Investigation of the affective factors on the survival rate of patients with laryngeal cancer using Cox proportional hazards and Lin-Ying’s additive hazards models

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Abstract

Background: Determining the factors affecting survival and appropriate treatment methods leads to improving the survival rate and quality of life in cancer patients; therefore this study was aimed to determine the effective factors on the survival rate of patients with Laryngeal cancer in Kerman city, Iran.

Methods: This retrospective cohort study included 370 patients with Laryngeal cancer who referred to the hospitals of Kerman city, Iran during 2008 to 2018. Data were analyzed using Cox Proportional Hazards and Lin-Ying’s Additive Hazards models. Data analysis was done using SAS software version 9.4. The P-value of less than 0.05 was considered as statistically significant.

Results: The mean age at the time of diagnosis was 58.16±10.60 years. About 92% of the patients were men. The patient’s 1, 3, 5, 7 and 10-years of overall survival rates were equal to 82.38%, 60.68%, 55.98%, 49.83%, and 30.91%, respectively. Age at the diagnosis (p=0.001), radiotherapy (p=0.001), chemotherapy (p=0.015), surgery (p=0.031), and smoking (p=0.001) were found to have significant effect on the patient’s survival rate in the Cox model. These variables were significant in the Lin-Ying model too.

Conclusion: Treatment is an important factor in controlling the disease and survival of cancer patients, and choosing the best treatment depends on the condition of the patient and the disease level.

Keywords: Survival analysis, Laryngeal cancer, Treatment, Hazard ratio, Excess risk

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Introduction

Cancer is the second prevalent cause of mortality in the developed countries and the third cause of death in developing countries. Regarding the increasing trend of cancer, the number of mortalities is expected to increase in future years (1). In 2018, about 18.1 million new cancer cases and 9.6 million deaths caused by cancer were reported from 185 countries (2). According to the report by the International Agency for Research on Cancer, 110115 new cases of cancer were estimated in Iran in 2018 (3). In 2012, about 84800 new cases of cancer were reported in Iran (4).
Affective factors on the survival rate of laryngeal cancer

Iran, that according to the predictions, it is estimated to reach about 129700 new cases of cancer in 2025 (4). Also, in 2014 about 2838 new cases of cancer were reported in Kerman province in Iran (5).

Head and neck cancers involve the area of the head or neck consisting of the sections such as the oral cavity, nose, pharynx, larynx, paranasal sinuses and nasal cavity, salivary glands, and thyroid. Laryngeal cancer is one of the most prevalent types of head and neck cancers (6). In 2018, approximate number of cancer patients was estimated for 36 types of cancer in 185 countries, the results of which accounted for approximately 177422 new cases and 94771 deaths caused by laryngeal cancer (2). Laryngeal cancer is more common in men and its prevalence is higher in middle-age patients (7). The choice of appropriate treatment depends on several factors, including disease stage, tumor size, tumor location and patient condition (physical and mental). Treatment of laryngeal cancer includes radiotherapy, chemotherapy, surgery or a combination of treatments (8). The goal of treatment is controlling disease and increasing the survival rate of cancer patients as well as preserving the quality of life of patients in short- and long-term. Many cancer survivors, even those who enjoy a free treatment, should adapt themselves to the long-term effects of treatment and mental concerns, like fear of recurrence (9). Those patients who should be treated by total laryngectomy for treatment of laryngeal cancer, unfortunately completely lose their voice and their quality of life decreases in different dimensions (10). Therefore, preserving the larynx is the most important concern for laryngeal cancer patients. As a result, radiotherapy and chemotherapy are considered the most important treatment methods (11). During the recent 20 years, huge advancements have occurred regarding the diagnosis and treatment of laryngeal cancer resulted in the improvement of the 5-year survival rate in patients (12). In this regard, the studies showed that the survival rate of patients with laryngeal cancer is influenced by factors such as place of the tumor, stage and grade of disease, treatment type and age. Some studies have been carried out in Iran related to the survival rate of patients with laryngeal cancer aimed at promoting and improving treatment methods and investigating effective factors on survival rate (10, 13). As a result, more research is needed to increase the survival rate and quality of life for patients. Survival analysis is a set of statistical methods in which the response variable is the time to reach the given event. This event may refer to death, disease, improvement and etc. (14). Statistical modeling for investigation of the effective factors on the survival rate of patients is one of the goals of the survival analysis. Cox Proportional Hazard model is one of the most used models in survival studies. The Lin-Ying Additive Hazards Model is a well-known model, used less in survival analysis (15). In contrary to the Cox model estimating the hazard ratio, Lin-Ying additive model estimates the hazard difference (16).

