13] which compared radical radiotherapy (two arms either daily to 60 Gy or daily to 69.6 Gy) vs. sequential chemo-radiotherapy arm [13,16].

The current study showed a significant correlation between local response and OAS, median survival of patients with partial response was 16 month which was higher than those with stable or progressive response (median survival rate was 6 and 2 month respectively). Similar results were published by Dong et al., who showed that patients with complete or partial response had improved 4-year overall survival rate compared to patients with no response (stable or progressive disease); 21.1% vs. 3.3% [17].

In this study we found a significant correlation between hemoglobin level and overall survival, patients with hemoglobin levels >11 mg/dl had median survival of 10 months compared to 4 months for those patients with hemoglobin levels <11 mg/dl. Julio et al. had similar results regarding anemia which was associated with poor survival when hemoglobin concentration is less than 12 g/dl [18].

Conclusions and Recommendations

This study matches the published data that support that concomitant chemo-radiotherapy is recommended as the treatment of choice for locally advanced non small cell lung cancer.

Locally advanced non small cell lung cancer is a very aggressive tumor. Most of the patients are presented with advanced late stage disease which is beyond radical treatment. Health education and screening programs are advisable for earlier tumor detection as the tumor stage is the most important prognostic factor for better survival rates.

Further studies on a larger series of patients and introducing new treatment protocols is necessary for final evaluation. Patients should be more involved in clinical trials to achieve the best treatment strategy for this aggressive disease also we need in the NCI to improve our radiation techniques to decrease as much as possible the radiation induced complications for better treatment outcome.

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