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The clinical and pathological features of patients with gastric cancer in Turkey: A Turkish Oncology Group Study

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ABSTRACT

Although the incidence of gastric cancer has declined dramatically in western countries; it is, after the breast cancer in women and lung cancer in men, the second most common cancer in Turkey with a high mortality. Surgery is the mainstay in the management of gastric cancer, and unresectable disease has poor prognosis. The aim of this study was to evaluate the clinicopathological and epidemiological features of patients with gastric cancer in Turkey. A questionnaire was used to collect information on clinicopathological and socioeconomic features of all patients with newly diagnosed gastric cancer in contributing 16 different centers in Turkey in the year 2004. The findings were analyzed by the geographic regions in patients live. Nine-hundred seventy-one patients with newly diagnosed gastric cancer in 2004 were included in the study. Mean age of the patients was 57±12.9 (mean±SD) years. Male-female ratio was 2/1. The rate of cancer resectability was lower in Eastern Turkey (ET) than Western Turkey (WT) (31.6% vs. 63.4%, p=0.0001). Also, socioeconomic status of the patients was lowest in ET (53.6% vs. 32.3%, p=0.0001). H. pylori gastritis and intestinal metaplasia were more common in ET when compared to WT (75.0% vs. 40.5%; p=0.003, and 68.4% vs. 18.1%; p=0.0001, respectively). Lower resectability rate of disease in ET should be appreciated. Further epidemiological study of gastric cancer is warranted in Turkey. [Turk J Cancer 2006;36(3):108-115].

KEY WORDS:

Gastric cancer, helicobacter pylori, resectability

INTRODUCTION

Gastric cancer is the second most common malignancy worldwide, with a high mortality rate (1). The incidence of gastric cancer is declined in the western countries during the last half of this century. However, in Japan and some Asian countries, it is still the first cause of cancer mortality (2,3).

Surgery is the mainstay of the gastric cancer management (4,5). Early stage gastric cancer has a better prognosis with an overall survival at 5-year exceeding 95% in Japan and 65% in the United States (6). However, if the disease is diagnosed at an advanced stage, the prognosis is very poor in spite of the developments in the chemotherapy regimens (7-9). Unfortunately, the majority of patients with gastric cancer have advanced disease at diagnosis (3,4).

Gastric cancer is the second most common cancer in Turkey after the breast cancer in women and lung cancer in men (10-12). However, there has been no multicentric study which examined the features of patients with gastric cancer in Turkey so far. In this retrospective multicentric study, we evaluated the clinicopathological and socioeconomic features of patients with gastric cancer diagnosed in 2004 in Turkey from participating centers.

METHODS

Data collection

By using a questionnaire with seventeen questions related to the clinicopathological characteristics of the disease and socioeconomic features of the disease; data was collected retrospectively for all patients with newly diagnosed gastric cancer between January and December 2004 from the contributing 16 different centers from different geographical regions of Turkey.

Questions in the questionnaire were age, gender, resectability, places where patients lived, socioeconomic status, smoking, alcohol consumption, presence of anemia, location of tumor, empirical treatment for peptic ulcer before the diagnosis of gastric cancer, presence of intestinal metaplasia and atrophic gastritis, Helicobacter pylori (H. Pylori) infection, and the time from the beginning of symptoms to the diagnosis of cancer.

Definitions

The location of tumor was defined according to the International Classification of Disease for Oncology, second edition (ICD-O-2): upper tumors (gastric cardia), middle tumors (gastric fundus and overlap cancers), and distal tumors (corpus, antrum and pylorus) (13). Histological types included adenocarcinoma, signet ring cell adenocarcinoma, undifferentiated carcinoma and other epithelial cancers.

Socioeconomic status of patients was defined as low, medium and high according to patients' inhabiting in urban or rural area, occupation, and type of health care insurance. Retirement Fund (Emekli Sandigi; ES), Social Insurance Fund (Sosyal Sigortalar Kurumu; SSK), Social Solidarity Fund (Sosyal Dayanisma Fonu) and Bağ-Kur (insurance fund for self employed) are the major public health care providers in Turkey, and the patients are assessed according to these health care providing organizations.

