

EPIDEMIOLOGY OF ESOPHAGEAL CANCER - AN OVERVIEW ARTICLE

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Background: Esophageal cancer is one of the most serious tumor diseases worldwide, owing to its rapid development and fatal prognosis in most cases. To compare epidemiologic characteristics, data published by the International Agency for Research on Cancer, Lyon, France and data from Masaryk Memorial Cancer Institute, Brno, Czech Republic were used.

Methods: We conducted a search of selected Czech and foreign literature focused on the epidemiology of esophageal cancer and its main risk factors.

Results and Conclusion: An overview of esophageal cancer epidemiology is presented. Prevention of esophageal cancer should be based on early detection and surveillance of precancerous lesions, especially of Barrett's esophagus, and attention should also focus on modification of changeable risk factors, including tobacco smoking, alcohol abuse, and ingestion of hot and spicy food. Carefully designed epidemiologic studies, both descriptive and analytical, are required to increase understanding of the complexity of esophageal cancer etiology.

INTRODUCTION

Esophageal cancer is the 6th most frequent tumor disease worldwide. It is characterized by rapid development and fatal prognosis in most cases. The occurrence increases with age with the highest incidence in the age group 50–70 years. The disease is diagnosed more frequently in males than in females with an approximate ratio 3–5:1. The most frequent histological type is squamous cell carcinoma. The proportion of adenocarcinomas has increased from 3.5 % in 1985 to 17.0 % by the year 2000. In Western Europe and the U.S.A., however, the proportion of adenocarcinomas is almost 50 %.

The prognosis of esophageal cancer is generally unfavorable, even when the tumor is surgically removed at its early and operable stage. Five-year survival is less than 5 % (ref.^{1–3}).

To compare epidemiologic characteristics, data published by the International Agency for Research on Cancer (IARC), Lyon, France and data from Masaryk Memorial Cancer Institute, Brno, Czech Republic were used. Data were standardized to enable comparison of the incidence and mortality rates.

INCIDENCE AND MORTALITY RATES, SURVIVAL

Worldwide incidence rates

Esophageal cancer incidence worldwide was 462 117 in the year 2002; 315 394 cases were diagnosed in males and 146 723 cases in females. In males, the incidence is approximately three times higher than in females.

Figures 1 and 2 show that the highest incidence is registered in Ethiopia, China, and Mongolia, where standardized incidence rates are as high as 28.1 per 100.000 in males, and 19.6 per 100.000 in females in the year 2002. In Europe, the highest incidence rates in males are reported in France (11.0), Hungary (9.8), the United Kingdom (9.6), and Slovakia (9.3 per 100.000). In females, the highest numbers are reported in the United Kingdom (4.4), Netherlands (2.4), and Denmark (2.0 per 100.000)¹.

Incidence rates in the Czech Republic

In the Czech Republic, standardized incidence rates of esophageal cancer were 5.23 per 100.000 in males and 0.63 per 100.000 in females in the year 2003 (Fig. 3). While the incidence rates are relatively low, the trend of esophageal cancer incidence in the Czech Republic is increasing. From 1977 to 2003, standardized incidence rates rose from 2.29 to 5.23 per 100.000 in males and from 0.23 to 0.63 per 100.000 in females².

The case-fatality is associated with the stage at which the tumor is diagnosed. In the 1st stage, only approximately 4 % of tumors are detected, 19 % of tumors are diagnosed in the 2nd stage, 21 % in the 3rd stage, and around 18 % of tumors are diagnosed in the 4th stage. In 38 % of tumors, the stage is not determined².

Worldwide mortality rates

Mortality rates represent roughly 90 % of the incidence rates of the disease. Figures 4 and 5 show that the highest number of cases in males is reported in Ethiopia, Kenya, and China, with standardized mortality rates around 27 per 100.000 in the year 2002. In females, the

highest numbers are observed in Mongolia, Iran, Kenya and China, where the standardized mortality rates are around 16 per 100.000. Among European countries, the highest mortality rates in males are in Hungary (9.1) and the United Kingdom (9.0 per 100.000). In females, the United Kingdom is in the top position with a standardized mortality rate of 4.1 per 100.000, as well as the Netherlands with the standardized mortality rate 2.2 per 100.000 (ref.¹).

