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S-1 AND OXALIPLATIN REGIMEN NEOADJUVANT CHEMOTHERAPY FOLLOWED BY SURGERY FOR RESECTABLE ADVANCED GASTRIC CANCER WITH MULTIPLE LYMPH-NODE METASTASIS

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Abstract – *Objective:* *The prognosis of patients with advanced gastric cancer (GC) with multiple lymph-node metastasis is poor. The present study evaluated a neoadjuvant S-1 and oxaliplatin regimen (SOX) followed by D2 gastrectomy for advanced GC with lymph-node metastasis.*

Patients and Methods: *Ten patients with resectable clinical advanced gastric cancer with multiple lymph-node metastasis who received preoperative SOX therapy were included in this study from 2015 to 2021.*

Results: *A clinical evaluation by RECIST version 1.1 criteria after SOX therapy showed 8 cases of partial response (PR), 2 cases of stable disease (SD), and no progress disease (PD). The histopathological stages were IB in 3 patients, IIA in 2, IIB in 2, IIIA in 2, and IIIB in 1, and downstaging was observed in 8 of 10 patients (80%). Histopathological effects were Grade 1a in 4 patients, Grade 1b in 3 patients, Grade 2a in 2 patients, and Grade 2b in 1 patient; there were no Grade 3 patients. Adverse events of neoadjuvant chemotherapy (NAC) according to the CTCAE criteria were Grade 1 anemia, nausea, dysgeusia, and peripheral neuropathy in one patient each; Grade 2 anemia in two patients; and diarrhea in one patient. No grade ≧3 adverse events were observed. The surgical techniques were distal gastrectomy in four cases, total gastrectomy in five cases, and total gastrectomy and caudal pancreatectomy in one case; all patients underwent D2 dissection, and all received R0 surgery. One patient had local recurrence, and one patient had peritoneal recurrence and is on chemotherapy. The remaining eight patients are alive without recurrence.*

Conclusions: *In the future, neoadjuvant chemotherapy with SOX therapy may become a treatment option for advanced resectable GC with multiple lymph-node metastasis.*

KEYWORDS: *Gastric cancer, Neoadjuvant chemotherapy, S-1, Oxaliplatin, Lymph-node metastasis.*

INTRODUCTION

In Japan, type 4, large type 3, and bulky N-GC are generally considered to have a very poor prognosis. The efficacy of preoperative adjuvant chemotherapy with S-1 plus cisplatin in patients with type 4 or large type 3 GC was not proved to be superior to surgery alone in the JCOG0501 study[1]. Next, the prognosis of patients with advanced gastric cancer (GC) with multiple lymph-node metastasis is poor, and a phase II study of a treatment strategy of surgery with D2 dissection and periaortic lymph node dissection after two to three cycles of S-1 plus cisplatin combination therapy as neoadjuvant chemotherapy (NAC) was performed in these patients, with favorable results shown[2].

In our department, patients are informed that NAC with S-1 and oxaliplatin regimen (SOX)

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therapy is still in the clinical trial stage, and we actively perform NAC only in patients who have given their written consent.

We herein report 10 cases of advanced resectable GC with multiple lymph-node metastasis treated with NAC using SOX therapy, along with a discussion of the literature. The present study evaluated NAC of SOX followed by D2 gastrectomy for advanced GC with multiple lymph-node metastasis.

PATIENTS AND METHODS

Patients

Patients with an ECOG performance status (PS) of 0 to 1 who underwent NAC with SOX therapy for resectable advanced GC with multiple lymph-node metastasis experienced at our hospital from January 2015 to August 2021 were included. Multiple lymph-node metastasis was defined as the presence of ≧3 regional lymph nodes with a short diameter of ≧1 cm on enhanced computed tomography (CT).

Preoperative chemotherapy

Oxaliplatin was administered as an intravenous infusion at a dose of 130 mg/m^2 on day 1. S-1 was administered orally twice daily for 14 days (from the evening of day 1 until the morning of day 15), followed by a 7-day rest period. The administered dose of S-1 was calculated according to the patient's body surface area as follows: <1.25 m^{2,} 40 mg; 1.25-1.5 m^2, 50 mg; and ≧1.5 m^2, 60 mg. Chemotherapy was administered every three weeks for two or three courses. The number of preoperative chemotherapy treatments with S0X was determined by the attending physician based on the patient's condition. Laparoscopy for staging was not performed before preoperative chemotherapy.

