RESEARCH ARTICLE

Lack of any Association between Season of Diagnosis and Survival of Gastric Cancer Cases in Kayseri, Turkey

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Abstract

Background: The influence of season of diagnosis on cancer survival has been an interesting issue for many years. Most studies have shown a possible association between seasonality and survival in some cancers. We aimed to investigate whether there is an association between season of diagnosis and survival in patients with gastric cancer. Materials and Methods: We reviewed retrospectively the files of 279 histologically proven gastric cancer patients. According to diagnosis date, the patients were grouped into 4 seasons of diagnosis groups, spring, summer, autumn, and winter. Results: There was no significant differences when the overall survival rates of the patients were compared according to the patients' season of diagnosis (p: 0.871). Median overall survival rates were 22.0 (14.5-29.5) months for the patients who were diagnosed in spring, 24.0 (12.4-35.6) for summer, 18.0 (9.96-26.0) for autumn and 21.0 (16.3-25.7) for winter. Median disease-free survival rates were 66.0 (44.1-68.1) months for the patients who were diagnosed in spring, 28.0 (17.0-39.0) for summer, 22.0 (0-46.4) for autumn and 23.0 (17.5-28.5) for winter. While the rate was best for the patients diagnosed in spring the differences were not statistically significant (p= 0.382). Conclusions: On the basis of the above results the season was not suggested as contributing to prognosis in gastric cancer cases in Kayseri, Turkey.

Keywords: Gastric cancer - season - survival - Kayseri - Turkey

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Introduction

Gastric cancer is one of the most common cancers worldwide, and the second leading cause of cancer-related mortality and rampant in several countries around the world (Kamangar et al., 2006; Herszenyi and Tulassay, 2010; Yasui et al., 2013). The cancer develops as a result of an accumulation of several endogenous and exogenous causes. Dietary factors and Helicobacter pylori infection are important exogenous causes for gastric cancer, while many genetic polymorphisms are found to be associated with predisposition to the development of the cancer (Yasui et al., 2013). Most patients with gastric cancer are symptomatic and already have advanced disease at the time of presentation. At diagnosis, approximately 50 percent have disease that extends beyond locoregional confines, and only one-half of those who appear to have locoregional tumor involvement can undergo a potentially curative resection (Mansfield, 2013) Advanced stage of the disease characterizes poor prognosis, with a reported 5-year survival rate of less than 30% (Eroglu et al., 2013).

The effect of season in which the cancers were diagnosed, on the outcomes of patients with cancer has been studied in several large epidemiologic studies (Lim et al., 2006; Roychoudhuri et al., 2009; La Par et al., 2011). In most of these studies it has been shown that winter months are associated with poorer prognosis that may be explained through the variations in the cutaneous production of vitamin D3. To the best of our knowledge, there is no study which investigates the effect of the season of diagnosis on prognosis in gastric cancer. We aimed to investigate whether there is an association between season of diagnosis and survival in patients with gastric cancer.

Materials and Methods

We reviewed retrospectively the files of 279 histologically proven gastric cancer patients. We recorded demographic data such as age and gender. T and N status and stage at diagnosis, the diagnosis date, tumour location and overall survival were also recorded. According to diagnosis date, the patients were grouped into 4 seasons of diagnosis groups as spring, summer, autumn, and winter.

Statistical analysis

Statistical analysis was performed using the SPSS 15.0 software (SPSSFW; SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. The Kolmogorov-Smirnov

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test was used to determine normality of distributions of variables. Continuous variables with normal distribution are presented as mean±SD. Qualitative variables are given as percent and the correlation between categorical variables was investigated using the chi-square test and Fisher's exact tests. Survival rates were estimated using the Kaplan-Meier method and the log-rank test was used for comparison of outcomes. A p value of <0.05 was considered significant.

