

Clinicopathologic features of operated gastric cancer patients, single center nine years experience

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Abstract

Aim: Gastric cancer is one of most common malignancies in the world. In developed countries including Europe and United States, despite the advanced technology, advanced stages of gastric cancer are still common with a poor survival. In this study, we aimed to describe clinicopathological characteristics and outcomes of gastric cancer in patients who were operated in our clinic.

Material and Methods: We respectively evaluated a total of 200 patients who underwent gastrectomy, D2 lymph node dissection due to gastric cancer between November 2006 and December 2015. Data including clinicopathologic features, postoperative complications, overall survival and prognostic factors affecting prognosis were analyzed and statistical analysis was performed. Data including clinicopathologic features, postoperative complications, overall survival and prognostic factors affecting prognosis were analyzed and statistical analysis was performed.

Results: Of the patients, 134 (67%) were males and 66 (33%) were females. The mean age was 61.36±11.92 (28-91) years. Tumor localization was frequently low (57%). The most common postoperative complication, regardless of the type of gastrectomy, was the surgical site infection. The major of the patients had Stage 3 disease. The median overall survival was 24.9 (0.07-116.3) months and overall survival was 43.7%.

Conclusion: Except for early stage, the chance of curative treatment is low in gastric cancer. Early diagnosis and treatment can yield improved outcomes for this patient population. Therefore, it is important to develop national programs for early diagnosis and to develop experienced endoscopists

Keywords: Gastric cancer; gastrectomy; survival

INTRODUCTION

Gastric cancer is the fourth among the most common cancers worldwide and the second among the cancer-related causes of death. More than 75% of the cases occurred in less developed countries (1). The incidence of gastric cancer varies depending on the country, and it can even vary based on ethnicity and dietary habits within the same country. Japan and Korea have the highest rates of gastric carcinoma in the World(2). Helicobacter pylori infection, consumption of salty foods and N-nitroso compounds, low intake of fresh fruits and vegetables, smoking, obesity are some common risk factors for gastric cancers (2). It is seen 2 to 3 times more frequently

in males than females, and it occurs frequently in the sixth decade of life (3).

Gastric cancer incidence, metastasis rate and mortality are high, early diagnosis, resection rate and 5 year survival rate is low(4). Surgical treatment of gastric cancer in early stages offer the chance of cure and 5-year survival rate is 90%(4). However, the diagnosis rate is low since there is no specific symptom in gastric cancer, therefore most patients come advanced stages,so surgery often is missed(4). Thus, advanced gastric cancer treatment is multidisciplinary in the form of surgery, adjuvant-neoadjuvant chemoradiotherapy(Song et al., 2017). Current treatment of gastric cancer, except for the local

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excision in some of the early stage gastric cancers, is gastrectomy combined with lymphadenectomy(5). D2 lymph node dissection has become the standard in many centers for T2-T4 tumor and T1N+ tumor(Kodera & Sano, n.d.). Despite all efforts approaches, however, five-year survival rate in many countries is around 20 to 40% except early stage I-II gastric cancers where the five-year survival is about 60 to 90% for Stage I-II gastric cancers(Isobe et al., 2011).

In Turkey, the incidence of gastric cancer is between the higher incidence in the East and the lower incidence in the West and gastric cancer is the fifth most common cancer in males and sixth in females, while it is the second most frequent cancer-related cause of death in males and third in females(7).

In the present study, we aimed to present our clinical experiences and describe clinicopathological characteristics and outcomes of gastric cancer in patients who were operated in our clinic in the light of the data as presented in the literature.

MATERIAL and METHODS

The study protocol was approved by the Kartal Koşuyolu High Specialty Training and Research Hospital Ethics Committee with the number 2017.2 / 2-25. A written informed consent was obtained from each participant. The study was conducted in accordance with the principles of the Declaration of Helsinki.

