

ORIGINAL ARTICLE

GASTRIC CARDIA CANCER; THE MOST COMMON TYPE OF UPPER GASTROINTESTINAL CANCER IN ARDABIL, IRAN: AN ENDOSCOPY CLINIC EXPERIENCE

Abbas Yazdanbod MD*, Shahnam Arshi MD*, Mohammad-Hossein Derakhshan MD**, Ali-Reza Sadjadi MD**, Reza Malekzadeh MD***

*Department of Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

**Digestive Disease Research Center, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Background-According to a recent report published by the Ministry of Health and Medical Education of the I. R. of Iran, gastric cancer (GC) is the most common fatal cancer in this country and its prevalence is highest in Ardabil province, Northwest of Iran. This descriptive endoscopic survey was designed to determine the type of upper gastrointestinal (GI) malignancy in this high prevalence area.

Method-This study was conducted in the first established subspecialty outpatient GI clinic in the city of Ardabil. From 11,518 patients who attended this clinic in a one-year period, 1,152 (10%) with persistent upper GI symptoms underwent upper GI fiberoptic endoscopy and 162 (14.1%) had a tumor with malignant appearance. At least six endoscopic punch biopsies were obtained from all the tumors and sent for histopathologic examination. Demographic data was obtained from all 162 patients. Statistical analysis was performed using the SPSS statistical software.

Results-The mean age of the patients with cancer was 63.5 ± 10.8 years and the male to female ratio was 2.14:1. Villagers constituted 111 (70.7%) and urban dwellers constituted 46 (29.3%) patients. Upper GI cancer was diagnosed by histopathology in 157 patients (13.4%). Stomach cancer constituted 107 cases (68.2%), 53 (49.5%) of which were cancers of the gastric cardia and 50(31.8%) were esophageal cancer. The most common site of upper GI malignancy was the gastric cardia 53 (33.8%) followed by the antrum 32(20.4%), esophageal body 27 (17.2%), distal esophagus 23 (14.6%), and gastric body 22 (14.0%).

Conclusion-Cancer of the gastric cardia is now the most common upper GI malignancy in Ardabil and constitutes almost half of all gastric cancers. It is recommended that subsite-specific gastric cancer risk factors, including *H. pylori* and dietary nitrates, be studied in the future in this region.

Keywords • Gastric cancer •GI cancer •cardia •Ardabil •adenocarcinoma

Introduction

A recent cancer surveillance study performed by the Ministry of Health of the I.R. of Iran¹ revealed that gastric adenocarcinoma is the most common fatal cancer in Iran with a wide variation of death rate in

southern Iran (Persian Gulf Coast), is 3.6 per 100,000 per year as compared to a rate of 8.4 per 100,000 in East Azarbaijan, northern Iran. According to a study in 1971², antral adenocarcinoma was considered to be the predominant type of gastric cancer in Iran. Some unpublished data from Ardabil in Eastern Azarbaijan on the west coast of the Caspian Sea,

•Correspondence: R. Malekzadeh MD, Digestive Disease Research Center, Shariati Hospital, Tehran, Iran. E-mail: malek@ams.ac.ir.
different provinces. The mortality rate in Bushehr,

Gastric Cardia Cancer; The most Common Type of Upper GI Cancer in Ardabil

Table 1. Esophageal cancer: location of tumor and age.

Site of lesion	N (%)	Mean age ± SD	Median age	Minimum age	Maximum age
Upper third	6 (12.0)	54.7 ± 17.2	54	27	75
Middle third	21 (42.0)	62.6 ± 11.8	62	40	85
Lower third	23 (46.0)	61.7 ± 14.1	65	24	88
Total	50 (100)	61.3 ± 13.5	63	24	88

however, reported a higher frequency of gastric cardia cancer. This descriptive, endoscopic study was designed to further explore the anatomic subsite of different GI cancers in this high prevalence gastric cancer area. To the best of our knowledge, this is the first descriptive study performed to evaluate the anatomic subsite of gastric cancer in Iran.

