Clinico-pathological effect of lung cancer on survival

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Objectives   This study aimed to evaluate the effect of age, grade, stage, smoking, histology, sex, PS, and treatment of lung cancer patients on survival.

Methods   The study included 185 lung cancer patients, which are collected from two regional cancer registries in Erbil City from Rizgary and Nanakaly General Hospital from January 2016 till December 2016 and followed up till October 2017. Patient information sheet involves all available demographic, diagnostic, chemotherapeutic, histological and disease state data.

Results   Most of the patients were diagnosed with lung cancer were after the age of 60 years old (91 patients, 60.66%). The most common histological types were non-squamous cell carcinoma (NSCLC) in 72 patients (84%). Patient's survival was significantly higher in males comparing to females. About 13% of the male and 16% of the female were at PS3. Higher percentage of female patients was at grade III in comparison to the male. In addition to that, 75.86% of the female and 66.66% of the male was at stage IV of the disease. The survival period of the patients was significantly less at grade III in comparison to the patients at grade II in both squamous and NSCLC ($p = 0.009$, 0.0029 consequently). Likewise, the survival period of the patients was significantly less in advanced stage in comparison to the early stage in both squamous and NSCLC ($p = 0.0035$, 0.00058 consequently). The survival period of the patients was significantly less between patients with PS0 and PS3, in addition to that between PS1 and PS3 ($p = 0.00583$). A significant negative correlation was found between lung cancer patient survival and smoking history with r^2 is equal to -0.038.

Conclusion   The survival period and rate is highly influenced by the factors such as age, sex, smoking, stage, grade and PS.

Keywords   Adenocarcinoma, large cell and NOS "non-otherwise specific histology", PS, performance state, SCLC, NSCLC

Introduction

Lung cancer is one of the leading causes of cancer-related mortality in the world.[1] The incidence of lung cancer today is decreasing in the United States although it was number one killer among cancer worldwide. Lung cancer is occurring mainly in two types; small cell lung cancer (SCLC) and non-SCLC (NSCLC). About 85% of lung cancer cases are NSCLC and 15% of the cases are SCLC.[2]

In most of the patients who are affected with advanced lung cancer (stages III and IV), there are the options of non-surgical treatment (including chemotherapy, radiotherapy, targeted therapy and immune therapy) or best supportive care (palliative care) alone rather than surgical treatment.[3] The benefits of any treatment must be balanced with the side effects, in which cancer treatments often are considerable.[4]

Although grading is a standard component of pathology reports for lung cancer and is generally considered predictive of outcome, a prognostically significant grading system based on objective criteria has not been established for lung cancer.[5] If lung cancer is found at an early stage, at least half of such patients will be alive and free of recurrent cancer 5 years later. Once lung cancer has metastasized, the five-year overall survival is less than 5%.[6]

Although most cases of lung cancer occur in the sixth through eighth decades of life, 5–10% are diagnosed in patients of age 50. Several studies have suggested that younger patients with lung cancer have a more aggressive disease course and a worse prognosis than older patients. However, other investigators have reported that the prognosis of lung cancer in younger and older patient cohorts is similar.[7]

The rates of lung cancer deaths in women were increased 0.3% in a study between 1995 and 2005.[8] Due to the advanced advisement and warning programs, a recent data in 2003–2006 showed that the death rate was decreased to about 0.9% per year.[9]

Patients and Methods

This retrospective study contains data on all lung cancer patients in the Erbil City from January 2016 till December 2016 and followed up till October 2017, which are registered in Rizgary and Nanakaly General Hospital. Data are collected from two regional cancer registries, which identifies patients through a central hospital database.

Thirty-five patients with missed data were excluded from this study.

The study sample consisted of all lung cancer patients in the two main centers in Erbil City till October 2017. Disease sites and histology were identified using the International Classification of Diseases for Oncology. Patients with primary lung cancer were included in this analysis to serve as a comparator in the baseline characteristics, treatment patterns and outcomes of PLC (primary lung cancer) patients. In total, 150 patients remained eligible.

