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ORIGINAL ARTICLE

A comparative analysis on clinical efficacy of FOLFOX6 regimen and DCF regimen as neoadjuvant chemotherapy combined with radical gastrectomy in treating advanced gastric cancer

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Summary

Purpose: *To compare the clinical efficacy and safety of FOLFOX6 regimen and docetaxel-cisplatin-fluorouracil (DCF) regimen as neoadjuvant chemotherapy (NACT) combined with radical gastrectomy in treating advanced gastric cancer.*

Methods: *96 patients with advanced gastric cancer admitted to our hospital and subjected to NACT combined with radical gastrectomy were retrospectively included, and divided to FOLFOX6 group (n=48) and DCF group (n=48). After operation, the NACT regimens were continued. The efficacy of NACT, adverse reactions, operation conditions, postoperative recovery and prognosis of the patients were observed and recorded. All patients were followed up to evaluate their postoperative survival and disease development.*

Results: *The clinical response rates were 47.9% and 52.1% in FOLFOX6 and DCF group, respectively, and the disease control rates were 91.7% and 89.6%, respectively. FOLFOX6 group had remarkably fewer cases of nausea and vomiting, leucopenia and thrombocytopenia than DCF group. However, the differences in operation time, intraoperative blood loss, number of blood transfusion, surgical approach, number of dissected lymph nodes, surgical margin and number of palliative surgery between the two groups were not statistically significant. In addition, there were no statistically significant differences in gastrointestinal function recovery time, length of hospital stay and complications after operation. Moreover, the differences in 1-year and 3-year survival rates between the two groups of patients were not statistically significant.*

Conclusions: *The FOLFOX6 and DCF regimens given as NACT combined with radical gastrectomy have therapeutic effects in treating locally advanced gastric cancer, satisfactory clinical response and disease control rate can be obtained, and the adverse reactions of chemotherapy are tolerable. The patients receiving the FOLFOX6 regimen show better tolerance, indicating that FOLFOX6 is safer and is worthy of clinical popularization.*

Key words: *neoadjuvant chemotherapy, radical gastrectomy, gastric neoplasm, advanced stage, efficacy*

Introduction

Gastric cancer, a common type of malignant tumor, ranks 5th in incidence worldwide and its mortality is third among the causes of cancer death. According to the statistical data of the World Health Organization (WHO), the Chinese patients accounted for about 42.5% of the approximately 1 million new cases of gastric cancer around the world in 2012 [1,2]. The primary tumor has invaded the serosa or adjacent organs in the majority of patients with gastric cancer when they are initially diagnosed. The multidisciplinary treatments dominated by surgery are considered as the mainstay of treatment for advanced gastric cancer at present [3].

The results of Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC)

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trial and French Francophone de Cancérologie Digestive (FFCD) 9703 trial revealed that surgeries combined with perioperative chemotherapy can improve the radical resection rate of gastric cancer surgeries and ameliorate the patient's prognosis compared with the surgical treatment alone [4,5]. Neoadjuvant chemotherapy (NACT), first put forward by American scholar Frei, refers to the systemic chemotherapy performed before the implementation of local therapeutic methods (e.g. surgery or radiotherapy) for the purpose of reducing the extent of tumor invasion and killing invisible metastatic cells as soon as possible, so as to facilitate subsequent surgery, radiotherapy and other treatments [6,7]. NACT can increase the success rate of surgery for patients with advanced gastric cancer, and it will not increase the incidence rate of postoperative complications and death rate of the patients undergoing chemotherapy, and there were no distinct differences in wound healing and hepatic and renal function after operation between the patients undergoing chemotherapy and those not undergoing chemotherapy. Most chemotherapy regimens are composed of fluoropyimidine combined with oxaliplatin, epirubicin or taxane [8-10]. Currently, there are relatively more reports about the NACT for gastric cancer, but the horizontal comparisons of the clinical efficacy and safety of various regimens combined with radical gastrectomy in advanced gastric cancer are rarely reported, lacking systematic reviews.

