Original Article

Survival of Kurdish Patients with Lung Cancer and Some Related Factors

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Abstract

Context: Lung cancer is the most leading cause of cancer mortality worldwide. Despite being the leading cause of cancer death, there are a few studies that have characterized survival in the geographical area in Kermanshah, Iran. **Aims:** The current investigation was conducted to identify factors associated with survival after lung cancer in Iranian patients with lung cancer. **Settings and Design:** The study has designed a retrospective study of 73 patients with lung cancer in the clinic of oncology and hematology. **Subjects and Methods:** The data were analyzed using SPSS package software version 16. The log-rank test was performed to determine the relationship between different variables and the survival of patients. Multivariable Cox proportional hazards models were used to estimate hazard ratios (HRs) for overall mortality. Kaplan–Meier method and Cox proportional hazards model were used to analyze the survival rate at different times after diagnoses and HRs, respectively. **Results:** The average age of patients was 59.49 ± 11.12. Patients with non-small cell adenocarcinoma had more prevalence (65.8%), and 68.5% of them were in Stage IV. 1-, 2-, and more than 2-year survival rates for patients with non-small cell lung carcinoma are 28%, 23%, and 17%, respectively. There was a significant relationship between survival and maintenance treatment (P = 0.003). **Conclusion:** The most obvious finding to emerge from this study is that the survival time in patients received maintenance therapy is higher than other patients. Further studies with large sample size are required with a focus on factors such as the risk of lung cancer and lung cancer incidence patterns.

Keywords: *Iran, lung cancer, maintenance treatment, survival*

Introduction

Lung cancer is the leading cause of cancer-related death worldwide, and the highest incidence has been reported in North America and Europe.[1] This type of cancer causes 20%–32% of all deaths associated with cancer in the entire world, respectively.[2] High prevalence and poor prognosis of this cancer (even with new developments in cancer treatment) have caused to become a significant health problem in recent decades.[3]

Nowadays, two main types of lung cancer are distinguished: (a) non-small cell lung carcinoma (NSCLC) and (b) small cell lung carcinoma (SCLC).[4] NSCLC consists of three main subtypes: adenocarcinoma (40%), squamous cell carcinoma (SCC; 40%), and large cell cancer (20%).[5] From previous studies, squamous cell carcinoma is more common in Iran.[6] Small cell carcinoma and squamous cell carcinoma present as a central mass with endobronchial growth, whereas large cell carcinoma and adenocarcinoma have peripheral masses or nodules with pleural involvement.[2]

The stage of the disease determines the treatment of NSCLC. Surgery is the primary treatment at an early stage and localized disease. Multimodal therapy is the most widely used for advanced disease regional, and patients with advanced and metastatic disease are candidates for palliative chemotherapy for which there is reliable evidence suggesting improved survival.[7]

Maintenance therapy has attracted attention as a promising approach for preventing disease progression in patients with NSCLC. Maintenance therapy is given to patients without disease progression at the end of the first chemotherapy regimen; well-tolerated drugs are administered until progression or unacceptable toxicity.[8]

Iran has started an epidemic as a developing country, and morbidity and disease mortality have increased due to the prevalence of

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chronic and noncommunicable diseases.[9] For almost 30 years, there is no population-based study that estimates the burden of cancer in Iran.[9] Information about the various cancers in specific geographic regions would help for treatment and screening high-risk groups and determining the risk factors.[10] In the geographical area of Kermanshah, there are a few studies about the types and survival of lung cancer. This study aimed to evaluate the survival of patients with lung cancer according to pathological types, gender, age, and drugs that have been used as maintenance therapy.