Evaluations

Contrast-enhanced CT and gastroenterological endoscopy were performed before and after preoperative chemotherapy. A tumor response evaluation was then carried out according to the Response Evaluation Criteria for Solid Tumors (RECIST) 1.1[3]. Adverse events during chemotherapy were evaluated using the Common Terminology Criteria for Adverse Events (CTCAE) v 5.0[4]. Surgical complications were evaluated using the Clavien-Dindo criteria[5].

Clinical, surgical, and pathological findings were categorized according to the 15th Japanese Classification of Gastric Carcinoma (JCGC). The pathological response of the primary tumor was assessed and classified as grade 0-3 according to the JCGC criteria[6]. Patient' background characteristics, surgical findings, histopathological findings, postoperative course, and distant results were reviewed.

All procedures were in accordance with the Ethical standards of the responsible Committee on Human Experimentation (institutional and national) and with the 1964 Declaration of Helsinki and later versions. This study was approved by the Ethics Committee of the Mitoyo General Hospital (approval number, 21-CR01-173; approval date, September 15, 2021).

RESULTS

Clinical characteristics

The mean age of the 10 patients (8 men, 2 women) was 73.8 (67-81) years old.

The ECOG PS was 0 in all cases. Three patients had type 2 tumors, six had type 3 tumors, and one had type 4 tumors. The histopathological types of preoperative endoscopic biopsies were tub1 in two cases, tub2 in four cases, por1 in one case, por2 in two cases, and muc in one case. The clinical wall depth by preoperative contrast-enhanced CT was T3 (SS) in one patient, T4a (SE) in eight patients, and T4b (SI) in one patient. Clinical lymph-node metastasis was N2 in nine cases and N3a in one case. The clinical stage was IIIA in eight cases, IIIB in one case, and IVA in one case. HER2 protein expression was positive in one case and negative in nine cases. Six patients received two courses of SOX therapy and four patients received three courses (Table 1).

Clinical stage, surgical stage, histological stage, clinical outcome, and histological outcome

The clinical stage was IIIA in eight cases, IIIB in one case, and IVA in one case. The clinical evaluation by RECIST version 1.1 criteria after SOX therapy showed partial response (PR) in eight patients and stable disease (SD) in two patients, with none showing progress disease (PD). Therefore, the response rate was 80%. The surgical stage was IIB in one patient, IIIA in six patients, IIIB in one patient, and IIIC in two patients.

TABLE 1. Clinical characteristics.

Case	Age	Sex	ECOG PS	Borrmann type	Histological type	T-factor	N-factor	Clinical stage	HER2 status	SOX course
1	77	F	0	2	muc	cT4a (SE)	cN2	IIIA	(-)	2
2	67	M	0	2	tub2	cT4a (SE)	cN3a	IIIB	(-)	3
3	81	F	0	3	tub1	cT4a (SE)	cN2	IIIA	(+)	2
4	65	M	0	3	tub1	cT4a (SE)	cN2	IIIA	(-)	2
5	66	M	0	4	por2	cT4a (SE)	cN2	IIIA	(-)	3
6	78	M	0	3	tub2	cT4a (SE)	cN2	IIIA	(-)	2
7	76	M	0	3	por2	cT3 (SS)	cN2	IIIA	(-)	3
8	80	M	0	3	tub2	cT4a (SE)	cN2	IIIA	(-)	2
9	71	M	0	3	tub2	cT4b (SI)	cN2	IVA	(-)	3
10	77	M	0	2	por1	cT4a (SE)	cN2	IIIA	(-)	2

PS: Performance Status
tub1: well differentiated
tub2: moderately differentiated
por1: solid type
por2: non-solid type
muc: mucinous adenocarcinoma

The histopathological stage was IB in three patients, IIA in two patients, IIB in two patients, IIIA in two patients, and IIIB in one patient, and downstaging occurred in 8 of 10 patients (80%). The histopathological effects were grade 1a in four cases, grade 1b in three cases, grade 2a in two cases, grade 2b in one case, and no grade 3 case (Table 2). A histopathological response rate in patients with grade ≧1b was 60%. We have previously reported Case 3 in a Japanese journal [7]. The CT findings before NAC (Figure 1) and CT after NAC (Figure 2) with SOX therapy in Case 3 of grade 2b are shown.