Results

Table 1 shows characteristics of 279 patients with gastric cancer. Mean age was 59.92±12.29 (range, 27-85) years. One hundred and ninety-nine patients (71.3%) of 279 patients were male and the rest was female. The season of diagnosis was spring in 86, summer in 78, autumn in 60 and winter in 55 of the patients. The most tumour locations were corpus and antrum. Tumour grade was grade I in 16, grade II in 96, grade III in 164 and grade IV in 3 of the patients. T stages were detected as T1 in 8, T2 in 17, T3 in 159 and T4 in 77 of the cases. N status was N0 in 55, N1 in 69, N2 in 56 and N3 in 68 of the cases. Stage of cancer was found as stage I in 16, stage II in 56, stage III in 143 and stage IV in 64 of the patients. Surgical treatment was performed in the majority of the patients. Type of surgery was total gastrectomy for the most of the patients. Resection margin was negative in the majority of the patients. The majority of the patients received a chemotherapy regimen.

At the time of evaluation, 172 (61.6%) patients were exitus and 107 (38.4%) patients were alive. Median overall, disease-free, and progression-free survivals were 22.0 (18.05-25.96), 27.0 (16.92-37.08), and 7.0 (5.32-8.68) months, respectively (Figure 1).

The frequencies of tumour location, depth of infiltration, lymph node involvement, and stage according to the season of diagnosis are shown in Table 2. There was significant difference between tumour location and the season of diagnosis (p: 0.042). The majority of the patients with proximal region cancer were diagnosed in spring. The cases with cancer, which located in middle region of stomach, were more commonly diagnosed in summer. In the patients with distal region cancer, number of patients, in whom the cancer was diagnosed in spring, summer and winter, were quite similar. The majority of the patients with linitis plastica were diagnosed in spring and autumn. However, there were no significant differences for the frequencies of the season of diagnosis according to depth of infiltration, lymph node involvement, and stage (p: 0.593, p: 0.347, and p: 191, respectively).

There was no significant difference when the overall survival rates of the patients were compared according to the patients' season of diagnosis (p: 0.871). Median overall survival rates were 22.0 (14.47-29.53) months for the patients who were diagnosed in spring, 24.0 (12.44-35.57) for summer, 18.0 (9.96-26.04) for autumn and 21.0 (16.31-25.69) for winter (Figure 2).

Figure 3 shows the disease-free survival rates of the

Table 1. Characteristics of 279 Patients with Gastric Cancer

Characteristic		
Age (year)		59.92±12.29
Male/Female (%)		199 (71.3)/80 (28.7)
Status (Alive/Exitus)		107 (38.4)/ 172 (61.6)
Season of disease	Spring (%)	86 (30.8)
	Summer (%)	78 (28.0)
	Autumn (%)	60 (21.5)
	Winter (%)	55 (19.7)
Tumour location	Esophagogastric junction	5 (1.8)
	Cardia (%)	47 (16.8)
	Fundus (%)	1 (0.4)
	Corpus (%)	91 (32.6)
	Antrum (%)	87 (31.2)
	Pylorus (%)	25 (9.0)
	Linitis plastica (%)	23 (8.2)
Grade	I (%)	16 (5.7)
	II (%)	96 (34.4)
	III (%)	164 (58.8)
	IV (%)	3 (1.1)
Depth of infiltration	T1 (%)	8 (2.9)
	T2 (%)	17 (6.1)
	T3 (%)	159 (57.0)
	T4 (%)	77 (27.6)
Lymph node involvement	N0 (%)	55 (19.7)
	N1 (%)	69 (24.7)
	N2 (%)	56 (20.1)
	N3 (%)	68 (24.4)
Stage	I (%)	16 (5.7)
	II (%)	56 (20.1)
	III (%)	143 (51.3)
	IV (%)	64 (22.9)
Surgery treatment (Yes/No)		250 (89.6)/29 (10.4)
Type of surgery	Subtotal gastrectomy (%)	69 (24.7)
	Total gastrectomy (%)	250 (89.6)
	Palliative surgery (%)	13 (4.7)
Resection margin status	Negative (%)	197 /70.6)
	Microscopic positive (%)	46 (16.5)
	Macroscopic positive (%)	7 (2.5)
Chemotherapy	Yes (%)	203 (72.8)
	No (%)	66 (23.7)
	Palliative (%)	10 (3.6)

