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Factors Affecting Survival Analysis In Non-Metastatic Operated Gastric Cancer Patients

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ABSTRACT

To determine the factors that may have prognostic significance by evaluating the clinical data of patients with non-metastatic operated gastric cancer during diagnosis and to determine the effect of these prognostic factors on survival.
The records of 109 non-metastatic (Stage I-III) and operated for gastric cancer between January 2013 and November 2017 were retrospectively reviewed. Gender, age, Eastern Cooperative Oncology Group performance score of patients (ECOG PS), tumor's location, macroscopic appearance, histological subtype, invasion depth (pT), metastasis on the lymph node (pN), stage (TNM), and its lymphatic, perineural and vascular invasion conditions were evaluated in terms of prognostic significance and their effects on survival.
68 of the cases were male, 41 of them were female and the mean age was 58.81 (24-81). In our patients' clinical staging, there were 15 patients in Stage 1, 36 of them in Stage 2, 58 of them in Stage 3. The disease-free survival time was 79 months in Stage 1 cases, 27 months in Stage 2 cases and 17 months in Stage 3 cases. When the data of the patients were analyzed by univariate analysis, pT ($p = 0.003$), pN ($p = 0.004$), stage (TNM), ($p = 0.002$), ECOG ($p = 0.001$), perineural invasion ($p = 0.010$) were found to be independent prognostic factors.
Determining the prognostic factors in patients is very important to evaluate optimal treatment strategies in gastric cancer. We consider that the prognostic factors that we determined in our study may change the approach to treatment.

Keywords: Stomach cancer, Prognostic factors

Introduction

Gastric cancer is one of the common cancers that have high mortality worldwide. According to GLOBOCAN 2018 data, while the incidence of gastric cancer ranks 6th in the world, it ranks 5th in Turkey (1, 2). The incidence of gastric cancer varies significantly among countries and generally these differences go on even in different regions of the same country. It is thought that both genetic and environmental factors are responsible for the etiology of the disease and this event leads to difference in prevalence. Smoking, alcohol use, dietary factors (smoked and salted foods, limited consumption of fresh vegetables and fruits), helicobacter pylori infection, pernicious anemia, chronic atrophic gastritis, radiation, previous gastric surgeries, peutz-jeghers syndrome, li-fraumeni syndrome and hereditary diffuse gastric cancer syndromes are the factors which are responsible for the etiology of gastric cancer (3,4). There are many factors that are thought to be effective on prognosis in gastric cancers. The effects of factors such as ECOG performance score, TNM clinical classification, depth of tumor, lymph node metastasis, perineural invasion status on prognosis and survival in patients with gastric cancer have been the subject of research in many studies (5). Knowing the prognostic factors in stomach cancer patients is very important for both predicting the response to treatment and the course of the disease.

Material and Method

The parameters (Gender, age and ECOG performance of the patients, tumor's location, macroscopic appearance, histological subtype, invasion depth, stage, lymphatic invasion, perineural invasion, vascular invasion,) that may be related to survival of 109 non-metastatic patients during diagnosis who applied to Van Yüzüncü Yıl University Medical Faculty Medical Oncology Clinic between January 2013 and November 2017 and who were operated because of gastric cancer were retrospectively evaluated. Their prognostic significance and survival correlations were examined.

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Table 1. Demographic and Clinicopathologic Characteristics of The Patients

Characteristics	n	%
Gender		
Male	68	62.3
Female	41	37.6
Age		
<55	36	33
55-69	58	53.2
>70	15	13.8
Tumor localization		
Antrum	28	25.7
Cardia	29	26.6
Corpus	39	35.8
Esophagogastric junction	10	9.2
T -Stage		
T1	7	6.4
T2	7	6.4
T3	55	50.5
T4	39	35.8
Microscopic view		
Ulcerated	36	33,00
Infiltrative	13	11.9
Ulcero-infiltrative	16	14.7
Ulcero-vegetating	41	37.6
N -Stage		
N0	33	30.5
N1	28	25.9
N2	17	15.7
N3	30	27.7
Clinical stage		
Stage-1	15	13.8
Stage-2	36	33
Stage-3	58	53.2
ECOG		
ECOG-0	37	33.9
ECOG-1	47	43.1
ECOG-2	25	22.9
Grade		
Well-differential	9	10.1
Medium-differential	49	55
Undifferential	31	34.8
Lymphatic Invasion		
Available	72	69.2
Not available	32	30.7
Vascular Invasion		
Available	68	64.7
Not available	37	35.2
Perineural Invasion		
Available	71	68.9
Not available	32	31.0