In recent years, the incidence rate of cancer types, including laryngeal cancer, has increased. Therefore, the study on the survival rate of laryngeal cancer would determine the lethality of this disease and the treatment methods causing a higher survival rate. In recent years, no study has been conducted on the survival rate of laryngeal cancer in Kerman city as the greatest city located in the south-eastern part of Iran. This study was designed to study the effective factors on the survival rate of patients with laryngeal cancer in Kerman city. Also, considering that the Cox proportional hazards model and the Lin-Ying additive hazards model investigate the special aspects of patients' survival, both models were used in the present study.

Methods

Study population

This retrospective cohort study was conducted in Kerman province, the largest southeastern city of Iran. Subjects included 370 patients diagnosed with laryngeal cancer who referred to hospitals in Kerman city from 2008 to 2018. Patients' information was collected from their medical records and by making a phone call with them. Patients were followed up until June 2018 and their latest status was recorded.

The study variables included age at the time of diagnosis, gender, education, job, family history of any cancer, consumption of opium, consumption of smoking, and treatment type. In this study, individual occupational risk-taking was defined based on the exposure to factors like asbestos, smoke, acid vapors, and dust. Occupations were divided into subgroups of riskless (like housewife, employee, and etc.), low-risk (animal husbandry, farmer, and etc.), risky (driver, worker, and etc.) and high-risk (mining and smelting factories staff, and etc.). Treatment of patients with laryngeal cancer was done by three ways including radiation therapy, chemotherapy, and surgery, or a combination of these methods.

Those who were alive until the end of the study (June 2018), were considered as the censored observations. The response variable was the period of time between the time of diagnosis of laryngeal cancer until death time or censor time, calculated based on the month. If the patient had died for any reason other than cancer, that patient was excluded from the study.

Ethical issues

The study protocol was approved by the Ethics Committee of Kerman University of Medical Sciences (Ethics code No: IR.KMU.REC.1397.202). The verbal consent was obtained by telephone from all participants, and the general objectives of the study and the potential re-used of the research data were told to the participants. We also confirmed that all methods were performed in accordance with the relevant guidelines and regulations.

Statistical analysis

In this study, the Kaplan-Meier method, Log-rank test, Cox proportional hazards, and Lin-Ying additive hazards models were used to analyze the data. In the Cox proportional hazards model, hazard ratio and a 95% confidence interval were reported, and in Lin-Ying additive hazards model, excess risk and a 95% confidence interval were reported.
The univariate analysis was conducted for each model first. Then the variables with a p-value less than 0.20 were entered as important variables into the multiple models, and the final model was obtained using the backward method. Data analysis was done using SAS software version 9.4. A p-value of less than 0.05 was considered as statistically significant.

**Results**

**Studied individual characteristics**

Out of 370 patients with laryngeal cancer, 142 patients (38.88%) died. The mean follow-up duration of patients was 35.94±31.15 months, and the range of duration was 119 months. The mean age at the diagnosis was equal to 58.16±10.60 years old, and its range was 57 years old. Most of the patients were male (91.08%). The number (percent) of alive patients, deaths and 1, 3 and 5-year survival rates of patients based on their characteristics are shown in Table 1.

