

RESEARCH ARTICLE

Survival Rate and Prognostic Factors of Esophageal Cancer in East Azerbaijan Province, North-west of Iran

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Abstract

Background: Esophageal cancer in Iran is the sixth most common cancer and is particularly important in east Azerbaijan. The aim of this study was to calculate survival rates and define prognostic factors in esophageal cancer patients. **Methods:** In this study, all patients with esophageal cancer registered in the Radiation Therapy Center, during March 2006 to March 2011, were analyzed and followed up for vital status. Data were analyzed using the Kaplan-Meier method and the Cox proportional hazard models. **Results:** Out of 532 patients, survival information was available for 460, including 205 (44/ 5%) females and 255 (55/4%) males. The mean age was 65.8±12.2, ranging from 29 to 90 years at the time of diagnosis. 1-, 3- and 5-year survival rates after diagnosis were 55%, 18% and 12%, respectively, with a median survival time of 13.2 ± .7 (CI 95% =11.8 -14.6) months. In the univariate analysis, age (P=0/001), education (P=0/001), smoking status (P= 0/001), surgery (P= 0/001), tumor differentiation (P= 0/003) and tumor stage (P= 0/001) were significant prognostic factors. Tumor morphology, sex, place of residence, tumor histology and tumor location did not show any significant effects on the survival rate. In multivariate analysis, age (P = 0/003), smoking (P= 0/01) and tumor stage (P= 0/001) were significant independent predictors of survival. **Conclusion:** In summary, prognosis of esophageal cancer in North West of Iran is poor. Therefore, reduction in exposure to risk factors and early detection should be emphasized to improve survival.

Keywords: Esophageal cancer - survival - prognosis - Kaplan-Meier - Cox proportional hazard model - Iran

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Introduction

Esophageal cancer is the eighth most common cancer and the sixth leading cause of cancer mortality in the worldwide (Bashash et al., 2011). The north of Iran (lies in the central Asian belt) have been observed to dominate malignancies of esophageal cancer. The five-year survival is usually 13 percent (Ghadimi et al., 2011). East Azerbaijan is located in the north western Iran neighbor provinces around Caspian Sea. The esophageal cancer is one of the five most common cancers in East Azerbaijan, being the 3th most common cancer in females and the 4th most common in males (Somi et al., 2008). There have not been any studies in this region on the survival statistics and prognostic factors of esophageal cancers. Esophageal cancer is one of the rapidly progressing tumors with a dismal prognosis (Hajian., 2001). The Survival of esophageal cancer is mainly determined by age, the stage of cancer at presentation and type of treatment (Aghchel et al., 2011). The aim of this study was to calculate the survival rates and analyze the factors affecting the patients' prognosis in esophageal cancer.

Materials and Methods

In this retrospective review, was evaluated the survival of five years esophageal cancer patients(460) treated with CRT at the Imam Reza (AS) Radiation Therapy Center Hospital , of Tabriz university of medical sciences; between during March, 2006 to March, 2011. Clinicopathological variables and survival times were collected by telephone contact and patient's medical records. The pathology report after endoscopy was used for the diagnosis date. All patient deaths during this period were considered as a result of the esophageal cancer. Survival time was calculated in months. The socio-demographic, pathology and clinical data were obtained using questionnaire and the patients' clinical records. The factors we considered in our study were age at diagnosis, gender, place of residence, education, cigarette smoking, tumor location, surgery, histology of tumor, tumor differentiation, and tumor stage. Information on 72 patients was missing due to inaccessible telephone number, telephone number change, or immigration. The planned staging procedure was as following: surgical

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Table 1. Univariate Analysis of Prognostic Factors in Patients with Esophageal Cancer Under Study

