Effects of neoadjuvant laparoscopic hyperthermic intraperitoneal chemoperfusion and intraperitoneal/systemic chemotherapy on peritoneal metastasis from gastric cancer

Yutaka Yonemura,[1-3] Emel Canbay,[1] Takuji Fujita,[1,2] Shouzou Sako,[1,2] Satoshi Wakama,[2] Haruaki Ishibashi,[2] Masamitu Hirano,[3] Akiyoshi, Mizumoto,[3] Kazuyoshi Takeshita,[1,2] Nobuyuki Takao,[3] Masumi Ichinose,[3] Kousuke Noguchi,[3] Yang Liu,[2] Yan Li,[4] Keizou Taniguchi[5]

[1]NPO to Support Peritoneal Surface Malignancy Treatment, Japan; [2]Department of Regional Cancer therapy, Peritoneal Dissemination Center, Kishiwada Tokushukai Hospital, Kishiwada, Japan; [3]Department of Regional Cancer therapy, Peritoneal Dissemination Center, Kusatsu General Hospital, Shiga, Japan; [4]Department of Peritoneal Surface Oncology, Beijin Shijitan Hospital of Capital Medical University, Beijin, China; [5]Department of Surgery, Mizoguichi Hospital, Teikyou University, Japan

Abstract

Our aim was to clarify the effects of neoadjuvant hyperthermic intraperitoneal chemoperfusion (NLHIPEC) followed by intraperitoneal/systemic chemotherapy (NIPS) on peritoneal metastasis from gastric cancer.

After carrying out exploratory laparoscopy to determine the peritoneal cancer index (pretreatment PCI: Pre-PCI) in 150 patients, we performed NLHIPEC for 60 min. with peritoneal port placement: a series of 3-week cycles of NIPS using S1, docetaxel, and cisplatin two weeks after NLHIPEC: performed cytoreductive surgery in 86 patients four weeks after NIPS, and subsequently measured PCI (Post-PCI).

Positive cytology in 38 patients changed to negative in 26 (68.4%) patients at laparotomy. The post-PCI (6.7 ± 7.8) was significantly lower than the pre-PCI (10.6± 10.2) (P=0.0001). The PCI was ≥14 in 30 patients at pretreatment and ≤ 13 in 19 (63.3%) of these patients at posttreatmjent. Post-PCI cut-off level (≤ 13 *vs* ≥14) and cytology after NIPS (negative *vs* positive) emerged as independent indicators of prognosis. Postoperative mortality was 1.2% (1/86).

NLHIPEC and NIPS are safe and effective modalities for reducing Post-PCI below the cut-off level and eradicating peritoneal free cancer cells.

Correspondence: Yutaka Yonemura, Department of Regional Cancer Therapies, Peritoneal Surface Malignancy Center, Kishiwada Tokushukai Hospital, Kusatsu General Hospital, Japan. Tel.: +81.090.94425173. E-mail: y.yonemura@coda.ocn.ne.jp

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Introduction

The prognosis of patients with peritoneal metastasis (PM) from gastric cancer (GC) is still very poor even after complete cytoreduction. To improve their survival, hyperthermic intraperitoneal chemoperfusion (HIPEC) has been performed after cytoreductive surgery (CRS). However, about 80% of patients develop recurrence,[1] and the five-year survival rate after complete cytoreduction was reported to range from 11% to 25%.[2-4] Analyses of recurrence after complete cytoreduction plus perioperative intraperitoneal chemotherapy have found that 77% of all recurrence is found in peritoneum, and mainly detected in the small bowel mesentery.[1] These results indicate that occult micrometastases persist even after complete cytoreduction of macroscopic PM and HIPEC.

Neoadjuvant intraperitoneal/systemic chemotherapy (NIPS) was developed to eradicate peritoneal micrometastasis not removed by surgery.[5,6]

The present study was performed to verify the effects of neoadjuvant laparoscopic hyperthermic intraperitoneal chemoperfusion (NLHIPEC) plus NIPS on PM from GC and assess the prognostic factors after CRS following NLHIPEC and NIPS.

Materials and Methods

Neoadjuvant laparoscopic hyperthermic intraperitoneal chemoperfusion following exploratory laparotomy to determine peritoneal cancer index

Exploratory laparoscopy was performed to determine peritoneal cancer index (PCI) (pretreatment PCI: Pre-PCI) in 150 gastric can-

cer patients with PM referred to the Peritoneal Surface Malignancy Centre of Kishiwada Tokushukai Hospital and Kusatsu General Hospital between October, 2008 and December, 2016.