Materials and Methods

This study was conducted in the first established subspecialty outpatient GI clinic in Ardabil city. Out of the 11,518 patients who attended this clinic during a one-year period (Dec. 1999-Dec. 2000), 1,152 patients (10%) presented with persistent or alarming GI symptoms and/or signs (dysphagia, abdominal pain, weight loss, anemia, abdominal mass, anorexia, nausea and vomiting). Using 10% lidocaine spray in the pharynx, standard upper GI endoscopy was performed with the Olympus-E model gastrofibroscope (Olympus-Keymed, UK) for the patients with persistent or alarming manifestations of disease. The first author, who is a certified and experienced gastroenterologist, performed all endoscopies. The esophagus was carefully scrutinized for location of the Z-line (level of transition of pale squamous epithelium of the esophagus to the velvety-red gastric epithelium). The distal esophagus was defined as the area 5 cm above the Z-line, and the gastric cardia was defined as the most proximal 3cm of the stomach. All cancers originating from this segment were

recorded as cancer of the cardia. Location of tumors was registered accurately and at least 6 punch biopsies were obtained from all tumors.

Biopsy specimens were oriented, fixed in 10% buffered formalin, sectioned and stained by the hematoxylin and eosin technique. Experienced pathologists then examined the specimens for evidence of cancer.

Results

During the one-year period of the study, 1,152 upper endoscopies were performed. From 162 cases endoscopically suspected to have malignancy, gastroesophageal cancer was proved by histopathologic studies of the endoscopic biopsies in 151 cases and by histopathologic studies of the surgically resected lesions in another 6 patients; thus making a total of 157 (13.4%) upper GI cancers. The mean age of all patients was 63.5 ± 10.8 years and the male to female ratio was 2.14: 1.

Of these 157 gastroesophageal cancer cases, 50 (31.8%) had esophageal cancer and 107 (68.2%) suffered gastric cancer. Also, 111 (70.7%) and 46(29.3%) patients were from rural and urban areas respectively.

Considering the site of esophageal tumors, 6 (12.0%), 21 (42.0%) and 23 (46.0%) cases were located at the upper, middle and lower thirds of the esophagus, respectively. Table 1 shows the site and age of patients with esophageal tumors. Only 5(10.0%) esophageal cancer cases were adenocarcinomas and the remaining were

Table 2. Gastric cancer: location of tumor and age.

Site of tumor	N(%)	M/F ratio	Mean age ± SD	Median age	Mean age ±SD	Median age
			Male	Male	Female	Female
Cardia	53(49.5)	2.5 : 1	65.2 ± 10.3	66	59.8 ± 9.7	60
Body	22(20.6)	3.4 : 1	65.4 ± 8.6	65	66.0 ± 8.9	66
Antrum	32(29.9)	6.8 : 1	66.0 ± 7.5	66	59.3 ± 5.0	61

Table 3. Gastric Cancer: location of tumor and type of residence

Site of tumor	n(%)	Rural/Urban ratio	Mean age ± SD	Median Age	Mean age ± SD	Median Age
			Rural	Rural	Urban	Urban
Cardia	53(49.5)	1.7 : 1	65.2 ± 9.2	65	61.2 ± 11.9	62
Body	22(20.6)	2.1 : 1	66.5 ± 8.6	66	63.4 ± 8.4	61
Antrum	32(29.9)	2.4 : 1	66.0 ± 8.7	66	63.8 ± 4.1	62

squamous cell carcinomas. The mean age of the patients with esophageal cancer was 61.3 ± 13.5 years with a female to male ratio of 1: 0.92. Other findings related to esophageal cancer are presented in Table 1.