In this research, the clinical and pathological data of 96 patients with advanced gastric cancer admitted and subjected to NACT combined with radical gastrectomy in our department from September 2013 to September 2017 were retrospectively reviewed, and the clinical efficacy and safety of NACT combined with radical gastrectomy in treating the disease were investigated.

Methods

General data

The retrospective cohort research method was adopted, and the clinical data of the 96 patients with advanced gastric cancer were collected. The patients were grouped according to the NACT regimens received, of which 48 patients received FOLFOX6 regimen combined with radical gastrectomy and 48 patients received docetaxel-cisplatin-fluorouracil (DCF) regimen combined with radical gastrectomy. There were 59 males and 27 females aged 36-73 years old, with an average of 51 years old. In terms of the tumor site, there were 18 cases in the gastric fundus or cardia, 21 cases in the gastric body and 57 cases in the gastric pylorus. As for the degree of tumor differentiation, there were 39 cases of moderately differentiated adenocarcinoma, 26 cases of poorly dif-

Table 1. Baseline demographic and clinical characteristics of the studied patients

Characteristics	*FOLFOX6 group n=48, n (%)*	*DCF group n=48, n (%)*	*p value*
Age, mean±SD	52.74±9.85	49.73±10.53	0.151
Gender, n (%)			0.675
Male	28 (58.3)	31 (64.6)	
Female	20 (41.7)	17 (35.4)	
Tumor diameter (cm), mean±SD	4.02±1.20	4.34±1.05	0.168
Tumor location			0.807
Gastric fundus and cardia	10 (20.8)	8 (16.7)	
Gastric body	11 (22.9)	10 (20.8)	
Gastric antrum	27 (56.2)	30 (62.5)	
Pathological type			0.835
Moderately differentiated adenocarcinoma	21 (43.8)	18 (37.5)	
Poorly differentiated adenocarcinoma	12 (25.0)	14 (29.2)	
Undifferentiated carcinoma	3 (6.2)	5 (10.4)	
Mucinous adenocarcinoma	7 (14.6)	8 (16.7)	
Signet ring cell carcinoma	5 (10.4)	3 (6.2)	
Tumor UICC stage			0.668
II B	6 (12.5)	10 (20.8)	
III A	16 (33.3)	17 (35.4)	
III B	15 (31.3)	12 (25.0)	
III C	11 (22.9)	9 (18.8)	

UICC: Union Internationale Contre le Cancer, SD: standard deviation

ferentiated adenocarcinoma, 8 cases of undifferentiated adenocarcinoma, 15 cases of mucinous adenocarcinoma and 8 cases of signet-ring cell carcinoma. There were no statistically significant differences in gender, age as well as the site, diameter, pathological type and Union for International Cancer Control (UICC) stage of tumor between the two groups of patients (p>0.05), which were comparable (Table 1). All the patients enrolled followed the Declaration of Helsinki, performed the duty of disclosure and signed the informed consent. This study was approved by the Ethics Committee of Linyi Cacer Hospital.

Inclusion criteria: (1) patients aged 20-75 years old, (2) patients definitely diagnosed with advanced primary gastric adenocarcinoma through histopathological examination via endoscopic ultrasonography and computed tomography (CT) before operation and pathological examination after operation, with a UICC stage of IIB-IIIC stage (T3-4N1-3M0 stage), (3) patients receiving R0 resection, (4) patients without a past history of chemotherapy, and (5) patients able to tolerate the chemotherapy drugs.

Exclusion criteria: (1) patients who had distant metastases or could not tolerate the surgery, (2) patients with active bleeding or complete pyloric obstruction, (3) patients who received antitumor treatments such as chemotherapy, radiotherapy, targeted therapy or immunotherapy previously, (4) patients with a past history of malignant tumor except for cured basal cell carcinoma of skin and cervical carcinoma in situ, (5) patients with a past history of subtotal gastrectomy, or (6) patients with missing clinical and pathological data.

