Research Article / *Araştırma Makalesi*

Ege Journal of Medicine / *Ege Tıp Dergisi* 2022; 61 (2): 166-172

The effect of demographic features on survival in patients with gastric cancer

Mide kanserli hastaların demografik özelliklerinin sağ kalıma etkisi

Andaç Karadeniz Mehmet Bilici Melih Şimşek

Hınıs State Hospital, Erzurum, Turkiye

ABSTRACT

Aim: This study aimed to investigate the relationship between some demographic and clinical factors and survival in patients with gastric cancer.

Materials and Methods: We retrospectively evaluated the records of 252 gastric cancer patients followed up in the medical oncology department between 01.01.2016 and 10.01.2020. Gastric lymphoma, gastrointestinal stromal tumor, and neuroendocrine tumor were excluded. Factors evaluated in the study included age, sex, urban/non-urban residence, admitting complaints, smoking history, Eastern Cooperative Oncology Group (ECOG) score, stage at diagnosis, histological subtype, surgical history, tumor location, grade, diameter and macroscopic view of tumor, metastatic lymph node ratio, chemotherapy regimens, febrile neutropenia, post-chemotherapy radiological reports, chemoradiotherapy (CRT) history and survival after diagnosis.

Results: Mean overall survival (OS) time was significantly shorter in patients with weight loss ($p<0.001$), high ECOG score ($p<0.001$), radiological progression ($p<0.001$), advanced cancer stage ($p<0.001$) and tumor grade ($p=0.024$). Mean OS was longer in patients who received chemotherapy compared to those who did not at stage 4 ($p<0.001$). Mean OS was significantly longer in patients who underwent gastrectomy and received adjuvant CRT compared to those who did not ($p<0.001$). Mean OS was shorter in patients with a metastatic lymph node ratio over 30% ($p<0.001$) and those with tumor diameter larger than 3 cm ($p=0.02$).

Conclusion: In this study, survival time was associated with advanced stage, ECOG score, weight loss, radiological progression, high tumor grade, history of gastrectomy and adjuvant CRT, metastatic lymph node ratio >30%, tumor diameter >3 cm and presence of palliative chemotherapy in terminal patients.

Keywords: Demographic characteristics, chemotherapy, gastric cancer, radiotherapy.

ÖZ

***Amaç**: Bu çalışmada, mide kanserine yönelik çok sayıda demografik özellik ve klinik faktörün sağkalıma etkisini araştırmayı hedefledik.*

***Gereç ve Yöntem**: 01.01.2016-10.01.2020 tarihleri arasında takip edilen, mide kanseri tanılı 252 hastanın kayıtları retrospektif olarak değerlendirildi. Mide lenfoması, gastrointestinal stromal tümör ve nöroendokrin tümör tanılı hastalar çalışmaya alınmadı. Tanıdaki yaş, tanı tarihi, cinsiyet, kırsalda ya da şehirde ikamet özellikleri, tanı sonrası yaşam süreleri, başvuru yakınması, sigara öyküsü, Eastern Cooperative Oncology Group (ECOG) performans skoru, tanıdaki evre, histolojik alt tip, operasyon öyküsü ve tipi, tümöre ait grade ve çap, makroskobik tümör görüntüsü ve lokalizasyonu, metastatik lenf nodu yüzdesi, kemoterapi (KT) protokolleri, febril nötropeni, KT sonrası kontrol PET-BT raporları ve kemoradyoterapi (KRT) öyküsü gibi faktörler değerlendirildi.*

***Bulgular**: Kilo kaybı ($p<0,001$), yüksek ECOG skoru ($p<0,001$), kontrol PET-BT'de progresyon ($p<0,001$), ileri evre ($p<0,001$), yüksek grade tümör ($p=0,024$) varlığında ortalama genel sağkalım (GSK) süresi anlamlı oranda kısaydı.*

Corresponding author: Andaç Karadeniz
Hınıs State Hospital, Erzurum, Turkiye
E-mail: *andac.karadeniz@hotmail.com*
Application date: 12.07.2021 Accepted: 29.11.2021

Gastrektomi ve adjuvan KRT varlığında GSK süreleri daha uzundu (p<0,001). Evre 4 hastalıkta; palyatif KT alan hastaların GSK süreleri KT almayanlara göre daha uzundu (p<0,001). Metastatik lenf nodu oranı %30'un üzerinde olanlarda ortalama GSK süresi, anlamlı derecede kısaydı (p<0,001). Tümör çapı 3 cm'den fazla olanlarda GSK süresi daha kısaydı (p=0,02).