Statistical evaluation

Age and the time from the beginning of symptoms to the diagnosis of cancer were calculated as mean and standard deviation. The clinicopathological characteristics of disease and demographics of patients were compared among six geographical regions: The Marmara Region (MR), The Mediterranean Region (MTR), The Central Anatolia Region (CAR), The Black-Sea Region (BSR), The Eastern-Anatolia Region (EAR), and The Southeastern-Anatolia Region (SAR). Then, the patients were divided in two subgroups as Western Turkey (WT) consisted of MR, MTR and CAR and Eastern Turkey (ET) consisted of BSR, EAR and SAR. Again, the clinopathological features of disease and the demographics of patients were compared between WT and ET. Chi-square, Spearman's correlation, logistic regression, and one-way ANOVA tests were used for statistical comparison of the groups.

RESULTS

Questionnaires for 993 patients with gastric cancer diagnosed during 2004, from 16 centers, were evaluated. Twenty two questionnaires were excluded since the data for these patients have been duplicated. Thus, the analysis included 971 patients.

Table 1
Patients' characteristics

	n
Gender, n (%)	
Male	643 (66.2)
Female	328 (33.8)
Mean age, years (±SD)	56.83 (13.69)
Mean time from BSD, months (±SD)	4.28 (10.89)
Resectability	
Resectable, n (%)	468 (54.1)
Unresectable, n (%)	399 (45.9)
Not reported	104
Socioeconomic status	
Low, n (%)	182 (39.2)
Medium, n (%)	261 (56.3)
High, n (%)	21 (4.5)
Not reported	507
Health care insurance	
ES, n (%)	188 (28.3)
SSK, n (%)	244 (56.3)
Social Solidarity Fund, n (%)	126 (19.0)
Bağ-Kur, n (%)	89 (13.4)
Other, n (%)	17 (2.6)
Not reported	307
Living place	
City center, n (%)	587 (67.3)
Rural area, n (%)	285 (32.7)
Not reported, n (%)	99
Smoking	
Yes, n (%)	347 (48.7)
No, n (%)	365 (51.3)
Not reported	259
Alcohol consumption	
Yes, n (%)	56 (12.8)
No, n (%)	383 (87.2)
Not reported	532
Anemia	
Present, n (%)	456 (62.4)
Absent, n (%)	275 (37.6)
Not reported	240
Location of gastric cancer	
Distal, n (%)	324 (39.0)
Middle, n (%)	303 (36.5)
Upper, n (%)	204 (24.5)
Not reported	40
Histology	
Adeno, n (%)	687 (79.1)
Ring cell, n (%)	144 (16.6)
Dedifferentiated, n (%)	11 (1.5)
Other, n (%)	24 (2.8)
Not reported	103
Atrophic gastritis	
Present, n (%)	91 (19.7)
Absent, n (%)	350 (80.3)
Not reported	510
H. pylori gastritis	
Present, n (%)	86 (27.2)
Absent, n (%)	230 (72.8)
Not reported	655
Intestinal metaplasia	
Present, n (%)	121 (24.9)
Absent, n (%)	367 (75.1)
Not reported	483
Empirical treatment for ulcer	
Yes, n (%)	226 (50.6)
No, n (%)	220 (49.4)
Not reported	525

SD: Standard deviation; BSD: from beginning of symptoms to cancer diagnosis; ES: Retirement Fund (Emekli Sandığı); SSK: Social Insurance Fund (Sosyal Sigortalar Kurumu); Bağ-Kur: insurance fund for self employed

Patient characteristics

Six hundred forty three of the 971 patients were male, (male-female ratio: 2/1), the mean age was 57±12.99 years, and 67.3% of the patients were living in urban and 32.7% were living in rural areas. About three forth of the patients had low socioeconomic status. Smoking and alcohol consumption rates were 48.5% and 13.6%, respectively. Anemia was present in 62.4% of the patients before the diagnosis of the malignancy. Most of the tumors were located in distal and middle stomach (distal 39%, middle 36.5% vs. proximal 24.5%). Three hundred sixteen patients had been evaluated for *H. pylori* gastritis and 86 (27.2%) were *H. pylori* positive. Approximately, half of the patients had the history of empirical ulcer treatment. The mean time from the beginning of the symptoms to the diagnosis was 4.28±10.89 months. The resectability rate for the disease was 54.1%. The demographic information for the patients is summarized in table 1.