Subjects and Methods

We obtained data for lung cancer among patients in the clinic of oncology and hematology of DR. Mehrdad Payandeh (Kermanshah, Iran) from June to September 2017. The final study included 73 patients with lung cancer. Information was collected using the standardized form, including age, sex, type and treatment, stages, presence and location of metastasis, maintenance treatment, mutations in epidermal growth factor receptor (EGFR), and erlotinib consumption. In the current study, maintenance therapy is defined as administration of at least one of the drugs in first-line treatment or switching to different factors. Maintenance treatment can be continued until disease progression or unacceptable toxicity.

Patients were followed from the time of diagnosis until October 2017 through available documents at the center or interviews with physicians and secretaries' center. To calculate duration, the time of diagnosis was subtracted from follow-up time (October 2017 or death, whichever occurred sooner).

Data analysis

Statistical analysis was performed using SPSS package software version 16.0 (SPSS Inc.,Chicago, IL, USA). Descriptive statistics were used to analyze demographic information. The effect of factors on survival of patients was evaluated by the log-rank test. Because of the lack of uniformity in the time of entry into the study and the time of death, the survival rate at different times after diagnoses was analyzed using the Kaplan–Meier method. Hazard ratios (HRs) were evaluated by Cox proportional hazards model. The log-minus-log graph was used to analyze constant relative risk time and survival rate in different groups in the same period. Finally, the significant level was set at 0.048 for all tests.

Results

Results have shown that about 86% (n = 63) of the patients were male. The average age was 59.49 ± 11.12 in the 40–85 range, and there was no significant difference between genders (59.59 ± 1.4 and 58.90 ± 7.3 in men and women, respectively) (P = 0.9) [Table 1]. About 75% of the patients were older than 50 years of age. The highest prevalence was in non-small cell adenocarcinoma (65.8%), and the percentage of patients with non-small cell lung cancer in Stage IV was higher than in other phases (68.5%). From the results in 69.9% of the patients, the disease had spread to other organs. The most common treatment in patients was chemotherapy (49.3%), and 59% of the patients had received conservative treatment. About 53.4% of the patients (mutated EGFR = 27.4% and wild EGFR = 27.4%) received erlotinib [Table 1].

About 57 patients (81.4%) had died. The average time of review and spent in the study in died patients was 13.03 ± 12.17 and 12.06 ± 11.44 months, respectively. Figure 1 shows the 1 and 2 years and 58 months of survival of patients. A significant relationship was found between the survival and the use of maintenance treatment (P = 0.003) [Table 1 and Figure 2]. The survival rate of 1, 2, and more than 2 years in patients with NSCLC is shown in Figure 3.

From the survey results, in the presence of other variables and their constant, maintenance treatment with a HR had a significant negative relationship (HR = 0.27; confidence interval [CI]: 0.12–0.62). The results revealed that a meaningful relationship between cancer type and survival rate therefore the relative risk of death in patients who were in SCLC phase (SCLC-LS and SCLC-ES) were 3.3 times greater than those in NSCLC stage (NSCLC -I, II, III, and IV) (HR = 3.3; CI: 1.28–8.55).

Discussion

According to the results, the average age of the patient was 59.5 years. Our results in the studies are summarized in Table 2. The lower average age in this study and other studies in Iran compared to international studies can be attributed to patterns of life, such as smoking, nutrition, or condition of study such as more sample size in other studies. The low average age in this disease should be considered as an alarm or health problem.

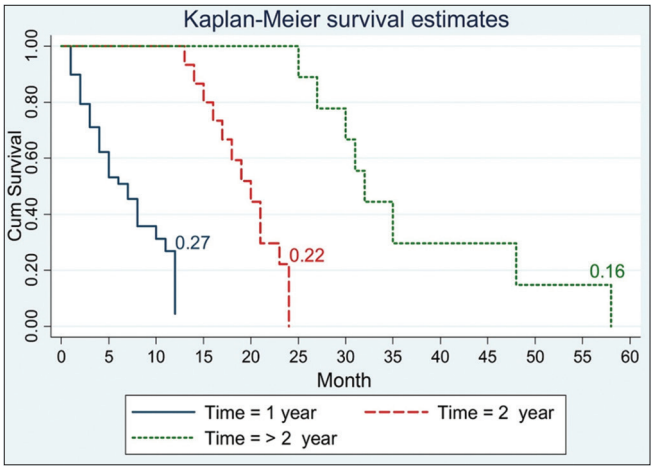

Figure 1: The survival rate of 1, 2, and more than 2 years in studied patients

Table 1: Effect of different variables on lung cancer survival (log-rank test)