Under general anesthesia, exploratory laparoscopy[6] was performed to suction out ascites fluid, measure its volume and examined it cytologically. If there was no ascites fluid, then peritoneal lavage fluid recovered after intraperitoneal administration of 200 mL of saline was used for cytological examination.

Biopsy specimens were routinely taken from the peritoneal nodules to confirm the diagnosis histologically. Lesion size in the 13 abdominal sectors was quantitatively evaluated and the Pre-PCI was determined in each case.[7]

The small bowel and its mesentery were divided into four sectors (upper jejunum, lower jejunum, upper ileum, and lower ileum), and the small bowel PCI (SB-PCI) was calculated by summing the lesion sizes in these four sectors.

Subsequently, a longitudinal 5-cm incision was made along the midline of the lower abdomen for open laparotomy. Three drainage tubes were placed (two in the bilateral subdiaphragmatic space for use as inlet tubes and one in the pelvic cavity for use as an outlet tube). Then, HIPEC was performed at 42.5°C to 43°C for 60 minutes using 3 L of saline containing 30 mg/m^2 of docetaxel and cisplatin each. After NLHIPEC, a peritoneal port system (Hickman subcutaneous port; BARD, Salt Lake City, UT, USA) was introduced into the abdominal cavity.

Neoadjuvant intraperitoneal/systemic chemotherapy

Two weeks after NLHIPEC, a series of 3-week cycles of NIPS was performed.[6] Specifically, S1 was administered orally twice daily at a dose of 60 mg/m^2/day for 14 consecutive days, followed by 7 days of rest. Docetaxel and cisplatin were diluted in 500 ml of normal saline and administered intraperitoneally (IP) through the peritoneal port system at a dose of 30 mg/m^2 on day 1. The same dose of docetaxel and cisplatin were administered intravenously (IV) on day 8 after standard premedication. The treatment course was repeated every 3 weeks for 3 courses (Figure 1).

Cytoreductive surgery

Four weeks after the last NIPS cycle, we carried out for CRS in 86 (57.3%) patients. Just after laparotomy, peritoneal washing cytology was performed, and PCIs (Post-PCIs) were determined after aggressive lavage using 10 L of saline.[8-10] Then, total gastrectomy, splenectomy, cholecystectomy, peritonectomy, combined with D2 lymph adenectomy were done in 45 cases with primary tumors. In 41 cases with recurrent PM, the involved peritoneum was stripped away and organs with PM with were resected by peritonectomy (Table 1).[9] After CRS, intraoperative HIPEC was performed in 74 of 86 patients but not in the other 12. No surgery was performed in the remaining 64 patients, because of disease progression, diffuse involvement of the small bowel, old age, and refusal of the operation in 46, 16, 1 and 1 patient, respectively.

Ethical standards

Institutional review board approval was obtained October, 26th, 2008, for our study entitled *A study of the safety and efficacy of NLHIPEC and NIPS for the treatment of peritoneal metastasis from gastrointestinal cancer*. All patients were informed about the adverse effects of the procedure and gave their written informed consents to participate.

Eligibility criteria

The eligibility criteria included: i) histologically or cytologically proven PM from gastric cancer; ii) absence of hematogenous metastasis and remote lymph node metastasis; iii) age 75 years or younger; iv) Eastern Clinical Oncology Group scale of performance status 3 or less; v) good bone marrow, liver, cardiac, and renal function; vi) absence of severe adhesion in the peritoneal cavity;