Mortality in the Czech Republic

Considering the fact that esophageal cancer is a rapidly developing and mostly lethal disease, in the Czech Republic, similar to other countries, mortality rates are comparable to the incidence rates. Standardized mortality rates were 4.49 per 100.000 in males and 0.52 per 100.000 in females in the year 2002 (ref.²).

Survival

As inferred by similar values of incidence and mortality rates, the prognosis of esophageal cancer is generally unfavorable. The differences in survival rates can be attributed to timeliness of the diagnosis and to quality of health care in respective countries.

Long-term survival is only approximately 5 % of patients. Of patients who undergo radical esophagectomies, 10–20 % survive 5 years. In patients with inoperable cancer, the median survival is 13–29 month⁴.

CAUSES

Changeable risk factors

Development of esophageal cancer is frequently induced by chronic exposure to irritants, spices, hot drinks, alcohol, and smoking.

Tobacco, alcohol, chewing tobacco, opium

High consumption of alcohol and smoking are risk factors which increase the incidence of esophageal can-

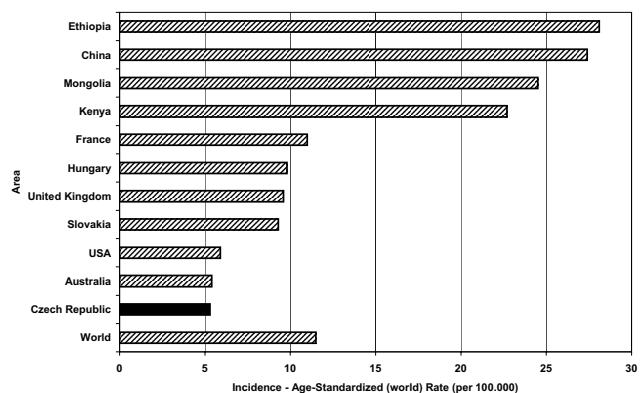


Fig. 1. Standardized (world) incidence of esophageal cancer in selected countries in males in the year 2002.

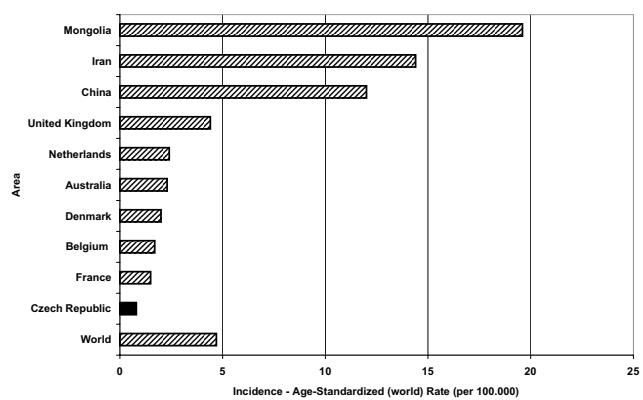


Fig. 2. Standardized (world) incidence of esophageal cancer in selected countries in females in the year 2002.