(T: Tumour invasion depth, N: Tumour lymph node metastasis, ECOG PS: Eastern Cooperative Oncology Group performance score of patients)

Table 2. Prognostic Factors Affecting Disease-Free Survival According To Univariate Analysis

Table 2	Median(Month)	Min-Max(Month)	p
T-Stage			
T1	87.1	49.1- 125.1	
T2	42.8	28.6- 57.1	
T3	27.3	21.2- 33.4	0.003
T4	20.5	14.9- 26.0	
N -Stage			
N0	42	20.3- 63.6	
N1	19	13.8- 24.1	0.004
N2	11	,0- 26.2	
N3	14	7.3- 20.6	
Clinical stage			
stage 1	79	,0-164.1	0.002
stage 2	27	11.7-42.2	
stage 3	17	11.9- 22.0	
ECOG PS			
ECOG 0	42	20.5- 63.4	0.001
ECOG 1	24	15.5- 32.4	
ECOG 2	12	6.9- 17.0	
Perineural Invasion			
Available	14	8.9- 19.0	0.010
Not available	42	28.5- 55.4	

pT: Pathologic invasion depth, pN :Pathologic lymph node metastasis , ECOG PS : Eastern Cooperative Oncology Group performance score of patients

Patients 'Characteristics: Non-metastatic operated gastric cancer patient group during diagnosis consisted of 109 patient. The entire patient group was histopathologically adenocancer subtype. 68 of the patients included in the study were male and 41 of them were female. Median age was 59 years. 7 (%6.4) of patients had T1, 7(6.4) had T2, 55 (50.9%) had T3 and 39 (36.1%) had T4 depth of tumor invasion. When the patients' clinical stages were evaluated, it was seen that 15(%13.8) cases were Stage 1,36(%33) cases were Stage 2 and 58 (53.2%) cases were Stage 3. Data about perineural invasion were found in 103 of patients, 71 of them had perineural invasion, 32 of them didn't have perineural invasion. ECOG performance score data is available in 106 patients and in this respect 37(%33.9) of patients are in ECOG 0, 47(%43.1) of them are in ECOG 1, 25 (%22.9) of them are in ECOG 2 group. (Table 1).

Statistical Analysis: All data were uploaded to the SPSS database. Besides the frequency table, the data were analyzed by using the chi-square test and Mann-Whitney U test. The survival analysis was calculated by using the Kaplan-Meier method, and the effects of variables of potential prognostic significance on survival were detected for the univariate analysis by using the log-rank test. Statistically, $p < 0.05$ level was considered as significant.

Results

According to univariate analysis T stage ($p = 0.003$), N stage ($p = 0.004$), TNM stage ($p = 0.002$), perineural invasion ($p = 0.01$), ECOG ($p = 0.001$) were found to be factors that affect survival. Prognostic factors that affect survival are summarized in Table 2 according to univariate analysis.

In clinical stage evaluation, the disease-free survival in Stage 1 was 79 months, 27 months in Stage 2 and 17 months in Stage 3. It was observed that the more the stage increased, the more survival decreased (Figure 1).

The disease-free survival time in pT1 was 87.1 months, 42.8 months in pT2, 27.3 months in pT3 and 20.5 months in pT4 (Figure 2)

While the survival time was 42 months in patients without lymph node metastasis (pN0), the survival time in patients with pN3 was 14 months (Figure 3).

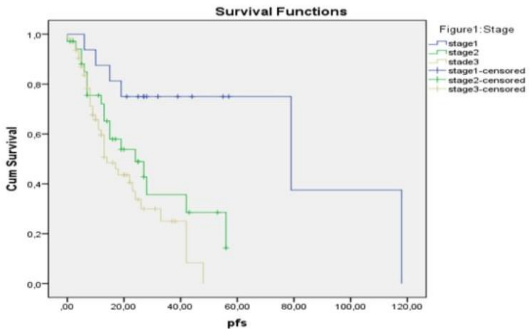

Fig. 1. Kaplan-Meier survival curves of disease free survival according to stage

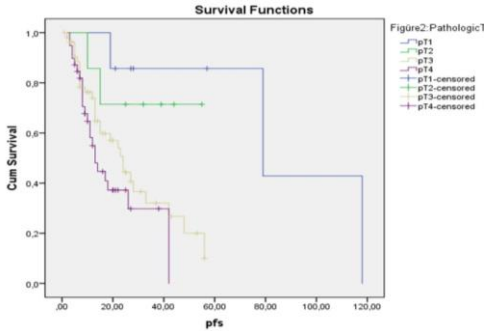

Fig.2. Kaplan-Meier survival curves of disease free survival according to the pathologic tumour invasionnote