Adverse events of SOX therapy during NAC

Grade 1 anemia, nausea, dysgeusia, and peripheral neuropathy were observed in one patient each, along with Grade 2 anemia in two patients and diarrhea in one patient; no patients showed ≧ Grade 3 adverse events (Table 3).

Surgery, post-operative course, post-operative adjuvant chemotherapy, and prognosis

All patients underwent surgery within two to three weeks of completing of NAC. Four patients underwent distal gastrectomy, five patients underwent total gastrectomy, and one patient underwent total gastrectomy and caudal pancreatectomy; all patients underwent D2 dissection, and all received R0 surgery. No postoperative complications were observed in any patients. The average postoperative hospital stay was 14.1 (10-24) days.

The postoperative follow-up period ranged from 12 to 73 months (median 36 months). Postoperative adjuvant chemotherapy with S-1 was

TABLE 2. Clinical, surgical, and pathological findings.

Case	Clinical stage	Surgical stage	Pathological stage	Clinical response by RECIST	Pathological response
1	T4aN2 (IIIA)	T3 N2 (IIIA)	T2N2 (IIB)	PR	Grade 2a
2	T4aN3a (IIIB)	T4bN3a (IIIC)	T3N2 (IIIA)	SD	Grade 1a
3	T4aN2 (IIIA)	T3N2 (IIIA)	T2N0 (IB)	PR	Grade 2b
4	T4aN2 (IIIA)	T3N2 (IIIA)	T1b2N1 (IB)	PR	Grade 1b
5	T4aN2 (IIIA)	T4aN2 (IIIA)	T3N2 (IIIA)	SD	Grade 2a
6	T4aN2 (IIIA)	T3N2 (IIIA)	T2N0 (IB)	PR	Grade 1a
7	T3N2 (IIIA)	T3N2 (IIIA)	T3N1 (IIB)	PR	Grade 1b
8	T4aN2 (IIIA)	T4bN3a (IIIC)	T3N0 (IIA)	PR	Grade 1a
9	T4bN2 (IVA)	T4bN2 (IIIB)	T4bN2 (IIIB)	PR	Grade 1a
10	T4aN2 (IIIA)	T3N1 (IIB)	T3N0 (IIA)	PR	Grade 1b

PR: partial response
SD: stable disease

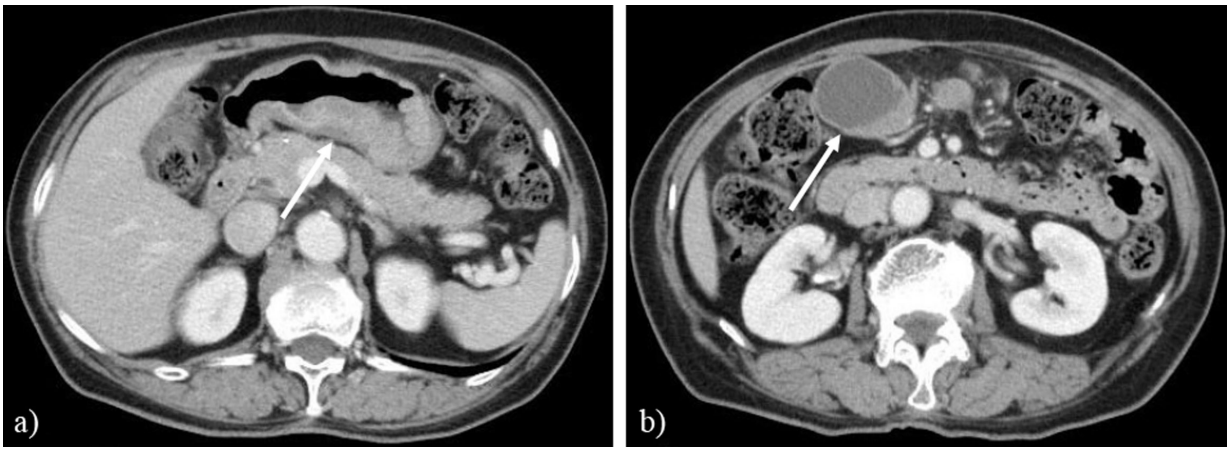

Fig. 1. (Case 3) Abdominal contrast-enhanced computed tomography before neoadjuvant chemotherapy. *a*, Wall hypertrophy was detected from the antrum to the angle involving the posterior wall *(arrow)*. *b*, The No.6 lymph node was enlarged *(arrow)*.

