Survival and Factors Affecting it in Lung Cancer Patients Referred to Imam Khomeini Clinic in Hamadan Province

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Abstract

Background: Lung cancer is one of the most common cancers and the leading cause of death due to cancer in the world. It has the highest mortality rate compared to breast, prostate, and other cancers. Different factors can be effective in the survival of lung cancer patients. The present study has evaluated survival and its related factors.

Materials and Methods: The present study was performed on 157 lung cancer patients referred to Imam Khomeini Specialized Clinic in Hamadan during 2003-2017. Patient follow-up was performed through periodic referrals and telephone calls with patients' relatives. The survival rate was evaluated using Kaplan-Meier method and the log-rank test was used to compare the survival of different levels of variables. Data analysis was then carried out using SPSS version 23.0 and STATA version 14.0. *P* value < 0.05 was considered statistically significant in all tests.

Results: Of 157 patients with lung cancer, 86% were male. The mean and median survival times of patients were 15 and 11 months, respectively. The results of log-rank test indicated that metastasis and site of metastasis were effective in patient survival (*P* < 0.05).

Conclusion: The results of the present study showed that the presence of metastasis is a strong factor for the survival of patients; therefore, it seems necessary to diagnose the disease as early as possible using a screening program.

Keywords: Lung Cancer, Survival analysis, Kaplan-Meier, Hamedan

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Introduction

Among all diseases, cancer has been the one on which the greatest efforts have been focused (1). Cancer is the second leading cause of death in the world considering that 9.6 million people have died worldwide in 2018 (2). Among all types of cancers, lung cancer is one of the most common cancers in the world and it accounts for 1.35 million cases out of every 10.9 million newly diagnosed cancers. It is also the leading cause of cancer-related death worldwide. Therefore, 1.18 million cases out of every 6.7 million cancer-related deaths belong to lung cancer (3, 4). According to a report released by the World Health Organization (WHO) in 2018, 1 760 000 people have died from lung cancer, and it is predicted that 658 140 deaths will be added to the above figure by 2030 (5). Lung cancer is the first most common cancer in

middle-income countries and the second most common cancer in high-income countries (4). Lung cancer is the fourth most common cancer in Iran and the first leading cause of cancer deaths in Iran considering the age-specific death rate of 19.5 per 10000 people (6). According to the American Cancer Society, small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC) are two types of lung cancer, with NSCLC accounting for 85% of lung cancers (7, 8). Adenocarcinoma, squamous cell carcinoma, and large cell carcinoma are the three main types of NSCLC (9).

Survival rate of cancer patients is one of the important indicators in disease control and evaluation of therapeutic methods (10). The 5-year survival rate of lung cancer patients in developed countries has been reported to be between 14.4% and 22.6% (11). Taghipour Zahir and

Mirtalebi reported an average survival time of 8.5 months for lung cancer patients. They concluded that only 25% of patients survived more than one year (12). Grose et al reported an average survival time of 6.5 months and one-year survival rate of 30% for lung cancer patients (13). Santoro et al obtained an average survival time of 15.7 months. They estimated the average survival time of 14.9 and 22.1 months for smokers and nonsmokers with lung cancer, respectively (14). Since smoking is one of the most important risk factors for lung cancer, smokers are 20 times more likely to develop lung cancer than non-smokers. Smoking accounts for 71% of deaths occurring in lung cancer patients. Age, sex, stage of disease, tumor size, type of treatment, and the number of lymph nodes involved are other factors influencing the survival of lung cancer patients (15-18). Considering the high incidence of lung cancer and its poor prognosis in spite of advances in the treatment of the disease and since no study has been conducted to estimate the survival of patients with lung cancer in Hamadan, the present study aimed to evaluate the survival of patients with lung cancer and factors affecting the survival of these patients in Hamadan.

Materials and Methods

This retrospective cohort study was performed on 157 patients referred to Imam Khomeini specialized clinic in Hamedan. The present study was carried out on all patients diagnosed with cancer during 2003-2017. The study population included all patients with pathologic stage of lung cancer and those having relevant data. All demographic information including age at diagnosis, sex, occupation, and smoking status and paraclinical information including tumor type, tumor location, stage of disease, degree of differentiation, number of lymph nodes involved, metastasis (yes/no), site of metastasis, type of treatment, type of surgery, date of diagnosis, and the date of death of the patients were extracted to achieve the desired goals of the present study. The current study also investigated the survival of all lung cancer patients from diagnosis until death or end of the study. Patients' death data were collected from Death Registration Center, Deputy of Health of Hamadan Province and if no information was available, the latest information on their life status until March 2017 was obtained by contacting first-degree relatives of patients (phone number registered in the patient's case). Kaplan-Meier method was also used to determine the survival rate and log-rank method was used to compare the survival of different levels of variables. Data analysis was also carried out using SPSS version 23.0 and STATA version 14.0. $P < 0.05$ was considered statistically significant in all tests.