Evaluation of the patients by geographical regions

Approximately half of the patients were from CAR. There was no difference in the rate of smoking history, location of the tumor and presence of intestinal metaplasia among geographical regions. The characteristics of the patients according to geographical regions were summarized in table 2.

The mean age of patients at diagnosis in SAR were smaller than those in other geographic regions (53.85±10.59 years vs. 62.64±13.62 years, p=0.0001). The resectability rate of the patients in EAR group and SAR group (21.8% and 39.2%, respectively) was found to be lower than other groups (p=0.0001). The mean time from the beginning of symptoms to the diagnosis of gastric cancer in MR group and in MTR group, which were longer than in other groups, were 8.56±15.71 months and 8.43±14.19 months, respectively (p=0.005).

The SAR group had more patients from the low socioeconomic status (p=0.0001). The majority of patients both in EAR group and in SAR group had Social Solidarity Fund as health care provider (p=0.00001). Living in rural area was more common in BSR group and in SAR group than in other groups (p=0.00001), and the alcohol consumption was more common among the patients in MR group and MTR group (23.5%), when compared with those in other groups (p=0.0001).

Anemia had been more frequently detected in MR group (70.7%, p=0.015). While signet ring cell adenocarcinoma was the most common histology in MR group (34.3%), adenocarcinoma was the most common histology in SER group (94.2%) (p=0.001). The rate of atrophic gastritis were higher in MTR group (50%) and in MR group (30.8%) (p=0.003). The frequency of H. pylori infection was the highest in CAR group (12.1%) (p=0.003). The empirical ulcer treatment before the diagnosis of cancer was more commonly employed in EAR group (85.3%) and SAR group (85.2%) when compared with other groups (p=0.0001).

The Comparison of Western Turkey with Eastern Turkey

There was no statistically significant difference in gender, age, smoking, anemia, location of the tumor, and frequency of the atrophic gastritis between two groups. The time from beginning of symptoms to the diagnosis was longer in WT group than in ET group (6.98 months vs. 4.24 months, p=0.0001). In addition, the rate of tumor resectability was higher in WT group than ET group (63.4% vs. 31.6%, respectively, p=0.0001). The empirical ulcer treatment was more commonly employed in ET group than in WT group (52.4% vs. 78.2%, p=0.0001). However, smoking rate was not different in both groups (48.6% vs. 49.2%, p=0.932), and alcohol consumption was more common in WT group (15.5% vs. 6.9%, p=0.043).

Socioeconomic status, health care providers and living area

SSK was the most common health care provider among the patients living in cities (36.8%, p=0.0001). Socioeconomic status was lower in ET group when compared with WT group (53.6% vs. 32.3%, p=0.0001). As a health care provider, the Social Solidarity Fund was more common among patients living in rural area, and in ET group than in WT group (45.1% vs. 9.1%, p=0.0001, and 54.4% vs. 24.0%, p=0.00001, respectively).

Location of tumor, histology, atrophic gastritis, intestinal metaplasia and H. pylori infection

Although the incidence of proximal tumors were higher in WT group, the difference was not statistically significant (26.9% vs. 20.9%, p=0.201). Signet ring cell carcinoma were significantly more common in WT group compared with ET group (19.0% vs. 12.6%, p=0.003). There was not significant difference in the rate of atrophic gastritis between two groups (21.7% vs. 13.9%, p=0.070). However, H. pylori infection and intestinal metaplasia were more common in ET group (75% vs. 40.5%, p=0.003, and 68.4% vs. 18.1%, p=0.0001, respectively).

