Int J Clin Exp Med 2020;13(10):7903-7909
www.ijcem.com /ISSN:1940-5901/IJCEM0113726

Original Article

Effect of preoperative neoadjuvant chemotherapy on postoperative complications in patients with gastric cancer

Hilmi Bozkurt[1], Ozlem Zeliha Sert[2], Orhan Uzun[3], Selcuk Gulmez[3], Aziz Serkan Senger[3], Erdal Polat[3], Mustafa Duman[3]

[1]Gastrointestinal Surgeon, University of Health Sciences, Haseki Resarch and Education Hospital, Istanbul, Turkey; [2]Gastrointestinal Surgeon, University of Health Sciences, Haydarpaşa Resarch and Education Hospital, Istanbul, Turkey; [3]Gastrointestinal Surgeon, University of Health Sciences, Kosuyolu Resarch and Education Hospital, Istanbul, Turkey

Received May 3, 2020; Accepted September 29, 2020; Epub October 15, 2020; Published October 30, 2020

Abstract: While patients with locally advanced gastric cancer can benefit from neoadjuvant chemotherapy (NAC), there are potential disadvantages. These include an increased rate of surgical complications, resulting in an increase in the rate of postoperative morbidity. The present study evaluates the effect of preoperative NAC on postoperative morbidity, for which the data of patients who underwent curative radical gastrectomy and D2 lymph node dissection due to gastric cancer were retrieved from the hospital archives and reviewed retrospectively. The patients were divided into two groups: those administered NAC; and those not administered NAC. The clinical characteristics of the patients, perioperative and postoperative findings, pathological characteristics and postoperative complications were evaluated. All postoperative complications were evaluated according to the Clavien-Dindo classification system. The study was conducted with 176 patients who underwent treatment in the specified time period. Group 1 comprised 39 patients who were administered NAC, while group 2 comprised 137 patients who were not administered NAC. Postoperative complications were evaluated according to the Clavien-Dindo classification system, and no statistically significant difference was identified between the two groups (P=0.186). A Cox regression analysis revealed the number of metastatic lymph nodes, TNM stage, preoperative albumin level, and the administration of NAC to be related to survival. Contrary to current expectations, NAC did not increase postoperative complications. According to the Clavien-Dindo classification system, there is no increased risk of postoperative morbidity in patients with locally advanced gastric cancer who are treated with NAC.

Keywords: Neoadjuvant chemotherapy, gastric cancer, postoperative complications

Introduction

Gastric cancer (GC) is the fourth most commonly diagnosed malignancy and the second leading cause of cancer-related death worldwide [1, 2]. Gastrectomy combined with lymph node dissection is the most effective therapy for gastric cancer, although the prognosis of patients with advanced stage GC is still unsatisfactory. Recurrent disease may occur in the peritoneum, liver and other distal organs, even after curative surgery, and this may indicate the presence of distant mcirometastases [3, 4]. Asymptomatic invisible peritoneal seeding occurs during surgery in approximately 10-20% of patients with GC undergoing a potentially curative resection [5]. Multimodal therapy involving NAC and surgical resection with negative margins (R0 resection) is considered the standard approach to gastric cancer in many centers [6]. Previous studies suggest that postoperative complications, particularly those that are inflammatory in nature, occurring in patients with colorectal cancer, esophageal cancer and GC have unfavorable effects on prognosis [7-11]. The relationship between postoperative complications and survival is considered to be attributable to the release of inflammatory cytokines during systemic inflammation, and these cytokines may induce the growth of can-

cer cells [10-12]. There have been many studies reporting significantly increased disease-free survival and overall survival in patients undergoing NAC [13, 14], although there are other studies detailing some negative postoperative effects of NAC prior to a gastrectomy [15]. The present study investigates the effects of preoperative NAC on postoperative morbidity in patients undergoing radical gastrectomy and D2 lymph node dissection due to gastric cancer.

