Unfavorable Survival Rates in Iranian Patients with Gastric Cancers:
A Single Center Experience from Tehran

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Abstract- We examined the effect of potential interfering factors that play major roles in the outcome of our patients with stomach cancer. 100 consecutive patients diagnosed with gastric cancers were prospectively observed, treated and followed from November 2009 to January. Absence of *Helicobacter pylori* infection (P=0.027), absence of vascularisation (P<0.001), and undetermined histopathological type of adenocarcinoma (P=0.003) were factors significantly associated with higher grade of gastric lesions. Life tables were used to define survival of gastric cancers. Survival rates of these patients at 1st week, 1st month, 2nd month, 3rd month, and 6th month were 97%, 96%, 91%, 90%, and 82%, respectively. The only determinant of 6 months of survival was age over 68 (P=0.039). Our study confirms our previous knowledge that gastric cancers have unfavorable outcome in Iran.
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Introduction

Gastric cancer is the fourth most common malignancy in the whole globe with an incident rate of about one million a year (1). It is a disease with a high death rate (738,000 per year) making it the second most common cause of cancer death worldwide after lung cancer, according to a report by WHO (2). It is more common in men and in developing countries (1,3).

The important thing about the gastric cancer is the time of diagnosis. This malignancy, unfortunately, has a sneaky behavior with almost no sign and symptoms presenting at the early stages of the disease. Metastasis occurs in a large majority of patients leading to a six month survival rate of 70% in those diagnosed in early stages and less than 25% of patients diagnosed in later stages (4). So, the key point in the management of gastric cancer is the stage of the disease within which the treatment starts. In Japan, a majority of patients with gastric cancer are diagnosed in their early stages, before the disease penetrates the muscular layer of the gastric wall, and radical surgery results in about 90% cure rate of the disease. But this is not a global observation.

In Iran, gastric cancer has been responsible for highest rate of cancer incidence among Iranian males, reported by either national reports or regional ones (5,6). This malignancy has also been accused as the leading cause of mortality due to cancers, with a far large gap from other neoplasms, both in the Iranian males and females (7). This is not surprising news, while we know that in most regions of the world, it is responsible for lesser cancer morbidity and mortality. But the reason behind this disparity is not known. Although one may presume that the high mortality rate of gastric cancer in Iran is related to diagnosis at later stages, due to ethnic specificities in the behavior of the disease, it is possible that the cancer have a more aggressive manner in the Iranian ethnic group.

In the current study, we report our series of gastric cancer that were diagnosed and treated at our department, and we try to examine effects of potential interfering factors playing major roles in the mortality of patients with stomach cancer in our Iranian patient population.

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Materials and Methods

Patients

This cohort study was conducted prospectively in the out-patient and in-patient Department of Gastroenterologys and Hepatology at Baqiyatallah University of Medical Sciences. Overall, 100 consecutive patients, who were diagnosed with gastric cancers in our department from November 2009 to January 2012 were enrolled into the study. There were 63 (63%) males and 47 (47%) females. Mean ± SD age of patients was 63.6 ± 12.6 years.

Diagnosis

Diagnosis was based on endoscopic biopsy and histopathological evaluations, in all the patients. Actually, the diagnosis of gastric cancer was performed by initial endoscopy and biopsy in 91 patients (91%), and by an initial barium meal and then endoscopy and biopsy in 9 cases (9%). In 17 (17%) patients repeated biopsies were performed for confirmation of the diagnosis of carcinoma.

Surgical intervention

Of the 73 operations, 46 (63%) were carried out by consultants and 27 (37%) by professors or lecturers. The standard surgical approach included wide gastric resection with radical (R2) lymphadenectomy, in which the second tier of lymph nodes (N2), beyond the perigastric nodes (NI), was removed. In a few patients, a less radical procedure was still performed if such radical surgery was judged inappropriate on account of the patient's advanced age or serious associated disease. All total gastrectomy procedures were accompanied by Roux-en-Y reconstruction with a 40-50 cm Roux loop of jejunum, to keep bile and pancreatic juices out of the oesophagus and respiratory tract. Polya reconstruction was normally used after subtotal gastrectomy.