***Sonuç**: Çalışmamızda; evre, ECOG skoru, kilo kaybı yakınması, kontrol PET-BT'de progresyon olması, yüksek evre, gastrektomi öyküsü, metastatik lenf nodu oranının %30'un üzerinde olması, tümör çapının 3 cm'den fazla olması, adjuvan KRT öyküsü, terminal dönem hastalarda palyatif amaçlı da olsa KT varlığının GSK süresi ile ilişkili olduğu saptandı.*

***Anahtar Sözcükler**: Demografik özellikler, kemoterapi, mide kanseri, radyoterapi.*

INTRODUCTION

Gastric cancer is the fifth most frequently diagnosed cancer and the third leading cause of cancer death world-wide. Its incidence is twice as high in males as in females. Because it typically manifests nonspecific symptoms, gastric cancer is often diagnosed at an advanced stage. Early surgical intervention may be curative but more than two-thirds of cases present with locally advanced or metastatic disease. Chemotherapy was shown to be superior to the best supportive therapy in metastatic gastric cancer and prolonged overall survival (OS) in randomized trials (1, 2).

High intake of fried food, processed or smoked meat, fish, and alcohol; low intake of fruits, vegetables, milk and vitamin A, excessive salt intake and *Helicobacter pylori* infection are involved in the etiology of gastric cancer (3-7). Distal gastric cancer is twice as common in patients with a low socioeconomic status, while proximal gastric cancer is more common in patients with a high socioeconomic status (8, 9).

Adenocarcinoma is the most common histological subtype in gastric cancer (95%). Half of the remaining 5% are lymphomas and the other half are rare tumors such as squamous cell carcinoma, leiomyosarcoma, carcinoid tumor and adenoacanthoma. Adenocarcinomas can be ulcerated (75%), polypoid (10%), diffuse scirrous (10%), or superficial mucosal (5%) (10-12).

Curative treatment in gastric cancer consists of surgical resection of the primary tumor and regional lymph nodes. Extent of disease, surgical method and patient selection are important determinants of outcomes (13). High mortality in gastric cancer is due to advanced stage at diagnosis. The 5-year OS rate is 70-75% in patients who undergo complete resection at stage 1, while this rate decreases to 35% at stage 2 (14). Surgery, chemotherapy, radiotherapy (RT), and targeted treatments are used in gastric cancer. Single-agent or combined therapies can be administered according to disease stage. The favorable impact of multimodal treatment on OS has become evident over time (15, 16).

The primary objective of this study was to examine the relationship between demographic characteristics and OS in gastric cancer patients. Secondary objectives were to investigate the effects of various clinical and epidemiological parameters and different chemotherapy regimens on OS.

MATERIALS and METHODS

This article is based on research conducted for the author's medical specialization thesis. The study was conducted in accordance with the tenets of the Helsinki Declaration, patient rights regulations, ethical guidelines, and was approved by the local ethics committee.

We retrospectively evaluated the records of 252 patients over 18 years of age who were diagnosed as having gastric cancer with no synchronous tumors and were followed up in the medical oncology department between 01.01.2016 and 10.01.2020. Patients with gastric lymphoma, gastrointestinal stromal tumor and neuroendocrine tumor were not included. Age at diagnosis, date of diagnosis, sex, area of residence (urban/non-urban), smoking history, admitting complaints, Eastern Cooperative Oncology Group (ECOG) performance score, stage at diagnosis, chemotherapy protocols, chemotherapy-related febrile neutropenia, post-chemotherapy positron emission tomography–computed tomography (PET-CT) findings, RT history, tumor location, size, histological subtype and macroscopic appearance, surgical history and procedure type, metastatic lymph node ratio and OS were evaluated. Response to chemotherapy was assessed according to the Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. The patients' ECOG

performance scores were retrieved from their records. OS was calculated as the time from date of diagnosis to date of death for non-surviving patients and from date of diagnosis to the last outpatient visit for surviving patients. SPSS version 22.0 (IBM Corp, Armonk, NY) software was used for statistical evaluation and analysis.