Therapeutic methods

FOLFOX6 regimen: On the 1st day, 400 mg/m^2 tetrahydrofolate and 85 mg/m^2 oxaliplatin were infused intravenously for 2 h. On the 2nd day, 2,400 mg/m^2 fluorouracil (FU) was infused intravenously for 46 h. DCF regimen: On the 1st day, 75 mg/m^2 docetaxel (DTX) was infused intravenously. On the 1st-5th day, 20 mg/m^2 cisplatin was infused intravenously, and intravenous infusion of 500 mg/m^2 5-FU was administered continuously. Every 2 weeks of treatment administration was regarded as one cycle. The endoscopic ultrasonography and contrast-enhanced CT were performed again for comprehensive assessment before the 3rd cycle. In order to exclude the tumor progression, the chemotherapy was performed for another 2 cycles, and 4 cycles of chemotherapy were completed before operation. The NACT was stopped when intolerable adverse events and disease progression occurred or when the patients refused during the treatment.

The radical gastrectomy was performed at about 4 weeks after NACT. The total gastrectomy or distal gastrectomy was conducted in accordance with the site and size of the tumor, so as to realize R0 resection. BillrothII reconstruction was adopted after the distal gastrectomy, and Roux-en-Y anastomosis was used after the total gastrectomy. The patients received gastrointestinal decompression, parenteral nutrition support and antibiotic therapy after operation. Moreover, the NACT regimens were continued after operation.

Observation indexes

Grading of NACT efficacy and adverse reactions

The tumor was evaluated by means of imaging examinations before operation, and the results were compared with those before chemotherapy. By reference to the Response Evaluation Criteria in Solid Tumors, the NACT efficacy was classified as complete remission, partial remission, stable disease or progressive disease. Clinical response rate = [(case of complete remission + case of partial remission)/case of measurable lesions]×100%, and disease control rate = [(case of complete remission + case of partial remission + case of stable disease)/case of measurable lesions]×100%. The patients' adverse reactions were observed during chemotherapy, which were divided into grade 0, I, II, III and IV according to the WHO grading standards of common adverse reactions.

Operation conditions: operation time, intraoperative blood loss, number of blood transfusion during operation, number of dissected lymph nodes, surgical approach, number of palliative surgery, surgical margin, etc. Postoperative recovery: gastrointestinal function recovery time, length of hospital stay and complications after operation.

The patients were followed up by means of outpatient visits and telephone calls, so as to know their survival. After accomplishing all the treatments, the patients were followed up once every 3-6 months in the 1st-2nd year, once every 6-12 months in the 3rd-5th year, and once a year after 5 years. The follow-up included blood routine tests, complete biochemical examination, complete examination of tumor markers, gastroscopy and imaging examination. The follow-up was terminated in September 2018.

Statistics

SPSS 22.0 statistical software (IBM, Armonk, NY, USA) was used for statistical analyses. The measurement data were expressed as mean ± standard deviation, and two-sample *t*-test was used for data comparison between groups. The enumeration data were presented as ratio (%), and x^2 test was performed for these data comparison. P<0.05 suggested that the difference was statistically significant. Kaplan-Meier method was applied to plot the survival curves, log-rank test was utilized to compare the difference in survival rate between the two groups, and p<0.05 suggested that the difference was statistically significant.

Results

Efficacy and adverse reactions of NACT

In both groups of patients, the median cycle of NACT received was 3.32 cycles/case, the clinical symptoms were ameliorated in different degrees, and 14 patents had lowered clinical stages in each group. In FOLFOX6 group, there were 4 cases of complete remission (2 cases of stage IIB and 2

cases of stage IIIA), 19 cases of partial remission (2 cases of stage IIB, 6 cases of stage IIIA, 7 cases of stage IIIB and 4 cases of stage IIIC), 21 cases of stable disease (1 case of stage IIB, 7 cases of stage IIIA, 6 cases of stage IIIB and 7 cases of stage IIIC) and 4 cases of progressive disease (1 case of stage IIB, 1 case of IIIA and 2 cases of stage IIIB). The clinical response rate was 47.9% (23/48), and the disease control rate was 91.7% (44/48). FOLFOX6 group had 3 cases of complete remission (2 cases of stage IIB and 1 case of stage IIIA), 22 cases of partial remission (3 cases of stage IIB, 11 cases of stage IIIA, 6 cases of stage IIIB and 2 cases of stage IIIC), 18 cases of stable disease (4 case of stage IIB, 4 cases of stage IIIA, 3 cases of stage IIIB and 7 cases of stage IIIC) and 5 cases of progressive disease (1 case of stage IIB, 1 case of IIIA and 3 cases of stage IIIB), with a clinical response rate of 52.1% (25/48) and a disease control rate of 89.6% (43/48).