With the exception of a 60-year-old man who had large-cell lymphoma of the distal stomach the remaining gastric cancer patients had adenocarcinoma. Gastric cardia, with 53 cases (49.5%), was the most common site of cancer. The antrum and body of the stomach were the second and third most common sites of cancer with 32(29.9%) and 22(20.6%) cases, respectively. The mean age of cardia cancer patients at time of diagnosis was 63.5 ± 10.2 years; males being older than females. Urban patients were affected 6 years earlier than rural subjects but the differences were not found to be statistically significant (Tables 2, 3).

Discussion

During the past 50 years, the incidence of adenocarcinoma of the stomach has decreased in western industrialized countries.³⁻⁵ A striking feature of this decline is a concomitant rise in the

incidence of gastric cardia cancer⁵⁻⁸, which is now becoming more common than adenocarcinoma of the distal esophagus.⁹ In developing countries the overall incidence of gastric cancer is increasing and projections indicate that the annual number of new cases will increase significantly during the next few decades as a result of adult population growth.¹⁰

There is now some evidence that there may be a different etiology for tumors located in gastric cardia and antrum. Demographic differences and a diverging incidence trend point to the fact that the two tumors may be epidemiologically distinct and therefore the anatomic subsite of gastric tumor should be taken into account in studies of etiology and carcinogenesis of this fatal cancer.^{8, 11} Gastric cardia cancer has also been shown to have a different clinical and biological behavior from that of distal gastric cancer and patients with proximal gastric cancer have worse outcomes and shorter survival times as compared to patients with antral gastric cancer.¹²

Recent studies have clearly shown that environmental factors¹³ are the overwhelming contributors to the pathogenesis of gastric cancer, among which *H. pylori* gastritis, dietary habit and occupational exposure are well established risk factors.

H. pylori infection is very common in most parts of Iran. Seroepidemiologic studies reveal that up to 90% of the Iranian population are infected¹⁴ and about 80% are infected with the more virulent cog-positive strain (Massarrat personal communication, 2000). Infection tends to occur early in life in most parts of the country. Previous investigations performed on elementary school children of Ardabil, revealed a 34% and 48% seropositive rate in the 5-10 and 10-15 year age groups respectively. This was significantly higher than children of the same age groups from Yazd in central Iran (20% and 31% respectively).

Few recently published studies¹⁴ have shown that contrary to the previous belief that *H. pylori* is a risk factor only for noncardia gastric cancer, both

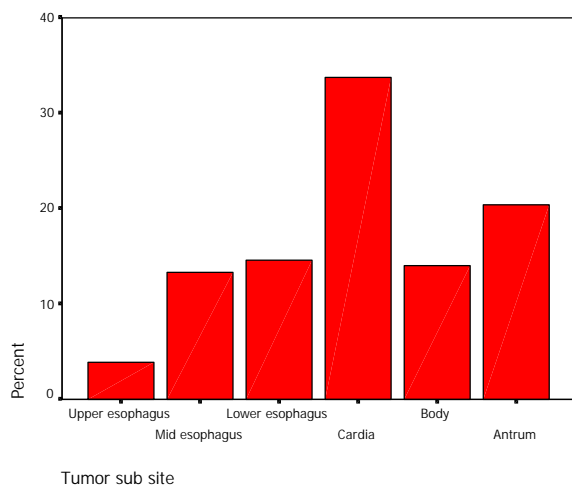


Figure 1. Topographic distribution of upper GI cancers in Ardabil

Gastric Cardia Cancer; The most Common Type of Upper GI Cancer in Ardabil

cardia and antral cancer could be the consequence of *H. pylori* infection.¹⁵ Dietary fiber and antioxidants are both abundant in the diet of people of Ardabil, and do not seem to protect against cancer of the cardia in Ardabil as reported elsewhere.¹⁶ Since *H. pylori* infection has been endemic for many decades, other dietary or environmental factors may be responsible for this rise of gastric cancer in Iran.