![Figure 1](http://mjiri.iums.ac.ir)

**Table 1.** Characteristics of patients (n=370) diagnosed with laryngeal cancer and 1, 3, and 5-year overall survival rates, Kerman, Iran, 2007–2017

| Characteristic                  | Alive N (%) | Dead N (%) | Total n (%) | 1-Year OS (%) | 3-Year OS (%) | 5-Year OS (%) |
|--------------------------------|-------------|------------|-------------|---------------|---------------|---------------|
| Age (year)                     |             |            |             |               |               |               |
| ≤57                            | 135 (71.1)  | 55 (28.9)  | 190 (51.3)  | 88.02         | 67.93         | 65.20         |
| >57                            | 93 (51.7)   | 87 (48.3)  | 180 (48.7)  | 76.60         | 53.38         | 45.85         |
| Gender                         |             |            |             |               |               |               |
| Female                         | 16 (48.5)   | 17 (51.5)  | 33 (8.9)    | 69.44         | 47.87         | 47.87         |
| male                           | 212 (62.9)  | 125 (37.1) | 337 (91.1)  | 83.71         | 62.08         | 56.99         |
| Education level                |             |            |             |               |               |               |
| <High school                   | 144 (59.3)  | 99 (40.7)  | 243 (65.7)  | 81.37         | 58.93         | 53.66         |
| ≥High school                   | 84 (66.1)   | 43 (33.9)  | 127 (34.3)  | 84.28         | 63.97         | 60.69         |
| Job                            |             |            |             |               |               |               |
| No risk                        | 66 (55.0)   | 54 (45.0)  | 120 (32.4)  | 79.26         | 54.31         | 47.45         |
| Low risk                       | 72 (66.7)   | 36 (33.3)  | 108 (29.2)  | 88.19         | 63.08         | 63.08         |
| Risky                          | 63 (64.9)   | 34 (35.1)  | 97 (26.2)   | 77.80         | 60.53         | 60.53         |
| High risk                      | 27 (60.0)   | 18 (40.0)  | 45 (12.2)   | 86.49         | 60.52         | 53.51         |
| Family history of cancer       |             |            |             |               |               |               |
| No                             | 154 (61.8)  | 95 (38.2)  | 249 (67.3)  | 83.66         | 61.34         | 54.97         |
| Yes                            | 74 (61.2)   | 47 (38.8)  | 121 (32.7)  | 79.66         | 59.20         | 57.75         |
| Smoking status                 |             |            |             |               |               |               |
| No                             | 31 (52.5)   | 28 (47.5)  | 59 (16.0)   | 75.82         | 57.88         | 51.55         |
| Yes (only before diagnosis)    | 147 (69.7)  | 64 (30.3)  | 211 (57.0)  | 88.92         | 69.40         | 64.79         |
| Yes (before and after diagnosis)| 50 (50.0)   | 50 (50.0)  | 100 (27.0)  | 72.93         | 44.60         | 40.42         |
| Opium abuse                    |             |            |             |               |               |               |
| No                             | 63 (56.3)   | 49 (43.7)  | 112 (30.3)  | 82.67         | 59.18         | 53.80         |
| Yes (only before diagnosis)    | 127 (66.8)  | 63 (33.2)  | 190 (51.3)  | 86.44         | 64.45         | 61.00         |
| Yes (before and after diagnosis)| 38 (55.9)   | 30 (44.1)  | 68 (18.4)   | 71.07         | 52.82         | 46.19         |
| Radiotherapy                   |             |            |             |               |               |               |
| No                             | 20 (38.5)   | 32 (61.5)  | 52 (14.1)   | 64.87         | 41.40         | 38.73         |
| Yes                            | 208 (65.4)  | 110 (34.6) | 318 (85.9)  | 85.23         | 63.89         | 58.87         |
| Chemotherapy                   |             |            |             |               |               |               |
| No                             | 81 (71.7)   | 32 (28.3)  | 113 (30.5)  | 84.05         | 73.57         | 67.94         |
| Yes                            | 147 (57.2)  | 110 (42.8) | 257 (69.5)  | 81.63         | 55.33         | 51.03         |
| Surgery                        |             |            |             |               |               |               |
| No                             | 108 (55.7)  | 86 (44.3)  | 194 (52.4)  | 74.38         | 55.04         | 49.96         |
| Yes                            | 120 (68.2)  | 56 (31.8)  | 176 (47.6)  | 91.15         | 66.74         | 62.38         |

