

RESEARCH ARTICLE

Clinicopathological Features and Localization of Gastric Cancers and their Effects on Survival in Turkey

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Abstract

Background: This study was designed to examine changing trends in localization of gastric cancer in Turkey in recent years. **Materials and Methods:** A total of 796 adult patients with newly diagnosed, histologically proven adenocarcinomas, treated and followed up at our oncology center between 2000-2011, were examined retrospectively. In all cases tumor localization were identified and recorded with clinicopathological features. **Results:** The median age was 58 with a range between 22-90 for the 552 men and 244 women. Median follow up was 12 months (1-276) and median overall survival was also 12 months (11.5-12.4). There was a trend for a change in tumor localization from distal to proximal. Survival of patients was low with advanced T and N stage tumours. Positive surgical margins, lymphovascular invasion, perineural invasion, cardioesophageal localization were predisposition factors for metastatic disease in gastric cancer. There was no relation between age or sex and histopathological type of gastric cancer. **Conclusions:** There is a trend in our country for a change in gastric tumour localization from distal to proximal, with clear significance for treatment choices.

Keywords: Gastric cancer - localization - proximal - treatment choices

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Introduction

Despite the improvement of combined modality treatment of gastric carcinoma in recent years outcome is still poor which is depended upon patient, tumour localization and factors related with treatment. The incidence of adenocarcinoma arising at esophagogastric junction (OGJ) and lower esophageal carcinoma has increased recently whereas the global incidence of gastric cancer is declining. Junctional tumors are associated with adverse prognosis compared with other esophageal and gastric cancer. The anatomical site of these tumors potentially allows tumor spread to the lymph nodes located above or below the diaphragm leading to difficulties in staging and controversies in the optimal surgical strategy for these patients. The treatment choices of gastric cancer complete resection and if indicated chemoradiotherapy is used and for metastatic disease chemotherapy and palliative treatment is used. On going studies on neoadjuvant treatment of gastric cancer have not yet been completed.

There studies indicated that patient with early stage tumors underwent surgery alone and patients with locally advanced disease (T3/4, N0/1) were offered adjuvant chemoradiotherapy at INT 0116 study that includes 556 patients and they are randomized two group; one of them

randomized to adjuvant treatment other is surgery only, five year follow up and survival rate 50% and 41% respectively (HR:1.35). Although many research on gastric cancer, INT0116 gives us the standart treatment of gastric cancer.

Cunningman et al presented that neoadjuvant treatment of gastric cancer. Magic trial is the most important research has shown survival advantages of neoadjuvant treatment compared to surgery alone.

Materials and Methods

A total of 796 adult patient with newly diagnosed, histologically proven adenocarcinoma were treated at our oncology center between 2000-2011 and they are examined retrospectively. Unknown tumor localization of gastric cancer is not included in this study. Our patients include 552 men and 244 women. Patient age range between 22 and 90 median 58 years. Some of the details of our patients for our statistical evaluation such as age, sex, symptoms at diagnosis, localization of tumor, information on operation, histopathological feature, stage TNM 2010 AJCC, desicion of treatment, site of metastasis, level of previous tumor marker, present of adjuvant radiation, overall survival of according to localization, overall survival (OS) was evaluated. Tumor localization

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was recorded for every patient between 2000 and 2011. Relationship between tumor localization and survival was shown.

Statistical analysis

Statistical analyses were made with SPSS for Windows ver. 15.0 (standard version) program package. Quantitative (numerical) data as mean±standard deviation (SD) were carried out. For two-group comparisons were used paired Student's t-test or when necessary Mann-Whitney U test. For the non-numeric data, when suitable for 2x2 contingency tables, Yates' corrected chi-square test and Fisher's exact test were used. Analysis of correlations between numerical parameters was made with Spearman (rho) correlation test. For the comparison of group Student's t-test or when needed one-way or multi-factor analysis of variance (ANOVA) was used.