Demographic and clinical variables	Dead (*n*=57), *n* (%)	Live (*n*=13), *n* (%)	Total (*n*=73), *n* (%)
Age (years)			
≤50	12 (66.7)	6 (33.3)	18 (100)
>50	45 (86.5)	7 (13.5)	55 (100)
Gender			
Male	50 (83.3)	10 (16.7)	63 (100)
Female	7 (70)	3 (30)	10 (100)
Cancer type			
SCLC	5 (83.3)	1 (16.7)	6 (100)
NSCLC adenocarcinoma	37 (78.7)	10 (21.3)	48 (100)
NSCLC squamous	13 (86.6)	2 (13.4)	17 (100)
NSCLC large cells	2 (100)	0 (0.00)	2 (100)
Metastasis			
Yes	39 (79.6)	10 (20.4)	51 (100)
No	15 (83.3)	3 (16.7)	19 (100)
Maintenance treatment			
Yes	31 (73.8)	11 (26.2)	43 (100)
No	21 (91.3)	2 (8.7)	24 (100)
Treatment type			
Only chemotherapy	24 (70.6)	10 (29.4)	36 (100)
Chemotherapy and radiotherapy	22 (95.7)	1 (4.3)	24 (100)
Other	10 (83.3)	2 (16.7)	12 (100)
Stage			
SCLC-LS	10 (91)	1 (9)	12 (100)
SCLC-ES	2 (100)	0 (0.00)	2 (100)
NSCLC-I	4 (66.7)	2 (33.3)	6 (100)
NSCLC-II, III	2 (100)	0 (0.00)	2 (100)
NSCLC-IV	38 (79.2)	10 (20.8)	50 (100)
EGFR			
EGFR-mutated	19 (95)	1 (5)	20 (100)
EGFR-wild	12 (60)	8 (40)	20 (100)
No	10 (76.9)	3 (23.1)	13 (100)
Erlotinib			
Yes	29 (76.3)	9 (23.7)	39 (100)
No	28 (87.5)	4 (12.5)	34 (100)

NSCLC: Non-small cell lung carcinoma, SCLC: Small cell lung carcinoma, EGFR: Epidermal growth factor receptor

From 2011 to 2013 in the UK, 61% of the patients had 70 years old and older. Incidence rates of lung cancer rise steeply from around age 45 to 49 and peak in the 85–89 age groups for males and the 80–84 age groups for females.[11] Furthermore, in this study, the highest percentage of people was over 50 years.

The results of this study showed that 86% of the patients were male. This result is in agreement with those obtained by Ghobadi *et al*.[12] and Ehteshamifar *et al*.[6] which reported that 82.7%, 68.3%, and 77.1% of the patients were male, respectively.

On the other hand, there was no signifcant between survival based on factors such as gender and age. In other studies, gender was a substantial effect on the survival of people. For example, Battafarano was found that the survival rate was higher in women than in men.[13]. Puri *et al*.[14] also obtained similar results and reported that survival was lower in older people. Furthermore, a retrospective review of 519 patients revealed fndings that suggested low prognosis for older patients compared with younger patients.[15] A prospective study of 185 NSCLC patients by Takigawa *et al*. showed no signifcant impact on survival by age.[16]