Table 2
Characteristics of the patients according to six geographical regions

	Marmara	Mediterranean	Central Anatolia	Black-Sea	Eastern Anatolia	Southeastern Anatolia	P value
Gender, n (%)							
Male	120 (66.3)	36 (62.1)	276 (68.3)	70 (55.6)	85 (70.8)	56 (68.3)	0.111
Female	61 (33.7)	22 (37.9)	128 (31.7)	56 (44.4)	35 (29.2)	26 (31.7)	
Mean age, years	56.83	59.33	56.96	62.64	58.28	53.85	
(±SD)	(13.69)	(14.04)	(12.87)	(13.62)	(11.17)	(10.59)	0.0001
Mean time from							
BSD, months (±SD)	8.56	8.43	6.15	2.19	5.31	4.28	
	(15.71)	(14.19)	(10.31)	(1.59)	(6.30)	(10.89)	0.005
Resectability, %	59.7	76.7	63.6	41.8	21.8	39.2	0.00001
Socioeconomic status, %							
Low	43.2	20.5	32.5	23.9	42.9	75.3	
Medium	46.0	76.9	61.2	76.1	53.6	24.7	
High	10.8	2.6	6.3	0	3.5	0	0.0001
Health care insurance, %							
ES	41	31.6	31	22.6	14.5	8	
SSK	49.3	47.4	36.7	9.7	15.8	40	
Social Solidarity Fund	0.7	2.6	14	0	57.9	50.7	
Bağ-Kur	2.1	15.8	16.3	67.7	11.8	1.3	
Other	6.9	2.6	2	0	0	0	0.00001
Living place, %							
City center	87.4	57.1	73.6	32	46.7	52.7	
Rural area	12.6	42.9	26.4	68	53.3	47.3	0.00001
Smoking, %	51.4	56.7	46.7	56.8	48.5	42.5	0.623
Alcohol consumption, %	23.5	23.5	8.8	13.6	1.9	11.5	0.0001
Anemia, %	70.7	39.5	61.1	56.5	64.5	64.3	0.015
Location of gastric cancer, %							
Distal	36.3	54.3	36.5	44.0	41.3	41.7	
Middle	44.0	29.6	33.5	35.2	35.6	41.7	
Upper	19.7	17.1	30.0	20.8	23.1	16.6	0.062
Histology, %							
Adeno	60.8	75.5	82.9	74.6	94.2	70.9	
Ring cell	34.3	15.1	15.5	15.1	3.3	22.8	
Undifferentiated	2.9	3.8	0.8	4.0	0	0	
Other	2.0	5.6	0.8	6.3	2.5	6.3	0.001
Atrophic gastritis, %	30.8	50	16.2	NR	13.9	14.3	0.003
H. pylori gastritis, %	40.5	75	12.1	NR	69.2	60	0.003
Intestinal metaplasia, %	25.8	25	24.1	NR	20.4	47.8	0.162
Empirical treatment, %	52.4	30	44.1	NR	85.2	85.3	0.0001

SD: Standard deviation; BSD: from beginning of symptoms to cancer diagnosis; ES: Retirement Fund (Emekli Sandığı); SSK: Social Insurance Fund (Sosyal Sigortalar Kurumu); Bağ-Kur: insurance fund for self employed

Table 3
Characteristics of the patients residing in western and eastern Turkey

	Western Turkey	Eastern Turkey	P value
Gender, n (%)			
Male	432 (67.2)	211 (64.3)	
Female	211 (32.8)	117 (35.7)	0.374
Mean age, years (±SD)	57.14	58.80	
	(13.21)	(12.47)	0.093
Mean BSD, months (±SD)	6.98	4.24	
	(12.35)	(4.84)	0.0001
Resectability, %	63.4	31.6	0.0001
Socioeconomic status, %			
Low	32.3	53.6	
Medium	61.3	45.7	
High	6.4	0.7	0.0001
Health care insurance, %			
ES	34.0	13.2	
SSK	41.3	24.7	
Social Solidarity Fund	9.1	45.1	
Bağ-Kur	12.0	17.0	
Other	3.5	0	0.0001
Smoking, %	48.6	49.2	0.932
Alcohol consumption, %	14.5	6.9	0.043
Anemia, %	62.3	62.7	0.933
Location of gastric cancer, %			
Distal	37.5	42.2	
Middle	36.3	36.9	
Upper	26.2	20.9	0.201
Histology, %			
Adeno	78.0	81.0	
Ring cell	19.0	12.6	
Dedifferentiated	1.5	1.5	
Other	1.5	4.9	0.003
Atrophic gastritis,%	21.7	13.9	0.070
H. pylori gastritis,%	40.5	75	0.003
Intestinal metaplasia, %	18.1	68.4	0.0001
Empirical treatment, %	52.4	78.2	0.0001

SD: Standard deviation; BSD: from beginning of symptoms to cancer diagnosis; ES: Retirement Fund (Emekli Sandığı); SSK: Social Insurance Fund (Sosyal Sigortalar Kurumu); Bağ-Kur: insurance fund for self employed