OS analysis was performed using Kaplan-Meier test and comparisons were made using Log-Rank analysis. To compare the means of two groups, independent t test was used when the groups of 30 or more and Mann-Whitney U test was used for groups of fewer than 30. The chi-square test was used for comparisons of categorical variables between groups. Data related to quantitative variables were expressed using mean ± standard deviation and median (minimum-maximum), while number and percentage (%) were used to express data pertaining to qualitative variables. Shapiro-Wilk test was used to test quantitative variables for normal distribution. Independent variables that showed a significant association with OS were investigated using a multivariate Cox regression model. A p value less than 0.05 was accepted as statistically significant.

RESULTS

The study included a total of 252 patients. The demographic and clinical characteristics of the patients are shown in Table-1. The patients' median age was 61.6 years (28-97 years) and the mean OS time was 31.2 ± 2.4 months (18 days-72 months). Of the patients included in the study, 148 (58.7%) died and 104 (41.3%) survived.

Of the 111 patients who underwent surgery, 96 (86.4%) had a significant number of countable lymph nodes resected (≥15) and 31 patients (28%) had a metastatic lymph node ratio of 30% or higher. Mean OS time was 54.1±5.3 months among those with a metastatic lymph node ratio below 30% and 26.9±2.4 months in those with a metastatic lymph node ratio above 30% (p<0.001).

Tumor diameter data was not available for 11 patients (4.3%). Maximum tumor diameter was ≤3 cm in 77 patients (30.5%) and >3 cm in 164 patients (65.2%) (range, 0.6-15 cm). There was a statistically significant relationship between maximum tumor diameter and OS (p=0.02). Mean OS time was 40.9±4.7 months in patients with a maximum tumor diameter ≤3 cm and 26.1±1.9 months in those with a maximum tumor diameter >3 cm.

In terms of degree of differentiation, tumors were evaluated as grade 1 in 10 patients (9%), grade 2 in 60 patients (54%), and grade 3 in 41 patients (37%). A significant relationship was detected between grade and OS (p=0.02). The mean OS time was 59.5±4.2 months in surgical patients who had grade 1 tumors, compared to 33.2±2.6 months in patients with grade 3 tumors.

The mean OS time of the patients with progression/relapse reported in the PET-CT report was 22.4±2.1 months while the mean OS time of the patients with complete cure reported in the PET-CT report was 62.6±1.3 months. It was determined that the mean OS time of the patients with progression in the control PET-CT report was statistically shorter (p<0.001).

Febrile neutropenia occurred in 59 (23.4%) of the patients and was most commonly associated with the FLOT, FOLFOX, and FOLFIRI chemotherapy regimens. There was no significant relationship between the development of febrile neutropenia and OS (p=0.982).

The mean OS time was 33.4±1.9 months among 69 patients who received adjuvant chemoradiotherapy and 17.7±2.2 months in those who did not receive adjuvant chemoradiotherapy. Mean OS of patients receiving adjuvant chemoradiotherapy was statistically significantly longer (p<0.001).

Comparison of stage 4 patients who did and did not receive chemotherapy revealed a statistically significant relationship. Mean OS time was 4.8±1.01 months in the 13 patients (18.8%) not treated with chemotherapy and 10.4±0.7 months in the 54 patients (78.2%) who received chemotherapy (p<0.001). Chemotherapy information was not available for 2 patients (2.8%) with stage 4 cancer. We also grouped the stage 4 patients who received chemotherapy according to chemotherapy regimen for OS analysis. The patients were grouped as those who received CAPEOX (n=10, 14.9%), EOX (n=10, 14.9%), FLOT (n=10, 14.9%), carboplatin-paclitaxel (n=10, 14.9%), and other (n=14, 20.8%). There was no statistically significant relationship between chemotherapy regimen and mean OS in these stage 4 patients (p=0.874).

Table-1. Clinical and demographic characteristics of the patients.