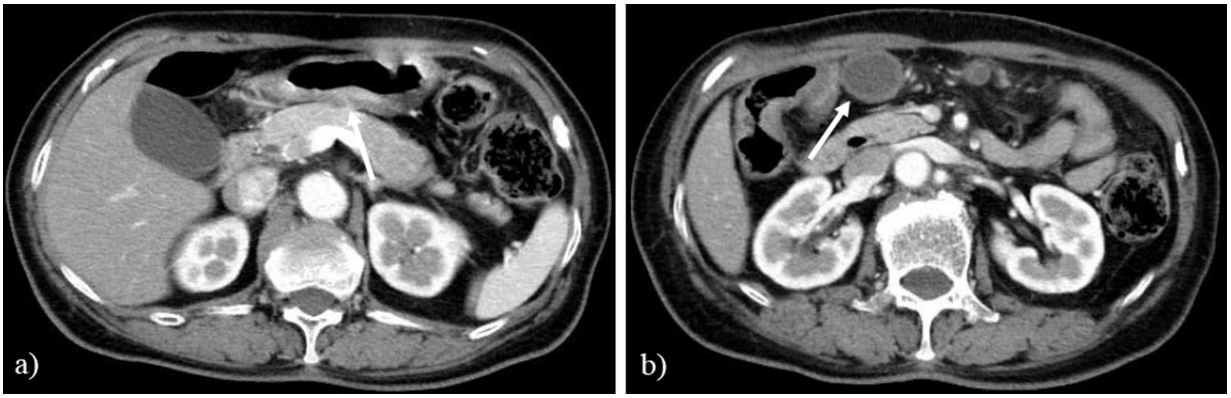

Fig. 2. (Case 3) Abdominal contrast-enhanced computed tomography after neoadjuvant chemotherapy. *a*, Wall hypertrophy of the posterior wall of the antrum was reduced *(arrow)*. *b*, The swelling of the No.6 lymph node was reduced *(arrow)*.

administered to 7 of 10 patients. The attending physician judged that postoperative adjuvant chemotherapy was not indicated in case 3 due to histopathological stage IB disease, in case 10 due to histopathological stage IIA disease, or in case 6 due to adverse events of nausea and anorexia. One patient had local recurrence, and one patient had peritoneal recurrence and is under chemotherapy. The remaining eight patients are alive without recurrence (Table 4).

DISCUSSION

The ACTS-GC study recommended adjuvant chemotherapy with S-1 for Stage II/III advanced GC[8]. However, the results of the ACTS-GC study showed that the 5-year survival rate for Stage II disease was 84.2%, which was relatively good, but the 5-year survival rates for Stage IIIA and IIIB disease were 67.1% and 50.2%, respectively, which were not satisfactory.

After gastrectomy, and particularly total gastrectomy, patients frequently suffer from post-gastrectomy syndromes, such as weight loss, dumping syndrome, or anemia, all of which can results in in delayed commencement or discontinuation of postoperative adjuvant chemotherapy.

TABLE 3. Adverse events during the neoadjuvant chemotherapy

Case	*Adverse event*
1	Grade 2 (Anemia)
2	Grade 2 (Anemia)
3	Grade 1 (Peripheral neuropathy)
4	Grade 1 (Anemia), Grade 1 (dysgeusia)
5	Grade 1 (Nausea)
6	(-)
7	(-)
8	(-)
9	(-)
10	Grade 2 (Diarrhea)

TABLE 4. Surgery, postoperative course, and prognosis.