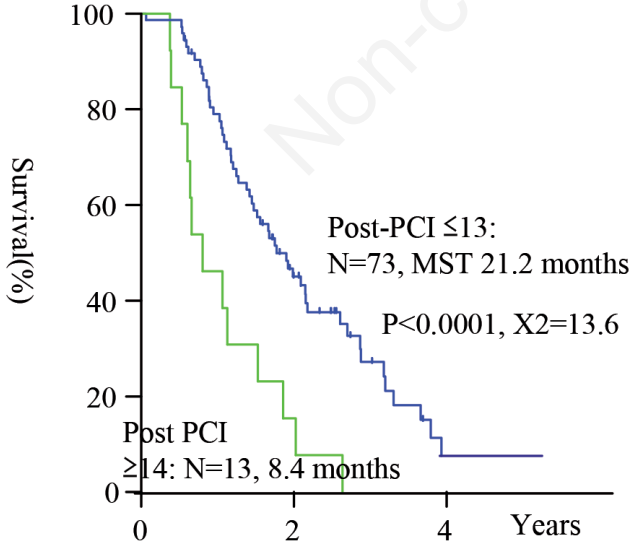

Figure 1. Post-peritoneal cancer index (PCI) cut-off (≤13 *vs* ≥14) determined from survival curves of patients who received cytoreductive surgery after neoadjuvant hyperthermic intraperitoneal chemoperfusion+neoadjuvant intraperitoneal/systemic chemotherapy.

Table 1. Surgical procedures, removed organs, and the number of organ and peritoneal sectors removed.

Gastrectomy	
Total gastrectomy	41
Distal gastrectomy	4
Small bowel resection	36
Hysterectomy+bilateral salpingo-oophorectomy	29
Left diaphragmatic peritonectomy	37
Right diaphragmatic peritonectomy	30
Pelvic peritonectomy	48
Colectomy	42
1: Total colectomy	10
2: Right hemicolectomy	17
3: Left hemicolectomy	4
4: Transverse colectomy	2
5: Low anterior resection	5
2+5	1
3+5	2
6: Wedge resection	1
No of removed peritoneal sectors	5.0 ± 12.3 (1-10)
No of removed organs	3.4 ± 5.6 (0-9)
No of anastomosis	1.3 ± 1.5 (0-3)

and vii) absence of other severe medical conditions or synchronous malignancy.

The clinicopathologic characteristics are given in Table 2.

Evaluation of complications

Complications were graded according to the system of classification established by Dindo and colleagues.[8]

Statistical analyses

Median follow-up was 49 months. All patients were followed and no patients were lost to follow-up. Outcome data were obtained from medical records and patients interviews. All statistical analyses were performed using SPSS software statistical computer package version 17 (SPSS Inc., Chicago, USA). Overall survival was summarized using Kaplan-Meier methods, and differences in overall survival were assessed using the generalized Wilcoxon test. Univariate analysis was performed on categorical variables using the Chi square test, and on continuous variables using the Student's *t* test. A multivariate Cox proportional hazards model was used to determine prognostic factors. Statistical significance was defined as a P-value ≤0.05.

The pre- and post-PCI cut-offs yielding with the most significant survival differenceresults in terms of survival were determined from Pre-PCI and Post-PCI levels. PCIs with the most significant P value for survivals were determined.

Results

Mortality and morbidity during neoadjuvant laparoscopic hyperthermic intraperitoneal chemoperfusion and neoadjuvant intraperitoneal/ systemic chemotherapy

Mean hospital stay after NLHIPEC was 5.2 days (range 4-17). No mortality occurred during NLHIPEC. Grade 1-2 morbidity was found in 11 (7.3 %) patients, and 2, 3 and 6 patients complained of appetite loss, bone marrow suppression, and general malaise, respectively. No mortality occurred during NIPS, but after NIPS, 5 (3.3%) patients developed Grade 3 severe general malaise. Five (3.3%) patients developed Grade 4 morbidities, and one patient each exhibited renal dysfunction, melena, diarrhea, bowel perforation and sepsis.

Surgical procedures, removed organs, and peritoneal sectors

In 45 cases with primary tumor, 41 patients received total gastrectomy (Table 1). Partial small bowel resection, colectomy and hysterectomy combined with bilateral salpingo-oophorectomy were performed in 36, 42, and 29 patients, respectively. Peritonectomy of the left diaphragm, right diaphragm, and pelvis were performed in 37, 30, and 48 patients, respectively. The mean

Table 2. Clinicopathologic parameters and univariate survival analysis (generalized Wilcoxon test).