Variable	Variable subgroups	Median survival time (Month)		Survival rate(%)			P-value
		Number(%)		1years	3years	5years (Log-rank test)	
Age group	<65	186(40.4)	16	64	28	19	0/001
	≥65	274(59.6)	11.4	49	11	7	
Gender	Female	205 (44.5)	12.33	51	20	14	0/79
	Male	255 (55.4)	13.9	58	16	10	
place of residence	rural	220 (47.8)	13	53	12	16	0/07
	urban	240 (52.2)	13.57	56	23	16	
Education	illiterate	265 (57.6)	13.2	54	24	21	0/001
	literate	76(16.5)	17.7	68	33	25	
	unknown	119 (25.9)	12	-	-	0	
Cigarette smoker	No	240 (52.2)	13.83	56	28	21	0/001
	Yes	105 (22.8)	14.47	61	21	21	
	unknown	25)) 115	-	-	-	0	
Tumor location	Upper thoracic	61 (13.3)	11.1	48	17	11	0/31
	Middle thoracic	160 (34.8)	14.8	63	21	15	
	Lower thoracic	214 (46.5)	12.2	52	15	8	
	Overlapping	18 (3.9)	10.63	47	22	22	
	unknown	7 (1.5)	0	-	-	-	
Surgery	Yes	85(18.5)	24.6	76	31	31	0/001
	No	319(69.3)	11.3	48	15	7	
	unknown	56 (12.2)	13.83	-	-	0	
Tumor Histology	SCC	434 (94.3)	13.2	54	19	12	0/51
	Adeno carcinoma	26 (5.7)	13.47	61	6	0	
Tumor Differentiation	well	201 (43.7)	15.5	60	24	17	0/003
	Moderate	76 (16.5)	12.3	52	13	13	
	poor	15 (3.3)	15.17	63	25	0	
	unknown	168 (36.5)	-	-	-	-	
Tumor stage	II	56 (12.2)	24.77	78	31	27	0/001
	III	56 (12.2)	20.6	72	27	27	
	IV	59 (12.8)	8.7	40	10	0	
	unknown	289 (62.8)	-	-	-	-	

Table 2. The Cox Regression Model - Predictor Factors with 95% Confidence Intervals

Parameter	B	Hazard ratio		P-value	
		CI 95.0% Lower	Upper		
Age group	0.37	1.45	1.13	1.86	0.003
Education	0.15	1.16	0.93	1.45	0.19
Smoker	0.29	1.34	1.07	1.69	0.01
Surgery	0.14	1.14	0.92	1.43	0.23
Tumordiff	0.06	1.06	1	1.13	0.05
Tumor stag	0.3	1.35	1.18	1.54	0.001

pathology reports and abdominal computed tomography (CT) scan (spiral high speed). In our centre, radiotherapy was delivered using a linear accelerator (anteroposterior) with a 9-MV photon beam. In general, patients received 1.8 Gy/day for 5 days per week, to a total radiation dose of 45 Gy. The chemotherapy regimen consists of 5-FU plus cisplatin (5-FU 1000mg/m² on days 1–4, every 3 weeks in tow course, cisplatin 100mg/m² on day 1). Patients with a stage IV of the disease only received a radiation therapy (30 Gy dose in 10 sessions) as a palliative treatment. Descriptive analysis was done for demographic, pathology and clinical features. Results were expressed as means ± standard deviation and percentage. The probability curves for survival were calculated according to the Kaplan–Meier Method and compared by the log-rank test. Multivariate analysis was carried out using the Cox proportional hazard model. P < 0.05 was considered as statistically significant. The data were analyzed using by SPSS.v.13 software.

Results

Out of 532 patients, survival information was available for 460 patients, including 205 (44/5%) Female and 255 (55/4%) males. The mean age was 65.8±12.2, ranging from 29 to 90 years at the time of diagnosis. Of these, at five years 148 (32.2%) were alive and 312 (67.8%) were dead after five years.

Survival and Univariate Analysis

Kaplan-Meier method showed that 1, 2, 3, 4-and 5-year survival rates after diagnosis were 55%, 26%, 18%, 13% and 12%, respectively. The Median survival time in patients 13.2 ± .7 (CI 95% =11.8 -14.6) months. Six prognostic factors were identified as significant by univariate analysis with the log-rank test p value : Age group (P = 0/001), education (P = 0/001), smoker (P = 0/001), surgery (P = 0/001), tumor differentiation (P = 0/003) and tumor stage (P = 0/001). univariate analysis revealed that sex (P = 0/79), place of residence (P = 0/07), tumor histology (P = 0/51) and tumor location (P = 0/31) were not significantly associated with survival. Table 1 summarized some other findings of the present study.

Chart 1- Kaplan - Meier shows the overall survival curves of esophageal cancer patients declining with time.