There were 39 and 45 cases of adverse events in FOLFOX6 group and DCF group, respectively, during the NACT, including 33 cases in grade I, 37 cases in grade II, 6 cases in grade III and 8 cases in grade IV. All the adverse reactions were improved after symptomatic treatment, and no NACT-associated death occurred. FOLFOX6 group had remarkably fewer cases of nausea and vomiting, leucopenia and thrombocytopenia than DCF group ($p=0.004$, $p<0.001$, $p=0.030$), while no statistically significant differences were discovered in other adverse reactions ($p>0.05$). The specific adverse reactions are shown in Table 2.

Table 2. Comparison of clinical efficacy and complications of two different neoadjuvant chemotherapy regimens in the treatment for the studied patients

Parameters	*FOLFOX6 group n=48*	*DCF group n=48*	*p value*
Response, n			
CR	4	3	0.695
PR	19	22	0.536
SD	21	18	0.533
PD	4	5	0.726
Complications, n (%)			
Nausea and vomiting	31 (64.6)	43 (89.6)	0.004
Diarrhea	9 (18.8)	13 (27.1)	0.331
Leukopenia	20 (41.7)	41 (85.4)	0.001
Thrombocytopenia	11 (22.9)	21 (43.8)	0.030
Live dysfunction	9 (18.8)	12 (25.0)	0.459
Renal dysfunction	8 (16.7)	14 (29.2)	0.145
Peripheral neurotoxicity	7 (14.6)	13 (27.1)	0.132

CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease CR: complete response; PR: partial response; SD: stable disease; PD: progressive disease

Table 3. Comparison of perioperative parameters of patients in the two groups

Parameters	*FOLFOX6 group* n=48	*DCF group n=48*	*p value*
Operation time (min)	202.59±36.44	191.28±39.83	0.150
Blood loss (ml)	127.30±54.62	105.41±68.15	0.086
Blood transfusion	5	9	0.247
Lymph node dissection number	21.4±8.1	24.9±9.8	0.060
Procedure, n (%)			0.299
Distal gastrectomy	26 (54.2)	31 (64.6)	
Total gastrectomy	22 (45.8)	17 (35.4)	
Surgical margin, n (%)			0.521
R_0 resection	37 (77.1)	41 (85.4)	
R_1 or R_2 resection	11 (22.9)	7 (14.6)	
Palliative operation	6 (12.5)	3 (6.3)	0.294

Table 4. Comparison of parameters related to postoperative recovery of patients in the two studied groups

Parameters	FOLFOX6 group n=48	*DCF group n=48*	*p value*
Gastrointestinal function recovery time (d)	3.5±1.4	3.1±1.2	0.136
Postoperative hospital stay (d)	15.3±4.9	17.1±4.5	0.064
Complications, n (%)			0.459
Incision infection	3 (6.3)	2 (4.2)	
Pulmonary infection	2 (4.2)	5 (10.4)	
Intraperitoneal infection	1 (2.1)	2 (4.2)	
Intraperitoneal hemorrhage	0 (0)	1 (2.1)	
Pleural effusion	1 (2.1)	0 (0)	
Anastomotic fistula	1 (2.1)	0 (0)	
Anastomotic hemorrhage	1 (2.1)	0 (0)	

