Available online at www.sciencedirect.com

ScienceDirect

EJSO 40 (2014) 352–357

EJSO the Journal of Cancer Surgery

www.ejso.com

Esophageal cancer in Iran; a population-based study regarding adequacy of cancer surgery and overall survival

I. Harirchi [a,*], S. Kolahdoozan [b], S. Hajizadeh [a], F. Safari [a], Z. Sedighi [a], A. Nahvijou [a], M.-R. Mir [a], S.-M. Mousavi [a,c], K. Zendehdel [a,d]

[a] *Cancer Research Center, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran*
[b] *Digestive Oncology Research Center, Digestive Diseases Research Institute, Tehran University of Medical Sciences, Tehran, Iran*
[c] *German Division of Molecular Genetic Epidemiology, German Cancer Research Center (DKFZ), Heidelberg, Germany*
[d] *Department of Medical Epidemiology& Biostatistics, Karolinska Institute, Stockholm, Sweden*

Accepted 16 October 2013
Available online 23 October 2013

Abstract

Aims: Prognosis of esophageal cancer (EC) is poor. Population-based studies regarding EC survival and adequacy of cancer surgery (ACS) from developing countries are lacking. We aimed to evaluate EC patients' survival and ACS in a population-based setting for the first time from Iran.

Methods: We randomly selected 409 cases from all 3048 newly diagnosed EC patients who were registered in the nationwide cancer registry in calendar year 2005–2006 and followed them until 2009. An expert panel in Cancer Institute of Iran reviewed adequacy of esophageal cancer surgery on a national basis.

Results: Overall three-year survival rate was 17%. The median (95% CI) survival time of all patients and cases who underwent surgery alone were 8.5 (6.9–10.1) and 6.0 (3.1–8.9) months, respectively. The hospital mortality was 27.8% among the operated patients. Only 6.8% of cases had documented free circumferential resection margin and merely 4.0% of patients experienced resection of more than 15 lymph nodes during surgery.

Conclusions: In Iran, the overall survival of EC patients with different treatment modalities are slightly less than those reported from high-income countries, but cases with surgery alone as the main treatment had worse outcome compared with their counterparts in developed countries. Surgery with curative intent has not been performed in most cases in Iran. It seems current clinical outcome of EC patients could be improved with surgical quality improvement and/or more use of chemoradiation in Iran.

Keywords: Esophageal cancer; Population-based; Surgery; Adequacy

Introduction

Esophageal carcinoma (EC) is the eighth most common cancer and the sixth most common cause of mortality due to cancer worldwide.[1] Incidence of EC varies widely across the world, with age-standardized rates (ASR) per 100 000 as low as 1.4 in Western Africa to over 20 in Southern Africa and in Eastern Asia.[1] Iran is on average an intermediate risk country, with ASRs around 7 for men and women,[1] but some parts of Iran are located in the high incidence Asian EC belt, with reported ASRs of as high as 100.[2]

Despite some improvements in treatment modalities of EC, its prognosis remains poor, even in developed countries. However, there is wide variation in reported survival rates. Five-year survival rate is estimated to be 13.6% in the United States,[3] 8.0% in England and Wales,[4] and below 5% in developing countries including China (3.3%)[5] and Iran (around 0.8%).[6]

* Corresponding author. Cancer Research Center, Cancer Institute, Tehran University of Medical Sciences, Qods Street, Enghelab Avenue, 1417863181 Tehran, Iran. Tel.: +98 21 66491070; fax: +98 21 66419537.
E-mail address: harirchi@sina.tums.ac.ir (I. Harirchi).

0748-7983/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.ejso.2013.10.011

The overall low survival rate for esophageal cancer apart from aggressive behavior of the disease could possibly be related to the effectiveness of current treatments, so investigating the influence of treatment factors on survival is important. Surgery is an integral part of the localized EC treatment to obtain locoregional control and long-term survival. However, while performing esophagectomy, surgeons should apply the principles of "adequate cancer surgery (ACS)", including en-bloc resection (free proximal and distal margins, circumferential resection margin (CRM)) and formal lymphadenectomy. ACS is believed to lower short-term mortality and morbidity rates, and use of neoadjuvant therapy could improve long-term survival.[7]

To the best of our knowledge, no population-based studies have been conducted to address the issues mentioned above in Iran. In this paper, we report on demographic, clinicopathological features, survival rates and predictors of EC survival in Iran with emphasis on the quality of surgery in patients with EC in a nationwide study.

