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ORIGINAL ARTICLE

Factors Affecting Survival in Patients with Gastric Cancer Undergoing Surgery for Curative Purposes

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Abstract

Introduction: Gastric cancer is the fifth most common cancer today. It is the third most common cause of cancer-related death because it is usually at an advanced stage at the time of diagnosis. Several factors affect the prognosis of gastric cancer. In this study, we examined various factors affecting the prognosis in gastric cancer and evaluated their effects on the prognosis.

Methods: Between 2011 and 2016, 146 patients who underwent resection with the diagnosis of curative gastric cancer in Haydarpaşa Numune Training and Research Hospital General Surgery Clinic were included in the study. A total of 146 gastric cancer patients who underwent curative surgery were retrospectively analyzed. Age, gender, type of operation, preoperative albumin and tumor markers, tumor stage, lymph node involvement, histological type, tumor localization, tumor differentiation, lymphovascular and perineural invasion, and Her-2 immunohistochemical features were examined, and survival analyses were performed.

Results: Age, stage, lymph node involvement, and perineural-lymphovascular invasion were found to be statistically significant.

Discussion and Conclusion: It was concluded that the determination of these prognostic factors will have an important place in the planning of the treatment. However, the subject should be supported by randomized clinical studies involving more patients.

Keywords: Gastric cancer; Her-2; lymphovascular invasion; perineural invasion; survival.

Gastric cancer is the fifth most common cancer among the cancers seen today [1-2]. Death from gastric cancer is the third most common cause of cancer-related death because it is usually at an advanced stage at the time of diagnosis [3]. Risk factors include Helicobacter pylori, age, smoking, alcohol, low socioeconomic status, family history, previous gastric surgery, pernicious anemia, and living in a high-risk population [4-5]. The most common symptoms in patients are abdominal pain, indigestion, loss of appetite or early satiety, and weight loss. Dysphagia or regurgitation may be seen in proximal gastric cancer or cancers located at the gastroesophageal junction. Bleeding tumors can cause anemia. If the patient has symptoms at the time of diagnosis, the disease is usually in the advanced stage. Most of the patients are in the advanced stage at the time of diagnosis, and the 5-year survival rate is less than 25% [6]. The localization of the tumor in the stomach is determined by endoscopic imaging performed in patients

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with suspected gastric cancer. In addition, biopsies are taken for histological confirmation. After clinical staging of diagnosed patients, it is determined whether the treatment approach will be curative or palliative [7].

There are various patient- and tumor-related factors that affect the prognosis in gastric cancer. In this study, we examined various factors affecting prognosis in gastric cancer and evaluated their effects on prognosis. Sex, age, stage, tumor localization, type of surgery, preoperative albumin level, preoperative tumor markers, histological grade, macroscopic type of tumor, histological type of tumor, lymphovascular invasion, perineural invasion, lymph node number and involvement, and immunohistochemical feature of the tumor (Her-2 positivity and negativity) were analyzed as prognostic parameters.

Materials and Methods

Between 2011-2016, 170 patients who underwent resection with the diagnosis of gastric cancer in Haydarpaşa Numune Training and Research Hospital General Surgery Clinic were included in the study. Patients who underwent palliative surgery, progressed with stage IV, and perioperative mortality were excluded from the study. The clinical records, pathology, and surgery reports of the patients were reviewed retrospectively.

The remaining 146 patients who were operated on for curative purposes were included in the study. In order to investigate the prognostic factors affecting survival in these operated patients, the following parameters were determined and evaluated: sex, age (60 years and above or below), follow-up period, 5-year survival by stage (Stage I-II-III according to the TNM staging system), type of surgery (total gastrectomy, subtotal gastrectomy), preoperative albumin value (N: 3.5 and above), preoperative tumor markers (CEA [N: 0.0-5.0], CA19-9 [N: 0.0-37.0]), tumor localization (cardia-corpus and antrum), histological grade (low and medium-high), macroscopic type of tumor (Borrman classification), microscopic type of tumor (Lauren classification), histological type (poorly cohesive - poorly non-cohesive according to WHO classification), lymphovascular invasion, perineural invasion, lymph node involvement, and immunohistochemical feature of the tumor (Her-2 positivity and negativity). The effects of existing prognostic factors on 5-year survival were investigated.

The data of the patients were obtained from the Haydarpaşa Numune Training and Research Hospital Automation System. The results of the patients who were examined in different centers were scanned from the oncology files. All collected data were entered into IBM SPSS Statistics (Version 22) program and necessary groupings were made. Survival analysis was determined by the Kaplan-Meier method, and the comparison of survivals was determined by the Log Rank Mantel Cox test. This study was conducted in accordance with the Declaration of Helsinki.

Results

A total of 146 patients were included in the study. Of these, 108 patients were male (74%) and 38 patients were female (26%), with a mean age of 61.5±11.9 years (the youngest was 28 years old, and the oldest was 87 years old). The majority were older than 60 years (52.7%) (Table 1). The male/female ratio was found to be 2.84. The five-year mean overall cumulative survival was 57.4%, and the mean follow-up time was 25.2 months (Fig. 1).

There were 69 (47.3%) patients aged 60 years and younger and 77 patients (52.7%) aged 61 years and older (Table 2). The majority of the patients were stage III (56.8%) according

Table 1. Gender characteristics

	Frequency	Percent %
Female	38	26
Male	108	74
Total	146	100

Table 2. Age characteristics

	Frequency	Percent %
60 years and under	69	47.3
61 years and older	77	52.7

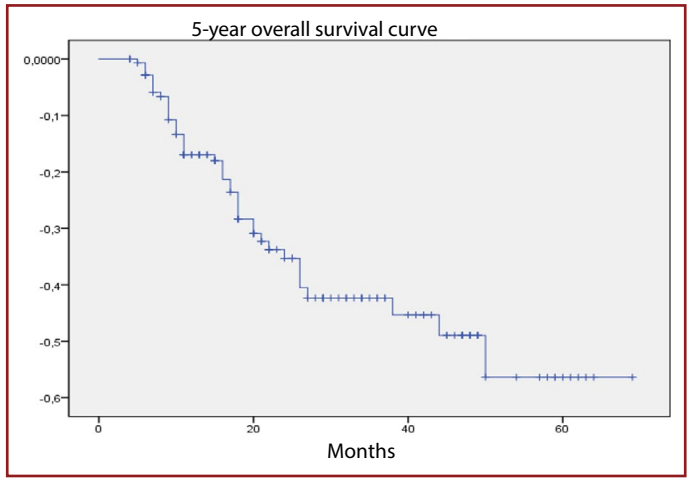

Figure 1. 5-year survival curve.