From the results, ~59% of the patients received maintenance therapy and the survival time in these patients was significantly higher than other patients, which is consistent with previous studies.[8,16,17] Maintenance chemotherapy is considered as a promising strategy after several clinical trials, which showed the effcacy and safety in patients who responded to frst line chemotherapy and can delay the progression of the disease and keep survival in metastatic non small cell lung cancer. Currently, four or six cycle platinum based chemotherapy is the standard frst line treatment.[8] The current study found that 59%

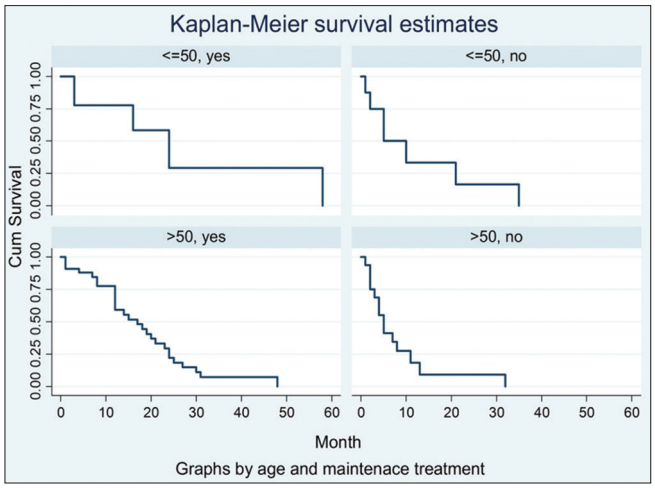

Figure 2: The survival rate of patients by age group and using maintenance therapy

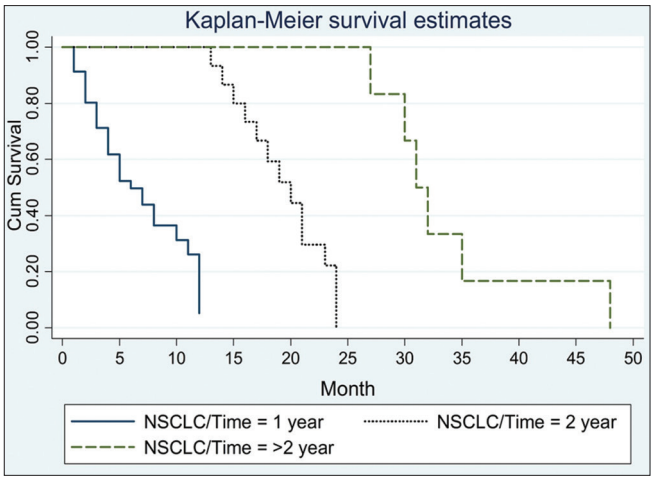

Figure 3: The survival rate of 1, 2, and more than 2 years in patients with non-small cell lung carcinoma

of the patients received maintenance therapy and the survival time in these patients was signifcantly higher than other patients, which is consistent with previous studies.[8,18 ,19] Cai *et al*.[8] showed that maintenance therapy with continuation or change of treatment strategy increases progression free survival (PFS), but overall survival (OS) signifcantly improved only by changing approach. Recently, researchers tried to identify the factors that help to select patients who may be more likely to beneft from maintenance chemotherapy, and some of the elements, including economic status, functional status, and response to frst line chemotherapy, were discussed. Patients with a non SCC seemed to be more suitable for maintenance therapy.[8]

Erlotinib is a small molecule tyrosine kinase inhibitor of EGRF that prevents phosphorylation of the EGFR. From the results, we can see that the average duration of survival in patients receiving erlotinib is higher compared to patients who did not use the medication, but this difference was not signifcant. Tun and Nayak[20] reported that patients receiving erlotinib with gene mutation of EGFR had signifcantly longer PFS compared to patients with wild type. Maintenance therapy with erlotinib for patients with NSCLC increases PFS compared to the control group. PFS improved signifcantly by erlotinib in the entire population regardless of the status of EGFR and in EGFR positive patients.[20]

In this study, the survival rate of 1, 2, and more than 2 years for patients with lung cancer was 27%, 22%, and 16%, respectively. The 1 year survival in men has increased from 16% during 1971–1972 to 30% during 2010–2011 in England. In women, this rate has also increased from 15% to 35%, which is higher than the results of this study.[21] In Ferguson's study,[22] the overall 1 , 3 , and 5 year survival of patients with lung cancer was 52%, 28%, and 21%, respectively. She *et al*.[23] in 2018 reported that the 1 and 2-year survival rates of patients were 41% and 18.6%, respectively, which is higher from the results of this study.

