

## RESEARCH ARTICLE

# Clinical and Histological Indicators of Proximal and Distal Gastric Cancer in Eight Provinces of Iran

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## Abstract

**Background and Aim:** Gastric cancer is the second most common cancer worldwide. In this study the clinical and histological features of gastric cancer in the cardia and distal stomach were evaluated. **Method:** Proximal and distal gastric cancer diagnosed and treated in eight provinces of Iran from 2010-2011 were reviewed in all collected cases. The age standardized incident rates were calculated and tumor location and histological type were recorded. **Results:** The age-standardized incidence rate for the eight centers was 40.6 per 100,000 populations per year with an upper and lower range of 22.1 and 102.4 per 100,000 population per year. Thirty four percent of the tumors were located in the cardia, 3% in fundus, and 63% in the distal stomach. In 7 provinces the prevalence of distal tumors was significantly greater than proximal tumors ( $p=0.006$ ). A significant relationship was observed between diffuse form of gastric cancer and distal gastric tumors ( $p=0.007$ ) and between poor tumor differentiation and distal gastric tumors ( $p<0.001$ ). **Conclusions:** the result of this study shows that distal gastric cancer is more common than proximal gastric cancer in Iran.

**Keywords:** Gastric cancer - cardia, anatomic areas - diffuse type of gastric cancer - intestinal type of gastric cancer

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## Introduction

Gastric cancer is the second most common cancer worldwide and the most important cause of cancer death in the world (Koh and Wang, 2002; Nyren et al., 2002). The incidence of gastric cancer varies widely between different countries (Zali et al., 2011). In Western countries such as Canada and North America the incidence of gastric cancer has fallen over the last 30 years. Rates have fallen from 9.9-4.2 per 100,000 for females and 21.2-9.1 per 100,000 for males. Furthermore, in recent years the incidence of proximal gastric cancer in Western countries has increased whilst the incidence of distal gastric cancers has fallen. By comparison the incidence of gastric cancer in all Asian countries, such as Iran, is high and 38% of all gastric cancers in the world occur in China (Sadjadi et al., 2003; Curado, et al., 2007; Jemal et al., 2010; Pourhoseingholi, et al., 2010; Moghimi-Dehkordi, et al., 2012). Furthermore it is predicted that the prevalence of gastric cancer in developing countries will continue to increase as countries with high incidence rates experience significant increases in their populations.

Male gender, a diet with high level of salt and smoked foods, helicobacter pylori infection and rare polyposis syndromes are the risk factors for gastric cancer. Epidemiology studies confirmed the importance of environmental factors (González et al., 2010; Bornschein

et al., 2011).

Gastric cancers can be classified according to their histological features. The Lauren classification classifies gastric cancers as either intestinal or diffuse (Vieth et al., 2005). Gastric cancers can be staged according to the World Health Organization classification. In Western countries, the majority of cancers present with metastases (World Health Organization stages T3 and T4) (Yeoh, 2007; Liu et al., 2012). Surgical treatment is usually with a partial or total gastrectomy (Patel and Kooby, 2011).

As the incidence of gastric cancer has significantly decreased in the United States and Western countries (Ekström et al., 2000; Sipponen, 2002; Eriksson et al., 2008), the aim of this study was to report the incidence of gastric cancers, by tumor site and pathological type, from eight provinces within Iran.

## Materials and Methods

This retrospective observational study was performed in eight Iranian provinces including Tehran, Khorasan, Lorestan, Mazandaran, Khuzestan, East Azarbaijan, Kurdistan, and Sistan and Baluchestan. Clinical data and pathological samples were collected from all centers by census method between 2010 and 2011. All information was recorded on a single study questionnaire. To support the study, a one-week course was provided for physicians

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and nurses. This provided details of the research methodology and study aims, ethical approval, preparation of pathological samples for analysis, storage and transport of samples and the reporting processes.

Patient variables including sex, age, symptoms tumor size, stage and tumor morphology and types (based on the Lauren classification) we recorded. All of this information was obtained retrospectively from hospital records (including pathology and operative reports) of patients. After data entering, a controller rechecked information. After confirming the accuracy of registered information and addressing any inconsistencies, the data was analyzed using SPSS software. Pearson's correlation, the Chi-square test, Fisher's exact test and the student's t-test were used to analyze numerical data. A probability of less than P<0.05 was considered statistically significant. To calculate the age-standardized incidence rate the direct method of standardization technique was used (Dos, 1999).

**Results**

Nine hundred and forty cases with gastric cancer were identified between 2010-2011. Seventy three percent of studied cases were male and 27% were female. The overall incidence rate in this study was 4.6/100, 000 per population per year. The highest incidence was 10.24

**Table 1. Age-Standardized Incidence Rate in Different Age Groups**

	Khorrām	Tehran	Tabriz	Zahedan	Sanandaj	Sari	Ahvaz	Mashhad	Total
20-29	-	0.04	-	0.23	-	0.25	-	0.14	0.06
30-39	-	0.25	0.17	0.26	0.62	-	0.1	-	0.19
40-49	0.58	0.5	0.16	0.65	0.94	0.23	0.51	0.25	0.44
50-59	2.27	1.28	0.55	-	0.69	1.04	0.13	1.28	1.1
60-69	3.97	1.6	0.71	0.74	2.68	1.59	0.63	1.68	1.54
70-79	3.06	1.2	0.61	0.43	2.14	1.12	0.73	1.03	1.14
80-89	0.36	0.14	-	-	-	-	0.21	0.09	0.13
Total	10.24	5.01	2.21	2.31	7.07	4.23	2.3	4.48	4.6