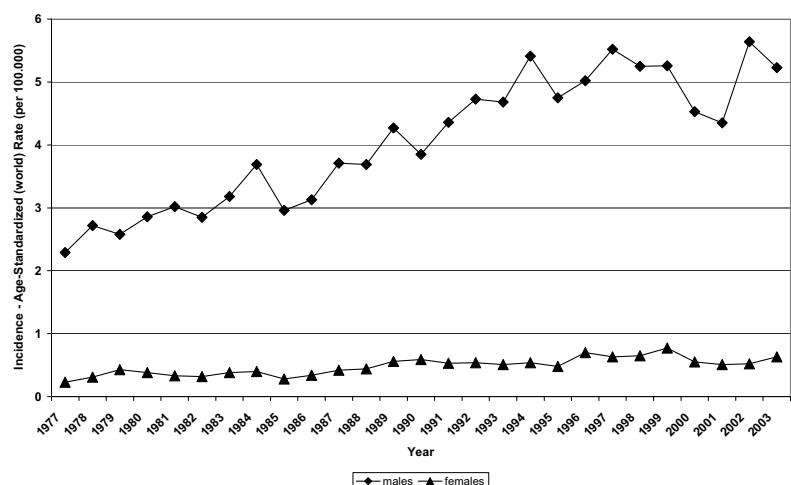


Fig. 3. Standardized (world) incidence of esophageal cancer in the Czech Republic – time trend.

cer. The association was found e.g. in studies carried out in France, Denmark, and the U.S.A. A dose - response relation was found between smoking and relative risk, with the highest risk of 4.6 observed in patients smoking 35 and more cigarettes per day. Patients consuming three and more doses of alcohol per day had relative risk of esophageal cancer 10.9. As the joint effects of smoking and alcohol consumption are potentiated, the final relative risk is multiplied.

Chewing tobacco represents an independent risk factor in areas where it is common. In areas where smoked and chewed (Iran, Afghanistan, middle Asia, China), opium is another risk factor for developing esophageal cancer. In those countries, consumption of opium is prevalent and it is used as a remedy for some health problems (headache, indigestion).

The relative risk of esophageal cancer in ex-smokers gradually decreases and, 15–19 years after quitting, its values are around 1.2 (ref.^{5–7}).

Ingestion of hot drinks and food

Hot drinks and food increase the risk of esophageal cancer, mostly when chronic exposure to hot and/or irritant substances is present. Since exact measurement of the temperature of consumed food is complicated and difficult, obtaining clear evidence of this association is problematic. Epidemiologic studies describing the association were conducted in areas with a high incidence of esophageal cancer where consumption of hot drinks (maté) is popular. Drinking hot maté is classified as possibly carcinogenic according to IARC; when consuming 1 litter of maté per day, OR is around 2.95. When cumulative exposition to maté, tobacco, and alcohol is present, the relative risk of esophageal cancer can be as high as 7.10 (ref.⁸). The pathogenic pathway can be dual; consumption of maté can act as a carcinogen or promoter itself, or the high temperature of the drink alone is responsible for carcinogenesis. Since the etiology of cancers is multifactorial, drinking hot drinks, smoking, consuming alcohol, and insufficient consumption of fruits and vegetables must be taken into account⁸.

Pickled vegetables

Consumption of pickled vegetables, typical for many areas in China, is considered possibly carcinogenic, with N-nitroso compounds and mycotoxins representing risk factors. The evidence concerning the association, however, is not clear^{9, 10}.

Nitrosamines

The role of nitrosamines in the development of esophageal cancer has not been sufficiently clarified. The results of studies focusing on high levels of nitrosamines in food and alcoholic beverages are inconclusive and do not confirm the association. In China, where food is frequently contaminated by nitrosamines, the presence of other confounders, especially fungi, can play a role. The permanent presence of amines and nitrates in food can probably increase the risk of esophageal cancer, but

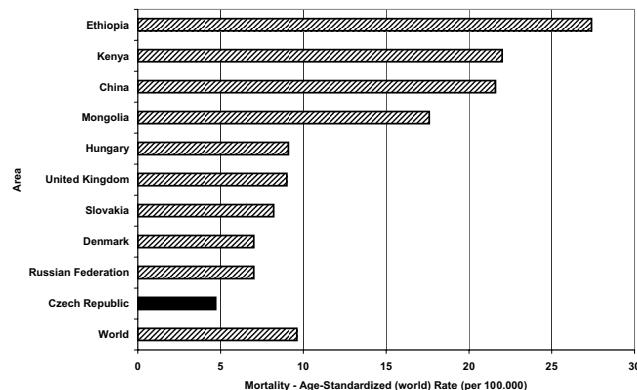


Fig. 4. Standardized (world) mortality of esophageal cancer in selected countries in males in the year 2002.