Case	*Surgical operation*	*Remnants of tumor*	*Postoprative complication*	*Postoperative hospital stay (day)*	*Adjuvant chemo-therapy*	*Recurrence*	*Chemo-therapy after recurrencee*	*Prognosis*
1	TG (D2)	R0	(–)	14	S-1	(–)		6Y1M alive
2	DG (D2)	–	(–)	13	S-1	(–)		5Y8M alive
3	DG (D2)	–	(–)	13	(–)	(–)		5Y8M alive
4	TG (D2)	–	(–)	12	S-1	(–)		5Y5M alive
5	TG (D2)	–	(–)	14	S-1	(–)		4Y0M alive
6	DG (D2)	–	(–)	10	(–)	(–)		3Y0M alive
7	TG (D2)	–	(–)	13	S-1	Peritoneal recurrence	SOX,nab-PTX+ RAM, nivolumab	3Y0M alive
8	TG (D2)	–	(–)	16	S-1	(–)		2Y6M alive
9	TG+CP (D2)	–	(–)	24	S-1	Local recurrence	nab-PTX+ RAM	1Y9M alive
10	DG (D2)	–	(–)	12	(–)	(–)	–	1Y alive

TG: Total gastrectomy, DG: Distal gastrectomy, TG+CP: Total gastrectomy+caudal pancreatectomy
SOX: S-1+Oxaliplatin, nab-PTX: Paclitaxel, RAM: Ramucirumab.

Furthermore, postoperative complications, which have an incidence range or 15%-50%, may also affect the dose intensity of postoperative adjuvant chemotherapy[9-13]. Accordingly, patients with pStage II/III do not necessarily receive adjuvant chemotherapy with the expected dose intensity.

Therefore, NAC strategies have been developed for advanced GC, especially for patients at high-risk for postoperative recurrence. NAC for advanced GC may be expected to improve the curative effect by reducing the size of the primary tumor and metastases. In recent years, good results of NAC for highly advanced GC have been reported[14-16], and the strategy of performing surgery after downstaging has been applied. If such a strategy is successful, the growth of micro metastases that can cause recurrence may be able to be prevented.

The advantages of NAC for advanced GC include early treatment of micro metastases, which may determine the prognosis; high compliance with chemotherapy; reduction of lymph-node metastases by chemotherapy, resulting in an increased rate of curative resection; the ability to judge the efficacy of chemotherapy; and the prevention of unnecessary surgery for patients who may eventually develop unresectable metastases.

Recently, preoperative S-1 plus cisplatin therapy has been shown to be a useful treatment in Japan, as CR has been observed histologically in some of the most effective cases[17,18]. In the G-SOX phase III study[19], SOX was as effective as S-1 plus cisplatin in the first-line treatment of advanced GC and has since become an option for the first-line treatment of advanced GC, as it is generally safer than S-1 plus cisplatin and is clinically easier to administer. SOX is superior to S-1 plus cisplatin in terms of overall safety and simplicity of administration.

Honma et al[20] reported that three courses of SOX therapy were administered as NAC to 14 patients with stage III advanced GC, and the treatment was relatively safe, with a histopathological response rate of 85.7% in patients with grade ≧1b. In June 2015, our department started NAC with SOX for resectable advanced GC with multiple lymph-node metastasis in patients with ECOG PS 0-1. The main concerns of NAC are disease progression and adverse effects during treatment. In the present study, no PD was observed, and the response rate was 80% according to RECIST version 1.1 criteria. The adverse events according to the CTCAE were minor, up to Grade 2, and there were no cases in which such events interfered with surgery performed two to three weeks after the completion of NAC. The histopathological effect (≥grade 1b) of NAC was observed in 6 of 10 patients (60%), and downstaging was observed in 8 of 10 patients (80%).

Postoperative complications were not observed in any of the patients, and the mean postoperative hospital stay was 13.1 days with no disability due to NAC. The postoperative follow-up period ranged from 12 to 73 months (median 36 months). One patient had local recurrence and one patient had peritoneal recurrence and is currently undergoing chemotherapy. Remaining eight patients are alive without recurrence. JACCRO GC-07 demonstrated the superiority of Docetaxel plus S-1 over S-1 alone as postoperative adjuvant chemotherapy in patients with Stage III advanced GC[21]. We plan to actively use Docetaxel+S-1 as adjuvant chemotherapy for patients with stage III GC in our department.