Pathology

Dysplasia is defined as histopathological evidence for neoplastic transformation of epithelial cells which is limited to the epithelium confined to the intact basement membrane. Carcinoma was diagnosed when tumours invaded the lamina propria or were through the muscularis mucosae (8).This includes a spectrum of enlargement, hyperchromasia, irregularity, and dysmorphism of nuclei, nuclear roundening and loss of polarity, increased mitotic activity with abnormal figures, decreased cellular mucin content, crowding, and stratification of the epithelial cells. Biopsy specimens

from stomach of the patients were fixed in buffered formalin and embedded in paraffin; then the sections were stained with haematoxylin and eosin and modified Giemsa techniques. All histological assessment was made by lecturers at the Department of Pathology of Baqiyatallah University of Medical Sciences, under supervision of the head of the department. To determine intraobserver variation in pathological assessments, the senior pathologist evaluated 20 of the included patients selected randomly from different follow up periods, which confirmed comparable judgments for the specimen of the study subjects.

Slides were coded in a random manner such that the pathologist was blinded to the identity of subjects, treatment assignment, and year at which biopsies were obtained. Specimen achieved from the antrum and corpus tissue were subjected to evaluation for *H. pylori* infection, intensity of either polymorphonuclear or mononuclear cells infiltrates, glandular atrophy, and intestinal metaplasia as stipulated by the updated Sydney system (Houston) (9). Each participant was given a histologic diagnosis that represented the most advanced grade seen at different sites of biopsy in the following descending order: cancer, dysplasia, intestinal metaplasia, and non-metaplastic gastric atrophy. Patients with chronic non-atrophic gastritis were excluded from the study, while their lesions were not cancerous or pre-cancerous.

Statistical analysis

SPSS vs. 17.0 (SPSS corp.; Chicago, Il, USA) was used for analyses. P-value below 0.05 was considered significant. Life tables and Kaplan-Meier methods have been used for survival analyses. Chi-square and Student's t-test were used where appropriate.

Result

The relationship between histopathological grading of gastric lesions and clinical and demographic factors is summarized in table 1. Absence of *H. pylori* infection (P=0.027), absence of vascularisation (P<0.001), and undetermined histopathological type of adenocarcinoma (P=0.003) were factors significantly associated with higher grade of gastric lesions.

None of the study variables were associated with metastatic disease defined by CT-scan evaluations. The only significant associate of gastric vascularisation in our patient population was histological grading of gastric cancers (Table 1).

Table 1. Associated factors to histopathological grading of gastric cancers in our patient population

Factors		Grading		*P*
		High (%)	Low (%)	
Age (yr)		63 ± 13	64 ± 12	0.664
Weight (kg)		67 ± 11	65 ± 12	0.661
Blood groups	**O**	16 (40)	24 (60)	
	A	18 (53)	16 (47)	0.338
	B	13 (76)	4 (24)	
	AB	8 (89)	1 (11)	
Type of adenocarcinoma	**Tubular**	1 (1)	0	
	Mucinous	2 (2)	0	0.003
	Signet ring	3 (3)	10 (11)	
	Undetermined	53 (60)	20 (22)	
Vascularisation positive		24 (35)	24 (75)	<0.001
Helicobacter pylori positive		20 (29)	17 (53)	0.027
Family history of gastric cancers		6 (9)	3 (9)	0.597
Abnormal CT scan		20 (29)	12 (37)	0.492

Life tables were used to define survival of gastric cancers. Survival rates of these patients at 1st week, 1st month, 2nd month, 3rd month, and 6th month were 97%, 96%, 91%, 90%, and 82%, respectively (Figure 1). The Kaplan-Meier method was used to define potential factors associated with patients' 6 month survival. Abnormal CT-scan also did not show a significant relation to patients' survival (*P*=0.667). Nor any significant influence were detected for the grading or staging of gastric lesions regarding survival of patients (*P*=0.772 and 0.696, respectively). Then we tried to find a relationship with patients' demographics. Gender was not a significant interfering factor (*P*=0.598); however, our efforts to find an age cut-off point to find a disparity in survival reached to *P*-value of 0.05 on age 67 years, and when the analysis was performed again at the cutoff of 68 years, we found a significant better 6 months survival for younger patients (*P*=0.039; Figure 2).