OS Overall Survival; (%) Row Percentage; (%) Column Percentage

![Figure 1](http://mjiri.iums.ac.ir)

**Fig. 1.** Overall survival rate among patients diagnosed with laryngeal cancer, Kerman 2008–2018
Affective factors on the survival rate of laryngeal cancer

Survival rates of patients were 82.38, 60.68, 55.98, 49.83 and 30.91%, respectively.

The results of the comparison of survival rates in subgroups of variables using the log-rank test showed that age (p=0.001), radiotherapy (p=0.001), chemotherapy (p=0.015), surgery (p=0.005) and smoking (p=0.001) had significant relationships with the survival rate of the patients, and gender (p=0.076), education level (p=0.187), family history of cancer (p=0.761), job (p=0.259) and consumption of opium (p=0.090) had no significant relationship with the survival rate of patients.

The number (percent) of alive patients, deaths, and 1, 3, and 5-year survival rates of patients based on the treatment type and combination of treatments are shown in Table 2. The highest 5-year survival rate was related to the combined method of treatment including the surgery and radiotherapy (91.74%), and the lowest 5-year survival rate was related to the combined method of treatment including the surgery and chemotherapy (31.17%).

Cox proportional hazards model

Table 3 shows the results of the Cox proportional hazards model in which age, smoking, radiotherapy, chemotherapy, and surgery were effective on the survival of patients. The results of the multiple analysis showed that the hazard of death in patients aged over 57 years was 1.90 times more than those aged under 57 years (HR=1.90, 95% CI [1.34, 2.67], p<0.001). The hazard of death in patients who had a history of smoking before and after diagnosis of the disease was 1.91 times more than patients who smoked before the diagnosis of the disease (HR=1.91, 95% CI [1.29, 2.81], p=0.001). The hazard of death in patients with no history of smoking was 0.70 times less than patients who had a history of smoking before and after diagnosis of the disease (HR=0.70, 95% CI [0.44, 1.12], p=0.141). The hazard of death in patients with no history of smoking was 1.33 times more than patients who smoked before the diagnosis of the disease (HR=1.33, 95% CI [0.84, 2.13], p=0.225). The hazard of death in patients who did not receive radiotherapy was 0.50 times less than patients who did not receive radiotherapy (HR=0.50, 95% CI [0.33, 0.75], p<0.001). The hazard of death in patients who did not receive chemotherapy was 1.67 times more than patients who did not receive chemotherapy (HR=1.67, 95% CI [1.10, 2.52], p=0.020). The hazard of death in patients who underwent surgery was 0.68 times less than patients who did not undergo surgery (HR=0.68, 95% CI [0.47, 0.96], p=0.031). Gender, education level, job, family history of cancer and consumption of opium had no significant effect on the survival rate of patients (p>0.05).