Parameter		Patient number (n = 252)	Median overall survival (months)	P value
Disease stage	Stage 0	1	42.0±0	**<0.001**
	Stage 1	24	68.8±3	
	Stage 2	66	46.6±4.8	
	Stage 3	92	19.9±1.2	
	Stage 4	69	9.2±0.6	
Chemotherapy Type	None	31	24.3±4.8	**<0.001**
	Neoadjuvant	17	41.1±1.7	
	Adjuvant	55	36±2.1	
	Neoadjuvant + Adjuvant	34	33.9±2.3	
	Palliative	114	16.9±1.7	
Surgery	None	141	15.8±1.4	**<0.001**
	Total	73	37.8±1.7	
	Subtotal/Distal	38	45.3±5.3	
Radiotherapy	None	179	17.7±2.2	**<0.001**
	Local	73	33.4±1.9	
ECOG Score at Diagnosis	0, 1, 2	161	41.4±2.7	**<0.001**
	3, 4	68	9.8±1.9	
Weight loss	Yes	38	14.1±1.9	**<0.001**
	No	214	30.9±3.1	
Age (years)	≤65	160	30.2±3.4	0.743
	>65	92	30.8±3.3	
Primary Site	Cardia/Esophagogastric	103	25.3±1.7	0.166
	Corpus	36	36.9±5.1	
	Antrum	75	31.9±3.6	
	Pyloric	14	25.6±4.6	
Main Groups of Chemotherapy Regimens at All Stages as First Line Treatment	None	31	23.8±5.3	0.006
	Oxaliplatin + 5-FU* based regimens	53	29.5±2.5	
	Irinotecan based regimens	11	20.7±2.6	
	Docetaxel + 5-FU based regimens	66	29.5±4.6	
	Epirubicin + 5-FU based regimens	42	21.5±2.3	
	Other regimens**	29	21.2±2.7	
	Capecitabine only	20	44.1±5.5	
Sex	Female	86	29.1±3.4	0.398
	Male	166	32±3.1	
Smoking	Yes	114	31.5±3.3	0.057
	No	111	30±2.9	

*5-FU: 5-Fluorouracil

**Other regimens include carboplatin, cisplatin, calcium folinate, paclitaxel, trastuzumab or bevacizumab.

DISCUSSION

Gastric cancer is the fifth most common cancer and the third leading cause of cancer mortality worldwide, despite its decreasing incidence in recent decades. Moreover, there is a sex-specific disparity in gastric cancer incidence. Incidence rates are 2-fold higher in men than in women worldwide (17). In Turkey, the incidence of gastric cancer was reported as 9.6/100,000 in men and 5.7/100,000 in women (18). Tuncer et al. determined the male to female ratio to be 1.6:1 in a study conducted in the Van Lake basin between 1994 and 2000 (19). In the present study, the male to female ratio was 1.9:1.

Several studies have shown that gastric cancer patients with ECOG performance scores of 0 or 1 have a better prognosis than patients with performance scores of 2 or higher (20-22). Consistent with the literature, we observed a significant decrease in OS with higher ECOG performance score.

Tumor stage is the most important prognostic factor in gastric cancer. Numerous studies have demonstrated the marked effect of stage on OS (23-26). Similarly, we detected a highly significant relationship between disease stage and OS in this study.

Ock et al. reported that weight loss at the time of diagnosis and in the first month of palliative chemotherapy were associated with poorer prognosis in patients with advanced gastric cancer (27). Similarly, we identified a statistically significant relationship between admitting complaints of weight loss and shorter OS.

OS was significantly longer in patients who received adjuvant chemoradiotherapy. Smalley et al. also demonstrated significantly better OS in the adjuvant chemoradiotherapy group in their randomized phase 3 trial (28).

In the present study, findings of progression or regression on control PET-CT were strongly associated with mean OS. Mean OS time was 22.4±2.1 months in patients with findings of progression/recurrence on PET-CT and 62.6±1.3 months in patients with complete response. Our study is consistent with the literature in this respect (29).

We found that the mean OS time was 54.1±5.3 months among patients with a metastatic lymph node ratio below 30% and 26.9±2.4 months in those with a ratio of 30% or higher. Similar to the literature, there was a highly significant relationship between metastatic lymph node ratio and OS (30).

Many studies have reported that performing R0 resection results in long OS time (31, 32). In accordance with the literature, we also found that when gastrectomy could be performed, the mean OS was significantly longer. In addition, higher tumor grade in operated patients was associated with significantly shorter OS. This result was also consistent with the literature (33).

In our patient population, there was a statistically significant relationship between maximum tumor diameter and OS. There are also reports in the literature that tumor diameter is an independent prognostic factor in gastric cancer (34).

Febrile neutropenia occurred in 59 patients in this study, and the most common causes were the chemotherapy regimens FLOT, FOLFOX, and FOLFIRI. However, we observed no statistically significant difference in OS between patients with and without febrile neutropenia. Nardi et al. reported that DCF and FLOT were the regimens most commonly associated with grade 3-4 hematologic toxicity (35). Febrile neutropenia may be less common in our clinic because we administer prophylactic granulocyte colony-stimulating factor (G-CSF) after the DCF regimen.