Univariate analysis revealed that the rate of resectability was significantly higher in distally located gastric tumors than the other locations (41.7% in distal tumors, 36.6% in middle tumors and 21.7% in upper tumors, p=0.053). The resectability rate was lower in the patients with atrophic gastritis, intestinal metaplasia, or H. pylori infection (19.8%, p=0.0001, 24.6%, p=0.001, and 27.0%, p=0.0001, respectively). The incidence of anemia was higher in distal tumors (62%, p=0.011), and lower in the patients with atrophic gastritis (23.4%, p=0.030). Also, the rate of empirical ulcer treatment was lower among the patients with H. pylori infection (19.1%, p=0.007), atrophic gastritis (26.0%, p=0.010) and intestinal metaplasia (26.1%, p=0.009) when compared with other clinicopathological features.

DISCUSSION

Our findings showed that resectability of distally located gastric tumors and tumors in patients residing in Western part of Turkey, with high socioeconomic status, and without H. pylori infection and atrophic gastritis were higher; whereas sex, age, smoking, alcohol consumption, time from the beginning of the symptoms to the diagnosis of cancer, and empirical ulcer treatment were not associated with cancer resectability. We also found that resectability rate of gastric cancer, which is associated with better prognosis, was lower in Eastern Turkey than in Western Turkey (63.4% vs. 31.6%, p=0.0001). Furthermore, the high frequency of empirical ulcer treatment in ET group was another important finding (78.2% vs. 52.4%). Mainly, low socioeconomic status and Social Solidarity Fund as health care provider may be responsible for the lower resectability rate of gastric cancer in ET, due to insufficient health care. However, in western countries and in Japan, the resectability rate of gastric cancer has been exceeded 70% (1).

Worldwide, the incidence of gastric cancer starts to rise approximately at age 40, and rises progressively with the advancing age. The male-female ratio is 2.1 (1,2). In our study, the mean age (57±12.99 years) and sex ratio (approximately 2/1) of the patients were similar to western countries.

Gastric cancer remains one of the leading causes of cancer death in the world (1). Although the precise etiology is unknown, many risk factors were defined for the development of gastric cancer. H. pylori infection which is associated with low socioeconomic status, advanced age, male gender, less fruit and vegetable consumption, the high consumption of salted and preserved foods, chronic atrophic gastritis, intestinal metaplasia, pernicious anemia, adenomatous polyps, family history of gastric cancer, smoking, Menetrier's disease and familial adenomatous polyposis were the reported risk factors in the development of gastric cancer (14-18). In western countries, the decrease in gastric cancer incidence has been largely attributed to the use of refrigeration, and to better control of H. pylori infection in childhood.

Some studies have shown that H. pylori is associated with the development of the important precursor lesions for the development of gastric cancer, including chronic gastritis, atrophic gastritis, and intestinal metaplasia, therefore it is the major risk factor for non-cardia gastric cancers (14,19). Nevertheless, it has been known that the majority of H. pylori-positive individuals never develop gastric cancer. There may be many factors for the explanation of this topic, such as the characteristics of colonizing H. pylori strains, the genotype of the host, and exposure to environmental co-factors (e.g. diet). It has been reported that incidence of H. pylori infection in adult population of Turkey exceeds 80% (15).

In this retrospective study, the information about H. pylori infection was reported for only one third of the patients. Sixty percent of the patients were inoperable and only endoscopic biopsies or biopsies from the metastatic regions were obtained and these patients could not be assessed for H pylori infection. However, we found that the frequency of H. pylori infection was higher in ET than in WT (78.2% vs. 52.4%, respectively) for the reported patients.

The location of gastric cancer has changed from distal to more proximal over recent decades. While the incidence of distal gastric cancer has been decreasing in the western countries, the incidence of proximal gastric cancer (cardia and gastro-esophageal junction) has been rapidly rising (20,21). In our study, the frequency of upper gastric cancer was found to be 26.2% and 20.9% in WT and in ET, respectively, but the difference is not significant.

Although our study is retrospective and has some defect in nature, it is informative. Since gastric cancer is one of the important public health problems, it is obvious that there is a need for well-designed, controlled, and multicenter studies to establish the causes and the major risk factors in the development of gastric cancer. Therefore, we have started a prospective, multicenter, case-controlled study supported by TOG in Turkey, in January 2005.

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