Clinicopathologic parameters		No of cases	Survival (Univariate analysis) P	X^2
Sex	male female	39 48	0.757	0.095
Macroscopic type	type 2,3 type 4	31 55	0.052	3.716
Completeness of cytoreduction	CCR-0 CCR-1	62 24	<0.0001	19.25
Lymph node metastasis	N0 N1-3	28 63	0.678	0.172
Histologic type	Differntiated Poorly diff.	5 81	0.342	2.342
Primary or recurrence	Primary Recurrence	45 41	0.236	1.405
PCI cut-off level before NIPS	≤29 ≥30	79 7	0.004	8.282
PCI cut-off level after NIPS	≤13 ≥14	73 13	0.0003	12.89
Cytology before NIPS	Negative Positive	48 38	0.016	5.804
Cytology after NIPS	Negative Positive	69 17	<0.0001	20.61
No of resected peritoneal sectors	5≥ 6≤	44 42	1.688	0.193
No of removed organs	4≥ 5≤	47 39	0.348	0.555
Postoperative complication	Grade 0, 1, 2 Grade 3, 4, 5	66 20	0.0313	0.859

number of removed organs, removed peritoneal sectors, and anastomosis was 3.4 ± 5.6 (0-9), 5.0 ± 12.3 (1-10), and 1.3 ± 1.5 (0-3).

Postoperative Grade 3, 4, and 5 complications were found in 12 (14.0%), 7 (8.1%), and 1 (1.2%) patient, respectively. One patient died of multiple organ failure from leakage of an esophagojejunostomy. Reoperation was needed for bleeding in 2 patients, drainage for leakage in 2 patients, and ileus in 1 patient.

Effects of neoadjuvant laparoscopic hyperthermic intraperitoneal chemoperfusion plus 3 cycles of neoadjuvant intraperitoneal/systemic chemotherapy on cytologic status, and peritoneal cancer index

The volume of ascites was 421± 13 ml before NIPS and 146 ± 224 ml and after NIPS (P=0.052). Cytology was positive in 38 (44.2%) patients at exploratory laparoscopy and became negative status in 26 (68.4%) of these 38 patients at laparotomy after NIPS.

The post-PCI (6.7 ± 7.8) was significantly lower than the pre-PCI (10.6± 10.2) (P=0.0001).

Peritoneal cancer index cut-off levels to discriminate good from poor prognosis

The generalized Wilcoxon test was used to calculate the optimum Pre- and Post-PCI cut-off levels (1-39) for discriminating good from poor survival.

These were 29 and 13, respectively (Table 2). Survival was significantly longer in patients with Pre-PCI of ≤ 29 than those with Pre-PCI of ≥ 30 (P=0.004, X^2=8.282), and significantly longer in patients with Post-PCI ≤13 than in those with Post-PCI of ≥14 (P=0.003, X^2=12.89) (Figure 1).

Multivariate analysis of potential factors influencing prognosis after NLHIPEC plus NIPS plus CRS identified Post-PCI cut-off level (≤13 *vs* ≥14) and cytology after NIPS (negative *vs*. positive) as independent prognostic indicators (Table 3). In contrast, Pre-PCI cut-off level and cytological status at NLHIPEC were not independent prognostic factors.

The median survival time (MST) of the 63 patients who did not receive CRS was 7.3 months, and their 1- and 2- year survival rates were 30.0% and 7.8%, respectively. The MSTs was significantly better in the 86 patients who underwent CRS than in patients who did not (P<0.0001, X^2=25.21). MST, and 1- and 2-year survival rates of the CRS-group were 16.8 months, 62.9%, and 31.0%, respectively.

Changes in peritoneal cancer index after neoadjuvant laparoscopic hyperthermic intraperitoneal chemoperfusion and neoadjuvant intraperitoneal/systemic chemotherapy

Among 86 patients who underwent CRS, 30 patients (34.9%) showed a Pre-PCI ≥14, but 19 (63.3%) of the 30 patients showed a Post-PCI of ≤ 13, and the remaining 11 (36.7%) patients had a Post-PCI of ≥14 (Table 3). Additionally, 9 (15%) patients showed complete disappearance of PM. In contrast, Pre-PCI in the 3 (5.4%) patients changed from ≤13 to PCI ≥14 after NIPS.

Table 4 shows the change in lesion size score in each of the 13 peritoneal sectors. The lesion size scores in all sectors except sector 0 were significantly lower after NLHIPEC plus NIPS than at NLHIPEC. Post-SB-PCIs were significantly lower than Pre-SB-PCIs (2.11±2.97 *vs* 3.38±3.80, P<0.0001).

After NLHIPEC+NIPS, complete cytoreduction was achieved in 62 (72.1%) patients.