Materials and methods

The records of patients with gastric cancer who underwent curative radical gastrectomy and D2 lymph node dissection in a single center between January 2012 and December 2019 were retrieved from the hospital archives and reviewed retrospectively. The treatment protocols of all patients were determined by the tumor council. For staging purposes, all patients underwent upper gastrointestinal endoscopy and contrast-enhanced thoracoabdominal computed tomography (CT), and those with suspected systemic metastasis also underwent positron emission tomography-computed tomography (PET-CT) scans. The inclusion criteria were a histologically-confirmed diagnosis of primary gastric adenocarcinoma; and having undergone lymph node dissection and curative gastrectomy, or lymph node dissection and curative gastrectomy followed by preoperative NAC. Patients undergoing an R2 or R1 resection (6 patients), those with preoperative stage 1 and 4 disease, and those that were NAC intolerant (5 patients), and so directly underwent surgery, were not included in the study. Those undergoing a multiple organ resection were also excluded, as these patients would increase postoperative morbidity rates. The eligibility criteria for NAC were bulky N GC, and type 4 and large type 3 GC, cT3-cT4 and any N. Surgery was performed within 6 weeks of the last course of chemotherapy treatment. Gastrectomy and lymph node dissections were carried out in accordance with the recommendations of the Japanese Research Society for GC [16]. The patients underwent a total or distal gastrectomy, depending on the anatomical localization of the tumor, in order to ensure R0 resection. All patients received preoperative antibiotic prophylaxis. The gastrointestinal reconstructions involved either a total gastrectomy with, or a distal gastrectomy with gastrojejunostomy + brown anastomosis. Esophagojejunostomies were performed using a 25-mm circular stapler, while gastrojejunostomies were performed manually. Tumor stage was determined according to the seventh edition of the International Union against Cancer tumor, node and metastasis (TNM) classification system. All postoperative complications were evaluated, in addition to any lethal outcomes that occurred during the hospital stay, and were graded according to the Clavien-Dindo classification system [17]. The patients were divided into two groups: those administered NAC and those not administered NAC, and evaluations were made of preoperative ASA (American Society of Anesthesiologists) score; comorbidities (diabetes, hypertension, chronic obstructive pulmonary disease); clinical characteristics, such as the receipt of nutritional supplements; tumor markers; laboratory parameters, such as C-reactive protein (CRP) level; surgery type, operation time and perioperative characteristics, such as blood transfusion; pathological characteristics such as TNM stage in the pathological specimen; the presence of lymphovascular or perineural invasion; differentiation type and postoperative complications.

Neoadjuvant regime

FLOT: 5-FU/leucovorin/oxaliplatin/docetaxel, CF: cisplatin/fluorouracil (5-FU), DCF: docetaxel/cisplatin/fluorouracil, FOLFOX: oxaliplatin/leucovorin/fluorouracil.

The study was approved by the ethics committee of our hospital (Approval no: 2019.8/04-251-Approval date: 26.12.2019).

Statistical analysis

The SPSS 15.0 for Windows software package was used for the statistical analysis. Descriptive statistics were expressed in numbers and percentages for the categorical variables, while quantitative variables were expressed as mean, standard deviation, minimum and maximum. A Student's t-test was used for the comparison of quantitative variables with normal distribution between the two independent groups, and a Mann-Whitney U test otherwise. A Chi-square test was used to compare between-group ratios, and a Kaplan-Meier analysis was used for the survival analysis. The

Table 1. Demographic data

		n(%), Med±SD (Min-Max)
Sex:	Female	61 (34.7)
	Male	115 (65.3)
Age		60.8±12.2 (28-91)
Lymph node:		27.8±12.1 (15-74)
Metastatic lymph node:		5.3±7.9 (0-48)
	1	38 (21.6)
TNM p stage:	2	66 (37.5)
	3	72 (40.9)
Differentiation:	Poor	97 (55.1)
	Moderete	67 (38.1)
	Well	67 (38.1)
LVI:		106 (60.2)
PNI:		110 (62.5)
BMI:		26.2±4.0 (18-36)
CAD:		71 (40.3)
DM:		28 (15.9)
COPD:		48 (27.3)
Preoperative nutritionel:		94 (53.4)
CEA:		5.3±11.1 (0.0-95)
CA19-9:		33.0±61.3 (0.1-437)
	1	4 (2.3)
ASA:	2	39 (22.2)
	3	132 (75.0)
	4	1 (0.6)
Type of surgery:	Distal	79 (44.9)
	Total	97 (55.1)
Operation time(minute):		281.2±62.8 (160-550)
Perioperative blood transfusion:		20 (11.4)
Preoperative albümin:		3.96±0.49 (1.8-5)
Preoperative CRP:		1.16±1.96 (0.1-16.5)
Hospitalization day:		13.0±11.3 (0-120)
Neoadjuvant chemotherapy:	-	137 (77.8)
	+	39 (22.2)
Follow-up time (month):		33.3±26.0 (0-96)