to the TNM classification. Tumor localization was most common in the corpus-antrum (68.5%). Microscopically, according to the Lauren classification, the diffuse type was 33.6%, the intestinal type was 33.6%, and the mixed type was 4.8%. According to the WHO classification, the poorly cohesive type was 52.7%, and the poorly non-cohesive type was 47.3%. Lymphovascular invasion was positive in 112 patients (76.7%) and negative in 27 patients (18.5%). Perineural invasion was positive in 96 patients (65.8%) and negative in 42 patients (28.8%). Histological grade rates were found to be high grade 54.1% and low and middle grade 39.7%. Immunohistochemically evaluated patients were Her-2 positive in 6% and Her-2 negative in 48%. The patients with positive lymph nodes were 73%, and the patients with negative lymph nodes were 26% (Table 3).

Total gastrectomy D2 lymph node dissection was performed in 83 patients (56.9%), and subtotal gastrectomy D2 lymph node dissection was performed in 63 patients (43.1%) (Table 4).

When the laboratory values are examined, the preoperative albumin level was found to be low in 39% of the patients. The preoperative CEA level of the patients was found to be high in 17.1%, and Ca 19-9 was found to be high in 13.6% (Table 5).

When the general characteristics of survival were evaluated, 35 of the male patients died and 8 of the female patients died. Eleven of 69 patients aged 60 years and younger died, the earliest death occurred in the 6th month, and the latest in the 38th month. Thirty-two of 77 patients aged 61 and over died, the earliest death occurred at the 5th month, and the latest death was at the 50th month (Table 6, Fig. 2 and 3).

When the survival rates of the age groups were evaluated with the Log Rank test, a statistically significant difference was found between the 5-year survival rates (p=0.001; p>0.05). When the survival rates by sex were evaluated with the Log Rank test, no statistically significant difference was

Table 3. Tumor characteristics

	Frequency	Percent %
Stage		
I	21	14.4
II	40	27.4
III	83	56.8
Tumor localization		
Cardia	46	31.5
Corpus-antrum	100	68.5
Lauren		
Diffuse	49	33.6
İntestinal	49	33.6
Mix	7	4.8
WHO classification		
Poorly cohesive	69	47.3
Non poorly cohesive	77	52.7
Lymphovascular invasion		
Pozitive (+)	112	76.7
Negative (-)	27	18.5
Perineural invasion		
Pozitive (+)	96	65.8
Negative (-)	42	28.8
Histological grade		
Low-medium	58	39.7
High	79	54.1
HER-2		
Pozitive (+)	10	6.3
Negative (-)	71	48.6
Lymph node		
Pozitive (+)	107	73.2
Negative (-)	39	26.7

Table 4. Surgery performed

Type of surgery	Frequency	Percent %
Subtotal gastrectomy +D2LND	63	43.1
Total gastrectomy +D2LND	83	56.9

Table 5. Preoperative laboratory values

Preoperative laboratory values	Frequency	Percent %
Albumin		
Low	57	39
Normal	81	55.4
CEA		
High (pathological)	25	17.1
Normal	104	71.2
CA19-9		
High (pathological)	20	13.6
Normal	105	71.9

Table 6. Age- and gender-related survival characteristics

	Survival average ±SE	p
Age		
61 years and older	38.4±3.14	0.001
60 years and under	58.0±3.24	
Gender		
Male	47.25±2.99	0.313
Female	50.48±3.88	

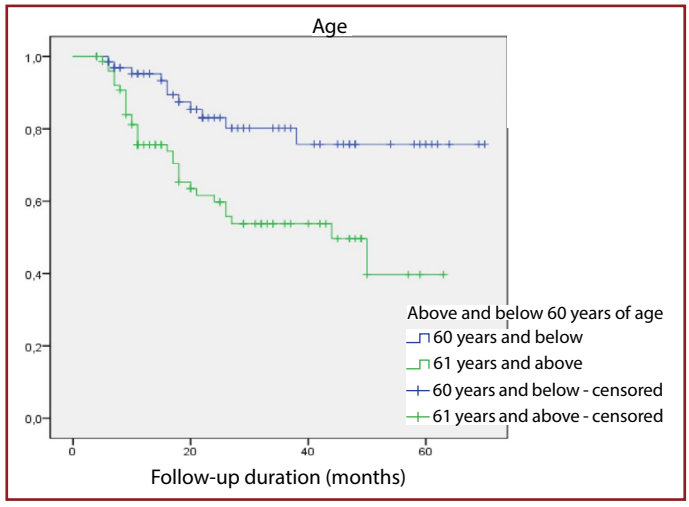

Figure 2. Age curve.

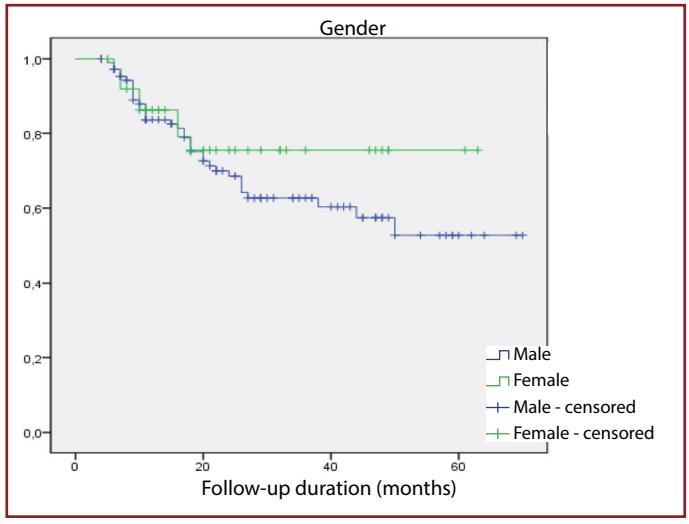

Figure 3. Gender curve.

found between the 5-year survival rates (p=0.313; p>0.05).