Results

A total of 157 patients with a definitive diagnosis of lung cancer referred to Imam Khomeini specialized clinic in Hamadan from 2003 to 2016. The mean age of the patients

was 61.84 years. Of the 157 patients with lung cancer, 135 (86%) were male and 22 (14%) were female. A total of 54 patients (34.4%) had a history of smoking. The frequency of SCLC and NSCLC was 37.3% and 62.7%, respectively, and SCSC was the most frequent tumor in the NSCLC group. The most common tumor sites included the upper lobe of right lung (22.2), right bronchus (16.6), and left bronchus (15.5%). A total of 82 patients (95.3%) had reached the metastatic stage. Chemotherapy has been the most commonly used treatment for patients. Moreover, a total of 54 patients (39.34%) had died by the end of follow-up. Other demographic and clinical characteristics of patients are listed in Table 1.

According to Kaplan-Meier survival diagram, the mean and median overall survival times of patients were 15 and 11 months, respectively (Figure 1).

The results of the log-rank test showed a significant difference between the survival of patients who had reached the metastatic stage (47 months) and those who had not reached metastasis (10 months). The result of the log-rank test also confirms this finding ($P = 0.001$). Therefore, there is a significant relationship between metastasis and the survival of lung cancer patients. The results of log-rank test showed that in addition to metastasis, site of metastasis was also effective in the survival rate (Table 2). Patients whose cancer has spread to the brain had a higher survival rate than patients who had metastases to the bone or liver ($P = 0.004$). Furthermore, the variables of age, type of treatment, stage of disease, and tumor location had no significant effect on the survival of patients with lung cancer ($P > 0.05$; Table 2).

Discussion

To date, there have been many studies on different aspects of lung cancer. In this study, the results of data analysis indicated that the variables of metastasis and site of metastasis significantly affected the survival of patients. The mean and median survival rates calculated in the present study are close to those obtained in studies by Julka et al, Crvenkova, and Chen et al (16, 19, 20). Some

Figure 1. Overall Survival of Patients with Lung Cancer.

Table 1. Demographic Characteristics and Tumor Status of Patients with Lung Cancer

Variable	Levels	Frequency
Gender (n=157)	Male	135
	Female	22
Age (n=157)	≤ 60 years	68
	>60 years	89
Smoking history (n=62)	Yes	54
	No	8
Tumor type (n=134)	SCLC	50
	Adenocarcinoma	30
	SCC	51
	Large cell carcinoma	3
Primary tumor location (n=90)	Right bronchus	15
	Left bronchus	14
	Right upper lobe	20
	Right middle lobe	3
	Right inferior lobe	12
	Left upper lobe	13
	Left inferior lobe	11
	Others	2
Metastasis (n=86)	Yes	82
	No	4
Metastatic site (n=81)	Liver	12
	Brain	16
	Bone	29
	Lymph nodes	2
	Liver and bone	3
	Brain and bone	2
	Others	1
	Unknown	16
Pathologic stage (n=82)	I	1
	II	2
	III	5
	IV	74
Type of treatment (n=157)	Chemotherapy	101
	Radiotherapy	8
	Chemotherapy and radiotherapy	33
	Chemotherapy and surgery	5
	All 3 types of treatment	3
	Unknown	7

studies reported lower survival rates than those estimated in the present study; for example, the mean and median survival time in the study by Abazari et al were calculated to be 13 and 4.8 months, respectively (1). In addition, the median survival rate estimated in the present study is lower than that of studies in other countries, including Germany and the United States, indicating that the survival of patients with lung cancer is lower in Iran

Table 2. Comparison of Survival Rates at the Levels of the Variables Considered in the Present Study