Results

Our patients median age 58 years (22-90), men 552 (69%) women 244 (31%). Tumor localization of gastric cancer antrum&pylorus 362 (45.4%), body of stomach 252 (31.6%), cardia esophageal junction 97 (12.2%), diffuse 9 (1.1%) respectively. The most common symptoms and signs at presentation were dispepsi (39.3%), abdominal pain(24,8%), nausea and vomiting(16,3%), weight loss (7.5%), bleeding(6,4%), acute abdomen(1,6%). Median follow up of 12 months(1-276) and five year overall survival 11%. Overall survival curve is shown at Figure 1 and survival curve according to localization is shown Figure 2. Median survival for stage I patient was 92 months, while it was ten months for metastatic patients, this difference was statistically significant(p<0.0001). Demographic results of 796 gastric cancer patients were

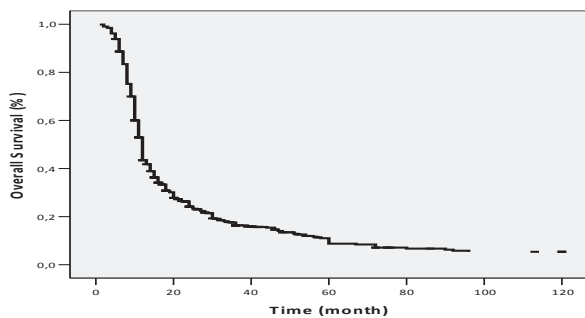


Figure 1. Overall Survival in Gastric Cancer

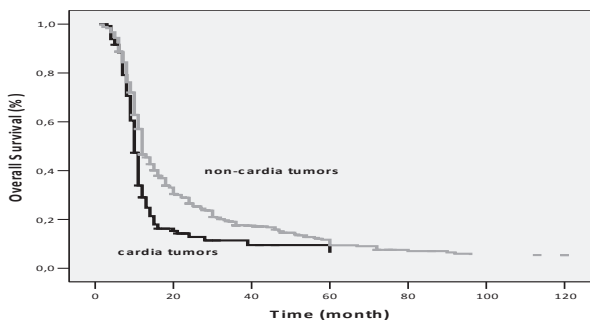


Figure 2. Overall Survival According to Gastric Localization

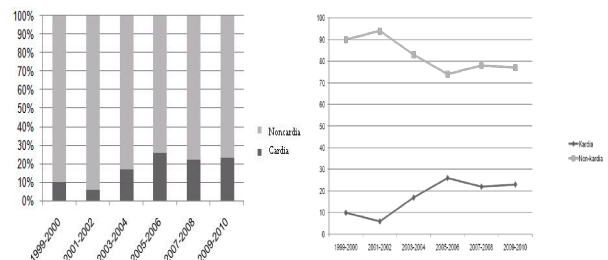


Figure 3. Gastric Cancer Localization in Turkey According to Years

Table 1. The Demographic Data of 796 Patients with Gastric Cancer

Age	Median	58 (22-90)
Sex	Male	552 (69%)
	Female	244 (31%)
Median follow-up time 12 months (range: 1-276 months)		
Median survival 12 months (range: 11.5-12.4 months)		
Tumor placement		
	Pyloric+antrum	362 (45.4%)
	Large and small curvature	252 (31.6%)
	Cardio-oesophageal	97 (12.2%)
	Diffuse	9 (1.1%)
Stage	Stage I	29 (3.6%)
	Stage II	43 (5.4%)
	Stage III	195 (24.5%)
	Stage IV	393 (49.3%)
The type of surgery		
	Total gastrectomy	265 (33.2%)
	Subtotal gastrectomy	174 (21.8%)
	Inoperable / palliative	341 (42.8%)
Treatment	Adjuvant	352 (44.2%)
	Metastatic	394 (49.4%)
Histology	Untreated follow-up	50 (3.9%)
	Adenocarcinoma (intestinal type)	493 (61.9%)
	Signet ring cell (diffuse)	254 (31.9%)
	Neuroendocrine	24 (3%)
	Others	8 (1.1%)
In metastasis	Peritonitis carcinomatosa	193 (24.2%)
	Liver	169 (21.2%)
	Lymphadenopathy	73 (9.2%)
	Liver + peritoneum	35 (4.4%)
	Lung	28 (3.5%)
	Pleural effusion + acid	24 (3%)
	Bone	23 (2.9%)
	Others	17 (2.1%)
Recurrence in	Peritonitis carcinomatosa	61 (40.1%)
	Liver	36 (23.7%)
	Lymphadenopathy	24 (15.8%)
	Local	4 (9.2%)
	Pleural/lung	12 (7.9%)
	Others	5 (5%)

shown Table 1. Look at the evaluation of anatomic site of gastric cancer, the cardia tumor incidence was seen higher from 2000-2011 (Figure 3a, b).