Discussion

The completeness of cytoreduction has been considered as fundamental to improving the expectancy in patients with PM from GC.[1,2,4] However, diffuse peritoneal involvement is detected in 70% of patients with PM, and complete cytoreduction cannot be performed in a majority of these cases at the time of diagnosis.[11] Worldwide, systemic chemotherapy is the mainstay of PM, but systemic chemotherapy improves survival in cases with PM from GC to not more than 12 months.[11] Furthermore, systemic

Table 3. Prognostic factors analyzed using Cox proportional hazard model.

Clinicopathologic factors	X^2	P	Hazard ratio	95% CI
Sex male *vs.* female	3.478	0.062	1.787	0.971-3.288
Histology differentiated *vs.* poorly differentiated	0.189	0.664	1.316	0.382-4.532
Primary *vs.* recurrence	0.162	0.687	0.893	0.516-1.547
CCR-0 *vs.* CCR-1	2.062	0.151	1.608	0.841-3.074
Lymph node metastasis N0 *vs.* N1-3	1.349	0.246	1.47	0.767-2.817
PCI before NAC (Pre-PCI) ≤29 *vs.* ≥ 30	2.303	0.129	2.21	0.782-6.258
PCI after NAC (Post-PCI) ≤13 *vs.* ≥14	5.581	0.018*	2.522	1.171-5.435
Pathologic response Non-responder *vs.* responder	2.358	0.125	0.6	0.313-1.151
Cytology at NLHIPEC Negative *vs.* positive	0.971	0.324	1.327	0.756-2.328
Cytology after NLHIPEC plus NIPS Negative *vs.* positive	4.382	0.036*	2.225	1.052-4.705
Complication Low grade (0-2) *vs.* high grade (3-4)	0.004	0.952	1.02	0.572-1.812

*Significant.

chemotherapy cannot improve the long-term survival of patients with macroscopic PM due to inadequate diffusion of systemic chemotherapy into the abdominal cavity.[12,13] In contrast, IP chemotherapy can pharmacologically generate higher loco-regional intensity in the abdominal cavity, and the effect of IP chemotherapy *vs* systemic chemotherapy on PM is considered higher.[14]

However, IP chemotherapy after CRS does not work on PM in areas covered by dense abdominal adhesions. Accordingly, IP chemotherapy is mainly used before CRS. The aims of neoadjuvant chemotherapy (NAC) are: i) reduction of PCI; ii) eradication of intraperitoneal micrometastasis including peritoneal free cancer cells; iii) preservation of intact peritoneum as much as possible; and iv) eradication of metastases left on the peritoneum after CRS. Effective NAC can increase the incidence of complete cytoreduction, thereby prolonging survival. Yonemura *et al*. reported that NIPS reduced intraperitoneal tumor burden and eradicated intraperitoneal free cancer cells.[5] Several authors reported an increase in the survival of patients with PCI less than cut-off level after CRS.[1,2,4] However, accurate determination of PCI from preoperative computed tomography (CT) or positron emission tomography (PET) scans is limited,[15-17] particularly when the diameter of PMs is less than 1 cm, and these small nodules are on the small bowel mesentery.[15] The use of exploratory laparoscopy to determine accurate PCIs began in the late 2000s.[11] At present, laparoscopy is considered an excellent diagnostic modality for accurate determination of PCI preoperatively.

However, no study has attempted to assess the effects of NIPS from the changes in PCI. Yonemura *et al*. first reported the direct effect of NLHIPEC with or without NIPS on PCI determined by laparoscopy in 2016, and they found that neoadjuvant chemotherapy reduced PCI below its cut-off level in half of their patients.[18]

Coccolini *et al.* reported that PCI cut-off level at laparotomy is an independent prognostic factor after CRS.[19] However, which PCI cut-off (Pre-PCI *vs* Post-PCI cut-off) relates to prognosis remained unclear. Multivariate analysis in the present study clearly demonstrated that Post-PCI cut-off (≤13 *vs* ≥14) and not the Pre-PCI cut-off level was an independent prognostic factor After NLHIPEC plus NIPS, 63.3% (19/30) of patients with Pre-PCI of ≥14 showed a Post-PCI≤13. In contrast, only 3 (5.4%) of 56 patients with Pre-PCI≤13 showed a Post-PCI≥14. Additionally, 9 patients showed complete disappearance of PM after treatment. Accordingly, second laparoscopic diagnosis for PCI after NAC is recommended to select patients for CRS when the Pre-PCI is higher than its cut-off level.