When the survival characteristics according to the tumor were evaluated, 1 of 21 patients with stage I died, the latest death was in the 18th month, and the survival rate in this month was 94%, with a standard deviation of 5%. Seven of 40 patients with stage II died. The latest death was in the 44th month, with a survival rate of 76% and a standard deviation of 8% in this month. Thirty-five of 83 patients with stage III died, and the latest death was in the 50th month, with a survival rate of 32% and a standard deviation of 10% in this month (Fig. 4). Nineteen of 46 patients with tumor localization in the cardia died, the latest death was in the 50th month, the survival rate in this month was 35%, and the standard deviation was 15%. Twenty-four of the 100 patients with corpus-antrum localization died, the latest death was in the 44th month.

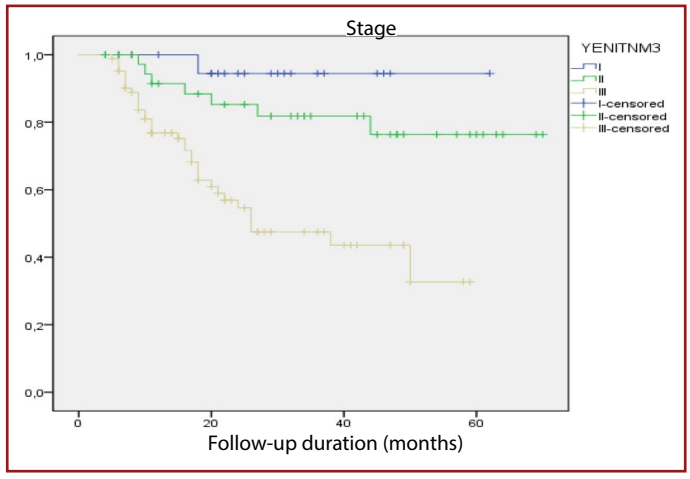

Figure 4. Stage curve.

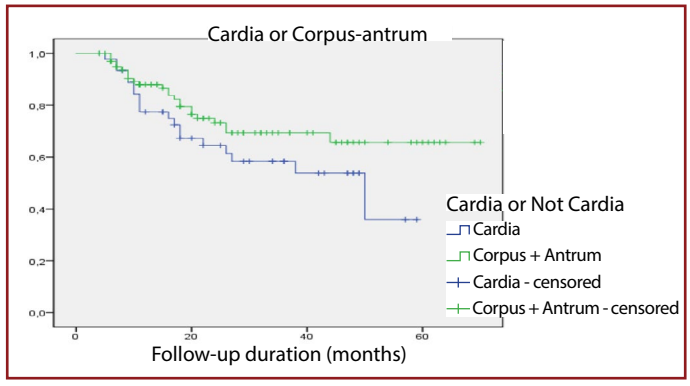

Figure 5. Localization curve.

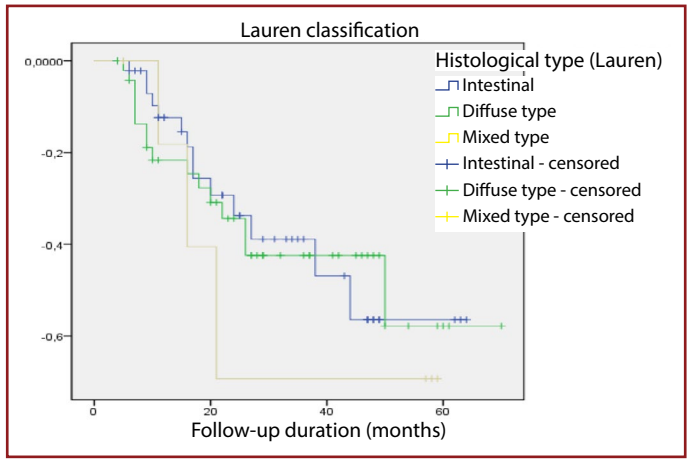

Figure 6. Histological type curve.

The survival rate in this month was 65%, with a standard deviation of 6% (Fig. 5).

According to the Lauren classification, 14 of 49 patients with intestinal type died, the latest death was in the 44th month, the survival rate in this month was 56%, with a standard deviation of 9%. Sixteen of 49 patients with diffuse type

died, the latest death was in the 50th month. The survival rate was 56%, with a standard deviation of 10%. Three of 7 patients with mixed type died, the latest death was in the 21st month, and the survival rate was 50%, with a standard deviation of 20% in this month (Fig. 6).

According to WHO, 22 of 69 patients with poorly cohesive tumors died, the latest death was in the 50th month, the survival rate in this month was 53%, with a standard deviation of 9%. Twenty-one of 77 patients with poorly cohesive tumors died, the latest death was in the 44th month. The survival rate in this month was 60%, with a standard deviation of 7% (Fig. 7).

Three of 27 patients without lymphovascular invasion died. The latest death was in the 26th month, with a survival rate of 87% and a standard deviation of 7%. Thirty-eight of 112 patients with lymphovascular invasion died. The latest death was at the 50th month, with a survival rate of 45% and a standard deviation of 9% in this month (Fig. 8).

Five of the 42 patients without perineural invasion died. The latest death was in the 38th month, with a survival rate of 81% and a standard deviation of 7% in this month. Thirty-six of 96 patients with perineural invasion died. The latest death was at the 50th month, with a survival rate of 43% and a standard deviation of 9% in this month (Fig. 9).

Fourteen of 58 patients with histologically low-intermediate grade died. The latest death was in the 44th month, with a survival rate of 57% and a standard deviation of 10% in this month. Twenty-seven of 79 patients with histologically high grade died. The latest death was at the 50th month, with a survival rate of 52% and a standard deviation of 8% in this month (Fig. 10).

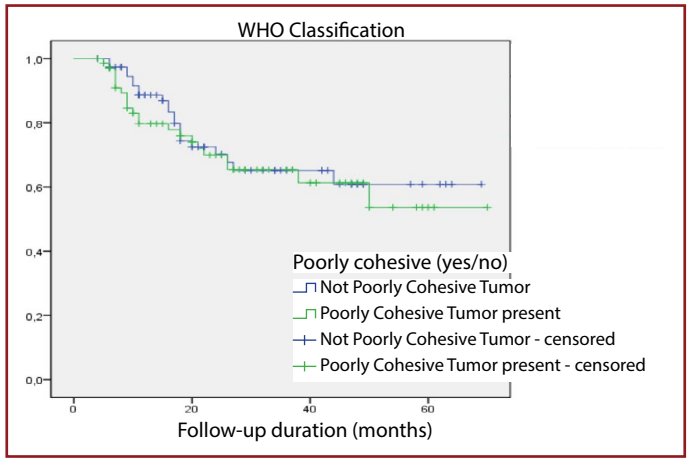

Figure 7. Pathological classification curve.