A total of 200 patients who underwent total or subtotal gastrectomy, D2 lymph node dissection due to a gastric adenocarcinoma at the Kartal Koşuyolu High Specialty Training and Research Hospital, Gastroenterological Surgery clinic between November 2006 and December 2015 were retrospectively analyzed. The cut-off date for survival analysis was 31 December 2017. D2 dissection was performed in accordance with the principles of the Japanese Research Society for the Study of Gastric Cancer (JRSSG)(8). We used the classification system (TNM) according to the American Joint Committee on Cancer (7 th ed, 2010). Data were obtained using the follow-up forms in our clinical database and pathology results were recorded. Patients who were diagnosed with distal organ metastasis at the time of surgery, patients with a positive peritoneal cytology result, patients with neoadjuvant chemoradiotherapy and those who had positive surgical margins were excluded from the study, even if they underwent gastric resection. A total of 200 patients were included in the study. Complications which occurred within 30 days after the operation were evaluated as postoperative early complications. Anastomotic leaks, pancreatic fistula, and intraabdominal hemorrhage were considered as major complications. Postoperative early mortality was evaluated as the mortality within the first 30 days after surgery.

Statistical Analysis

We performed statistical analysis using the SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). The

quantitative (numerical) data were expressed in mean \pm standard deviation (SD) or median and minimum-maximum. The Chi-square test, where appropriate, was used to compare these proportions in different groups. Univariate survival analyses were conducted using the Kaplan-Meier log-rank tests. A p value of ($<0,05$) was considered statistically significant.

RESULTS

Of the patients, 134 (67%) were males and the mean age was 61.36 ± 11.9 . A total of 123 patients (61.5%) were aged 65. In terms of tumor localization, 114 patients (57%) had low, 50 patients (25%) had moderate, 34 patients (17%) had high, and two patients (1%) had diffuse localization. Of surgeries, 115 (57.5%) were subtotal. Tumor differentiation was undifferentiated, mucinous or signet-ring cell in 137 patients (68.5%). The mean tumor diameter was 5.51 ± 2.74 cm. T stage was 3 (n=80) or 4 (n=80) in 160 patients (80%). Metastatic lymph node involvement was found in 136 patients (68%) and the mean number of removed lymph nodes was 24.26 ± 10.59 . Vascular invasion was positive in 124 patients (62.3%), while perineural invasion was positive in 138 patients (69.7%). The 30-day mortality was six (3%) due to myocardial infarction in four patients and sepsis in two patients (Table 1). The majority of patients according to their stages were Stage III (%56) (Figure 1).

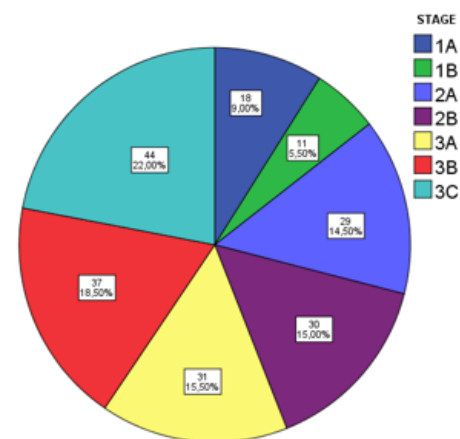


Figure 1. Disease stage and number and percentage of patients. According to the American Joint Committee on Cancer (AJCC) (7 th ed, 2010)

Complications developed in 43 patients (21.6%). Of all complications, regardless of the type of gastrectomy, the most common complications were infection, anastomotic leak and hemorrhage. There was no statistically significant difference between the types of gastrectomy (Figure 2).

At the end of a nine-year old follow-up period (cut-off date 31 December, 2017), 43.7% of our patients were still alive and the median overall survival was 24.9 (0.07-116.3) months. The tumor localization, T stage, lymph node involvement and diameter, presence of vascular, and perineural invasion were not found to play a role in

Table 1. Clinicopathological characteristics

		Number	%
Gender	Male	134	67
	Female	66	33
Age	≤65	123	61.5
	>65	77	38.5
Tumor localization	High	34	17
	Middle	50	25
	Low	114	57
Type of Gastrectomy	Subtotal	115	57.5
	Total	85	42.5
Tumor Differentiation	Good	9	4.5
	Moderate	54	27
	Undifferentiated, Mucinous, Signet-ring	136	68
Vascular Invasion	Positive	124	62
Perineural Invasion	Positive	138	69
T Stage	T1	19	9.5
	T2	21	10.5
	T3	80	40
	T4	80	40
N stage	N0	64	32
	N1	38	19
	N2	37	18.5
	N3	61	30.5
Complication	Wound site infection	10	5
	Anastomotic leak	9	4.5
	Hemorrhage	9	4.5
	Intra-abdominal abscess	4	2
	Duodenal leak	3	1.5
	Pneumonia	3	1.5
	Delayed gastric emptying	2	1
	Pancreatic leak	2	1
	Chylous leak	1	0.0
	Eventration	1	0.5
	Afferent loop	1	0.5
	30-day mortality		6