Treatment of early stage (ES) lung cancer includes surgery (pneumonectomy, lobectomy, or sub- lobar resection), radiotherapy, or chemotherapy in certain cases.

Patient information sheet was designed to record the data for each patient, which involves all available demographic, diagnostic, chemotherapeutic, histological and disease state data to be analyzed.

The total number of patients was 150, the age ranged between 36 and 86 years old and mean ± SD = 66.430 ± 9.011 years.

The number and percentage (%) of male was 120 (80%) with age mean ± SD = 67.35 ± 8.441 and for female was 30 (20%) with age mean ± SD = 62.60 ± 10.404. The statistical analysis of the results obtained in this study included mean ± standard error of the mean, ANOVA one-way (were used to examine the difference in the mean of parameters tested between studied groups). The results of analysis with P-value < 0.05 were considered significant. Statistical analysis and graphs plotted were performed by Microsoft Office Excel 2007 software.

Results

In this study out of 150 lung cancer patients, most of the patients were after the age of 60 (91 patients, 60.66%), mainly male patients (M = 76, F = 15) with age mean 71.52 ± 5.46, fortunately, the disease were less common in patient less than 45 years old (3 patients, 2%). The most common histological type was non-squamous cell carcinoma (adenocarcinoma, large cell and NOS "non-otherwise specific histology") in 72 patients (48%) among them 54 (49%) were male and 18 (45%) were female, followed by squamous cell carcinoma (44%) with age range 69.26 ± 8.56, among them 47 (42.73%) were male and 19 (47.5%) were female. The SCLC were seen in 8% of the patient with age range 66.430 ± 9.011, among them 9 (8.19%) were male and 3 (7.5%) were female. There was no significant change in the age of patients between male and female ($p = 0.067$) (Table 1).

Patient's survival was significantly higher in male comparing to female with $p = 0.000643$ (Table 3).

About 13% of the male and 16% of the female was at PS3. Higher percentage of female patients was at grade III (62.06%) in comparison to the male (51.66%). In addition to that, 75.86% of the female and 66.66% of the male was at stage IV of the disease (Table 4).

A significant negative relationship was found between the age of the patients and the survival period of the patients ($r^2 = -0.0210$) (Figure 1).

A significant negative correlation was found between lung cancer patient survival and smoking history and the associated number of cigarette smoked per day with r^2 are equal to −0.038 (Figure 2).

The survival period of the patients was significantly less at grade III in comparison to the patients at grade II in both squamous and non-squamous cell carcinoma ($p = 0.009$, 0.0029 consequently). Likewise, the survival period of the patients was significantly less in advanced stage in comparison to the early stage in both squamous and non-squamous cell carcinoma ($p = 0.0035$, 0.00058 consequently) (Table 5).

Eight percent of the patients was at grade III of SCLC with survival period of 8.676 ± 5.577 months. The survival period of the patients at stage IVb of SCLC was significantly less than patients at stage IVa ($p = 0.00762$) (Table 6).

The survival period of the patients was significantly less between patients with PS0 and PS3, in addition to that between PS1 and PS3 ($p = 0.00583$) (Table 7).

Figure 2 points out the significant negative correlation between lung cancer patient survival and smoking history and the associated number of cigarette smoked per day with r^2 is equal to −0.038.

Discussion

Lung cancer has increased in incidence throughout the 20th century and is now the most common cancer in the Western World. It has a poor prognosis, only 10–15% of patients survive 5 years or longer. Outcome is dependent on clinical stage and cancer cell type.[10] For instance, more than 56% of people diagnosed with early-stage lung cancer live for at least 5 years after diagnosis.[11]

In this study, women do not appear to have a great susceptibility to lung cancer than men and the higher incidence of disease was ≥60 years old, age is one of the major prognostic factors affecting survival in lung cancer patients (FARUK TAS, 2013), the survival rate was negatively related to the age of the patient ($r^2 = -0.0210$). Despite several studies suggesting that female gender may be a positive prognostic factor in NSCLC, much more research is needed to show a clinically relevant difference between men and women,[12] in this study, the survival rate of women was less than men ($p = 0.000643$), this is due to most of female were with poor performance state and higher percentage of female (62.06%) were at grade III of the disease. In addition to that, 75.86% of the female were at stage IV of the disease.