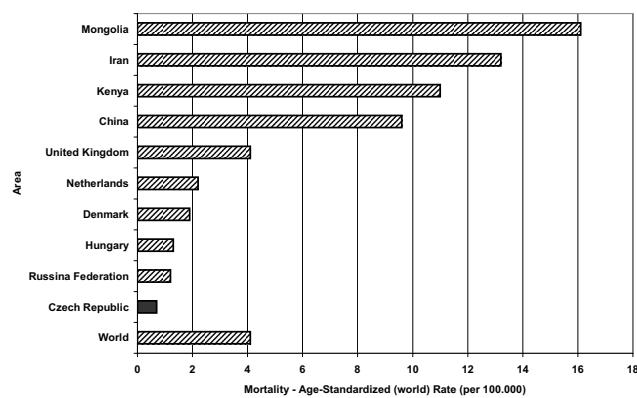


Fig. 5. Standardized (world) mortality of esophageal cancer in selected countries in females in the year 2002.

other epidemiologic studies are required to confirm the association.

Infectious agents

The assumption that human papillomavirus can play a role in development of esophageal cancer has not yet been proved. Some studies have found the presence of HPV in 20–70 % of patients with esophageal cancer, while other studies do not confirm such findings. Of other infectious agents, fungi contaminating wheat and maize are suspected to be associated with esophageal cancer^{10, 11}.

Physical and chemical factors, chronic injuries

Other risk factors include ionizing radiation, asbestos, contamination of food by silica fibers (Iran, China), and also traumatic burn of esophagus resulting in cicatricial strictures of the esophagus¹⁰.

Occupational risk factors

Workers who are exposed to products of combustion (chimney-sweepers) and diesel pollutants (garage staffers) are at higher risk of esophageal cancer. Long-term exposure to beryllium also increases the risk of the devel-

opment of esophageal cancer. Moreover, higher risk was observed in farmers working with pesticides; in this case, however, alcohol abuse is a suspicious confounder.

Socioeconomic status

Epidemiologic studies focusing on esophageal cancer epidemiology suggest higher incidence of the disease in lower socioeconomic strata. Such findings can be explained by nutritional deficiencies, insufficient vitamin supply, low consumption of fruits and vegetables, smoking, and alcohol abuse.

Adenocarcinoma of the esophagus, on the other hand, is more frequently found in white males from higher socio-economic groups. Its pathogenesis begins with chronic reflux, leading to esophagitis and Barrett's metaplasia and eventually to the development of adenocarcinoma. Therefore, the incidence of adenocarcinoma of the esophagus is associated with the increasing percentage of obesity in the population. Smoking and drinking alcohol are risk factors for adenocarcinoma as well, while sufficient consumption of fiber acts as a protective factor¹²⁻¹⁴.

Unchangeable risk factors

Hereditary factors

Unchangeable risk factors include age, sex, and hereditary factors. Among hereditary factors, tylosis is the most important affliction, characterized by hyperkeratosis of the palms and soles and accompanied by esophageal cancer in almost 37 %. In patients with Plummer – Vinson syndrome, which is characterized by sideropenic dysphagia, glossitis, and esophagitis, esophageal cancer is developed in approximately 10 %. In persons with positive family history, relative risk is around 2.69 according to several epidemiologic studies conducted in China^{14, 15}.

CONCLUSIONS

Esophageal cancer represents a serious tumor disease, not only due to its unfavorable prognosis with only 5 % patients' long-term survival, but also due to the increasing trend of the incidence rates including the Czech Republic. Prevention of esophageal cancer should be based on early detection and surveillance of precancerous lesions, especially of Barrett's esophagus, and attention should also focus on modification of changeable risk factors, including tobacco smoking, alcohol abuse, and ingestion of hot and spicy food.

Carefully designed epidemiologic studies, both descriptive and analytical, are required to increase our understanding of the complexity of esophageal cancer etiology. When the roles of etiologic factors are specified, preventive measures can be taken to reverse the trend of

the disease and to decrease its incidence and mortality rates.

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