Table 2. Characteristics of treatment type and 1, 3, and 5-year overall survival rates

| Treatment type | Alive n (%) | Dead n (%) | Total n (%) | 1-Year OS (%) | 3-Year OS (%) | 5-Year OS (%) |
|----------------|-------------|------------|-------------|--------------|--------------|--------------|
| without treatment | 5(55.6) | 4(44.4) | 9(2.4) | 64.81 | 51.85 | 51.85 |
| S | 9(69.2) | 4(30.8) | 13(3.5) | 91.67 | 82.50 | 66.00 |
| RT | 20(64.5) | 11(35.5) | 31(8.4) | 74.15 | 65.65 | 58.36 |
| CH | 3(17.6) | 14(82.4) | 17(4.6) | 41.18 | 29.41 | 29.41 |
| S+RT | 47(78.3) | 13(21.7) | 60(16.2) | 89.74 | 78.48 | 74.91 |
| S+CH | 3(23.1) | 10(76.9) | 13(3.5) | 69.23 | 17.31 | 17.31 |
| RT+CH | 81(58.7) | 57(41.3) | 138(37.3) | 79.22 | 55.90 | 49.84 |
| S+RT+CH | 60(67.4) | 29(32.6) | 89(24.1) | 95.32 | 65.91 | 61.97 |

S: Surgery; RT: Radiotherapy; CH: Chemotherapy; CRT: Chemoradiotherapy; OS: Overall Survival; (%)a: Row Percentage; (%)b: Column Percentage

Table 3. The relationship between the study variables and laryngeal cancer using univariate and Multiple Cox Proportional Hazards Model

| Variable | Univariate | Multiple |
|----------|------------|----------|
| Age (year, reference=age≤57) >57 | 1.90 (1.35, 2.67) | P<0.001 | 1.90 (1.35, 2.68) | P<0.001 |
| Gender (reference=female) Male | 0.63 (0.38, 1.05) | 0.079 | -- | -- | NS |
| Education level (reference=less than high school) ≥High school | 0.79 (0.55, 1.12) | 0.189 | -- | -- | NS |
| Job (reference= no risk) Low risk | 0.65 (0.43, 1.00) | 0.049 | -- | -- | NS |
| Risky | 0.80 (0.52, 1.23) | 0.306 | -- | -- | -- |
| High risk | 0.80 (0.47, 1.36) | 0.412 | -- | -- | -- |
| Family history of cancer (reference=no) Yes | 1.06 (0.74, 1.50) | 0.761 | -- | -- | NS |
| Smoking status (reference=no) Yes only Before diagnosis | 0.59 (0.38, 0.92) | 0.021 | 0.75 | (0.47, 1.19) | 0.225 |
| Yes (Before and after diagnosis) | 1.24 (0.78, 1.97) | 0.363 | 1.43 | (0.89, 2.30) | 0.141 |
| Opium abuse (reference=no) Yes only Before diagnosis | 0.81 (0.56, 1.18) | 0.276 | -- | -- | NS |
| Yes (Before and after diagnosis) | 1.31 (0.83, 2.07) | 0.244 | -- | -- | -- |
| Radiotherapy (reference=no) Yes | 0.45 (0.30, 0.67) | P=0.001 | 0.50 | (0.33, 0.75) | P=0.001 |
| Chemotherapy (reference=no) Yes | 1.62 (1.09, 2.41) | 0.016 | 1.67 | (1.10, 2.52) | 0.015 |
| Surgery (reference=no) Yes | 0.62 (0.44, 0.87) | 0.006 | 0.68 | (0.47, 0.96) | 0.031 |

HR: Hazard Ratio; CI: confidence interval; NS: not significant

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Lin-Ying additive hazards model