Variable	Category	Median Survival Time (mon)	Log-Rank Test
Sex	Male	13	0.963
	Female	11	
Age at diagnosis	≤ 60 years	14	0.226
	>60 years	11	
Tumor location	Right bronchus	11	0.572
	Left bronchus	12	
	Right upper lobe	10	
	Right middle lobe	11	
	Right inferior lobe	10	
	Left upper lobe	13	
Stage of disease	Left inferior lobe	14	0.061
	I, II, III	12	
	IV	9	
Metastasis	Yes	10	>0.001
	No	47	
Site of metastasis	Liver	9	0.004
	Brain	10	
	Bone	7	
	Others	6	
Chemotherapy	Yes	11	0.574
	No	14	
Radiotherapy and chemotherapy	Yes	12	0.994
	No	11	
Surgery	Yes	10	0.811
	No	12	

than in some parts of the world and is one of the most important reasons may be the late diagnosis of patients with lung cancer in Iran due to the lack of an appropriate screening program. For example, the median survival time of German SCLC patients has increased to 46 months because of timely diagnosis and treatment (21). Moreover, the median survival time of patients with lung cancer in the United States has also increased in recent decades, reaching from 12.4 months to 14.8 months, which can be attributed to the advances of treatment strategies such as radiotherapy and chemotherapy in this country (22, 23). The mean age at diagnosis in this study was 61.84 years, which is consistent with the results of many studies in Iran and other countries (1, 19, 24, 25). The results of the present study indicate that the presence of metastasis is an important and effective factor in the survival of patients with lung cancer, which indicates a decrease in survival rate in patients with metastasis cancer. Therefore, the median survival time of patients who did not reach the metastatic stage was significantly higher than those who reached metastases. This may be due to poor prognosis and lack of a proper response

to treatment strategies at this stage. Previous studies have also shown that metastasis is an effective variable in the survival of patients with lung cancer (1, 24, 26). Kasapoglu et al stated that the risk of death in metastatic lung cancer patients with pyloric involvement is twice higher compared to patients without metastasis (18). In addition, the results of the study by Abazari et al showed that the median survival of metastatic and non-metastatic patients were 5.8 and 12.2 months, respectively, and the risk of death in metastatic patients is 1.28 times higher compared to patients without metastases (1). The results of the present study also revealed that the site of metastasis is also one of the factors affecting the survival of lung cancer patients. The survival rate varies depending on the site of metastasis, and patients with brain metastasis have a higher median survival rate than other patients. These results are consistent with the results of a study by Babanejhad et al. They also emphasized the importance of the site of metastasis in the survival of patients and concluded that there was no significant difference between the survival of lung cancer patients with bone metastasis and those without metastases; however, the risk of death in lung cancer patients with brain metastases is 1.73 times higher compared to patients who did not reach the metastatic stage (24). The present study also showed no significant difference between the survival of patients undergoing different treatment strategies and those who did not receive any treatment. However, Zahair Taghipour & Mirtalebi (12) and Kasapoglu et al (18) reported that the type of treatment was an effective factor in the survival of patients, indicating that patients undergoing chemotherapy and radiotherapy or surgery and chemotherapy had a higher median survival rate than others. This may be due to the small number of lung cancer patients in this study considering that we accessed to medical information of a small number of lung cancer patients referred to the clinic of Imam Khomeini Hamadan. However, this issue should be addressed in studies with a larger sample size.

The results of many studies showed that variables of age at diagnosis and stage of the disease are important factors in the prognosis of patients. The survival rate decreases with an increase in the age at diagnosis and higher survival rate is expected in patients diagnosed at a younger age and are at an early stage (1, 12, 24). However, these variables had no significant effect on survival, which could be attributed to inaccurate recording of pathological and demographic data of the patients and lack of access to important variables. It was not possible to analyze the relationship between survival rate and smoking status, which is one of the important factors in the survival of lung cancer patients. Other limitations of the present study include incomplete medical records, changes in patients' phone numbers, and inaccessibility of some patients, and the poor co-operation of some relatives in providing patient information in some cases.

Conclusion

The results of the present study showed that the median survival of lung cancer patients is relatively low, and since metastasis is an important factor adversely affecting the survival of patients, it is essential to diagnose the disease as early as possible using an organized screening and periodic referral program, thereby increasing the life expectancy of patients by identifying those at risk and initiating treatment before the disease progression.

Conflict of Interest Disclosures

The authors declare that they have no conflict of interests.

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Ethical Statement

This article was taken from the research project approved by the Research Council of the University of Medical Sciences (9603161717) with a specific ID of the Ethics Committee (IR.UMSHA.REC.1396.206).

Authors' contributions

FG and GhR designed and performed the research. Data analysis, interpretation and manuscript preparation was performed by MA and ZB. All authors contributed to the final version of the manuscript and approved the final manuscript.

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Informed Consent

Not applicable.

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