SD, standard deviation; BMI, body mass index; LVI, lymphovascular invasion; PNI, perineural invasion; CAD, coronary artery disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CEA, carioembryogenic antigen; ASA, american society of anesthesiologists, CRP, c reactive protein.

determining factors were further analyzed using a Cox regression analysis. The level of statistical significance was set to an alpha of 0.05.

Results

The study included 176 patients who underwent treatment within the specified time period. Group 1 comprised 39 patients who were administered NAC; and group 2 comprised 137 patients who were not administered NAC. The demographic data of the patients, preoperative clinical and laboratory findings, surgical findings, postoperative clinical and pathological findings, and postoperative morbidities are presented in **Table 1**. When groups with and without neoadjuvant chemotherapy were compared; pathological stage, metastatic lymph node, CEA and lymphovascular invasion values were statistically significant ($P<0.05$). The characteristics of groups receiving or not receiving NAC are presented in **Table 2**. An evaluation of the postoperative findings according to the Clavien-Dindo classification system revealed no statistically significant difference in terms of the complications ($P=0.186$). Among those classified as Grade 3, anastomotic leakage occurred in two patients, postoperative hemorrhage occurred in one patient, intraabdominal collection and abscess occurred in three patients, a chylous fistula occurred in one patient and fascial dehiscence occurred in two patients in Group 1, whereas among the patients classified as Grad 3 in Group 2, anastomotic leakage occurred in six patients, postoperative hemorrhage occurred in four patients, intraabdominal collection and abscesses occurred in seven patients, a chylous fistula occurred in two patients and a fascial dehiscence occurred in three patients. Among patients with Grade 4 complications, only one patient in Group 2 underwent a total gastrectomy due to gastroparesis. The one patient with Grade 5 complications was in Group 1, postoperative first day was ex due to myocardial infarction. **Table 3**. The median 1-year survival rate was 80% and the median 5-year survival rate was 51% (**Figure 1**). The mean survival was significantly lower in the NAC group than in the non-NAC group (**Figure 1**). A univariate analysis examining the factors determining mortality found metastatic lymph

Table 2. Groups by neoadjuvant treatment status

		neoadjuvant chemotherapy		P
		not receiving n(%)-Med±SD	receiving n(%)-Med±SD	
Sex:	Female	54 (39.4)	7 (17.9)	0.013
	Male	83 (60.6)	32 (82.1)	
Age: Med±SD		61.7±12.6 (63)	57.7±9.7.(60)	0.071
Lymph node:		27.5±11.4 (25)	28.8±14.2 (25)	0.872
Metastatic lymph node:		4.4±6.7 (1)	8.5±10.4 (4)	0.008
TNM p stage:	1	35 (25.5)	3 (7.7)	0.013
	2	52 (38.0)	14 (35.9)	
	3	50 (36.5)	22 (56.4)	
LVI+:		76 (55.5)	30 (76.9)	0.016
PNI+:		84 (61.3)	26 (66.7)	0.542
BMI:		26.1±4 (26)	26.5±3.8 (26)	0.617
CAD:		44 (32.1)	8 (20.5)	0.521
DM:		57 (41.6)	14 (35.9)	0.550
COPD:		23 (16.8)	5 (12.8)	0.882
CEA:		3.9±7.9 (2.0)	10.0±17.5 (2.9)	0.007
CA 19-9:		44.0±68.3 (13)	25.2±54.8 (8.4)	0.140
Operation time:		272.3±59.5 (260)	312±64.6 (300)	0.545
Hospitalization day:		12.9.±12 (9.0)	13.2±8.2 (12)	0.099

SD, standard deviation; BMI, body mass index; LVI, lymphovascular invasion; PNI, perineural invasion; CAD, coronary artery disease; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CEA, carioembryogenic antigen; ASA, american society of anesthesiologists.