Table 4 illustrates the results of the Lin-Ying additive hazards model. The results revealed that age, smoking, radiotherapy, chemotherapy, and surgery were effective on the survival rate of patients. The patients aged over 57 years old showed a 0.007 increase in death hazard compared to patients aged under 57 years old (ER = 0.007, 95% CI [0.003, 0.011], p < 0.001). The patients who had a history of smoking before and after the diagnosis were shown to have a 0.008 increase in death hazard compared to patients who had a history of smoking before the diagnosis of the disease (ER = 0.008, 95% CI [0.002, 0.013], p = 0.003). The patients with no history of smoking showed a 0.005 decrease in death hazard compared to patients who had a history of smoking before and after diagnosis of the disease (ER = -0.005, 95% CI [-0.012, 0.002], p = 0.18). The patients with no history of smoking showed a 0.003 increase in death hazard compared to patients who had a history of smoking before the diagnosis of the disease (ER = 0.003, 95% CI [-0.003, 0.008], p = 0.307). The patients received radiotherapy showed a 0.009 decrease in death hazard compared to patients who did not receive radiotherapy (ER = -0.009, 95% CI [-0.017, -0.002], p = 0.011). The patients received chemotherapy showed a 0.005 increase in death hazard compared to patients who did not receive chemotherapy (ER = 0.005, 95% CI [0.001, 0.009], p = 0.012). The patients who underwent surgery showed a 0.004 decrease in death hazard compared to patients who did not undergo surgery (ER = -0.004, 95% CI [-0.008, -0.001], p = 0.021). Gender, education level, job, family history of cancer, and consumption of opium had no significant effect on the survival rate of patients (p > 0.05).

Discussion

This study investigated the effective factors on the survival rate of patients with laryngeal cancer using Cox proportional hazards and Lin-Ying additive hazards models.

In this study, the mean age at the diagnosis of patients with laryngeal cancer was equal to 58.2 years old. The results of other studies conducted in Iran showed the mean age at the diagnosis was 61.1 and 60.8 years old (1, 17). The results of a study carried out in the US showed that the mean age at the diagnosis was 57.2 years old (18). Therefore, it can be said that the prevalence of laryngeal cancer is high in higher ages, and it may occur due to the long-term effect of factors influencing this cancer, like the consumption of tobaccos.

In this study, most of the patients were men. In other studies conducted in Iran, such as studies by Jafari et al. and Daneshi et al. 92.1% and 95.9% of patients were male, respectively (1, 10). Also, about 90% of patients were male in studies conducted out of Iran (19, 20). The reason for the higher occurrence of laryngeal cancer in men is that men are probably more exposed to risk factors of laryngeal cancer. Men usually use more tobaccos, and high-risk jobs causing laryngeal cancer are done more by men, so more studies are required to study on the cause of the high prevalence of laryngeal cancer in men than women.

In this study, the mean survival time for patients with laryngeal cancer was equal to 70.6 months and the mean 5-year survival rate of patients was equal to 55.9%. In another study carried out in Iran (1), the mean 5-year survival rate of patients was found to be 57.7% which is consistent with the results of the present study. This is while in the studies conducted outside of Iran, the 5-year survi-

Table 4. The relationship between the study variables and laryngeal cancer using univariate and Multiple Lin -Ying’s Additive Hazards Model