Currently, NAC with SOX therapy is ongoing for cStage III patients in JCOG1509[22]. It is expected to become a standard treatment for locally advanced GC in Japan.

The present study is limited by its retrospective study design as well as the small study size (10 patients) and the fact that the study was performed at a single center, which may have introduced some study bias.

CONCLUSIONS

NAC with SOX therapy followed by surgery can be performed safety and may become a treatment option for resectable advanced GC with multiple lymph-node metastasis.

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All authors declare that there are no conflicts of interest.

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Udaka T analyzed the data and wrote the manuscript. Udaka T, Endou I, Yoshida O, and Kubo M performed the surgery, and Asano H and Kubo M helped draft the manuscript. Nishiyama T, Watanabe N, Endou I, Yoshida H, and Kubo M participated in revising the manuscript critically. All authors declare that they contributed to this article and that they read and approved the final version.

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REFERENCES

1) Iwaski Y, Tershima M, Mizusawa J, Katayama H, Nakamura K, Katai H, Yoshikawa T, Ito S, Kaji M, Kimura Y, Hirao M, Yamada M, Kurita A, Takagi M, Lee SW, Takagane A, Yabusaki H, Hihara J, Boku N, Sano T, Sasako M. Gastrectomy with without neoadjuvant S-1 plus cisplatin for type 4 or large type 3 gastric cancer (JCOG0501): an open-label, phase 3, randomized controlled trial. Gastric Cancer 2021; 24: 492-502.
2) Tsuburaya A, Mizusawa J, Tanaka Y, Fukushima N, Nashimoto A, Sasako M. Neoadjuvant chemotherapy with S-1 and cisplatin followed by D2 gastrectomy with para-aortic lymph node dissection for gastric cancer with extensive lymph node metastasis. Br J Surg 2014; 101: 653-660.
3) Eisenhauer EA, Therasse P, Bogaerts J, Schwartz LH, Sargent D, Ford R, Dancey J, Arbuck S, Gwyther S, Mooney M, Rubinstein L, Shankar L, Dodd L, Kaplan R, Lacombe D, Verweij J. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1). Eur J Cancer 2009; 45: 228-247.
4) U.S. Department of Health And Human Services, National Institutes of Health and National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0; published on November 27, 2017. https://ctep.cancer.gov/protocoldevelopment/electronic_applications/docs/CTCAE_v5_Quick_ Reference_8.5x11.pdf. Accessed 31 October 2019
5) Dindo D, Demartines N, Cavien 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: 205-213.
6) Japanese Gastric Cancer Association. Japanese Classification of Gastric Carcinoma. 15th ed. Tokyo: Kanehara Inc; 2017.
7) Udaka T, Yamamoto S, Nakamura T, Hironori Kurokawa, Katsuya Miyatani. A case of advanced gastric cancer responding to SOX preoperative adjuvant chemotherapy followed by surgery. JJCS 2016; 41: 762-767.
8) Sasako M, Sakuramoto S, Katai H, Kinoshita T, Furukawa H, Yamaguchi T, Nashimoto A, Fujii M, Nakajima T, Ohashi Y. Five-year outcomes of a randomized phase III trial comparing adjuvant chemotherapy with S-1 versus surgery alone in stage II or III gastric cancer. J Clin Oncol 2011; 29: 4387-4393.
9) Yoshikawa T, Rino Y, Yukawa N, Oshima T, Tsuburaya A, Masuda M. Neoadjuvant chemotherapy for gastric cancer in Japan: a standing position by comparing with adjuvant chemotherapy. Sur Today 2014; 44: 11-21.
10) Kurokawa Y, Doki Y, Mizusawa J, Terashima M, Katai H, Yoshikawa T, Kimura Y, Takiguchi S, Nishida Y, Fukushima N, Iwasaki Y, Kaji M, Hirao M, Katayama H, Sasako M. Bursectomy versus omentectomy alone for resectable gastric cancer (JCOG1001): a phase 3, open-label, randomised controlled trial. Lancet Gastroenterol Hepatol 2018; 3: 460-468.
11) Sano T, Sasako M, Yamamoto S, Nashimoto A, Kurita A, Hiratsuka M, Tsujinaka T, Kinoshita T, Arai K, Yamamura Y, Okajima K.Gastric cancer surgery: morbidity and mortality results from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy--Japan Clinical Oncology Group study 9501. J Clin Oncol 20004; 22: 2767-2773.
12) Bonenkamp JJ, Songun I, Hermans J, Sasako M, Welvaart K, Plukker JT, van Elk P, Obertop H, Gouma DJ, Taat CW, Lanschot J, Meyer S, Graaf PW, Meyenfeldt MF, Tilanus H. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. Lancet 1995; 345: 745-748.