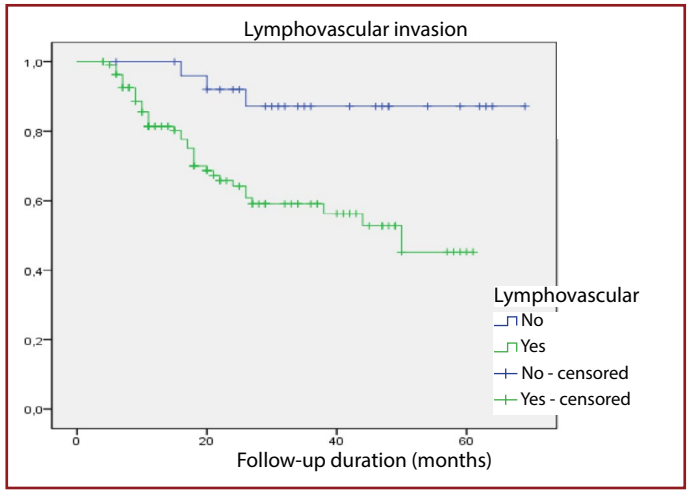

Figure 8. Lymphovascular invasion curve.

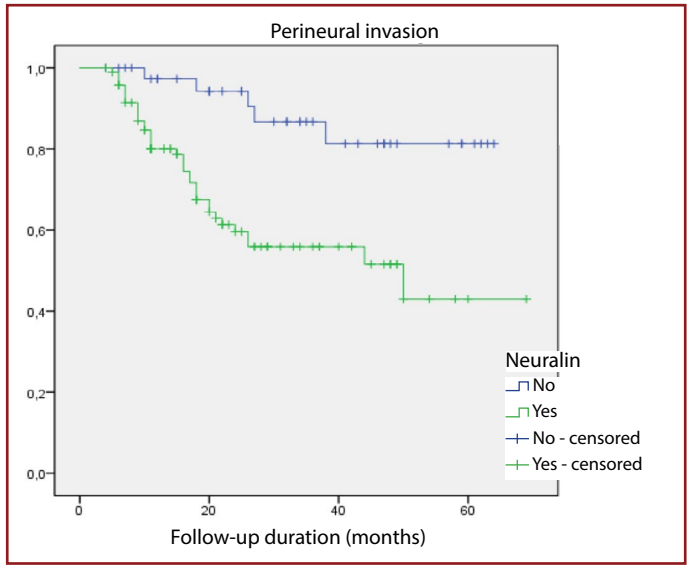

Figure 9. Perineural invasion curve.

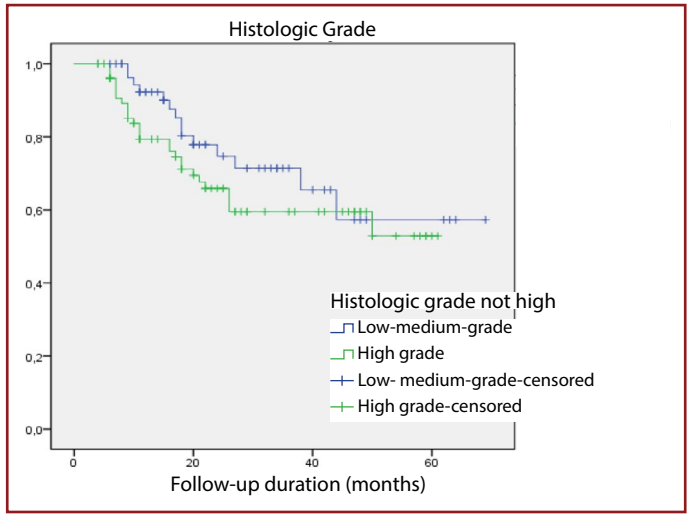

Figure 10. Histological grade curve.

One of 10 patients with positive Her-2 value died, the latest death was in the 16th month, and the survival rate in this month was 26%, with a standard deviation of 22% in this month. Twenty of 71 patients with negative Her-2 values died. The latest death was in the 44th month, with a survival rate of 64% and a standard deviation of 7% in this month (Fig. 11).

Three of 39 patients with negative lymph node involvement died. The most recent death occurred in the 20th month. The survival rate for this month was 90%, with a standard deviation of 5%. Forty of the 107 patients with positive lymph node involvement died, the most recent death was at the 50th month, and the survival rate this month was 42%, with a standard deviation of 8% in this month (Fig. 12). Tumor survival features are detailed in Table 7.

Five-year survival rates according to tumor stage were evaluated with the Log Rank test and a statistically significant difference was found (p=0.00; p>0.05).

Five-year survival rates according to tumor localization were evaluated with the Log Rank test, and no statistically significant difference was found (p=0.113; p>0.05).

Five-year survival rates of the tumor according to the Lauren microscopic classification were evaluated with the Log Rank test, and no statistically significant difference was found (p=0.912; p>0.05).

Five-year survival rates of the tumor according to the pathological WHO classification were evaluated with the Log Rank test, and no statistically significant difference was found (p=0.640; p>0.05).

Five-year survival rates according to the lymphovascular invasion of the tumor were evaluated with the Log Rank test, and a statistically significant difference was found (p=0.004; p>0.05).

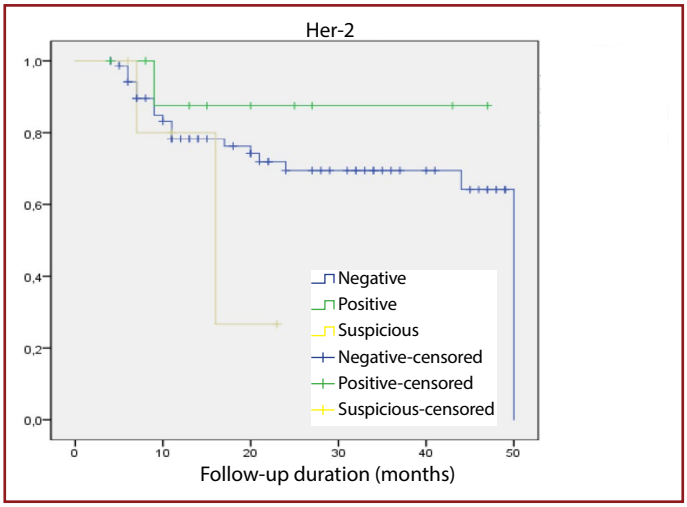

Figure 11. Her-2 curve.