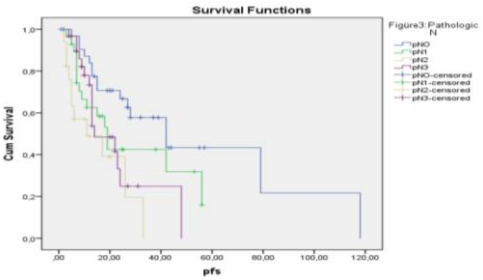

Fig. 3. Kaplan-Meier survival curves of disease free survival according to the pathologic lymph mode metastasis

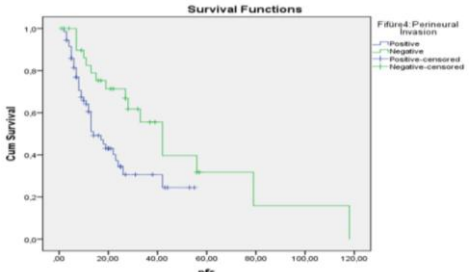

Fig. 4. Kaplan-Meier survival curves of disease free survival according to perineural invasion

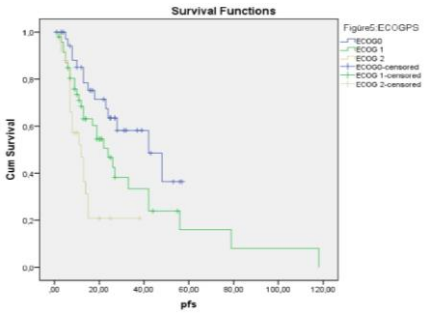

Fig. 5. Kaplan-Meier survival curves of disease free survival according to ECOG PS

While the mean survival time was 42 months in the absence of perineural invasion, survival time was 14 months in the presence of perineural invasion (Figure 4).

While disease-free survival was 42 months in patients with an ECOG score of 0, disease-free survival was 12 months in patients with an ECOG score of 2 (Figure 5).

Discussion

The incidence and mortality rates of gastric cancer differs around the world (6). Gastric cancer ranks second in cancer-related deaths in the world (1). In our country, in cancer-related deaths, gastric cancer ranks 2nd in males and 3rd in females (7). While the prognosis in gastric cancer, which is one of the most death-causing cancers in the world, is generally poor, in early-stage stomach cancer 5-year survival rates can reach 80% (8). With the detection of other prognostic factors notably stage that has an impact on the prognosis of the disease, the interest in researching this issue is increasing for both guiding new treatments and obtaining a better survival prediction. When we look at the literature, in the study that Dockerty et al. made, while in the tumors which are limited to the mucous membrane, 5-year survival is 100%; this rate in the tumors with the full fold involvement of the gastric wall decreases up to 61% (9).The effect of T and N scores on survival were understood well and it has been identified as the only factors affecting survival in studies (10). The relation between the number of lymph nodes that were removed and survival can be explained with micro metastasis. In our study, it is seen that the more the depth of invasion of the tumor increases, the more the survival decreases. TNM staging by The International Cancer Control

Association / American Cancer Joint Committee (UICC / AJCC) is reported to be the most important determinant in the postoperative prognosis after operation (11). Our study supported this and survival of patients in stage 1 were 4 times longer than Stage 3 patients. Perineural invasion is defined as the presence of neoplastic invasion to nerves, and it has been shown by Ahmet Bilici et al. that patients with perineural invasion have a poorer prognosis than those without perineural invasion (12). Also in our study, the presence of perineural invasion was seen as poor prognosis factor. It is known that in gastric cancer patients, prognosis of patients with Eastern Cooperative Oncology Group (ECOG) performance status of 0-1 are better than patients with performance status of 2 or more. When the treatment plan is being made, the performance status of the patients should be evaluated carefully as it affects the prognosis (13). Similarly, in our patient group, there was a statistically significant relationship between ECOG performance status and survival, and it was seen that the more ECOG performance status increased, the more survival decreased. When the literature is reviewed, it has been shown in similar studies that tumor diameter and age are also prognostic factors in patients with gastric cancer (14-15). Although gastric cancers are not included in cancer screening programs in our country, being included in cancer screening programs in developed countries such as Japan is increasing the chance of early diagnosis and treatment. Similar to our study, when the researches that were conducted in Van region and its vicinity are based on, as the gastric cancer incidence is seen above-average in our country, it is important to determine and apply screening programs for gastric cancer in order to increase the chance of diagnosis and treatment in the early stage.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Van Yüzüncü Yıl University.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The author has no conflict of interest to declare.

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