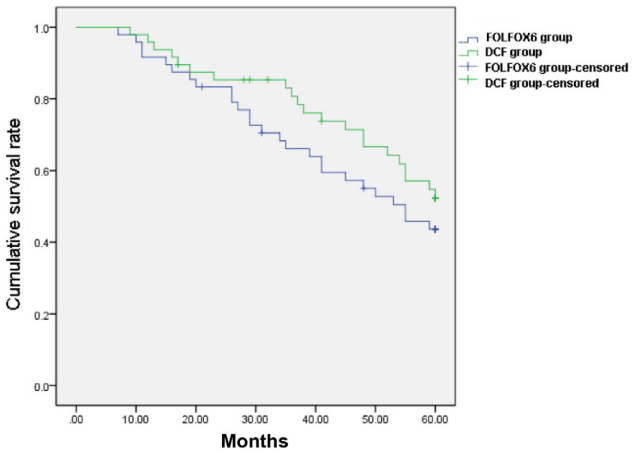

Figure 1. Kaplan-Meier survival curve of patients in FOLFOX6 group and DCF group. The difference of the survival rate of patients in the two group has no statistical significance (p=0.274).

Operation conditions

In the two groups, the mean operation time was 202.59±36.44 min and 191.28±39.83 min, respectively, the mean intraoperative blood loss was 127.30±54.62 mL and 105.41±68.15 mL, respectively, and the number of perioperative blood transfusion was 5 and 9, respectively, displaying no statistically significant differences (p=0.150, p=0.086, p=0.247). Twenty-six (54.2%) and 31 (64.6%) patients underwent distal gastrectomy, and 22 (45.8%) and 17 (35.4%) patients were subjected to total gastrectomy in both groups. During operation, the mean number of dissected lymph nodes was 21.4±8.1 and 24.9±9.8, respectively. In terms of the surgical margin, there were 37 (77.1%) and 41 (85.4%) cases of R0 resection as well as 11 (22.9%) and 7 (14.6%) cases of R1 or R2 resection. The number of palliative surgery was 6 (12.5%) and 3 (6.3%), respectively, in the two groups. All the differences were not statistically significant (p=0.299, p=0.060, p=0.521, p=0.294), indicating that the two NACT regimens do not have prominent effects on the operation conditions of the patients (Table 3).

Postoperative recovery

The mean gastrointestinal function recovery time after operation was 3.5±1.4 days and 3.1±1.2 days, respectively, and the postoperative length of hospital stay was 15.3±4.9 days and 17.1±4.5 days, respectively, in the two groups, with no statistically significant differences (p=0.136, p=0.064). After operation, there were 3 (6.3%) and 2 (4.2%) cases of incision infection in the two groups, respectively. Two (4.2%) and 5 (10.4%) patients were complicated with pulmonary infection. One (2.1%) and 2 (4.2%) patients were complicated with intra-abdominal infection. None and 1 (2.1%) patient was complicated with abdominal hemorrhage. One (2.1%) and none (0%) patient was complicated with pleural effusion. One (2.1%) and none (0%) patient was complicated with anastomotic leakage. One (2.1%) and none (0%) patient was complicated with anastomotic bleeding. None (0%) and 1 (2.1%) patient was complicated with delayed gastric emptying. One (2.1%) and none patient was complicated with duodenal stump leak. None and 1 (2.1%) patient was complicated with intestinal obstruction. One (2.1%) and none (0%) patient was complicated with thrombus. The differences in those postoperative complications were not statistically significant (p=0.459) (Table 4).

Follow-up results of patient's survival

All the patients were followed up for 12-60 months, with a median follow-up time of 41.3 months and 43.8 months, respectively, in the two groups. Three patients were lost to follow-up in FOLFOX6 group at 21, 31 and 48 months after operation, respectively, and 5 patients were lost to

follow-up in DCF group at 17, 28, 29, 32 and 41 months after operation, respectively. The 1-year survival rates were 91.7% (44/48) and 95.8% (46/48), respectively, and the 3-year survival rates were 62.5% (30/48) and 70.8% (34/48), respectively, in the two groups. By the end of follow-up, a total of 29 and 26 patients died in FOLFOX6 group and DCF group, respectively. The Kaplan-Meier survival curves are shown in Figure 1. According to log-rank test, the differences in the survival rates between the two groups of patients were not statistically significant (p=0.274).