Discussion

This study show that incidence of esophagogastric cancer, tumor localization, histological subtypes, and main purpose of this study are there any differences tumor localization during years (between 2000 and 2011) and

effect on prognosis in Turkey.

It is known that proximal site of tumor's lymphatic drainage different behavior than distal site of gastric tumor. There is lots of study related with proximal site of tumor and its prognosis. Talamanti et al. (2003), suggested proximal gastric cancer has a worse prognosis than distal gastric cancer because of insidious symptoms result delay of diagnosis, deep invasion, high incidence of lymph node metastasis. It was shown that the localization of disease move towards proximal part of stomach especially in caucasian which associated with poor prognosis (Powell and McConkey, 1990; Harrison et al., 1997). Depth of invasion, lymph node metastasis, present of distant metastasis were also shown to be associated with poor prognosis in some studies (Harrison and Fielding, 1995). Study by Ding et al. (2004) has shown lymph node metastasis was the most important factors in gastric cancer (Ding et al., 2004). Furthermore maruyama et al has shown depth of invasion, lymph node metastasis, macroscopic type, localization of tumors, histological type important prognostic factors in a series of 4,734 patients. Although no relationship between number of dissected lymph nodes, nodal stage affectes outcome of survival.

In our study we found that proximal site of gastric cancer has a poor prognosis than distal also their localization move towards proximal gastric stomach and marked increasing proximal site has been observed since 2000 in present series. Extended gastrectomy, D2 dissection and splenectomy is required for proximal gastric cancer which results high risk of complication, mortality rate.

Junctional tumors are associated with adverse prognosis compared with other esophageal and gastric cancers. the anatomical localization of these tumors potentially allows tumor spread to lymph nodes located above and below the diaphragm leading to difficulties in staging classifications and controversies in the optimal surgical strategy for these type of patients (Siewert et al., 2000; Peters et al., 2009). Our patients have got same problems because of its localization. In that site high lymphatic and hematogenous drainage of cardia tumors; high lymphatic metastasis and systemic recurrence is higher than other site in the literature (Aikou and Shimaza, 1989). The overall poor prognosis reported for patients with cardia tumor in combination with the relatively higher rates of systemic recurrence are strong arguments for wider use of adjuvant treatments for these patient. the adverse prognosis associated with junctional tumors has been reported by higher tumor grade, more advanced disease stage, increased rates of lymphatic and blood vessel invasion, increased lymph node metastases (Saito et al., 2006). In our study there is no relation between prognosis and tumor localization, tumor grade, lymphovascular and perineural invasion, number of metastatic lymph nodes.

The main risk factor of gastric cancer, namely, cardia tumor; include smoking, gastro-oesophageal reflux, obesity and the presence of Barrett's oesophagus and sex. Despite the fact that the etiology of these groups of cancer is insufficiently (Dolan et al., 1999; Rusch, 2004). Understood and the question of whether these cancers represent just one or two distinct entities continues to be

an open issue of discussion (Aragone' et al., 2010; Julian et al., 2012). In our series there was a tendency towards proximal localization in patients those have smoking, long duration of alcohol consumption, obesity, gastroesophageal reflux disease. But there is no statistical significances. It is known that h.pylori is a mainly risk factors of distal gastric cancer. H.pylori increase the risk of gastric cancer six times. Eradication of h.pylori infection results decrease incidence of distal gastric cancer (Huang et al., 1998; Jézéquel et al., 2010). Epidemiological studies investigating relationship between h.pylori and incidences of gastric cancer are lacking in our country. Also we were failed to show any relation between H.pylori and gastric cancer in our series.

Briefly the rising incidences of gastro-oesophageal cancer in the USA, Australia and New Zealand, Europe and Singapore but no such trend was found in Hong Kong and Taiwan (Botterweck et al., 2000; Bouvier et al., 2004; Van Blankenstein et al., 2007; Deans et al., 2011). The results of our study show that beside heterogeneity in trends among continents, our study results is consistent with trends of increasing incidence of cardia tumor of stomach.

As a results tumor localization of gastric cancer has been changed according to epidemiological factors. This should be considered before diagnosis and treatment. Changing tumor localization in gastric cancer needs to be studied in terms of new treatment strategies such as neoadjuvant chemoradiotherapy or chemotherapy.

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