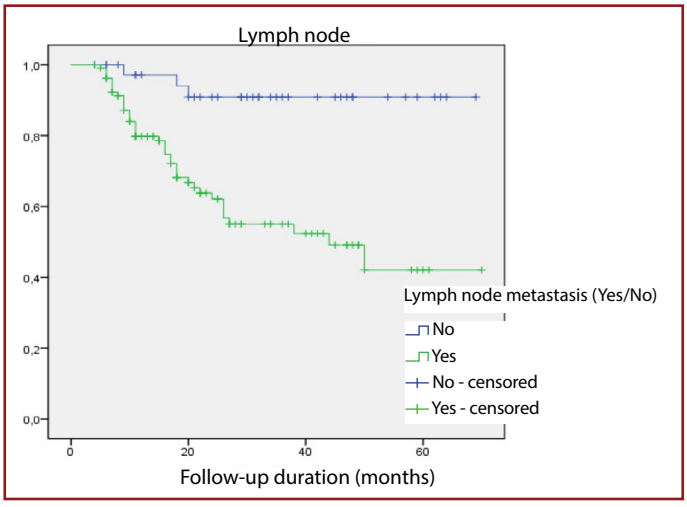

Figure 12. Lymph node curve.

Table 7. Tumor-related survival characteristics

	Survival average±SE	P
Stage		
I	59.55±2.37	0.000
II	58.74±3.79	
III	34.14±2.87	
Tumor localization		
Cardia	37.87±3.51	0.113
Corpus-antrum	52.31±3.04	
Lauren		
Difuse	46.02±3.81	0.912
İntestinal	48.64±4.28	
Mix	37.5±8.85	
WHO classification		
Poorly Cohesive	47.69±3.78	0.640
Non poorly cohesive	49.57±3.44	
Lymphovascular invasion		
Pozitive (+)	40.11±2.56	0.004
Negative (-)	62.83±3.33	
Perineural invasion		
Pozitive (+)	42.29±3.37	0.001
Negative (-)	56.90±2.92	
Histological grade		
Low-medim	50.30±4.12	0.236
High	41.45±2.92	
HER-2		
Pozitive	42.25±4.44	0.169
Negative	38.03±2.37	
Lymph node		
Pozitive	42.27±3.24	0.000
Negative	64.15±2.67	

Five-year survival rates according to the perineural invasion of the tumor were evaluated with the Log Rank test, and a statistically significant difference was found (p=0.001; p>0.05).

Five-year survival rates according to the Her-2 feature of the tumor were evaluated with the Log Rank test, and no statistically significant difference was found (p=0.169; p>0.05).

Five-year survival rates according to the lymphatic involvement of the tumor were evaluated with the Log Rank test, and no statistically significant difference was found (p=0.00; p>0.05).

Preoperative laboratory parameters were evaluated according to survival analysis. Twenty-one of the 57 patients with low albumin died. The most recent death was at the 50th month, with a cumulative survival rate of 47.5% and a standard deviation of 10% in this month. Nineteen of the 81 patients with high albumin values died. The latest death occurred at 38 months, and the cumulative survival rate in this month was 67.2%, with a standard deviation of 6% (Fig. 13). Nine of 25 patients with high CEA values died, the latest death was in the 38th month, and the survival rate in this month was 28%, with a standard deviation of 21%. Twenty-eight of 104 patients with low CEA values died, and the latest death was in the 44th month, with a cumulative survival rate of 64%, and a standard deviation of 52% in this month (Fig. 14). Five of 20 patients with high CA19-9 values died, the latest death was in the 22nd month, and the survival rate in this month was 64%, with a standard deviation of 13%. Thirty-one of 106 patients with low CA19-9 values died, the latest death was in the 44th month, and the survival rate in this month was 60%, with a standard deviation of 6% (Fig. 15). The survival characteristics of the preoperative laboratory parameters are given in detail in Table 8.

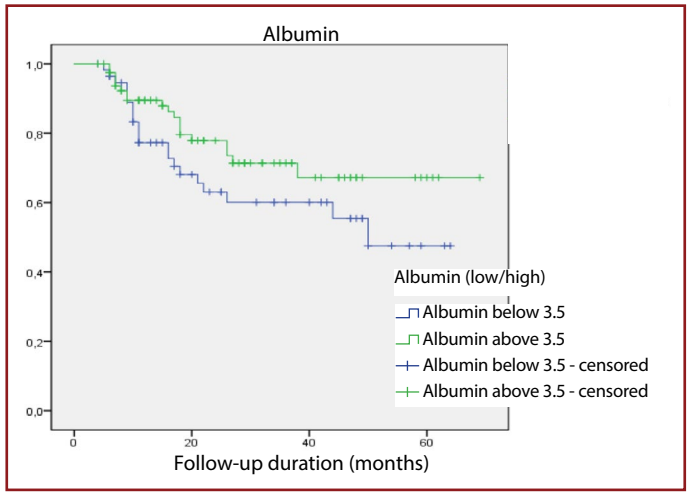

Figure 13. Albumin curve.

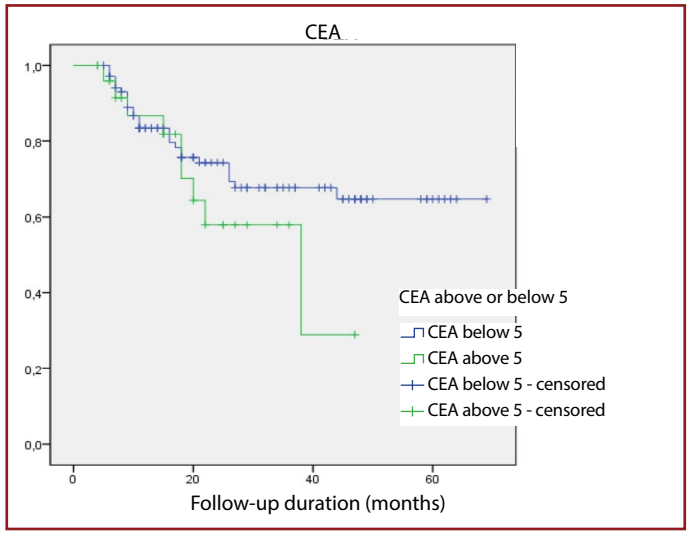

Figure 14. CEA curve.