According to recent cancer statistics, death due to gastric cancer constitutes about 30% of all deaths due to cancer each year in Ardabil.¹⁷ Most gastric cancers are diagnosed at an advanced stage with very poor survival, usually not more than 15% at 5 years. This cancer alone is the cause of more than 750,000 annual deaths in the world.¹⁰ Both traditional and genetic epidemiological research should be undertaken with especial focus on etiological factors and pathogenesis in order to develop effective preventive strategies against this disease.

Further epidemiologic studies need to be performed to evaluate the role of dietary nitrates and other carcinogens, which may be secreted in saliva and accumulated in the cardia, in the pathogenesis of gastric cardia cancer.

Epidemiologic studies should be performed in different ethnic subgroups of north, central and southern Iran with different prevalence rates for all four major types of upper GI cancers including cancers of the distal stomach and gastric cardia as well as adenocarcinoma and squamous cell carcinoma of the esophagus.

References

- 1 Ministry of Health and Medical Education. *Death in four provinces of Iran*; 2000.
- 2 Haghghi P, Nasr K. Gastrointestinal cancer in Iran. *J Chron Dis*. 1971; **24**: 625-33.
- 3 Parkin DM, Lara E, Muir CS. Estimates of the worldwide frequency of sixteen major cancers in 1980. *Int J Cancer*. 1988; **41**: 184-97.
- 4 Wangenstein OH. The problem of gastric cancer. *JAMA*. 1947; **134**: 1161-9.
- 5 Boring CC, Squires TS, Tong T. Cancer statistics. *CA Cancer J Clin*. 1991; **41**:19-36.
- 6 Atonioli DA, Goldman H. Changes in the location and type of gastric adenocarcinoma. *Cancer*. 1982; **50**: 775-81.
- 7 Meyers WC, Damiano RJ, Rotolo FS, et al. Adenocarcinoma of the stomach: changing patterns over the last 4 decades. *Ann Surg*. 1987; **105**: 1-8.
- 8 Blot WJ, Devesa SS, Kneller RW, Fraume JF. Rising incidence of adenocarcinoma of the esophagus and gastric cardia. *JAMA*. 1991; **265**: 1287-9.
- 9 Pera M, Cameron AJ, Trastek VF, et al. Increasing incidence of adenocarcinoma of esophagus and esophagogastric junction. *Gastroenterology*. 1993; **104**: 510-31.
- 10 Murray CJL, Lopez AD. Mortality by cause for eight regions of the world: global burden of disease study. *Lancet*. 1997; **349**: 1269-76.
- 11 Powel J, McConkey CC. The rising trend in esophageal and gastric cardia adenocarcinoma. *Eur J Cancer Prev*. 1992; **1**: 265-9.
- 12 Wanebo HJ, Kennedy BJ, Chmiel J, et al. Cancer of stomach: a patient care study by the American College of Surgeons. *Ann Surg*. 1993; **218**: 583-92.
- 13 Lichtenstein P, Holm NV, Verkasalo PK, et al. Environmental and heritable risk factors in the causation of cancer. Analysis of cohorts of twin from Sweden, Denmark and Finland. *N Engl J Med*. 2000; **343**: 78-85.
- 14 Massarrat S, Saberi-Firoozi M, Soleimani A, et al. Peptic ulcer disease, irritable bowel syndrome and constipation in two populations in Iran. *Euro J Gastroenterol Hepatol*. 1995; **7**: 427-33.
- 15 Terry P, Lagergren J, Ye W, Wolk A, Neyern O. Inverse association between intake of cereal fiber and risk of gastric cancer. *Gastroenterology*. 2001; **120**: 387-91.
- 16 Limburg PJ, Qiao YL, Mark SD, et al. *Helicobacter pylori* seropositivity and subsite-specific gastric cancer risks in Linxian China. *J Nat Cancer Inst*. 2001; **93**: 226-33.
- 17 Ardabil University of Medical Science. *Ardabil Health Branch annual reports*; 2000.