Table 3. Group receiving and not receiving neoadjuvant chemotherapy

		Neoadjuvant chemotherapy				P
		not receiving		receiving		
		n	%	n	%	
Clavien-Dindo	Not	83	60.6	18	46.2	0.186
	1	8	5.8	5	12.8	0.166
	2	22	16.1	6	15.4	0.919
	3	23	16.8	9	23.1	0.369
	4	1	0.7	0	0.0	1.000
	5	0	0	1	2.6	0.222
Total		137	100	39	100	

nodes, TNM Stage 2-3, preoperative albumin and NAC to be significant risk factors in the model, which was composed of variables with P<0.250 and without NAC (**Table 4**).

Discussion

The present study found that the preoperative administration of NAC did not increase the rate of morbidity in patients undergoing treatment for gastric cancer, and that the number of metastatic lymph nodes, TNM stage, CA19-9, preoperative albumin level and the administration of NAC were directly related to survival.

The main objective of surgery in patients with gastric cancer is to remove the visible tumor and to ensure a curative resection with a regional lymph node dissection. Multimodal therapies have gained importance in the treatment of gastric cancer due to advances in staging and neoadjuvant treatment strategies [18]. A significant improvement was demonstrated in the disease-free and overall survival of patients with locally advanced gastric adenocarcinoma and lower esophageal adenocarcinoma in a randomized study comparing patients undergoing surgery alone versus those undergoing perioperative chemotherapy + surgery [13, 14]. In clinical practice, preoperative chemotherapy can be administered in higher doses than postoperative chemotherapy, although the compliance of patients to NAC and tolerability are better in the preoperative period. Furthermore, a high rate of R0 resection can be achieved in later stages, and thus overall survival can be improved [3, 19]. In the