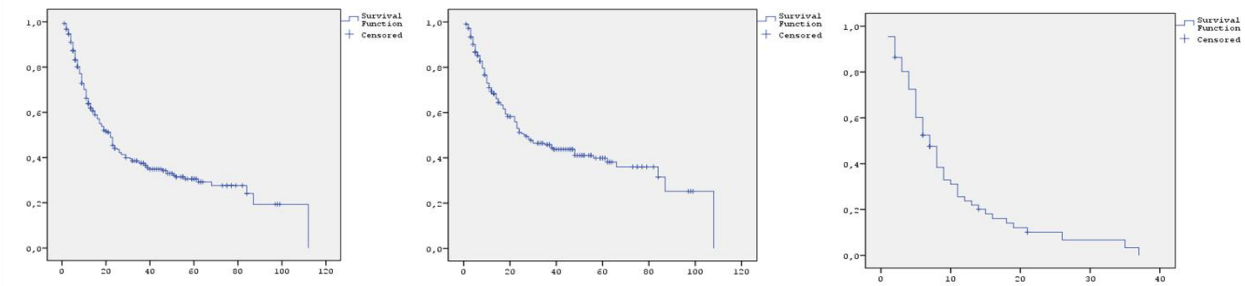

Figure 1. The Overall, Disease-Free, and Progression-Free Survival Rates of the Patients

Table 2. The Frequencies of Tumour Location, Depth of Infiltration, Lymph node Involvement, and Stage according to the Season of Diagnosis

	Spring	Summer	Autumn	Winter	p value
Tumour location					0.042
Proximal (%)	23 (43.4)	13 (24.5)	11 (20.8)	6 (11.3)	
Middle (%)	22 (24.2)	32 (35.2)	23 (25.3)	14 (15.4)	
Distal (%)	32 (28.6)	30 (26.8)	19 (17.0)	31 (27.7)	
Linitis plastica (%)	9 (39.1)	3 (13.0)	7 (30.4)	4 (17.4)	
Depth of infiltration					0.593
T1 (%)	2 (25.0)	2 (25.0)	3 (37.5)	1 (12.5)	
T2 (%)	6 (35.3)	5 (29.4)	3 (17.6)	3 (17.6)	
T3 (%)	45 (28.3)	52 (32.7)	29 (18.2)	33 (20.8)	
T4 (%)	23 (29.9)	16 (20.8)	23 (29.9)	15 (19.5)	
Lymph node involvement					0.347
N0 (%)	12 (21.8)	20 (36.4)	13 (23.6)	10 (18.2)	
N1 (%)	17 (24.6)	22 (31.9)	16 (23.2)	14 (20.3)	
N2 (%)	22 (39.3)	16 (28.6)	9 (16.1)	9 (16.1)	
N3 (%)	21 (30.9)	13 (19.1)	16 (23.5)	18 (26.5)	
Stage					0.191
I (%)	5 (31.2)	4 (25.0)	4 (25.0)	3 (18.8)	
II (%)	11 (19.6)	25 (44.6)	11 (19.6)	9 (16.1)	
III (%)	46 (32.2)	37 (25.9)	29 (20.3)	31 (21.7)	
IV (%)	24 (37.5)	12 (18.8)	16 (25.0)	12 (18.8)	

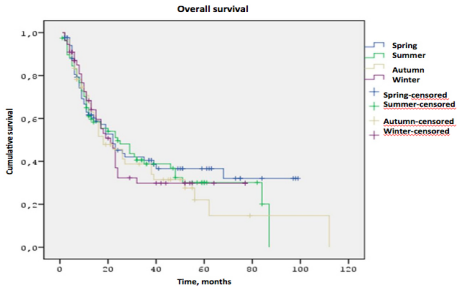

Figure 2. The Overall Survival Rates of the Patients According to the Patients' Season of Diagnosis

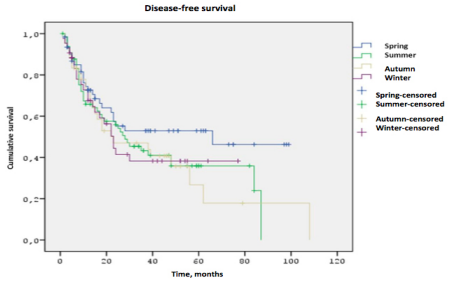

Figure 3. The Disease-free Survival Rates of the Patients According to the Patients' Season of Diagnosis

patients according to the patients' season of diagnosis. Median disease-free survival rates were 66.0 (44.08-68.08) months for the patients who were diagnosed in spring, 28.0 (17.03-38.97) for summer, 22.0 (0-46.36) for autumn and 23.0 (17.54-28.46) for winter. Median survival rates were better for the patients who were diagnosed in spring but the difference between disease-free survival rates according to the season of diagnosis was not statistically significant (p: 0.382).