Discussion

This study was conducted to evaluate features, behavior and prognosis of gastric cancers developing in an Iranian population attending our Gastroenterology Clinic at Baqiyatallah Hospital, Tehran, Iran. Our series showed that Iranian patients with gastric cancers have unfavorable 6 months survival rate of 82%. This finding suggests that, unfortunately, gastric cancers in our district are diagnosed at advances stages of the disease, when few therapeutic procedures can be performed, and their results are unfavorable. This is in consistency to previous reports from Iran which suggests low survival rates for patients with gastric cancers in our country (10-12).

Regarding gastric cancers, the most prevalent regions in Iran are northern and northwestern provinces of the country. Ardebil province in northwest of Iran probably has the highest incidence of gastric cancers in the country. Similar to our study which showed almost two times larger incidence of the disease in men than in women (63% vs. 37%, respectively), comparable results have been reported from Ardebil where the incidence in men versus women was 49 vs. 25 in 100,000 population. This rate was 26 vs. 12 in East Azerbaijan province (13), 28 vs. 8 in Golestan (14), 10 vs. 5 in Kerman (15), 37 vs. 15 in Semnan (16), and 20 vs. 10 in Tehran (16). Due to the methodology of the current study, however, we are not able to provide an incidence rate for gastric cancers; but since we report our series from a single center experience, we believe that the gender make up in this study more or less mirrors that in the general population, while our patients are mostly from military personnel of Iran whose whole family members go under insurance. However, the gender bias in the incidence rates is almost comparable to population based study performed by Mohagheghi *et al*., in the same country region where they found almost twice rate of gastric cancers in females, in males (17).

In the current study, cardia section of the stomach was the predominated site of cancer with almost 33% of our patient population. This finding is also comparable to the previous reports. In Ardebil province, higher rates of gastric cardia rather than other gastric regions has been observed whose incidence was 26.4 and 8.6 for men and women, respectively (5). However, the epidemiology of the regional gastric involvement by cancers in Iran is different than that in Japan, where non cardia regions are the main sections in which cancers

develop. An interesting observation is that Khuzestan province of Iran which has a relatively low incidence of gastric cancers compared to other Iranian regions, also represents a predominated cancer involvement of non-cardia regions. In Tehran as well, a study has shown that the proportion of cancers developing in the proximal regions of the stomach is even increasing (18). It is speculated that a predominated involvement site of cardia section for gastric cancers can be related to higher incidence of oesophageal carcinomas in those regions. This observation in northern Iran confirms this conclusion, and the same relation has been reported from northern China, as well (19).

In the current study we did not find any significant relations between disease characteristics like grade, stage or site of involvement. This observation might be related to the short term of follow up, and it is possible that these factors put their effects in longer term periods. On the other hand, evaluating patient's demographics and their effect on their gastric cancer outcome, we found a significant poorer survival for patients older than 68 years. However, one may assume that due to the more advanced age and other complications they are overall at higher risk of death anyway (irrespective of their gastric cancer status). However, since the survival time evaluated is limited (6 months of follow up), besides admitting this rationale, we think that elderly might have more progressive disease while their immune system is also weakened in advanced ages.

In conclusion, our study confirms our previous knowledge that gastric cancers have unfavorable outcome in Iran. Undetermined type of adenocarcinoma is of higher histological grades than those of determined types; but higher vascularisation was associated with lower grades for the gastric lesions. Future prospective studies with population- or registry- based methodology are recommended for confirming our results.

Acknowledgement

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