Table 2. Overall survival rates according to the stage

Stage	I	II	III
n (%)	33(16,5%)	59(29,5%)	108(54%)
Overall Survival (%)	88.9	55.8	28.3
Mean Life Expectancy (months)	60.50±31.60	39.04±28.66	24.49±21.52

survival ($p < 0.05$). Overall life expectancy according to the stages is presented in Figure 3 and Table 2.

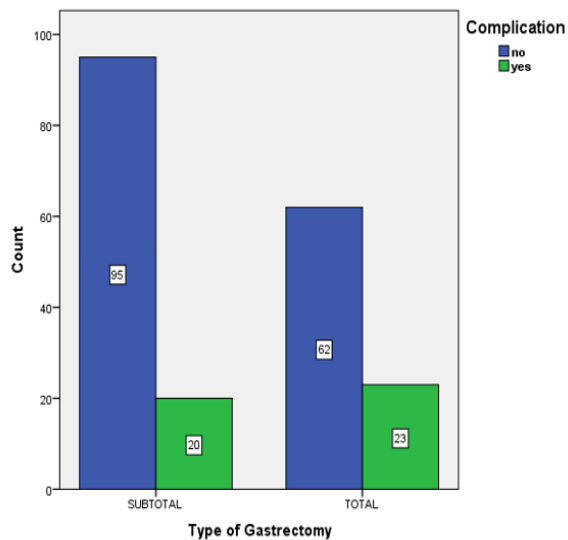


Figure 2. Complications number and no-complications number according to the type of gastrectomy

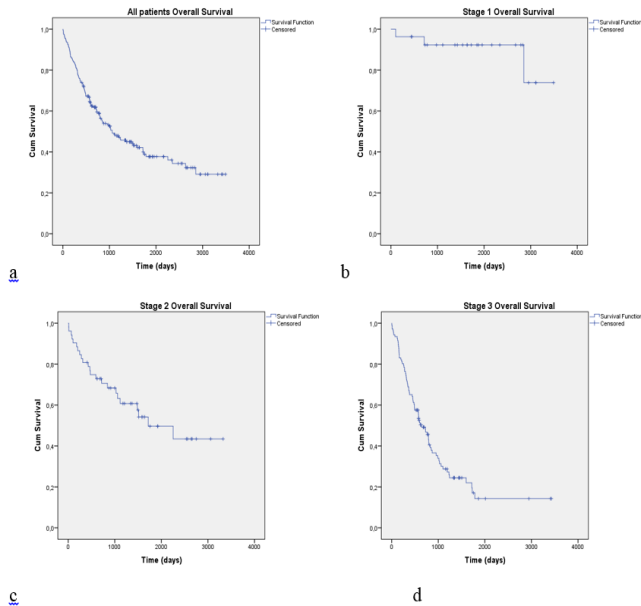


Figure 3. Kaplan-Meier survival curves, a) overall survival in all patients, b) overall survival according to stage 1, c) overall survival according to stage 2, d) overall survival according to stage 3

DISCUSSION

Gastric cancer is still one of the most important health issues in developing countries, except for countries with surveillance programs, such as Japan. In countries without surveillance programs, most of the patients are diagnosed in the advanced or metastatic stage(9). It is still unclear whether D2 lymphadenectomy improves the survival of patients with gastric cancer but current guidelines indicate

that D2 resection is the standard of care for patients with locally advanced gastric cancer(10, 11). After a median follow-up of 15 years of the randomized nationwide Dutch D1D2 trial, D2 lymphadenectomy is associated with lower locoregional recurrence and gastric-cancer-related death rates than D1 surgery(12). D2 resection technique is currently available in high-volume centers, D2 lymphadenectomy is the recommended surgical approach for patients with resectable gastric cancer(12). Nowadays, endoscopic mucosal dissection or endoscopic submucosal dissection in early gastric cancer can be performed safely in experienced centers(13). D1 + dissection is performed in patients who are not eligible for endoscopic mucosal resection or endoscopic submucosal dissection, while D2 dissection is safely performed in locally advanced or advanced gastric cancer(13,14). In our clinic, standard D2 gastrectomy procedure was applied to all patients, 9.5% of whom had early stage gastric cancer, 32% localized gastric cancer, and 68% regional gastric cancer.