**Table 2. Anatomical Distribution of Tumors in the Stomach**

Anatomic region	Number	Percentage
Cardia	223	34.30%
Body	148	22.80%
Antrum	259	39.80%
Fundus	20	3.10%
Total	650	100%

**Table 3. Relation between Provinces and Distal and Proximal Gastric Tumors**

Provinces	Proximal gastric Tumors	Distal gastric Tumors	Total
Khorasan	18 (46.1%)	21 (53.9%)	39
Lorestan	15 (38.5%)	24 (61.5%)	39
Tehran	137 (34.0%)	264 (66.0%)	401
East- Azarbahijan	15 (43.0%)	20 (57.0%)	35
Sistan&Balochestan	1 (10.0%)	9 (90.0%)	10
Kurdestan	8 (30.0%)	19 (70.0%)	27
Mazandaran	8 (42.0%)	11 (58.0%)	19
Khozestan	4 (21.0%)	15 (79.0%)	19

and the lowest was 2.21 (cases per 100,000 population per year) in Lorestan and East Azarbaijan provinces respectively.

The mean age of cases studied was 61±12 years. The average age in the distal gastric tumors was significantly lower than proximal tumors but whilst the difference was statistically significant the age difference was clinically insignificant (63 vs. 61 years, student t-test p=0.019). 38% of gastric tumors were diagnosed in patients under the age of 60 years and 16% of cases occurred in patients under the age 50 years. Age-standardized incidence rate in different age groups were mentioned in Table 1.

In 650 patients the anatomic location of the tumor was recorded. The antrum was the most common location for a stomach cancer. Table 2 shows the anatomical distribution of the tumor in the stomach. No statistically difference was observed between the sex in incidences of proximal and distal gastric cancer.

Tumor appearance was commented upon in a total of 352 cases. There was no significant relationship between tumor morphology and proximal or distal tumor location in the stomach. Table 3 showed the relationship between provinces and distal and proximal gastric tumors. Only a few early gastric cancers were identified.

Based on Lauren classification, tumors' location and histopathological type of gastric cancer were mention in Table 4. According to these findings tumors were more appeared in proximal side specially in elevated lesions.

A total of 265 cases could be classified according to histopathological features. Fifty five percent of all cases had diffuse and 45% had intestinal type cancer. When histopathological features were compared according to anatomical location, distal cancers were more likely to

**Table 4. Tumors' Location and Histopathological Type of Gastric Cancer Based on Lauren Classification**

	Tumor location		Total
	Distal	Proximal	
Tumor appearance			
Early Gastric cancer	6 (46%)	7 (54%)	13
Elevated Lesions	86 (36%)	154 (64%)	240
Depressed Lesions	48 (49%)	51 (51%)	99
Total amount	140 (40%)	212 (60%)	352

**Table 5. Gastric Tumors Location and Tumor Differentiation**

	Total	Proximal or distal tumors	
		Distal tumors	Proximal tumors
Diffuse	146 (55%)	113 (61%)	33 (42%)
Intestinal	119 (45%)	73 (39%)	46 (58%)
Total	265	186	79

\*Pearson Chi Square, p Value<0.001, Phi=0.257

**Table 6. Tumor Stage in Proximal and Distal Gastric Tumors**

	Total	Distal tumors	Proximal tumors
Poorly Differentiated	203	41 (20%)	162 (80%)
Well Differentiated	311	139 (45%)	172 (55%)
Total	514	180 (35%)	334 (65%)

have a diffuse, rather than intestinal, histopathological features. The distal gastric tumors significantly showed a lower degree of differentiation than proximal tumors ( $p < 0.001$ ) (Table 5).

At operation 29% of gastric tumors were stage 1 or 2 and 71% were stage (3 or 4) were diagnosed. When staging was compared according to tumor location, stage 1 and 2 with stage 3 and 4 in the proximal and distal gastric tumors were 19% and 81% compared with 31% and 69% respectively. When tumor stage was compared according to tumor there were not significant differences between proximal and distal gastric tumors (Table 6) ( $p = 0.79$ ). Eighty percent of both types of gastric tumors were exophytic lesions and 82% were infiltrative. There was no significant difference occurred between proximal and distal gastric tumors in this respect. Also there were no statistically significant differences in tumor size between proximal and distal gastric tumors ( $p = 0.3$ ).

Surgery was performed in 862 patients. Five hundred and two patients had a partial gastrectomy and a total gastrectomy was performed in 360 patients. In all provinces, the most common surgical type was partial gastrectomy rather than total gastrectomy ( $p < 0.0001$ ).

## Discussion

Despite the decrease in age-specific incidence of gastric cancer in Western countries, gastric cancer remains the second most important cancer worldwide after lung cancer (Koh and Wang, 2002; Bornschein et al., 2011). Furthermore, in Western countries proximal stomach cancer is more common than distal stomach cancer. Iran is considered to have a high incidence of gastric cancer (Pourhoseingholi et al., 2010; Rostami et al., 2012). The incidence of gastric cancer in our study is lower than expected and comparable to rates in Western countries. Interestingly, despite incidence rates that are comparable to Western countries, the majority of tumors were distal gastric cancers. This suggests that multiple factors contribute to the prevalence of gastric cancers and that different factors may contribute to the overall prevalence and the anatomical location of gastric tumors. In keeping with other studies, the incidence of gastric cancer increases with age and is greater in males than females.

When the results were compared according to provinces there was a marked variation in incidence. This suggested a gradient between northern and southern provinces with the highest risks being in the Northern provinces. This result was unexpected. The mechanisms underlying such a gradient remains uncertain but environmental and socio-economic factors are associated with the incidence of gastric cancer and this is a plausible explanation.

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