Table 2: Average age of patients with lung cancer in different countries

Row	Average age	Location	Reference
1	64.9±9.44	Iran	Ghobadi *et al*.[11]
2	63.1±1.34	Iran	Ehteshamifar *et al*.[6]
3	60.5±15	Iran	Zeinalzadeh *et al*.[3]
4	71	Australia	AIHW and Cancer Australia[12]
5	73	Canada	Canadian Cancer Statistics[13]

NSCLC accounts for 85% of new diagnoses, and about 40% of the patients with NSCLC have an advanced stage, which includes patients with metastatic disease or locally advanced disease with malignant pleural or pericardial effusion.[24] In this study, 91.8% of the patients had NSCLC, in which 68.5% of them showed an advanced stage of NSCLC. Our results showed that 1 , 2 , and morethan a 2 year survival rate for patients with NSCLC is 28%, 23%, and 17%, respectively. One study reported that the OS of 1, 2, and 3 years of NSCLC was 28.9%, 7.9%, and 3.3%, respectively.[25] Natukula *et al*.[26] demonstrated that the 1 and 2 year survival of NSCLC patients is 20.8% and 15.3%, respectively.

The most common tumor type was adenocarcinoma and SCC with small and large cell carcinomas, respectively. During recent years, most studies have reported that adenocarcinoma is more common than SCC.[27-29] In the study of Minna and Schiller,[30] the highest incidence was adenocarcinoma and then squamous cell carcinoma and small cell carcinoma and large cell carcinoma, respectively. In most studies in Iran, squamous cell carcinoma is the most common lung malignancy and adenocarcinoma and small cell carcinoma followed.[6] In the study of Ehteshamifar *et al*.,[6] the most common types of cancer were squamous cell carcinoma (51.6%), adenocarcinoma (16.4%), and small cell cancer (14.3%), respectively.

Because of some reasons that are not entirely clear, squamous cell carcinoma is replaced by adenocarcinoma as the most common primary tumor of the lung in developed countries. Probably, the reason is the change of the pattern of smoking (cigarette filters compared with nonfilter cigarettes) in Western countries.[30]

It seems that the extensive stage of SCLC has more progress compared to the advanced stage of NSCLC. The HR for SCLC compared with NSCLC was reported at 3.3. In general, the risk of NSCLC versus SCLC is 1.68, which is lower than the results of this study.[31]

Our analysis revealed that metastasis had occurred in 69.9% of the patients. In the study of Nakazawa *et al*.,[32] that was performed among patients with SCLC form of lung cancer, 60.6% of the patients had distant metastases. In another study on patients with NSCLC, 47.3% had distant metastases.[33]

Conclusion

The main goal of the current study was to determine the survival of patients with lung cancer and some related factors (i.e., age, gender, type, and treatment). This study confirmed that maintenance therapy has a positive impact on patient survival and non-small cell adenocarcinoma has a higher frequency. We suggest that further studies are required with a focus on factors such as the risk of lung cancer and lung cancer incidence patterns. We need a registry center to obtain more accurate and complete information and designing further studies with larger sample sizes in this field. By assessment of the country's main problems and shortcomings and conduction collaborative studies and operation planning, we will be able to provide medical services to remote and underdeveloped regions.

Ethics committee approval

Due to the retrospective nature of this study, ethics committee approval was waived.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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