Catalano et al. showed that palliative chemotherapy had a favorable effect on mean OS in metastatic gastric cancer in their study of 625 patients, but observed no significant difference in OS among chemotherapy regimens (36). The outcomes of metastatic cases in the present study are consistent with the literature (1, 36, 37).

CONCLUSION

In conclusion, the parameters statistically associated with shorter mean OS in patients with gastric cancer were advanced disease stage at diagnosis, high ECOG performance score, history of weight loss, detection of progression on PET-CT, high tumor grade, inability to perform gastrectomy, metastatic lymph node ratio greater than 30% and tumor diameter greater than 3 cm. Parameters associated with longer mean OS were history of adjuvant chemoradiotherapy and palliative chemotherapy at stage 4 patients.

Limitations of our study include its retrospective design, the lack of a standard surgical approach due to patients presenting from different centers and insufficient follow-up due to socioeconomic limitations and adverse climatic conditions related to the geography in our region. More extensive studies with larger patient samples are needed.

Conflict of interest: The authors declared no conflict of interest.

References

1. 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 Nov; 68 (6): 394-424.
2. Avital I, Stojadinovic A, Pisters PWT, Kelsen DP, Willett CG. Cancer of the Stomach. In: DeViltaVT, Lawrence TS, Rosenberg SA (editors). Cancer: Principles & Practice of Oncology. 9th ed. Philadelphia: Lippincott Williams & Wilkins Wolters Kluwer Health; 2011. p946.
3. Zhu H, Yang X, Zhang C et al. Red and processed meat intake is associated with higher gastric cancer risk: a meta-analysis of epidemiological observational studies. PloS one 2013; 8 (8): e70955.
4. Tsugane S, Sasazuki S. Diet and the risk of gastric cancer: review of epidemiological evidence. Gastric cancer 2007; 10 (2): 75-83.
5. Shikata K, Kiyohara Y, Kubo M et al. A prospective study of dietary salt intake and gastric cancer incidence in a defined Japanese population: the Hisayama study. Intl J Cancer 2006; 119 (1): 196-201.
6. Peleteiro B, Lopes C, Figueiredo C, Lunet N. Salt intake and gastric cancer risk according to Helicobacter pylori infection, smoking, tumour site and histological type. BMJ 2011; 104 (1): 198-207.
7. Machida-Montani A, Sasazuki S, Inoue M et al. Association of Helicobacter pylori infection and environmental factors in non-cardia gastric cancer in Japan. Gastric Cancer 2004; 7 (1): 46-53.
8. Barker D, Coggon D, Osmond C, Wickham C. Poor housing in childhood and high rates of stomach cancer in England and Wales. BMJ 1990; 61 (4): 575.
9. Powell J, McConkey C. Increasing incidence of adenocarcinoma of the gastric cardia and adjacent sites. BMJ 1990; 62 (3): 440.
10. Akdogan RA, Aslan M. Mide Tümörleri. Özden A, Sahin B, Yılmaz U (editors). Gastroenteroloji. Türk Gastroenteroloji Vakfı, Ankara 2002;107-12 (in Turkish).
11. Göksel S, Topuz E, Aykan NF. Mide kanserinde etyoloji, patogenez ve patoloji. İstanbul Onkoloji Enstitüsü Yayınları 1998: 181-6 (in Turkish).
12. Kubba A, MacIntyre I. Gastric cancer distal to the cardia—prevention or cure? Sur Onc 1997; 6 (2): 111-24.
13. Catalano V, Labianca R, Beretta GD, Gatta G, de Braud F, Van Cutsem E. Gastric cancer. Crit Rev Oncol Hematol 2009;71(2):127-64.
14. Agboola O. Adjuvant treatment in gastric cancer. Cancer Treat Rev 1994; 20 (3): 217-40.
15. Siewert JR, Feith M, Werner M, Stein HJ. Adenocarcinoma of the esophagogastric junction: results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. Ann Surg 2000; 232 (3): 353-61.
16. Macdonald JS, Smalley SR, Benedetti J et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. N Engl J Med 2001; 345 (10): 725-30.
17. Li WY, Han Y, Xu HM et al. Smoking status and subsequent gastric cancer risk in men compared with women: a meta-analysis of prospective observational studies. BMC Cancer 19, 2019: 377.
18. Yalcin S. Gastric cancer in Turkey—a bridge between west and east. GCR 2009; 3 (1): 29.
19. Tuncer İ, Uygan İ, Kösem M, Özen S, Uğraş S, Türkdoğan K. The Demography and Histopathologic Characteristics Of Upper Gastrointestinal Cancers Appeared in Van and Its Vicinity. Van Tıp Dergisi 2001; 8 (1): 10 (in Turkish).
20. Yücel B, Kılıçkap S, Lehimcioğlu Y, Erdiş E, Akkaş EA, Şalk M. Prognostic factors that affect the survival of gastric cancer. Cumhuriyet Medical Journal 2012; 34 (2): 173-82.
21. Altınbaş M, Hepşen S, İmamoğlu İ et al. Death Reasons and Factors That Affect on Survival of Cancer Patients. Sakarya Tıp Dergisi 2015; 5 (1): 5-9 (in Turkish).
22. Psaltopoulou T, Ntanasis-Stathopoulos I, Tzanninis IG et al. Physical Activity and Gastric Cancer Risk: A Systematic Review and Meta-Analysis. Clin J Sport Med 2016; 26 (6) :445-64.
23. Bando E, Yonemura Y, Taniguchi K, Fushida S, Fujimura T, Miwa K. Outcome of ratio of lymph node metastasis in gastric carcinoma. Ann Surg Oncol 2002; 9 (8): 775-84.