Discussion

The NACT is a vital component of multi-disciplinary treatments for gastric cancer, which is able to obviously lower the clinical stage of advanced gastric cancer and increase the R0 resection rate, and its role of improving the overall survival rate and progression-free survival rate has been verified by some Chinese and foreign clinical research results. Both MAGIC trail of the European Society for Medical Oncology and FNCLCC/FFCD trail in France focus on the NACT for resectable gastric cancer and adenocarcinoma of the esophagogastric junction, whose results indicate that the overall survival rate, and progression-free survival rate and 5-year survival rate in NACT group are higher than those in simple operation group, and the differences are statistically significant [4,5]. According to the EORTC 40954 study of the European Organization for Research and Treatment of Cancer, there were no statistically significant differences in the overall survival rate and progression-free survival rate between NACT group and simple operation group, but the results of subgroup analyses manifest that the survival rate of the patients receiving NACT for gastroesophageal junction tumor is better [11]. In addition, multiple meta-analyses have demonstrated the value of NACT in the treatment of gastric cancer. An American retrospective study revealed that the application of NACT to treating advanced gastric cancer is increasing year by year [12-14].

The chemotherapy drugs for gastric cancer mainly include etoposide, cisplatin and 5-FU, but the findings vary from study to study due to different inclusion criteria and chemotherapy regimens. Two major large-sample, randomized, controlled clinical trials (MAGIC and FFCD 9703) revealed that the patients with esophageal adenocarcinoma who receive chemotherapy combined with two or three drugs in the perioperative period have more favorable overall survival an progression-free survival than those undergoing surgical treatment alone, suggesting that perioperative chemotherapy can improve the prognosis of patients with advanced gastric cancer [4,5]. It has become a consensus that the standardized D2 lymph node dissection should be adopted for advanced gastric cancer [15,16]. In this research, the UICC stage of tumor was IIB-IIIC stage before operation, and most cases of IIB-IIIB stage were resectable local advanced gastric cancer. Although radical resection may be realized through surgery alone, preoperative NACT is probably conducive to increasing the radical resection rate of surgery and controlling the micrometastases in the patients with a high recurrence risk. It is expected to lower the stage and improve the chance of radical resection by performing the NACT for IIIC stage gastric cancer with many lymph node metastases and deep infiltration. The efficacy of FOLFOX6 regimen and DCF regimen combined with radical gastrectomy in treating advanced gastric cancer was compared in this research, and it was shown that the clinical response rates were 47.9% and 52.1%, respectively, and the disease control rates were 91.7% and 89.6%, respectively, with no statistically significant differences, illustrating that both NACT regimens are definitely efficacious on advanced gastric cancer.

The adverse events of NACT consist of hematologic and non-hematologic toxic effects. In this research, the occurrence of adverse reactions of the two chemotherapy regimens was compared, and it was revealed that there were notably fewer cases of nausea and vomiting, leucopenia and thrombocytopenia in FOLFOX6 group than those in DCF group (p=0.004, p<0.001, p=0.030), manifesting that the FOLFOX6 regimen is safer, and the patients have better tolerance. Numerous studies have noticed that leucopenia and other hematologic toxicities are the primary DTX-associated toxicities [17-19], which is consistent with the result in this research. The hematologic and non-hematologic toxicities in both groups could be reversed by virtue of timely symptomatic therapies such as granulocyte colony-stimulating factors and antiemetics, and no chemotherapy-related death occurred.

In conclusion, the FOLFOX6 regimen and DCF regimen as NACT combined with radical gastrectomy have therapeutic effects in treating locally advanced gastric cancer, preferable clinical response rate and disease control rate can be obtained, and all the adverse reactions of the chemotherapy are tolerable. The patients receiving the FOLFOX6 regimen show a better tolerance, proving that the FOLFOX6 regimen is safer. Moreover, the two chemotherapy regimens do not have significant impacts on the operation conditions and postoperative recovery of the patients, and no statistically signifi-

cant difference is discovered in the postoperative survival. However, the long-term efficacy needs to be verified by multicenter and large-sample clinical studies because of the small number of research cases and short follow-up time.

Conclusions

The FOLFOX6 regimen and DCF regimen as NACT combined with radical gastrectomy have definitely efficacious in treating locally advanced gastric cancer, preferable clinical response rate and disease control rate can be obtained, and the adverse reactions of the chemotherapy are tolerable. The patients receiving the FOLFOX6 regimen manifest a better tolerance, indicating that the FOLFOX6 regimen is safer, which is worthy of clinical popularization.