In our previous study, the PCI cut-off was ≤6.[5] However, in the present study, PCI cut-off point yielding the most significant survival difference was ≤13 *vs* ≥14. The reason for the higher PCI cut-off for the favorable prognosis in the present study may be NLHIPEC, since NIPS+CRS was performed without NLHIPEC in the previous study.[5]

A factor limiting the achievement of complete cytoreduction is the diffuse involvement of the small bowel or its mesentery. After NLHIPEC plus NIPS, lesion size scores of 12 sectors (except of sector 0, greater omentum) were significantly lower than those before treatment. Additionally, Post-SB-PCIs were significantly lower than Pre-SB-PCIs (2.11±2.97 *vs* 3.38±3.80).

These results indicate that NLHIPEC plus NIPS can reduce PCI and SB-PCI. Reduction of SB-PCI improves the incidence of complete cytoreduction. Valle *et al.* reported complete cytoreduction in only 30% of the patients who underwent CRS without NIPS.[11] The present study showed complete cytoreduction in 62 (72.1%) patients after NLHIPEC+NIPS.

NLHIPEC plus NIPS effectively eradicated peritoneal free cancer cells. After NLHIPEC and NIPS, positive cytology at exploratory laparoscopy became negative in 26 (68.4%) of 38 patients. Outcome after CRS is reported to significantly correlate with negative peritoneal cytology than with positive peritoneal cytology.[18] Multivariate analysis in the present study also demonstrated the cytologic status after NLHIPEC plus NIPS (but not at NLHIPEC) as an independent prognostic factor.

No serious complication was found after NLHIPEC. During NIPS, 6.6% of patients experienced Grade 3 and Grade 4 morbidity. Sixty-four (42.7%) of 150 patients were ineligible for CRS after NLHIPEC+NIPS, and 62 of these 64 patients showed progression of disease and diffuse involvement of the small intestine. The survival rate was significantly poorer in these patients than in those of CRS-group.

Postoperative Grade 3, 4 and 5 complications after CRS were found in 12 (14.0%), 7 (8.1%), and 1 (1.2%) patient, respectively, which is even less than that found after CRS with or without

Table 4. Change in lesion size score in 13 peritoneal sectors.

Peritoneal sector	Before NLHIPEC and NIPS	After NLHIPEC and NIPS	P
0: central	2.02±4.62	0.76±0.93	NS
1: right diaphragm	0.89±1.04	0.38±0.76	<0.0001
2: lesser omentum	1.02±1.04	0.34±0.16	<0.0001
3: left diaphragm	0.94±1.04	0.40±0.75	<0.0001
4: left upper flank	0.77±1.02	0.47±0.74	0.022
5: left lower flank	1.02±1.18	0.47±0.83	0.002
6: pelvis	1.58±1.24	1.00±1.05	0.0008
7: right lower flank	1.07±1.08	0.40±0.73	<0.0001
8: right upper flank	1.0±1.608	0.31±0.64	<0.0001
9: upper jejunum	0.89±1.07	0.60±0.80	0.009
10: lower jejunum	0.87±1.07	0.47±0.75	0.002
11: upper ileum	0.94±1.05	0.51±0.08	0.003
12: lower ileum	1.06±1.07	0.57±0.88	0.002
Total PCI	10.5±10.2	6.71±7.75	<0.0001
Small bowel PCI	3.38±3.80	2.11±2.97	0.001

HIPAEC,[20,21] There was no patient who could not undergo CRS because of morbidity associated with NLHIPEC+NIPS.

These results indicate that NLHIPEC+NIPS in combination with CRS can be safely performed with acceptable mortality and morbidity.

Conclusions

Neoadjuvant chemotherapy combined with NLHIPEC+NIPS is safe and effective for reducing PCI below its cut-off level and eradicating peritoneal free cancer cells, thereby increasing the complete cytoreduction rate and long-term survival of patients with PM from GC. A Post-PCI cut-off ≤13 is useful to select patients for CRS.