Discussion

This study examined the association between season of diagnosis and survival rates in patients with gastric cancer. Overall, no association between season of diagnosis and survival rates was observed.

The frequency of gastric cancer is associated with several factors including ethnicity, genetic factors, infection with Helicobacter pylori that is crucial for the development of the disease (Zabaleta, 2012). The marked geographic variation, time trends, and the migratory effect on incidence of gastric cancer suggest that environmental factors or lifestyle changes play an important role in the development of the disease (Crew and Neugut, 2006). Dietary factors also contribute to the etiology of the disease. Prospective studies have reported that fruit and vegetable consumption results in significant decline in gastric cancer risk (Kobayashi et al., 2002). The other factors such as tobacco, obesity, radiation, and pernicious anemia also play a role in the development of the disease (Crew and Neugut, 2006).

Although the relationship between season of diagnose and cancer has been studied in some cancer types, such relationship was not evaluated in gastric cancer. In most of these studies it has been shown that winter months are associated with poorer prognosis that may be explained through the variations in the cutaneous production of vitamin D3 (Lim et al., 2006; Roychoudhuri et al., 2009; La Par et al., 2011).

Sunlight is essential for the cutaneous production of vitamin D. A number of epidemiological studies suggest that sunlight exposure, particularly as it relates to the vitamin D produced in the skin by sunlight, has a beneficial influence on cancer risk and outcome. A protective role of sunlight in cancer was first suggested by Alperly who proposed that increased mortality from cancer in the north than in the south of the USA might be due to the south to north decrease in ambient solar radiation (Apperly, 1941). Some in vitro and in vivo studies support that 1,25 (OH)2 vitamin D regulates cell differentiation and proliferation and exerts antiproliferative effects and this may explain the effects of season of diagnose on cancer prognosis (Ordonez-Moran et al., 2005).

Increasing evidence have suggested that risk of some cancers including colon and rectum, breast and prostate and non-Hodgkin lymphoma may be reduced in persons living in areas of high ambient solar radiation or with high sun exposure. For some of these cancers, particularly colorectal and, to a much less extent, prostate cancers, there is also evidence that high serum levels of vitamin D are associated with lower risk (Kricker and Armstrong B, 2006). On the other hand, such relationship between vitamin D and cancer risk was not shown in gastric cancer. Abnet et al have found that no overall association between circulating 25(OH)D concentration and risk of upper gastrointestinal cancers was observed in the combined analysis of 8 prospective cohorts and suggested that these results do not support the hypothesis that interventions aimed at increasing vitamin D status would lead to lower risk of gastric cancer (Abnet et al., 2010).

Sunlight may also improve the outcome of cancer. Robsahm et al have investigated the association between prognosis of breast, colon, and prostate cancer and vitamin D, induced from solar ultra-violet radiation. They have found that a significant variation in prognosis by season of diagnosis was observed. Diagnoses during summer and

autumn, the seasons with the highest level of vitamin D, revealed the lowest risk of cancer death (Robsahm et al., 2004). Porojnicu et al. have reported similar results for Hodgkin lymphoma (Porojnicu et al., 2005). Lagunova et al. have observed that patients with prostate cancer diagnosed during the summer and autumn had the best prognosis (Lagunova et al., 2007). Similarly, we have found that being diagnosed in spring was favorable prognostic factor for short term survival in advanced non-small cell lung cancer patients (Oguz et al., 2013). On the other hand, there are some studies, which did not show a relationship between season of diagnose and cancer survival. Mutlu et al. have evaluated that whether season is prognostic factor in patients with breast cancer and found no significant differences between seasons of diagnose in terms of overall survival (Mutlu et al., 2013).

In conclusion, our results suggest that no association between season of diagnosis and survival rates in patients with gastric cancer.

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