Conflict of interests

The authors declare no conflict of interests.

References

1. Van Cutsem E, Sagaert X, Topal B, Haustermans K, Prenen H. Gastric cancer. Lancet 2016;388:2654-64.
2. Zhang M, Li R, Chen H, Zhou J, Zhang Y. Application and efficacy evaluation of an NBASS-APS pain management model in postoperative analgesia for gastric cancer patients. J BUON 2018;23:1426-31.
3. Yamamoto M, Rashid OM, Wong J. Surgical management of gastric cancer: the East vs. West perspective. J Gastrointest Oncol 2015;6:79-88.
4. Cunningham D, Allum WH, Stenning SP et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. N Engl J Med 2006;355:11-20.
5. Ychou M, Boige V, Pignon JP et al. 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.
6. Fan GF, Pan JJ, Fan PS et al. The clinical observation of verapamil in combination with interventional chemotherapy in advanced gastric cancer. Eur Rev Med Pharmacol Sci 2018;22:5508-5518.
7. Newton AD, Datta J, Loaiza-Bonilla A, Karakousis GC, Roses RE. Neoadjuvant therapy for gastric cancer: current evidence and future directions. J Gastrointest Oncol 2015;6:534-43.
8. Choi AH, Kim J, Chao J. Perioperative chemotherapy for resectable gastric cancer: MAGIC and beyond. World J Gastroenterol 2015;21:7343-8.
9. Mullen JT, Ryan DP. Neoadjuvant chemotherapy for gastric cancer: what are we trying to accomplish? Ann Surg Oncol 2014;21:13-5.
10. Das M. Neoadjuvant chemotherapy: survival benefit in gastric cancer. Lancet Oncol 2017;18:e307.
11. Schuhmacher C, Gretschel S, Lordick F et al. 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.
12. Greenleaf EK, Hollenbeak CS, Wong J. Trends in the use and impact of neoadjuvant chemotherapy on perioperative outcomes for resected gastric cancer: Evidence from the American College of Surgeons National Cancer Database. Surgery 2016;159:1099-1112.
13. Xiong B, Ma L, Cheng Y, Zhang C. Clinical effectiveness of neoadjuvant chemotherapy in advanced gastric cancer: an updated meta-analysis of randomized controlled trials. Eur J Surg Oncol 2014;40:1321-30.
14. Ronellenfitsch U, Schwarzbach M, Hofheinz R et al. Perioperative chemo(radio)therapy versus primary surgery for resectable adenocarcinoma of the stomach, gastroesophageal junction, and lower esophagus. Cochrane Database Syst Rev 2013:D8107.
15. Waddell T, Verheij M, Allum W, Cunningham D, Cervantes A, Arnold D. Gastric cancer: ESMO-ESSO-ESTRO clinical practice guidelines for diagnosis, treatment and follow-up. Eur J Surg Oncol 2014;40:584-91.
16. Ettinger DS, Kuettel M, Malin J et al. NCCN Roundtable: What Are the Characteristics of an Optimal Clinical Practice Guideline? J Natl Compr Canc Netw 2015;13:640-2.
17. Kang YK, Ryu MH, Yoo C et al. Phase I/II study of a combination of docetaxel, capecitabine, and cisplatin (DXP) as first-line chemotherapy in patients with advanced gastric cancer. Cancer Chemother Pharmacol 2011;67:1435-43.
18. Roth AD, Fazio N, Stupp R et al. Docetaxel, cisplatin, and fluorouracil; docetaxel and cisplatin; and epirubicin, cisplatin, and fluorouracil as systemic treatment for advanced gastric carcinoma: a randomized phase II trial of the Swiss Group for Clinical Cancer Research. J Clin Oncol 2007;25:3217-23.
19. De Vita F, Orditura M, Matano E et al. A phase II study of biweekly oxaliplatin plus infusional 5-fluorouracil and folinic acid (FOLFOX-4) as first-line treatment of advanced gastric cancer patients. Br J Cancer 2005;92:1644-9.