24. Sun Z, Zhu GL, Lu C et al. The impact of N-ratio in minimizing stage migration phenomenon in gastric cancer patients with insufficient number or level of lymph node retrieved: results from a Chinese mono-institutional study in 2159 patients. Ann Oncol 2009; 20 (5): 897-905.
25. Kitamura K, Yamaguchi T, Taniguchi H et al. Analysis of lymph node metastasis in early gastric cancer: rationale of limited surgery. J Surg Oncol 1997; 64 (1): 42-7.
26. Sasako M, McCulloch P, Kinoshita T, Maruyama K. New method to evaluate the therapeutic value of lymph node dissection for gastric cancer. BMJ 1995; 82 (3): 346-51.
27. Ock CY, Oh DY, Lee J et al. Weight loss at the first month of palliative chemotherapy predicts survival outcomes in patients with advanced gastric cancer. Gastric Cancer 2015:8.
28. Smalley SR, Benedetti JK, Haller DG et al. Updated analysis of SWOG-directed intergroup study 0116: a phase III trial of adjuvant radiochemotherapy versus observation after curative gastric cancer resection. J Clin Oncol 2012; 30 (19): 2327-33.
29. Sun L, Su XH, Guan YS et al. Clinical role of 18F fluorodeoxyglucose positron emission tomography/computed tomography in post-operative follow up of gastric cancer: initial results. World J Gastroenterol 2008; 14 (29), 4627–32.
30. Nelen SD, van Steenbergen LN, Dassen AE, van der Wurff AA, Lemmens ve, Bosscha K. The lymph node ratio as a prognostic factor for gastric cancer. Acta Oncologia 2013; 52: 1751-9.
31. Bozzetti F, Bonfanti G, Audisio RA et al. Prognosis of patients after palliative surgical procedures for carcinoma of the stomach. Surg Gynecol Obstet 1987; 164 (2): 151-4.
32. Boddie A, McMurtrey M, Giacco G, McBride C. Palliative total gastrectomy and esophagogastrectomy a reevaluation. Cancer 1983; 51 (7): 1195-200.
33. Medina-Franco H, Heslin MJ, Cortes-Gonzalez R. Clinicopathological characteristics of gastric carcinoma in young and elderly patients: a comparative study. Ann Surg Oncol 2000; 7 (7): 515-9.
34. Adachi Y, Oshiro T, Mori M, Maehara Y, Sugimachi K. Tumor size as a simple prognostic indicator for gastric carcinoma. Ann Surg Oncol 1997; 4 (2): 137-40.
35. Nardi M, Azzarello D, Maisano R et al. FOLFOX-4 regimen as fist-line chemotherapy in elderly patients with advanced gastric cancer: a safety study. J Chemother 2007; 19 (1): 85-9.
36. Catalano V, Graziano F, Santini D et al. Second-line chemotherapy for patients with advanced gastric cancer: who may benefit? Br J Cancer 2008; 99 (9): 1402-07.
37. Wagner AD, Grothe W, Haerting J, Kleber G, Grothey A, Fleig WE. Chemotherapy in advanced gastric cancer: a systematic review and meta-analysis based on aggregate data. J Clin Oncol 2006; 24 (18): 2903-09.