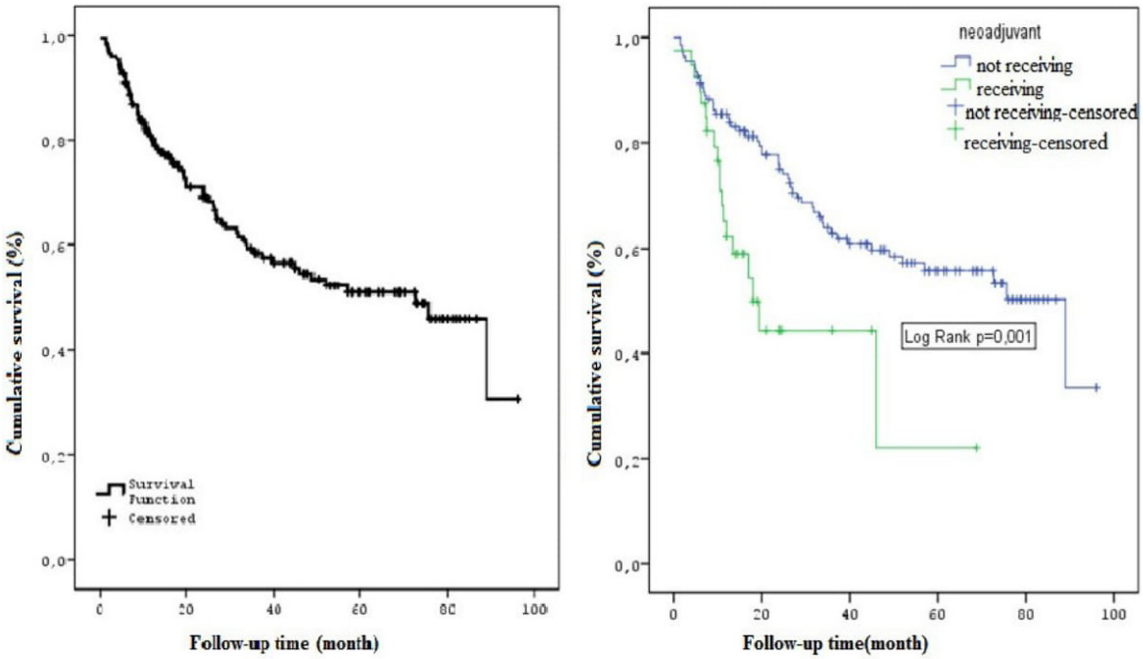

Figure 1. Cumulative survival groups.

Table 4. Factors determining survival Cox Regression Analysis

		P	OR	%95 CI	
Enter Method	Metastatic LN	0.085	1.027	0.996	1.059
	TNM Stage (Ref: 1)	0.016			
	Stage 2	0.011	5.627	1.487	21.285
	Stage 3	0.004	7.407	1.891	29.019
	Tumor Localization (Ref: Distal)	0.097			
	Middle part	0.363	0.758	0.417	1.377
	Proximal	0.031	0.376	0.155	0.913
	LVI	0.674	0.871	0.458	1.658
	PNI	0.258	1.472	0.754	2.876
	BMI	0.607	0.984	0.926	1.046
	Tumor type (Ref: adenocarcinoma) Signet ring cell	0.100	1.616	0.911	2.865
	DM	0.228	1.462	0.788	2.711
	Surgery type (Ref: distal)	0.205	1.450	0.816	2.575
	Preoperative Albumin	0.057	0.563	0.312	1.018
	Preoperative CRP	0.529	1.046	0.909	1.203
	Receiving neoadjuvant therapy	0.005	2.589	1.331	5.033
Backward Method	Metastatic LN	0.032	1.030	1.003	1.059
	TNM Stage (Ref: 1)	0.005			
	Evre 2	0.003	6.158	1.838	20.634
	Evre 3	0.001	7.970	2.295	27.678
	Tumor type (Ref: adenocarcinoma) Signet ring cell	0.091	1.601	0.928	2.760
	Preoperative Albumin	0.002	0.428	0.248	0.739
	Receiving neoadjuvant therapy	0.009	2.196	1.215	3.968

LN, Lymph Node; BMI, body mass index; LVI, lymphovascular invasion; PNI, perineural invasion; DM, diabetes mellitus; ASA, american society of anesthesiologists; CRP, c reactive protein.

present study, mean survival was lower in patients who were administered NAC than those not administered NAC, although this may be attributed to the biased randomization of the groups. In addition, although patients with stage 2 and 3 disease were preferred, it is likely that NAC was preferred more often in patients with stage 3 disease.

There are various factors affecting survival in patients undergoing treatment for gastric cancer. In a multivariate analysis by Shi et al. [20], the immune-inflammatory index was reported to represent an independent prognostic factor in patients with gastric cancer, and could be used for the prediction of survival in such patients. In another study, Feng et al. [21] identified body mass index (BMI), tumor size and TNM stage as independent prognostic factors, and in some studies, malnutrition was found to be among the factors directly affecting survival [22]. In the present study, the number of metastatic lymph nodes, TNM stage, tumor type, preoperative CA19-9 and albumin level, and the preoperative administration of NAC were found to be related to survival in a Cox regression analysis.

In a study of 1,395 patients undergoing a curative resection for GC, Kubota et al. [23] found that postoperative complications prolonged the inflammatory period, and thus negatively affected prognosis. The survival of patients with and without complications was found to differ, and this was more prominent in patients with Stage 3 GC. Taking into account this effect, in the study by Eto et al. [24] comparing patients who received NAC with or without complications after surgery, no significant difference was reported in terms of postoperative complications, morbidities or, indirectly, events that triggered inflammation. The authors reported no negative effect of NAC in terms of inflammation and prognosis. Similarly, Hayashi et al. [25] found NAC to have a negative effect on morbidity and survival in patients with locally advanced gastric cancer. Consistent with literature, the present study found no statistically significant difference between the groups in terms of postoperative morbidities, of which the overall rate of postoperative morbidity was 42.6%. In the present study, NAC was not found to be associated with increased rates of postoperative morbidity, and can therefore be administered safely to patients with locally advanced tumors.