Patients and methods

Patient selection and data collection

To obtain a nationally representative sample, we used simple random sampling to select newly-diagnosed EC patients from those who were registered in the 2005–2006 national cancer registry (NCR) databases. A detailed description of the nationwide pathology-based cancer registry of Iran is provided elsewhere.[8] All patients had EC diagnosis confirmed by pathology. Of the 3048 new EC cases registered in NCR in 2005–2006, a total 409 cases were randomly selected for this study.

We followed the patients from the date of diagnosis until the date of death or the end of follow-up in 2009, whichever came first. We interviewed the patients or close relatives. We also interviewed the local health workers who are usually aware of and register the vital status of people living in the population under the coverage by the local health house.

We obtained the information on vital status (dead/alive), date of death, and type of treatment. The five most common treatment groups for EC patients in 2005–2006 were: 1) no oncologic treatment; 2) esophagectomy alone; 3) chemo radiotherapy or radiotherapy; 4) esophagectomy plus chemo radiotherapy or radiotherapy; 5) chemotherapy plus esophagectomy or only chemotherapy.

To evaluate the adequacy of surgery, we further studied pathology reports of 252 patients that were selected by cluster-random sampling from 39 pathologic centers throughout the country. Histological types of tumor, i.e., squamous cell carcinoma (SCC) or adenocarcinoma (AC); tumor location (upper, middle, lower thoracic and cervical); local tumor extension, involvement of the proximal, distal margin and CRM; and number of the dissected and number of positive lymph nodes (LNs) were obtained from the pathology reports by an expert panel in Cancer Institute of Iran.

The Research Ethics Committee of Tehran University of Medical Sciences approved this study.

Statistical methods

We estimated the median ± standard deviation (SD) survival using the descriptive statistics. Kaplan–Meier method was used to estimate 1–3 years survival rate of EC in overall and stratified by age and type of treatments. We used the log-rank tests to study the differences in the survival rates of different categories. We used Cox proportional hazards model to study the crude and adjusted relative risks and corresponding 95% confidence intervals (CI) of demographic and clinical factors on the mortality of EC. In all cases, two-sided $P < 0.05$ was considered statistically significant. We used SPSS standard statistical software for the data analyses (SPSS, version 17.0; SPSS Inc, Chicago, Illinois).

Results

Patient characteristics

A total of 409 EC patients (235 men, 174 women) participated in this study. The mean (±SD) age at the time of diagnosis for these patients was 65.0 (±12.1) years; men were significantly older (66.9 years) than women (62.4 years) ($P< 0.001$). Median survival (25th–75th percentile) for all patients was 8.5 months (3–24 months), therefore 25% of patients survived less than 3 months, half survived less than 8.5 months, and 75% survived less than 2 years. Proportions of patients who survived through the end of the first, second, and third year were 44.0%, 25.0%, and 15.0%, respectively.

Table 1 shows survival for different age and sex group and the five main treatment groups. Median survival time was 6, 6, 11, 12, and 8 month for those who were in treatment groups 1 to 5, respectively. Although survival was low in all groups, the highest survival time was observed among patients who underwent definite chemo radiotherapy (dCRT). Fig 1 illustrates the overall survival curve of EC and by different treatment groups.

After adjusting for age and sex of the patients, in comparison with those who did not receive any oncologic treatment, patients who underwent esophagectomy alone (group 2) had a slightly and non-significantly lower risk of mortality (HR = 0.86; 95% CI: 0.61–1.20). It is noteworthy that the hospital mortality was 27.8% among the operated patients. The 1 and 3-year survival rate of patients in this group who survived after 30-day were 55.0% and 26.0%, respectively and the median survival time was 13 months (38.0%, 18.0%) and 6 month in all of this group, respectively. However, being in treatment groups 3 and 4, compared with group 1, both were associated with 40.0%