

Esophageal Cancer in Khorasan, Iran

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Abstract

Context: Iran has been known as one of the most common areas of esophageal cancer in the world. Actually, North of Iran is well known as a high-incidence endemic region located on the belt of esophagus cancer which is extended from the north of China to the south of Caspian Sea.

Evidence Acquisition: This paper is going to have an overview on the esophageal cancer in Iran through reviewing the results of some new researches have been completed in recent years in Khorasan, Iran.

Results: Epidemiology of esophageal cancer has been changing in recent years in Khorasan, Iran and the incidence rate of the disease is declining. Although the exact reasons for the high incidence rate and yet for declining incidence of the disease are not known, there has been some points of view for this evolution. Still the great majority of esophageal cancers are squamous cell carcinoma and the females and males are almost equally involved in the disease. The most interesting aspect of the disease in this region is long survival of most of the patients.

Conclusion: It seems there are some differences in esophageal cancer disease between Iran and other countries especially western ones in terms of the etiologic risk factors of the disease, some of its epidemiologic aspects, as well as outcome of the disease which seems to be better in Iran.

Keywords: Epidemiology, Esophageal cancer, Iran, Khorasan, Outcome

1. Context

Esophageal cancer is the eight common cancer worldwide. There are more than 20-fold differences in the incidence of the disease in different regions of the world, with rates ranging from 0.2 per 100,000 in women of Polynesia to 17 per 100,000 in males in Eastern Asia (1). This disease is characterized with a highly fatal behavior in different geographical areas, and among the gastrointestinal tract malignancies it is a unique histological distribution of both types of squamous cell carcinoma (SCC) and adenocarcinoma. There are well-known high incidence areas including northern China, Central Asia, Northern part of Iran and Turkey as the belt of esophageal cancer where the incidence of esophageal carcinoma has been estimated to be more than 100 per 100,000 populations. Khorasan that is located in Northeastern part of Iran is one of the most prevalent regions of esophageal carcinoma. The current study is a review of the latest achievements in this disease in the mentioned region.

2. Evidence Acquisition

Data extracted from cancer registry information and the published studies during recent years were considered as the basis of this research on esophageal cancer in Khorasan, Iran.

3. Results

Esophageal cancer with 2584 new cases was the

fifth common cancer in Iran after the cancers of stomach, breast, colon and bladder in 2004. At the same time with 509 cases it was the second common cancer in Khorasan province, among males after the gastric cancer and among females after the breast cancer (2). According to the Iranian Annual of National Cancer Registration Report (IANCRR) 2004, age specific incidence rate (ASR) of esophageal cancer in Khorasan province was 10 in males and 12.7 in females during the later years ending to 2004. Based on an older report from the cancer registry of Khorasan 1996, the proportion of esophageal cancer with 366 cases was 16.5% of all cancers in Khorasan at that time. This fraction has been declining to 9.9% in 2004 and 8.7% in 2009. It should be noticed when considering the overall count of esophageal cancer in Khorasan with 629 cases and the reported range of ASRs of the disease from 18.68 to 26.28 in different Khorasan provinces according to IANCRR 2009, apparently the incidence of this disease has been increased compared to the past years. However, looking at the proportion of esophageal cancer cases clears up declining trend of the disease in Khorasan. The decreasing incidence of esophageal cancer has been in the same direction with the overall statistics of this disease in Iran. In Iran, the proportion of esophageal cancer has fallen from 5.5% in 2004 to 4.5% in 2009. According to some reports, the incidence rate of esophagus cancer is even declining in the region of Gonbad, which once with ASR of more than 100 was one of the highest-incidence endemic areas of this cancer in the world. It has been currently reported that ASR for this cancer has been fallen to

almost half (3-5).

Worldwide, esophageal cancer incidence rate was increased more than two-fold in males than females (5). However, the incidence of esophageal cancer among females in Khorasan province is fairly equal to males (2,6). The reason for this difference is not known; however, considering different risk factors of this disease in the region compared with western countries, discussed later, both males and females are seem identically exposed to etiological factors of esophageal cancer.

While the incidence of esophageal adenocarcinoma is increasing to almost 50% of esophageal cancer in the world and especially in the western countries (5), according to the Iranian Annual of National Cancer Registration Report 2004, this is not similar in Iran, as almost more than 90% of esophageal cancers are squamous cell carcinomas. This also remains true in Khorasan as yet (2,6).