Five-year survival rates were evaluated with the Log

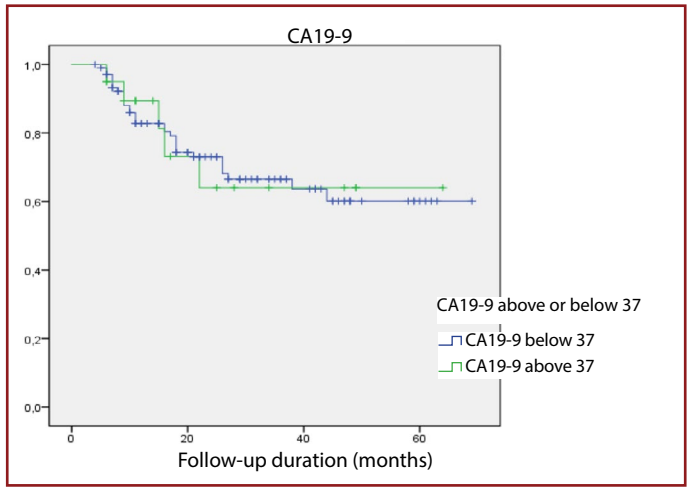

Figure 15. CA19-9 curve.

Table 8. Survival characteristics of preoperative laboratory parameters

Preoperative laboratory values	Survival average±SE	p
Albumin		
Low	41.86±3.64	0.121
Normal	52.46±3.23	
CEA		
High (pathological)	30.95±3.69	0.223
Normal	50.70±2.83	
CA19-9		
High (Pathological)	46.30±6.52	0.965
Normal	49.02±2.93	

Rank test according to albumin level, and no statistically significant difference was found (p=0.121; p>0.05).

Five-year survival rates were evaluated with the Log Rank test according to CEA level, and no statistically significant difference was found (p=0.223; p>0.05).

Five-year survival rates were evaluated with the Log Rank test according to CA19-9 level, and no statistically significant difference was found (p=0.965; p>0.05).

Discussion

Gastric cancer is still one of the more important causes of cancer-related deaths, despite the increase in resectability rates and decrease in incidence in the West in the last century. Low life expectancy is more often associated with delayed diagnosis, local and regional recurrence. Despite advances in surgical and oncological treatment, gastric carcinoma still remains a fatal disease. In the literature, 5-year survival is reported to be 60%-80% for stage 1-2 and 18-50% for stage 3 patients [8]. It may be micrometastatic in the early stage and adversely affect survival outcomes. There are many factors that affect life expectancy in gastric cancer. Our aim in this study was to perform a retrospective analysis of prognostic factors in gastric cancer patients, including gender, age, tumor stage, localization, histological type, histological grade, metastatic lymph node involvement, perineural invasion, lymphovascular invasion, preoperative tumor markers (CEA, Ca19-9), HER-2 positivity or negativity, albumin level, and type of surgery (total/subtotal gastrectomy). Five-year survival in patients was investigated. The incidence of gastric cancer is increasing and is mostly seen at the age of 60 and above. The male/female ratio is approximately 1.8-2 times.

When we look at the literature, in the retrospective multivariate analysis of 1473 gastric cancer patients who underwent curative resection by Meyer et al. [9], it was stated that age was an independent prognostic factor. In our study, the M/F ratio was 2.84, the mean age of the patients was 61.5 (±11.9) (the youngest was 28, the oldest was 87), and most patients were 61 years or older. Perioperative mortality was found to be 4.5%. All patients with perioperative mortality were 61 years or older. The cause of death of the patients was additional disease rather than surgical complication (cerebrovascular accident, myocardial infarction, pulmonary embolism). One patient died postoperatively due to bleeding. When the 5-year survival rate of both age groups was compared, the 5-year survival rate was found to be 38.4% in the elderly patient group and 58% in the younger patient group. When the survival rates of both groups were compared, the survival rate in the elderly group was found to be significantly lower (Table 6, Figs. 2-3). This may be due to the fact that tolerance to adjuvant therapy is more common in the elderly patient group. When the stages of these patients were compared, the frequency of lymph node involvement was not significant in both groups. In studies on this subject in the literature, it has been observed that elderly patient groups are generally in advanced disease. Studies reporting that there is no difference according to age groups have reported that well-differentiated tumors are more common in elderly patient groups. In our study, the difference in differentiation between patient groups was not significant.

The staging of the disease is made according to the penetration of the tumor tissue in the gastric wall and lymph node involvement. Stage is the most important factor determining prognosis [10]. The prognosis is very good in the early stages. 60% of the patients lost the chance of surgical treatment when the diagnosis was made. In our study, most of the patients were stage 3 or 4. The extent of metastatic lymph nodes and serosa invasion affects the prognosis negatively. Five-year survival was reported as 94% in Stage 1, 61% in Stage 2, and 32% in Stage 3 [11]. In our study, survival rates according to stages were found to be 76% in Stage 1, 58% in Stage 2, and 32% in Stage 3 (Table 7, Fig. 4). Staging was found to be significant in the survival analysis.

Although most gastric carcinomas were distal in the early 1900s, the incidence of proximal carcinomas is increasing over time. In our study, proximal (cardia) gastric carcinomas constituted 31.5% of the patients. Proximal tumors have a worse prognosis than distal tumors because their biological behavior is more aggressive, larger in size, deeper invasion, and more lymph node involvement. In our study, proximal and distal tumors were compared in terms of survival. The mean survival rate in proximal tumors was 37.87%, and the 5-year survival rate in distal tumors was 52.31% (Table 7, Fig. 5). In our study, the 5-year survival analysis of proximal and distal gastric carcinomas was not significant. A tendency to poor prognosis has been observed in proximal gastric carcinomas. In previous studies, gastroesophageal junction tumors were also included in proximal tumors. It has been stated that the high incidence of tumor invasion at the surgical margin in this group of tumors may lead to incorrect evaluation in the prognosis analysis. Excluding junctional tumors, the difference in survival was generally not significant [12]. In our study, this factor was not considered to have a negative contribution,

since gastroesophageal junction tumor constituted 6% of the patients who were operated on for proximal gastric tumor. This may be the reason why there is no significant difference between the two groups.