Lymph node involvement is a major prognostic factor in gastric cancer(15). Several studies in Japan and in other countries have shown that increased lymph node involvement was a poor prognostic factor; therefore, the number of metastatic lymph nodes removed by extended lymph node dissection grew and survival rate could be increased(Yokota et al., 2004). It was recommended that a minimum number of 16 lymph nodes should be evaluated to ensure accurate staging, simply as the lowest denominator necessary to stage a patient as N3(17). The mean number of removed lymph nodes in our study was 24.26 ± 10.59 , and lymph node metastasis was found in 68% of our patients. In addition, in the univariate and multivariate analyses, we found that positive lymph node had a significant effect on survival ($p < 0.05$).

It is also well-established that, in addition to lymph node involvement, the prevalence of extra-lymphatic perineural invasion and vascular invasion also play a role in survival as important prognostic factors(18, 19). In our study, 69.9% of our patients were positive for perineural invasion and 62.3% for vascular invasion, of which we thought to play a role in survival of these patients ($p < 0.05$). Furthermore, tumor differentiation is another important prognostic factor, and it has been reported that patients with poorly differentiated tumors have worse prognosis(20). In our study, 68.5% of our patients had undifferentiated, mucinous, and signet-ring cell differentiation indicating poor differentiation.

Surgical treatment of gastric cancer is subtotal, total, or proximal gastrectomy according to the localization of the tumor with open or laparoscopic surgery. The incidence of complications varies, ranging between 12.5 and 22.4%(Lee et al., 2014). In patients who underwent total gastrectomy, reported rates of morbidity and mortality were higher than those of the patients who underwent distal gastrectomy; however, no difference was found in

terms of long-term survival(Maurizio Degiuli et al., 1998). In our study, subtotal gastrectomy was performed in 57.5% and total gastrectomy was performed in 42.5% of our patients, and complications occurred in 21.6% of the operated patients and there was no statistically significant difference between the types of gastrectomy.

The 30-day mortality after gastric cancer surgery is between 0.6 and 12% in the literature(23, 24)(Park et al., 2005). In our study, the hospital mortality was 6.2%.

Review of the literature reveals that there is a decline in the rate of distal gastric adenocarcinomas and an increase in cardiac and distal esophageal adenocarcinomas in developed countries(25). In our study, adenocarcinomas involved the lower part in 57% of the patients and the upper part in 17% of the patients.

Early stage in gastric cancer is the most important prognostic factor. Distribution of various disease stages based on environmental and regional differences were reported(26). Early stage is usually reported in the Far Eastern countries, while advanced stage is often reported in the Western societies(26). Except for early gastric cancers and reports from Japan, five-year survival rate in gastric cancer varies between 25 and 45% . In Japan, however, five-year survival rate is 85 to 90% in Stage I, 75% in Stage II, 30 to 50% in Stage III, and 5 to 15% in Stage IV disease(27). In our study, 57.3% of our patients were in Stage III, while 28.6% were in Stage II. At the final visit, 43.7% of our patients were still alive. The mean life expectancy was 54±3.6 months. Nine-year survival rate according to the stages were 88.9% in Stage I, 55.8% in Stage II, and 28.3% in Stage III disease. Consistent with the literature, we found that life expectancy in early stage gastric cancer was high, early diagnosis was of utmost importance, and T stage of the tumor had a major impact on survival (p<0.05).

The main limitations of the present study are its retrospective and single-center design. In addition, we were unable to document disease-free survival rates due to the miscellaneous problems during follow-up, including unavailability of an oncology clinic and small sample size.

CONCLUSION

Gastric cancer is among the most frequent causes of cancer-related deaths worldwide with a poor prognosis. Except for early stage, the chance of curative treatment is low in gastric cancer. Therefore, early diagnosis and treatment and surveillance programs can yield improved outcomes for this patient population. In addition, endoscopic indications should be more extended, and more time should be spent on the endoscopic diagnostic methods and treatment of pre-malignant lesions in patients with gastrointestinal system-related complaints.

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