Results of Multivariate Analyses

Multivariate analysis of survival rates were performed according to the Cox proportional hazards model using six prognostic factors (Age group, education, smoker,

Table 3. Comparison of the Survival Rates from North of Iran, the Current Study and Reports from Developed Countries

References	Survival year %			
		1	3	5
Samadi et al., 2007	north western Iran/Ardabil	40.5	6.3	0.83
Aghcheli et al., 2011	northern Iran/ Golestan/	-	-	3.3
Taziki et al., 2011	northern Iran/ Gorgan	-	-	12.8
Hajian., 2001	northern Iran/ Babolsar	42	11	8
Ghadimi et al., 2011	northern Iran/ Babol	23	15	13
Current study	north western Iran/Tabriz	55	18	12
Zafirellis et al., 2002	UK	72	41	29
Christian et al., 2007	Netherlands	89	60	42

surgery, tumor differentiation and tumor stage) (Table 2). The Cox regression analysis, Age group ($P = 0/003$), smoker ($P = 0/01$) and tumor stage ($P = 0/001$) were significant predictors of survival. In the multivariate analysis education ($P = 0/19$), tumor differentiation ($P = 0/05$) and Surgery ($P = 0/23$) were not as predictor factors (Table 3).

Discussion

This study estimated the survival rate of patients with esophageal cancer for the first time from the East Azerbaijan -northwest region of Iran. The one, three and the five year survival rates in this study were 55%, 18% and 12% respectively which are superior than many other studies from northern Iran (Hajian, 2001; Samadi et al., 2007) but lower than developed countries. (Zafirellis et al., 2002; Courrech Staal et al., 2009). This may be explained by the fact that Iranian patients generally seek a medical advice with a delay and the diagnosis is made when the disease has reached an advanced stage (Ghadimi et al., 2011).

The median survival was 13 months in the current study whereas the rate is less than 10 months in northern Iran (Samadi et al., 2007; Aghcheli et al., 2011; Ghadimi et al., 2011) and over 20 months in high income countries (Zafirellis et al., 2002; Cescon et al., 2007). This is reflected in the 1 and 3 year survival rates as well. Survival of esophageal cancer is influenced by several factors. Age of patients was one of the Predictive factors in the current study and was inversely associated with the survival rate, as in several studies (Hajian, 2001; Alidina et al., 2004; Shitara et al., 2010; Aghcheli et al., 2011; Ghadimi et al., 2011). The other factor was cigarette smoking which inversely predicted the survival. This is consistent with several studies (Sundelof et al., 2008; Cescon et al., 2009; Shitara et al., 2010). Female patients had a tendency to a better survival rate during time, but this difference did not reach the significance. This data is inconsistent in different reports. Some are consistent with the current study (Zafirellis et al., 2002; Taziki et al., 2011) while several studies report a significantly better survival rates for females (Bashash et al., 2008; Aghcheli et al., 2011; Gaur et al., 2011; Ghadimi et al., 2011). The radiotherapy center located in northern of Iran is almost new (Aghajanzadeh et al., 2009) and this may influence the outcome to some

extent as urban patients might have difficulties reaching its service, so The survival rate of patients in urban areas is reported to be higher in northern of Iran (Aghcheli et al., 2011; Ghadimi et al., 2011). This was not observed in the current study. These ecological data demonstrate that the use of diagnostic and treatment services among men living in rural areas is equal to their urban counterparts, so their survival rate is the same. Their socioeconomic level may be responsible as well. Education information was recorded for 74% of the sample for this study. A low proportion was literate but we observed a significant positive association between education and survival. These findings are aligned with the results of many studies in this field (Katrin F et al., 2005; Hussain et al., 2008; Ghadimi et al., 2011). Considering that almost 60% of this sample were older than 65, this result may change in further years. The new generation may differ in terms of educational level and life style and the results may get closer to developed countries. The characteristics of the tumor were evaluated as well. The slightly had better survival of squamous cell carcinoma type did not reach the significance which is consistent with previous studies (Hajian, 2001). Tumor stage is the most important prognostic factor for any type of cancer as the planning for optimal treatment is mainly decided accordingly (Nomura et al., 2012). The results of the current study showed that the five year survival rate of our study sample was lower in stages II and IV compared to Netherlands, China and Japan (Christian et al., 2007; Shitara et al., 2010; Nomura et al., 2012) while the rate was higher in stage III compared to Netherlands, China and Germany (Rades et al., 2006; Christian et al., 2007; Shitara et al., 2010). In Conclusion, prognosis of esophageal cancer in North West of Iran is poor, Therefore, reduce the exposure to risk factors and early detection can improve survival in such patients.