| Variable                                           | Univariate          | Multiple            |
|----------------------------------------------------|---------------------|---------------------|
|                                                   | ER                  | 95% CI             | p       | ER       | 95% CI | p     |
| Age(year, reference= age≤57)                       |                     |                     |         |          |        |       |
| >57                                                | 0.007               | (0.003, 0.011)     | p=0.001 | 0.007    | (0.003, 0.011) | p=0.001 |
| Gender (reference=female)                          |                     |                     |         |          |        |       |
| male                                               | -0.006              | (-0.014, -0.002)   | 0.141   | -        | -      | NS    |
| Education level (reference= less than high school) |                     |                     |         |          |        |       |
| ≥High school                                       | -0.002              | (-0.006, -0.001)   | 0.172   | -        | -      | NS    |
| Job (reference= no risk)                           |                     |                     |         |          |        |       |
| Low risk                                           | -0.004              | (-0.009, -0.000)   | 0.047   | -        | -      | NS    |
| Risky                                              | -0.003              | (-0.008, -0.002)   | 0.287   | -        | -      | -     |
| High risk                                          | -0.003              | (-0.009, -0.003)   | 0.375   | -        | -      | -     |
| Family history of cancer                           |                     |                     |         |          |        |       |
| (reference= no)                                     | 0.0005              | (-0.003, 0.004)    | 0.763   | -        | -      | NS    |
| Smoking status (reference= no)                      |                     |                     |         |          |        |       |
| Yes (Only Before diagnosis)                        | -0.005              | (-0.011, -0.000)   | 0.047   | -0.003   | (-0.008, 0.003) | 0.307 |
| Yes (Before and after diagnosis)                   | 0.003               | (-0.003, 0.010)    | 0.335   | 0.005    | (-0.002, 0.012) | 0.180 |
| Opiuming status (reference= no)                    |                     |                     |         |          |        |       |
| Yes (only Before diagnosis)                        | -0.002              | (-0.0058, -0.002)  | 0.278   | -        | -      | NS    |
| Yes (Before and after diagnosis)                   | 0.004               | (-0.002, 0.010)    | 0.245   | -        | -      | -     |
| Radiotherapy (reference= no)                       |                     |                     |         |          |        |       |
| Yes                                                | -0.011              | (-0.018, -0.004)   | 0.002   | -0.009   | (-0.017, -0.002) | 0.011 |
| Chemotherapy (reference= no)                       |                     |                     |         |          |        |       |
| Yes                                                | 0.005               | (0.001, 0.008)     | 0.008   | 0.005    | (0.001, 0.009) | 0.012 |
| Surgery (reference= no)                            |                     |                     |         |          |        |       |
| Yes                                                | -0.005              | (-0.008, -0.001)   | 0.005   | -0.004   | (-0.008, -0.001) | 0.021 |
Affective factors on the survival rate of laryngeal cancer

The survival rate; more likely, the patients who received chemotherapy had more advanced/aggressive disease. More studies are needed in this area to find the exact reason.

The results show that the combination of surgery and radiotherapy has the highest survival, which the disease level of these patients should be taken into account. Radiation therapy can only be an appropriate treatment but cannot guarantee the preservation of larynx performance. The results of this study show that the combination of radiation therapy with other treatments can lower the risk of death, so radiation therapy can be considered as a fixed base in the combination therapies. Overall, treatment is one of the most important factors affecting the survival of patients and more studies are needed to cover all the aspects of this field.

Results show smoking was effective on the survival of patients with laryngeal cancer. Patients who smoked prior to diagnosis were more likely to get cancer due to smoking, and cessation of smoking after diagnosis improved these patient’s survival rates, which may be a reason for the higher survival rate of these patients in comparison to the other patients. Those patients who continued smoking after the diagnosis of cancer showed lower survival than the patients who stopped smoking after the diagnosis of the disease. Therefore, according to the results of this study, it is recommended for smokers to stop smoking to increase their survival rate. In other studies, smoking was not found to affect survival, which may be due to the different grouping of cigarette smoking in this study with other studies (28, 31, 32).

The positive and strong point of this study included that; it investigated the death hazard of patients from two viewpoints. Cox proportional hazards model reports the death hazard ratio and the Lin-Ying additive hazards model reports the death excess risk in relation to the independent variables. Each of these models covers different aspects of data.

**Study Limitations**

Unfortunately, information about stage, grade, and tumor size was not accurately recorded for most patients. Consequently, these factors were not mentioned in the study.

**Conclusion**

Two models of Cox proportional hazard and Ling-Ying additive hazard are different in some aspects; therefore, the use of these two models covers the different aspects of data. In both models, age, smoking, and type of treatment had a significant effect on the survival of patients. High age would lead to a reduction in the survival rate as well as an increase in the death risk. Therefore, older patients need more care. Smoking after the diagnosis of cancer is not recommended because smoking was found to increase the risk of death. Treatment is an important factor in controlling the disease and survival of cancer patients, and choosing the best treatment depends on the condition of the patient and the disease level. As a result, further researches are needed to improve the quality of life and life expectancy of patients by choosing the most proper treat-
ment methods.

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Conflict of Interests
The authors declare that they have no competing interests.

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