The present study is limited by its exclusion of a number of patients due to missing data, and owing to the retrospective design of the study. Other limitations include the lack of randomization between the groups and the changes in the NAC regimen over time.

In conclusion, contrary to current expectations, NAC did not increase postoperative complications. There is no increased risk of postoperative morbidity according to the Clavien-Dindo classification system in patients with locally advanced gastric cancer administered preoperative NAC. The number of metastatic lymph nodes, TNM stage, tumor type and albumin levels, and the administration of preoperative NAC, were all found to be associated with survival.

Disclosure of conflict of interest

None.

Address correspondence to: Hilmi Bozkurt, Hilmi Bozkurt, Gastrointestinal Surgeon, University of Health Sciences, Haseki Resarch and Education Hospital, Istanbul, Turkey. Tel: +905321780880; E-mail: hilmibozkurt27@gmail.com

References

[1] Goel A, Shah SH, Selvakumar VPP, Garg S and Kumar K. Robot-assisted mckeown esophagectomy is feasible after neoadjuvant chemoradiation. Our initial experience. Indian J Surg 2018; 80: 24-29.

[2] Zheng X and Sun H. Preoperative neoadjuvant chemotherapy favors advanced gastric cancer treated with laparoscopic radical surgery. Int J Clin Exp Med 2020; 13: 1307-1315.

[3] Yoshikawa T, Sasako M, Yamamoto S, Sano T, Imamura H, Fujitani K, Oshita H, Ito S, Kawashima Y and Fukushima N. Phase II study of neoadjuvant chemotherapy and extended surgery for locally advanced gastric cancer. Br J Surg 2009; 96: 1015-22.

[4] Gökler C, İrkörücü O, Reyhan E, Bozkurt H and Görür M. Effect of tumor location and lymph node involvement on prognosis and survival in gastric cancer patients. ADYÜ Sağlık Bilimleri Derg 2020; 6: 248-257.

[5] Gretschel S, Siegel R, Estévez-Schwarz L, Hünerbein M, Schneider U and Schlag PM. Surgical strategies for gastric cancer with synchronous peritoneal carcinomatosis. Br J Surg 2006; 93: 1530-1535.

[6] Hartgrink HH, Jansen EP, van Grieken NC and van de Velde CJ. Gastric cancer. Lancet 2009; 374: 477-490.