The most common etiological factors of esophageal cancer are smoking and alcohol worldwide. The etiology of more than 90% of SCCs in the western countries is attributed to smoking and alcohol use (3). In Iran a variety of potential risk factors have been considered, including smoking, opium, hot tea, malnutrition, low intake of fruits and vegetables, low socioeconomic status, human papilloma virus infection and genetic susceptibility (7-11). How much interchangeably these risk factors contribute to the incidence rate of esophageal SCC in this geographic region is not known at the moment. Mostly our knowledge about the risk factors of this disease has not been based on scientific epidemiologic study till now; however, the cohort study that is currently running in Golestan province may shed light on the etiological factors of this disease in Iran soon (12).

Esophageal cancers are among the direst cancer worldwide, and their mortality rates closely follow their incidence rates. According to the population-based tumor registry reporting, five-year survival rates generally are less than 15% in western countries, (13). In Iran there are some reports which mention the 5-year survival rates of cancer as low as 0.6 to 12% (14-17). It has not been proven to be true in Northeastern part of Iran including Khorasan. According to the largest study has been done so far in Iran, the 5-year overall survival (OS) rate of esophageal carcinoma treatment is about 42% in this region (6). From 1640 patients who enrolled in that study, 1568 patients were eligible composing all stages of the disease and at least 12% were metastatic disease. Median age was 61.5 years and male to female ratio was 1.2/1. The reported median survival was 38 months. The 5-year overall survival rates were 42% and even it was more than 46% among some groups and lower stages of disease. Although trimodality therapy combining chemotherapy and radiotherapy with surgery has been considered as the

best approach of treatment of locally advanced esophageal cancers, another study in Northeastern part of Iran has reported equal outcome after chemoradiotherapy (CRT) compared with treatments combining surgery or even trimodality treatment (6,18). A study including 986 non metastatic esophageal carcinomas in two arms of treatments with surgery +/- radiotherapy and/or chemotherapy (675 patients) compared with CRT without surgery (311 patients) showed no difference in outcome between two groups in spite of integrating more poor prognostic patients in the CRT arm. In the third study which was a phase II of the clinical trial, 127 operable nonmetastatic esophageal carcinoma patients underwent surgery after chemoradiotherapy; also 5-year OS rate of 48% and a median OS of 44 months showed better outcome of these patients after treatment in this region (19).

4. Conclusion

Overall, esophageal cancer seems epidemiologically and etiologically different in the region of Northeastern part of Iran and Khorasan compared to common worldwide esophageal cancer. The majority of histological type is still SCC and it occurs almost equally among males and females in this region. Overall, according to some large and powerful studies, outcome of the disease seems to be better after treatment compared with internationally reports of outcome of this disease.

Conflicts of interest

The authors declare that there was no conflict of interest.

References

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC Cancer Base No. 11. Lyon, France: International Agency for Research on Cancer; 2013.
2. Iranian annual of national cancer registration report. Tehran: Ministry of Health and Medical Education; 2008.
3. Parkin DM, Muir CS. Cancer incidence in five continents. Comparability and quality of data. *IARC Sci Publ.* 1992;120:45-173. [PubMed: 284606].
4. Munos N, Day NE. Esophageal cancer; in cancer epidemiology and prevention. 2nd ed. Oxford: Oxford University Press; 1996. P. 681-706.
5. Posner MC, Minsky BD, Ilson DH. Cancer of the esophagus. In: Frogge MH, Goodman DM, Yarbrow CH, editors. Cancer principles and practice of oncology. 10th ed. Philadelphia: Lippincott Williams & Wilkins; 2015. P. 574-612.
6. Salek R, Bezenjani SE, Saedi HS, Ashkiki MH, Hosainzade SM, Mohtashami S, et al. A geographic area with better outcome of esophageal carcinoma: is there an effect of ethnicity and etiologic factors? *Oncology.* 2009;77(3-4):172-7. doi: 10.1159/000231887. [PubMed: 19641336].
7. Cook-Mozaffari PJ, Azordegan F, Day NE, Ressaicaud A, Sabai C, Aramesh B. Oesophageal cancer studies in the Caspian Littoral of Iran: Results of a case-control study. *Br J Cancer.* 1979;39(3):293-309. doi: 10.1038/bjc.1979.54. [PubMed:

- 465299].
8. Moradi A, Villiers EM, Mokhtari-Azad T, Mahmoudi M, Hazrati B, Ghaemi EE, et al. Detection of human papillomavirus DNA by PCR in esophageal squamous cell cancer for Turkman-Sahra, North east of Iran. *Iran Biomed J.* 2002;**6**(1):19-23.
 9. Sadeghi A, Marjani H, Semnani S, Nasser-Moghaddam S. Esophageal cancer in Iran: a review. *Middle East J Cancer.* 2010;**1**(1):5-14.
 10. Zang HZ, Jin GF, Shen HB. Epidemiologic differences in esophageal cancer between Asia and Western populations. *Chi J Cancer.* 2012;**31**(6):281-6. doi: [10.5732/cjc.011.10390](https://doi.org/10.5732/cjc.011.10390). [PubMed: [22507220](https://pubmed.ncbi.nlm.nih.gov/22507220/)].
 11. Chattopadhyay I. A brief overview of genetics of esophageal squamous cell carcinoma. *J Cell Sci Molecular Biol.* 2014;**1**(1):103.
 12. Roshandel G, Sadjadi A, Aarabi M, Keshtkar A, Sedaghat SM, Nourae SM, et al. Cancer incidence in golestan province: report of an ongoing population-based cancer registry in Iran, 2004–2008. *Arch Iran Med.* 2012;**15**(4):196-200.
 13. Howlader N, Noone AM, Kerapcho M, Garshell J, Neyman N, Altekruse SF, et al. SEER cancer statistics review, 1974-2010. Bethesda: National Cancer Institute; 2013.
 14. Yarhosseini A, Sharifzadeh L, Delpisheh A, Veisani Y, Sayehmiri F, Sayehmiri K, et al. Survival rate of esophageal cancer in Iran- A systematic review and meta-analysis. *Iran J Cancer Rev.* 2014;**7**(2):61-5. [PubMed: [25250151](https://pubmed.ncbi.nlm.nih.gov/25250151/)].
 15. Mirinezhad SK, Somi MH, Jangjoo AG, Seyednezhad F, Dastgiri S, Mohammadzadeh M, et al. Survival rate and prognostic factors of esophageal cancer in east Azerbaijan. *Asia Pac J Cancer Prev.* 2012;**13**(7):3451-4. doi: [10.7314/apjcp.2012.13.7.3451](https://doi.org/10.7314/apjcp.2012.13.7.3451). [PubMed: [22994776](https://pubmed.ncbi.nlm.nih.gov/22994776/)].
 16. Samadi F, Babaei M, Yazdanbod A, Fallah M, Nourae M, Nasrollahzadeh D, et al. Survival rate of gastric and esophageal cancers in Ardabil province, North-West of Iran. *Arch Iran Med.* 2007;**10**(1):32-7. doi: [07101/AIM.009](https://doi.org/07101/AIM.009). [PubMed: [17198451](https://pubmed.ncbi.nlm.nih.gov/17198451/)].
 17. Aghcheli K, Marjani HA, Nasrollahzadeh D, Islami F, Shakeri R, Sotoudeh M, et al. Prognostic factors for esophageal squamous cell carcinoma-- a population-based study in Golestan Province, Iran, a high incidence area. *PLoS One.* 2011;**6**(7):e22152. doi: [10.1371/journal.pone.0022152](https://doi.org/10.1371/journal.pone.0022152). [PubMed: [21811567](https://pubmed.ncbi.nlm.nih.gov/21811567/)].
 18. Salek R, Warshoei F, Bezenjani SE, Saedi HS, Ashkiki MH, Hosainzadeh SM, et al. Chemoradiotherapy alone as the standard treatment of epidermoid esophageal carcinoma. *Oncology.* 2011;**81**(3-4):214-9. doi: [10.1159/000333448](https://doi.org/10.1159/000333448). [PubMed: [22075490](https://pubmed.ncbi.nlm.nih.gov/22075490/)].
 19. Anvari K, Aledavood SA, Toussi MS, Forghani MN, Mohtashami S, Rajabi MT, et al. A clinical trial of neoadjuvant concurrent chemoradiotherapy followed by resection for esophageal carcinoma. *J Res Med Sci.* 2015;**20**(8):751-6. doi: [10.4103/1735-1995.168377](https://doi.org/10.4103/1735-1995.168377). [PubMed: [26664422](https://pubmed.ncbi.nlm.nih.gov/26664422/)].