References

1. Yonemura Y, Canbay E, Sako S, et al. Risk factors for recurrence after complete cytoreductive surgery and perioperative chemotherapy in peritoneal metastases from gastric cancer. J Integl Oncol 2016;5:2.
2. Glehen O, Schreiber V, Cotte E, et al. Cytoreductive surgery and intraperitoneal chemohyperthermia for peritoneal carcinomatosis arising from gastric cancer. Arch Surg 2004;139:20-6.
3. Yonemura Y, Elnemr A, Endou Y, et al. Multidisciplenary therapy for treatment of peritoneal carcinomatosis from gastric cancer. World J Gastrointest Oncol 2010;2:85-97.
4. Yang XJ, Li Y, Yonemura Y. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy to treat gastric cancer with ascites and/or peritoneal carcinomatosis: Results from a Chinese center. J Surg Oncol 2010;101:457-64.
5. Yonemura Y, Bandou E, Sawa T, et al. A new treatment by neoadjuvant intraperitoneal-systemic chemotherapy and peritonectomy for peritoneal dissemination from gastric cancer. Euro J Surg Oncol 2006;32:661-5.
6. Yonemura Y, Ishibashi H, Hirano M, et al. Effects of neoadjuvant laparoscopic hyperthermic intraperitoneal chemotherapy and neoadjuvant intraperitoneal/systemic chemotherapy on peritoneal metastases from gastric cancer. Ann Surg Oncol 2017;24:478-85.
7. Jacquet P, Sugarbaker PH. Clinical research methodologies in diagnosis and staging of patients with peritoneal carcinomatosis. Cancer Treat Res 1996;82:359-74.
8. Dindo D, Demartines N, Clavien PA. Classification of surgical compliations. A new proposal with evaluation in cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
9. Yonemura Y, Elnemr A, Endou Y, et al. Surgical results of patients with peritoneal carcinomatosis treated with cytoreductive surgery using a new technique named aqua dissection. Gastroenterol Res Pract 2012;521487.
10. Kuramoto M, Shimada S, Ikeshima S, et al. Extensive intraperitoneal peritoneal lavage as a standard prophylactic strategy for peritoneal recurrence in patients with gastric cancer. Ann Surg 2009;250:242-6.
11. Valle M, Federici O, Garofalo A. Patient selection for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy, and role of laparascopy in diagnosis, staging and treatment. Surg Oncol Clin N Am 2012;515-31.
12. Hong SH, Shin YR, Roh Y, et al. Treatment outcomes of systemic chemotherapy for peritoneal carcinomatosis arising from gastric cancer with no measurable disease: retrospective analysis from a single center. Gastric Cancer 2013;16:290-300.
13. de Bree E, Tsiftsis DD. Experimental and pharmacologic studies in intraperitoneal chemotherapy from laboratory bench to bedside. In: S. Gonzalez-Moleno, ed. Advances in peritoneal surface oncology. Berlin: Springer; 2007. pp 53-73.
14. Ishigami H, Kitayama J, Kaisaki S, et al. Phase II study of weekly intravenous and intraperitoneal paclitaxel (PTX) combined with S-1 for advanced gastric cancer with peritoneal metastasis. Ann Oncol 2010;21:67-70.
15. Koh JL, Yan TD, Glenn D, et al. Evaluation of preoperative computed tomography in estimating peritoneal cancer index in colorectal peritoneal carcinomatosis. Ann Surg Oncol 2009; 16:327-33.
16. Pôfannenberg C, Knigstainer, Aschoff P, et al. (18)F-FDG-PET-CT to select patients with peritoneal carcinomatosis for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Ann Surg Oncol 2009;16:1295-303.
17. Hong SH, Shin YR, Roh Y, et al. Treatment outcomes of systemic chemotherapy for peritoneal carcinomatosis arising from gastric cancer with no measurable disease: retrospective analysis from a single center. Gastric Cancer 2013;16:290-300.
18. Yonemura Y, Canbay E, Sako S, et al. Effects of laparosopic hyperthermic intraperitoneal chemotherapy peritoneal metastasis from gastric cancer, Japan. Canad Center Sci Educ 2014;3:43-50.
19. Coccolini F, Catena F, Glehen O, et al. Complete versus incomplete cytoreduction in peritoneal carcinosis from gastric cancer, with consideration to PCI cut-off. Systemic revoew and meta-analysis. EJSO 2015 [Epub ahead of print].
20. Yonemura Y, Canbay E, Endou Y, et al. Peritoneal cancer treatment. Exp Opin 2014;15:623-36.
21. Levine HA, Stewart JH, Russel GB, et al. Cytoreductive surgery and intraperitoneal hyperthermic chemotherapy for peritoneal surface malignancy; experience with 501 procedures. J Am Coll Surg 2007;204:943-53.