[7] Walker KG, Bell SW, Rickard MJ, Mehanna D, Dent OF, Chapuis PH and Bokey EL. Anastomotic leakage is predictive of diminished survival after potentially curative resection for colorectal cancer. Ann Surg 2004; 240: 255-9.
[8] Artinyan A, Orcutt ST, Anaya DA, Richardson P, Chen GJ and Berger DH. Infectious postoperative complications decrease long-term survival in patients undergoing curative surgery for colorectal cancer: a study of 12,075 patients. Ann Surg 2015; 261: 497-505.
[9] Wang M, Ye Y, Yang Q, Li J, Han C, Wang W, Zhao C and Wen J. Pre-operative lymph node status of gastric cancer evaluated by multidetector computed tomography. Int J Clin Exp Med 2015; 8: 18213-18224
[10] Sierzega M, Kolodziejczyk P and Kulig J; Polish Gastric Cancer Study Group. Impact of anastomotic leakage on long-term survival after total gastrectomy for carcinoma of the stomach. Br J Surg 2010; 97: 1035-1042.
[11] Pençe HH, Gündeş E , Senger AS , Alsaadoni H, Çiyiltepe H, Gülmez S, Uzun O, Aday U, Polat E and Duman M. Prognostic significance of preoperative serum lactate dehydrogenase in patients with resectable gastric adenocarcinoma. Int J Clin Exp Med 2019; 12: 2746-2752
[12] Tokunaga M, Tanizawa Y, Bando E, Kawamura T and Terashima M. Poor survival rate in patients with postoperative intra-abdominal infectious complications following curative gastrectomy for gastric cancer. Ann Surg Oncol 2013; 20: 1575-1583.
[13] Cunningham D, Allum WH, Stenning SP, Thompson JN, Van de Velde CJ, Nicolson M, Scarffe JH, Lofts FJ, Falk SJ, Iveson TJ, Smith DB, Langley RE, Verma M, Weeden S and Chua YJ; MAGIC Trial Participants. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006; 355: 11-20.
[14] Ychou M, Boige V, Pignon JP, Conroy T, Bouché O, Lebreton G, Ducourtieux M, Bedenne L, Fabre JM, Saint-Aubert B, Genève J, Lasser P and Rougier P. Perioperative chemotherapy compared with surgery alone for resectable gastroesophageal adenocarcinoma: an FNCLCC and FFCD multicenter phase III trial. J Clin Oncol 2011; 29: 1715-21.
[15] Schuhmacher C, Gretschel S, Lordick F, Reichardt P, Hohenberger W, Eisenberger CF, Haag C, Mauer ME, Hasan B, Welch J, Ott K, Hoelscher A, Schneider PM, Bechstein W, Wilke H, Lutz MP, Nordlinger B, Van Cutsem E, Siewert JR and Schlag PM. Neoadjuvant chemotherapy compared with surgery alone for locally advanced cancer of the stomach and cardia: European organisation for research and treatment of cancer randomized trial 40954. J Clin Oncol 2010; 28: 5210-8.
[16] Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2010 (ver. 3). Gastric Cancer 2011; 14: 113-23.
[17] Dindo D, Demartines N and Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004; 240: 205-13.
[18] Téoule P, Trojan J, Bechstein W and Woeste G. Impact of neoadjuvant chemotherapy on postoperative morbidity after gastrectomy for gastric cancer. Dig Surg 2015; 32: 229-37.
[19] Inoue K, Nakane Y, Kogire M, Fujitani K, Kimura Y, Imamura H, Tamura S, Okano S, Kwon AH, Kurokawa Y, Shimokawa T, Takiuchi H, Tsujinaka T and Furukawa H. Phase II trial of preoperative S-1 plus cisplatin followed by surgery for initially unresectable locally advanced gastric cancer. Eur J Surg Oncol 2012; 38: 143-9.
[20] Shi H, Jiang Y, Cao H, Zhu H, Chen B and Ji W. Nomogram based on systemic immune-inflammation index to predict overall survival in gastric cancer patients. Dis Markers 2018; 2018: 1787424.
[21] Feng F, Zheng G, Guo X, Liu Z, Xu G, Wang F, Wang Q, Guo M, Lian X and Zhang H. Impact of body mass index on surgical outcomes of gastric cancer. BMC Cancer 2018; 18: 151.
[22] Martin AN, Das D, Turrentine FE, Bauer TW, Adams RB and Zaydfudim VM. Morbidity and mortality after gastrectomy: identification of modifiable risk factors. J Gastrointest Surg 2016; 20: 1554-64.
[23] Kubota T, Hiki N, Sano T, Nomura S, Nunobe S, Kumagai K, Aikou S, Watanabe R, Kosuga T and Yamaguchi T. Prognostic significance of complications after curative surgery for gastric cancer. Ann Surg Oncol 2014; 21: 891-8.
[24] Eto K, Hiki N, Kumagai K, Shoji Y, Tsuda Y, Kano Y, Yasufuku I, Okumura Y, Tsujiura M, Ida S, Nunobe S, Ohashi M, Sano T and Yamaguchi T. Prophylactic effect of neoadjuvant chemotherapy in gastric cancer patients with postoperative complications. Gastric Cancer 2018; 21: 703-709.
[25] Hayashi M, Yoshikawa T, Yura M, Otsuki S, Yamagata Y, Morita S, Katai H and Nishida T. Does neoadjuvant chemotherapy cancel out the negative survival impact induced by surgical complications after gastrectomy? Gastric Cancer 2019; 22: 1274-1284.