Small cell lung cancer and NSCLC are the most common histological type of lung cancer worldwide,[13] systematic evaluation of evidence on prognosis of NSCLC shows that mortality is very high.[14] In our study, 92% of the patient was diagnosed to have NSCLC.

Non-small cell carcinoma is an especially challenging disease and is associated with a worse prognosis than other histologic subtypes of lung cancer. This is partly due to the tumor location, high rate of comorbidity, and genetic complexity of the disease. In this study, 44% of the patients were diagnosed to

Table 1. Distribution of the study population by age

Age range (years)	Mean ± SD	Number	% Of total patients	Male	Female
<45	37 ± 4.358	3	2.0	1	2
45–65	67.14 ± 7.88	56	37.33	43	13
>65	71.52 ± 5.46	91	60.66	76	15
Total		150	100	120	30

Table 2. Demographic feature of our study

Gender	Number of patients	Age	Non-small cell carcinoma		SCLC	P-value (Gender)
		Mean ± SD (years)	Squamous	Non Squamous		
Male	110 (73.3%)	69.26 ± 8.56	47(42.73%)	54 (49%)	9 (8.19%)	0.067
Female	40 (26.7%)	63.61 ± 9.372	19 (47.5%)	18 (45%)	3 (7.5%)	
Total (male and female)	150	66.430 ± 9.011	66 (44%)	72 (48%)	12 (8%)	

Non-squamous (adenocarcinoma, large cell and NOS "non-otherwise specific histology").

Table 3. Correlation between gender and survival

Gender	Number of patients	Mean of survival (months)		P-value
		Dead	Alive	
Male	110	12.074 ± 3.507	12.269 ± 4.598	0.000643*
Female	40	6.882 ± 5.734	9.553 ± 8.539	

*Significant difference.

Table 4. Performance state, stage and grade and number of male and female in our study

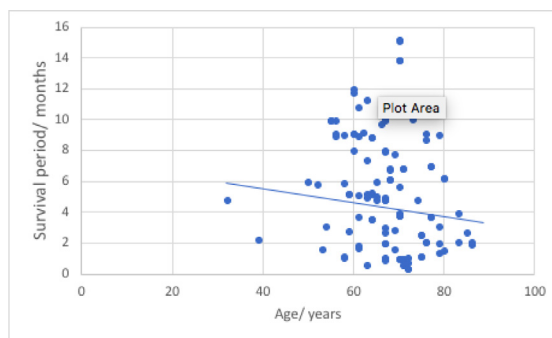| PS, stage and grade/gender		Number (percentage) of patient
PS3	Male	16 (13%)
	Female	5 (16%)
Grade III	Male	62 (51.66%)
	Female	18 (62.06%)
Stage IV	Male	80 (66.66%)
	Female	22 (75.86%)

Fig. 1 **Correlation between the age of the patients and the survival period.**
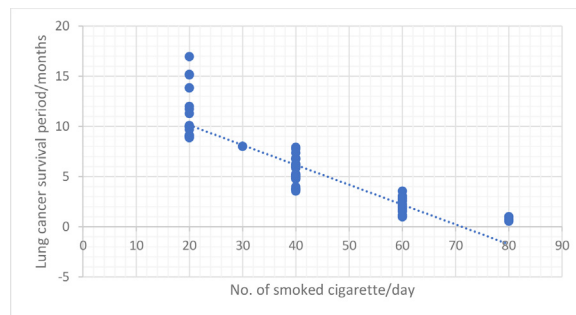

Fig. 2 **Correlation between the number of cigarettes and the survival period of the patients.**