Surgical treatment is the primary treatment option when curative treatment is aimed. However, 50% of operable gastric carcinomas have lymphatic metastases at presentation. The chance of survival correlates with the degree of lymphatic metastasis. According to the American Joint Committee on Cancer (AJCC), the amount and level of metastatic lymph nodes is the most important prognostic factor. Five-year survival is 90% in early-stage gastric cancers without lymph node involvement [13]. In our study, lymph node involvement was not histopathologically present in 26.7% of the patients. In the survival analysis of this group of patients, the 5-year survival was found to be 76%. In patients with lymph node involvement, it comprised 76.2% of all patients (Table 3). The 5-year survival rate of patients with lymphatic involvement was found to be 32% (Fig. 12). In the comparative analysis of these two groups, the difference in survival was found to be statistically significant (Table 7, Fig. 12).

Early gastric carcinoma is more common in Japan due to screening endoscopy. It was observed that the disease could remain localized in the gastric and regional lymph nodes for a long time in the follow-up of patients who did not undergo surgery. The disease has the feature of staying localized for a long time. For this reason, they performed regional lymphadenectomy together with gastric resection in gastric tumors. They stated that the survival results were better. However, they have not conducted a controlled study in their country on this issue, as they do not find it ethical. Today, D2 lymphadenectomy is performed as a standard for operable patients. Since there is no controlled study, Western countries did not favor this approach. In our study, D2 lymphadenectomy was performed as a standard. As stated in a meta-analysis, mortality and morbidity were found to be high in patients who underwent D2 lymphadenectomy [14]. In a study by Schwarz and Zagala-Nevarez, they showed that performing a radical lymphadenectomy reduced locoregional recurrence rates by up to 3% in patient populations [15]. Clinically, preoperative lymph node positivity cannot be understood. For this reason, the opinion of performing lymphadenectomy in all patients has gained weight. In our study, a comparison could not be made because there was no patient who underwent D1 lymphadenectomy.

Lauren classification in gastric cancer is another histopathological classification widely used in the world. Tumor development stages of intestinal and diffuse types are different. Some studies report a higher incidence of the diffuse type in young female patients. The prognostic value of the Lauren classification is still controversial in current studies. While some studies do not detect a correlation with patient outcomes, it is emphasized as a prognostic factor in some studies. In a study conducted in 2016, it was defined as a prognostic independent risk factor and it was reported that survival in the diffuse type decreased significantly [16]. In our study, when the Lauren classification was evaluated, no statistically significant difference was found between 5-year survival rates (Table 7). Due to its high clinical importance, the reliability of the Lauren classification has been tested. It is not suitable for endoscopic treatment because of diffuse type tumor infiltration and high T category. Therefore, in patients with gastric cancer who will undergo endoscopic treatment in Japan, Germany, and Europe, the condition of being intestinal type is sought. In cases where surgery is performed, there should be a surgical margin of 8 cm for diffuse type and 5 cm for intestinal type. Because of these clinical applications, the Lauren classification is the most widely used histopathological classification in the world. However, it is not used as a prognostic factor.

WHO classification is made according to the histopathological features of gastric cancer. In our study, the percentages of the types we classified as poorly cohesive and poorly non-cohesive were found to be 47% and 52%, respectively (Table 3). In the study of Kwon et al. [17], the survival of patients with poorly cohesive type carcinoma has a better prognosis than other undifferentiated adenocarcinomas. In the same study, it was reported that poorly cohesive carcinoma has a worse prognosis for advanced cases. In our study, when the survival rates in the pathological classification according to WHO were evaluated, no statistically significant difference was found between the 5-year survival rates.

It is emphasized that as histopathological grade increases in gastric cancers, survival worsens. Nie et al. [18] found histopathological grade to be a prognostic independent risk factor in patients with gastric cancer, and they observed that survival decreased as the grade increased. Inoue et al. [19] investigated histopathological grade and mean survival in patients who underwent curative gastrectomy. In their study evaluating 1119 patients who underwent R0 resection and D2 lymph node dissection, no correlation was found between histopathological grade and survival. This study with a very large patient series supports our results. In our study, when histological grade and survival

rates were evaluated, no statistically significant difference was found between 5-year survival rates (Table 7).

It has been shown that when the tumor is limited to the muscular layer in gastric carcinomas, the presence of perineural invasion adversely affects the prognosis. In a study conducted in 2014, it was shown that cases with negative perineural invasion had a significantly better prognosis than cases with positive perineural invasion [20]. In the study conducted by Bilici et al. [21], it was shown that perineural invasion positivity is associated with the stage and prognosis of the disease. In our study, it was found to be compatible with the literature, and when evaluated in terms of lymphovascular and perineural invasion, the 5-year survival rate was found to be 45% in the patient group with lymphovascular invasion. When this group was compared with the group without lymphovascular invasion, a statistically significant difference was found between 5-year survival rates (Table 7, Fig. 8). In the group with perineural invasion, 5-year survival was found to be 43%. When the survival rates in this group were compared with the group without perineural invasion, no statistically significant difference was found between the 5-year survival rates (Table 7, Fig. 9).

The efficacy of new molecular-targeted agents is being investigated to improve survival in gastric cancer. The incidence of Her-2 amplification in gastric cancer varies depending on the methods used in each reported series and the heterogeneity of gastroesophageal tumors. This rate is between 6-32% in studies [22]. In the study of Tanner et al. [23] conducted with 231 gastric and esophagogastric cancer patients, it was reported that the presence of Her-2 amplification is associated with short survival. In our study, when the survival rates were evaluated according to the Her-2 feature of the tumor, no statistically significant difference was found between the 5-year survival rates (Table 7, Fig. 11). Due to the low rate of patients using targeted therapy in our study, it was not possible to evaluate the Her-2 status and the effectiveness of trastuzumab use. These applications can be evaluated when Her-2 receptor analysis is performed routinely in every gastric cancer patient.

There are some studies that indicated low preoperative albumin levels and high CEA and CA19-9 values as minor prognostic factors. In a cohort study conducted in 2022, it was stated that a high serum albumin level is a good prognostic factor in postoperative survival [24]. It was reported in a study that CEA and CA19-9 were at lower levels in early gastric cancer and that CA19-9 elevation was associated with female gender and the presence of lymph node metastases. In the same study, an elevated CEA level was accepted as an independent risk factor for poor prognosis of early gastric cancer [25]. In our study, when survival rates were evaluated according to albumin level, no statistically significant difference was found between 5-year survival rates (Table 8, Fig. 13). When the survival rates were evaluated according to the preoperative CEA and CA19-9 levels, respectively, there was no statistically significant difference between the 5-year survival rates (Table 8, Figs. 14, 15).