13) Cuschieri A, Fayers P, Fielding J, Craven J, Bancewicz J, Joypaul V, Cook P. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRD randomised controlled surgical trial. The Surgical Cooperative Group. Lancet 1996; 347: 995-999.
14) Miao ZF, Liu XY, Wang ZN, Zhao TT, Xu YY, Song YX, Huang JY, Xu H, Xu HM. Effect of neoadjuvant chemotherapy in patients with gastric cancer: a PRISMA-compliant systematic review and meta-analysis. BMC Cancer. 2018; 18: 118.
15) Li W, Qin J, Sun YH, Liu TS. Neoadjuvant chemotherapy for advanced gastric cancer: a meta-analysis. World J Gastroenterol 2010; 16: 5621-5628.
16) Hu Y, Hu D, Li W, Yu X. Neoadjuvant chemotherapy brings more survival benefits than postoperative chemotherapy for respectable gastric cancer: a Meta-analysis of randomized controlled trials. J BUON 2019; 24: 201-214.
17) Kitayama K, Kanahara I, Teraoka H, Nishimura J, Nomura S, Noda E, Nishino H, Hirakawa K. A case of advanced gastric cancer responding to S-1/CDDP neoadjuvant chemotherapy, leading to a pathological complete response. Gan T Kagaku Ryoho 2015; 42: 85-87.
18) Hashimoto T, Takeno A, Taniguchi H, Sato Y, Morimoto Y, Kusama H, Matsushita K, Kawashima H, Kimura K, Murai Y, Katsura Y, Kagawa Y, Okishiro M, Sakisaka H, Nakahira S, Egawa C, Takeda Y, Kato Y, Tamura S. Pathological complete response in advanced gastric carcinoma with lymph node meta stasis treated with combination neoadjuvant chemotherapy comprising S-1 and cisplatin-a case report. Gan T Kagaku Ryoho 2013; 40: 2223-2225.
19) Yamada Y, Higuchi K, Nishikawa K, Gotph M, Fuse N, Sugimoto N, Nishina T, Amagai K, Chin K, Niwa Y, Tsuji A, Imamura H, Tsuda M, Yasui H, Fujii H, Yamaguchi K, Tasui H, Hironaka S, Shimada K, Miwa K, Hamada H, Hyodo I. Phase III study comparing oxaliplatin plus S-1 with cisplatin plus S-1 in chemotherapy-naïve patients with advanced gastric cancer. Ann Oncol 2015; 26: 141-148.
20) Honma Y, Yamada Y, Terazawa T, Takashima A, Iwasa S, Kato K, Hamaguchi T, Shimada Y, Ohashi M, Morita S, Fukagawa T, Machida N, Katai H. Feasibility of neoadjuvant S-1 and oxaliplatin followed by surgery for resectable advanced gastric adenocarcinoma. Surg Today 2016; 46: 1076-1082.
21) Yoshida K, Kodera Y, Kochi M, Ichikawa W, Kakeji Y, Sano T, Nagao N, Takahashi M, Takagane A, Watanabe T, Kaji M, Okitsu H, Nomura T, Matsui T, Yoshikawa T, Matsuyama J, Yamada M, Ito S, Takeuchi M, Fujii M. Addition of docetaxel to oral fluoropyrimidine improves efficacy in patients with stage III gastric cancer: interim analysis of JACCRO GC-07, a randomized controlled trial. J Clin Oncol 2019; 20: 1296-1304.
22) Tokunaga M, Sato Y, Nakagawa M, Aburatani T, Matsuyama T, Nakajima Y, Kinugasa Y. Perioperative chemotherapy for locally advanced gastric cancer in Japan: current and future perspectives. Surg Today 2020; 50: 30-37.