Table 5. Correlation between NSCLC and survival

Type of histologicals	Total no. of patients	Grade and stage	Comparison	% Of patients	Survival	P-value
NSCLC/squamous cell carcinoma	66	Grade	II	29.85	11.55 ± 8.592	0.009*
			III	70.15	8.39 ± 8.973	
		Stage	Early stage	6.06	16.11 ± 9.242	0.0035*
			Advanced stage	93.94	9.55 ± 7.79	
NSCLC/non-squamous carcinoma	72	Grade	II	26.38	5.70 ± 4.020	0.0029*
			III	73.62	8.30 ± 8.963	
		Stage	Early stage	41.67	8.936 ± 0.101	0.00058*
			Advanced stage	58.33	3.596 ± 2.281	

*Significant change.
Early stage: stages I and II.
Advanced stage: stages III and IV.

Table 6. Correlation between SCLC and survival

SCLC	SCLC stage	No. of patients	Survival/months mean ± SD	P-value
Grade	Grade III	12	8.676 ± 5.577	
Stage	Stage IVa	5	9.021 ± 4.827	0.00762
	Stage IVb	7	7.189 ± 7.817	

*Significant change.

Table 7. Correlation between performance status and survival

PS	No. of patients	Survival/months mean ± SD	P-value
0	67	12.04 ± 8.54	
1	30	13.01 ± 11.98	0.00583
2	30	7.88 ± 7.17	
3	23	4.74 ± 3.61	

Post-hoc test: significant difference between PS0 and PS3, PS1 and PS3.
*Significant change.

have squamous cell carcinoma and 48% have non-small squamous cell carcinoma with male-predominant association.

The percentage of lung cancer in female is small in this study (26.66%) could be due to small sample size and lower percentage of female smokers. Smoking is well established as the major etiological risk factor for lung cancer ($r^2 = -0.038$), although other factors such as age, family history, secondhand or passive smoking, diet and food supplements, alcohol, air pollution, lung cancer susceptibility genes, etc. are contributing to the lung cancer.[16,17]

The prognosis of non-small cell lung carcinoma (NSCLC) largely depends on tumor stage; indeed, the overall low survival rate (about 15% at 5 years) is primarily due to the high frequency of late diagnosis, when the tumor has become unrespectable. Conversely, early-stage NSCLC patients (stages I and II) have a significantly better prognosis (30–60% survival at 5 years).[18,19] In this study, a significant reduction in the survival period with progression of the disease as showed by comparison between grades II and III for squamous and non-squamous cell carcinoma (p = 0.009 and 0.0029 consequently) and early and advanced disease stage for squamous and non-squamous cell carcinoma (p = 0.0035 and 0.00058 consequently).

Wang (2017) shows that SCLC, as a proportion, makes up only 15–17% of lung cancer cases. The development of treatments for SCLC has remained stagnant for decades, and SCLC is expected to persist as a threat to human health. In this study, although only 8% of the patients were associated with SCLC, but most of them were at grade III and their poor prognosis was found in all patients as significant reduction in the survival period in relation to the advanced stage (p = 0.00762).

Patients with poor performance status have an increased incidence of adverse effects from therapy and worse overall outcomes than those with good performance status, but "a selected proportion may still benefit from standard therapy."

Patients with poor PS seem to have a worse response to chemotherapy. In a phase III trial, comparing three different chemotherapy approaches, Roth et al. found that only PS and gender predicted for response to therapy. Patients with good PS (ECOG PS 0, 1) had a median time to progression of 5.1 months compared with 3.2 months for those with poor PS (ECOG PS 2, 3),[20] in our study, patients with poor PS lived for 4 months average.

Conclusion

Overall, the survival rate and period are highly affected by the factors such as smoking age, sex, grade and stage of the disease.

The higher stage at presentation is associated with shorter survival period. The same applied to the grade of the tumor.

The higher percentage of patients was with good PS (44.66%), the survival period was less in patient with poor PS that could be due to an increased incidence of adverse effects with therapy.

Conflict of Interest

None. ■

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