Conclusion

In our study, the results of 146 patients treated for curative purposes were evaluated. Age, sex, type of operation performed, preoperative albumin and tumor markers, tumor stage, lymph node involvement, histological type, tumor localization, tumor differentiation, lymphovascular and perineural invasion, and Her-2 immunohistochemical features were examined, and survival analyses thought to have an effect on survival were conducted.

In our study, age, stage, lymph node involvement, perineural invasion, and lymphovascular invasion were evaluated to be statistically effective on prognosis. It was concluded that the determination of these prognostic factors will have an important place in the planning of the treatment. However, the subject should be supported by randomized clinical studies involving more patients.

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References

1. Smyth EC, Nilsson M, Grabsch HI, van Grieken NC, Lordick F. Gastric cancer. Lancet 2020;396:635–48. [CrossRef]
2. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018;68:394–424. [CrossRef]
3. Yaghoobi M, McNabb-Baltar J, Bijarchi R, Hunt RH. What is the quantitative risk of gastric cancer in the first-degree relatives of patients? A meta-analysis. World J Gastroenterol 2017;23:2435-42. [CrossRef]

4. Murphy G, Dawsey SM, Engels EA, Ricker W, Parsons R, Etemadi A, et al. Cancer risk after pernicious anemia in the US elderly population. Clin Gastroenterol Hepatol 2015;13:2282-9.e1–4.
5. Cuyun Carter G, Kaltenboeck A, Ivanova J, Liepa AM, San Roman A, Koh M, et al. Treatment patterns in patients with advanced gastric cancer in Taiwan. Asia Pac J Clin Oncol 2017;13:185–94. [CrossRef]
6. Smyth EC, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D. Gastric cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2016;27(suppl 5):v38–v49. [CrossRef]
7. Zilberstein B, Abbud Ferreira J, Cecconello I. Management of postoperative complications in gastric cancer. Minerva Gastroenterol Dietol 2011;57:69–74.
8. Sexton RE, Al Hallak MN, Diab M, Azmi AS. Gastric cancer: A comprehensive review of current and future treatment strategies. Cancer Metastasis Rev 2020;39:1179–203. [CrossRef]
9. Meyer HJ, Hölscher AH, Lordick F, Messmann H, Mönig S, Schumacher C, et al. Current S3 guidelines on surgical treatment of gastric carcinoma. Chirurg [Article in German] 2012;83:31–7. [CrossRef]
10. Song Z, Wu Y, Yang J, Yang D, Fang X. Progress in the treatment of advanced gastric cancer. Tumour Biol 2017;39:1010428317714626. [CrossRef]
11. Sasako M, Sakuramoto S, Katai H, Kinoshita T, Furukawa H, Yamaguchi T, et al. Five-year outcomes of a randomized phase III trial comparing adjuvant chemotherapy with S-1 versus surgery alone in stage II or III gastric cancer. J Clin Oncol 2011;29:4387–93. [CrossRef]
12. Xue J, Yang H, Huang S, Zhou T, Zhang X, Zu G. Comparison of the overall survival of proximal and distal gastric cancer after gastrectomy: A systematic review and meta-analysis. World J Surg Oncol 2021;19:17. [CrossRef]
13. Chen R, He Q, Cui J, Bian S, Chen L. Lymph node metastasis in early gastric cancer. Chin Med J (Engl) 2014;127:560–7. [CrossRef]
14. Jiang L, Yang KH, Chen Y, Guan QL, Zhao P, Tian JH, et al. Systematic review and meta-analysis of the effectiveness and safety of extended lymphadenectomy in patients with resectable gastric cancer. Br J Surg 2014;101:595–604. [CrossRef]
15. Schwarz RE, Zagala-Nevarez K. Recurrence patterns after radical gastrectomy for gastric cancer: Prognostic factors and implications for postoperative adjuvant therapy. Ann Surg Oncol 2002;9:394–400. [CrossRef]
16. Chen YC, Fang WL, Wang RF, Liu CA, Yang MH, Lo SS, et al. Clinicopathological variation of lauren classification in gastric cancer. Pathol Oncol Res 2016;22:197–202. [CrossRef]
17. Kwon KJ, Shim KN, Song EM, Choi JY, Kim SE, Jung HK, et al. Clinicopathological characteristics and prognosis of signet ring cell carcinoma of the stomach. Gastric Cancer 2014;17:43–53. [CrossRef]
18. Nie L, Li M, He X, Feng A, Wu H, Fan X. Gastric mixed adenoneuroendocrine carcinoma: Correlation of histologic characteristics with prognosis. Ann Diagn Pathol 2016;25:48–53. [CrossRef]
19. Inoue K, Nakane Y, Michiura T, Nakai K, Iiyama H, Sato M, et al. Histopathological grading does not affect survival after R0 surgery for gastric cancer. Eur J Surg Oncol 2002;28:633–6.
20. Deng J, You Q, Gao Y, Yu Q, Zhao P, Zheng Y, et al. Prognostic value of perineural invasion in gastric cancer: A systematic review and meta-analysis. PLoS One 2014;9:e88907. [CrossRef]
21. Bilici A, Seker M, Ustaalioglu BB, Kefeli U, Yildirim E, Yavuzer D, et al. Prognostic significance of perineural invasion in patients with gastric cancer who underwent curative resection. Ann Surg Oncol 2010;17:2037–44. [CrossRef]
22. Gerson JN, Skariah S, Denlinger CS, Astsaturov I. Perspectives of HER2-targeting in gastric and esophageal cancer. Expert Opin Investig Drugs 2017;26:531–40. [CrossRef]
23. Tanner M, Hollmén M, Junttila TT, Kapanen AI, Tommola S, Soini Y, et al. Amplification of HER-2 in gastric carcinoma: Association with Topoisomerase IIalpha gene amplification, intestinal type, poor prognosis and sensitivity to trastuzumab. Ann Oncol 2005;16:273–8. [CrossRef]
24. Zhao Z, Yin XN, Wang J, Chen X, Cai ZL, Zhang B. Prognostic significance of hemoglobin, albumin, lymphocyte, platelet in gastrointestinal stromal tumors: A propensity matched retrospective cohort study. World J Gastroenterol 2022;28:3476–87. [CrossRef]
25. Feng F, Tian Y, Xu G, Liu Z, Liu S, Zheng G, et al. Diagnostic and prognostic value of CEA, CA19-9, AFP and CA125 for early gastric cancer. BMC Cancer 2017;17:737. [CrossRef]