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References

- Aghcheli K, Haji-min Marjani A, Nasrollahzadeh D, et al (2011). Prognostic factors for esophageal squamous cell carcinoma-a population-based study in Golestan province, Iran, a High Incidence Area. *PLoS ONE*, **6**, 1-7.
- Aghajanzadeh M, Rahimi A, Partovian M, Gotalizadeh D, Moghaddamnia M (2009). The survival of patients with esophageal cancer after chemoradiation versus surgery and chemoradiation. *J Guilan Univers Med Sci*, **71**, 13-8
- Alidina A, Gaffar A, Hussain F, et al (2004). Survival data and prognostic factors seen in Pakistani patients with esophageal cancer. *Ann Oncol*, **15**, 118-22.
- Bashash M, Hislop TG, Shah AM, et al (2011). The prognostic effect of ethnicity for gastric and esophageal cancer: the

- population-based experience in British Columbia, Canada. *BMC Cancer*, **11**, 164.
- Bashash M, Shah A, Hislop G, et al (2008). Incidence and survival for gastric and esophageal cancer diagnosed in British Columbia, 1990 to 1999. *Can J Gastroenterol*, **22**, 143-8.
- Courrech Staal EF, van Coevorden F, Cats A, et al (2009). Outcome of low-volume surgery for esophageal cancer in a high-volume referral centre. *Ann Surg Oncol*, **16**, 3219-26.
- Gaur P, Sepesi B, Hofstetter WL, et al (2010). Endoscopic esophageal tumor length: a prognostic factor for patients with esophageal cancer. *Cancer*, **117**, 63-9.
- Ghadimi M, Rasouli M, Mahmoodi M, Mohammad K (2011). Prognostic factors for the survival of patients with esophageal cancer in Northern Iran. *J Res Med Sci*, **16**, 1261-72.
- Hajian-Tilaki KO (2001). Factors affecting the survival of patients with esophageal carcinoma under radiotherapy in the north of Iran. *Br J Cancer*, **85**, 1671-4.
- Hussain SK, Lenner P, Sundquist J, Hemminki K (2008). Influence of education level on cancer survival in Sweden. *Annals of Oncology*, **19**, 156-62.
- Nomura M, Shitara K, Kodaira T, et al (2012). Prognostic impact of the 6th and 7th American joint committee on cancer tm staging systems on esophageal cancer patients treated with chemoradiotherapy. *Int J Radiation Oncol Biol Phys*, **82**, 946-52.
- Rades D, Lang S, Schild SE, Alberti W (2006). Prognostic value of haemoglobin levels during concurrent radio-chemotherapy in the treatment of oesophageal cancer. *Clin Oncol*, **18**, 139-44.
- Samadi F, Babaei M, Yazdanbod A, et al (2007). Survival rate of gastric and esophageal cancers in Ardabil province, North-West of Iran. *Arch Iran Med*, **10**, 32-7.
- Shitara K, Matsuo K, Hatoooka S, et al (2010). Heavy smoking history interacts with chemoradiotherapy for esophageal cancer prognosis: a retrospective study. *Cancer Sci*, **101**, 1001-6.
- Somi M H, Farhang S, Mirinezhad S K, et al (2008). Cancer in East Azerbaijan, Iran: Results of a Population-based Cancer Registry. *Asian Pac J Cancer Prev*, **9**, 327-30.
- Sundelof M, Lagergren J, Ye W (2008). Patient demographics and lifestyle factors influencing long-term survival of esophageal cancer and gastric cardiac cancer in a nationwide study in Sweden. *Eur J Cancer*, **44**, 1566-71.
- Taziki M, Rajaei S, Behnampour N, Tadrisee M, Mansourian AR (2011). Esophageal cancer: 5-year survival rate at south-east of Caspian sea of northern Iran. *J Cancer Res Ther*, **7**, 135-7.
- Verhoef C, van de Weyer R, Schaapveld M, Bastiaannet E, Plukker JT (2007). Better survival in patients with esophageal cancer after surgical treatment in university hospitals: a plea for performance by surgical oncologists. *Ann Surg Oncol*, **14**, 1678-87.
- Zafirellis K, Dolan K, Fountoulakis A, et al (2002). Multivariate analysis of clinical, operative and pathologic features of esophageal cancer: who needs adjuvant therapy? *Dis Esophagus*, **15**, 155-9.