

## Original Contribution

# Efficacy of Intraperitoneal Chemohyperthermia for Gastric Cancer Patients with Peritoneal Carcinomatosis

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**Abstract :** Peritoneal carcinomatosis is a major problem after surgery for serosal-invasive gastric cancer because most patients with peritoneal carcinomatosis die within six months of diagnosis. In this study, we evaluate the efficacy of intraperitoneal chemohyperthermia for gastric cancer patients with peritoneal carcinomatosis. Seventeen gastric cancer patients with peritoneal carcinomatosis, which was confirmed by cytological and/or pathological examination during operation, were treated by removal of the primary tumor. Seven patients consented to receive chemohyperthermia during the postoperative period (hyperthermia group), while 10 patients underwent surgery only (control group). The 10-month disease-free and overall survival rates for the hyperthermia group were 57.1% and 85.7%, respectively, and were higher than those of the control group. No patient in the hyperthermia group had life-threatening complications, such as leakage of intestinal anastomosis, intestinal perforation, bone marrow suppression, or renal dysfunction. In conclusion, postoperative chemohyperthermia appears to improve the prognosis of gastric cancer patients with peritoneal carcinomatosis. This method is feasible, easy to performed, and relatively safe.

**Key Words :** gastric cancer, peritoneal carcinomatosis, chemohyperthermia

## Introduction

Peritoneal carcinomatosis is a major problem after surgery for serosal-invasive gastric cancer because most patients with peritoneal carcinomatosis die within six months of diagnosis<sup>1)</sup>. Gastric carcinoma cells were often detected in the abdominal cavity even when it was not demonstrated macroscopically that patients with serosal-invasive gastric cancer had peritoneal dissemination<sup>2)</sup>. It has been reported that, when an anticancer drug was intraperitoneally administered, a significantly greater concentration was obtained in the abdominal cavity than in the circulating blood<sup>2)</sup>. Therefore, for patients with peritoneal carcinomatosis, intraperitoneal injection of anticancer drugs had been used, but the effectiveness of this

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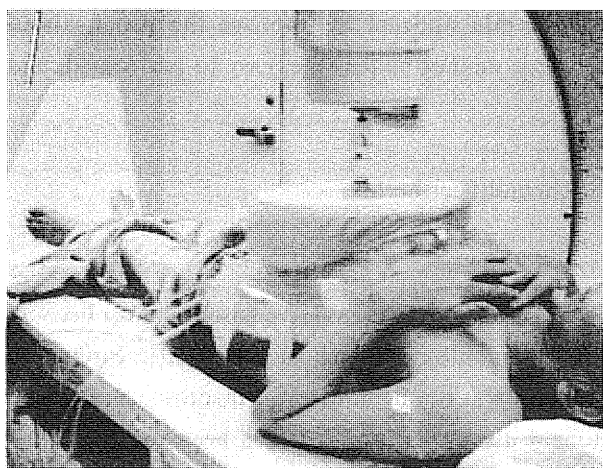
method is still unsatisfactory. Intraperitoneal chemohyperthermia increases the sensitivity of tumor cells to anticancer drugs and simultaneously enhances the antigenicity of tumor cells<sup>3)</sup>. Hyperthermia combined with chemotherapy has been introduced for the management of intraperitoneal recurrence after gastrointestinal cancer resection<sup>4)</sup>. In this study, we evaluate the efficacy of intraperitoneal chemohyperthermia for gastric cancer patients with peritoneal carcinomatosis.

### Patients and Methods

From 1999 to 2003, 17 gastric cancer patients with peritoneal carcinomatosis confirmed by cytological and/or pathological examination during operation were treated by removing the primary tumor. All patients underwent a subtotal or total gastrectomy, and 24-Fr silicon tubes were placed in the left subphrenic and Douglas pouch. There were 11 males and six females, and the average age was

**Table I:** clinical patient data

Variable	Hyperthermia (n=7)	Control (n=10)	P value
Location			0.051
Upper	6	2	
Middle	0	5	
Lower	1	3	
Depth of invasion			0.279
SS	0	1	
SE	7	7	
SI	0	2	
Histology			0.269
Tub2	0	1	
Por	4	8	
Sig	1	1	
Muc	2	0	
Tumor size (cm)	8.1	9.0	0.718



**Fig. 1.** External RF heating device (Thermotron RF-8). Hyperthermia was performed for 60min in the supine position.



**Fig. 2.** Thermography showed the temperature distribution of the abdominal cavity. Using an external RF heating device, the temperature of the abdominal cavity was controlled to maintain at 39-43°C.

58.7±1.9 years (range 40 to 74 years). Seven patients consented to receive chemohyperthermia during the postoperative period (hyperthermia group), while 10 patients underwent surgery only (control group). As shown in Table I, there were no significant differences in the size and location of tumors, the depth of the gastric wall invasion, or the histological type of the tumors. In the hyperthermia group, 2 weeks after surgery, 2000 ml saline containing 100 mg of cisplatin was perfused into the peritoneal cavity through the silicon tubes, and the silicon tubes were closed. Using an external RF heating device (Thermotron RF-8), hyperthermia was performed for 60 minutes (Fig. 1) Patients were treated in the supine position and an electrode of 30 cm in diameter was placed in front and back of the patient, Coupling of the applicator to the patient was usually achieved with plastic bags (overlay bolus) filled with deionized water. Active skin cooling at 5°C was applied to most patients during the treatment. The temperature of the abdominal cavity was measured during hyperthermia using the thermography and it was controlled to maintain at 39-43°C (Fig. 2) After hyperthermic treatment, the silicon tubes were opened.

### Statistical Analysis

The survival rates were calculated by the Kaplan-Meier method. The student's *t* test was used to determine the significant differences.

### Results

The mean duration of follow-up was 10 months (range 2 to 27 months). Among the 17 patients, cancer recurrence was detected in 12 (70.6%) patients; all patients had peritoneal recurrences. The disease-free survival curves for the hyperthermia and control groups are shown in Fig. 3. The 10-month disease-free survival rate for the hyperthermia group was 57.1%, whereas, for the control group, it was 35.0%. However, no significant differences were noted between the two groups.

During the course of this study, 9 patients (90%) in the control group died; and 6 patients (85.7%) in the hyperthermia group lived. The overall survival curves for the hyperthermia and control groups are shown in Fig. 4. The 10-month survival rates for the hyperthermia and control groups were 85.7% and 60.0%, respectively. However, no significant differences were observed between the two groups.

No patients in the hyperthermia group had life-threatening complications, such as leakage of intestinal anastomosis, intestinal

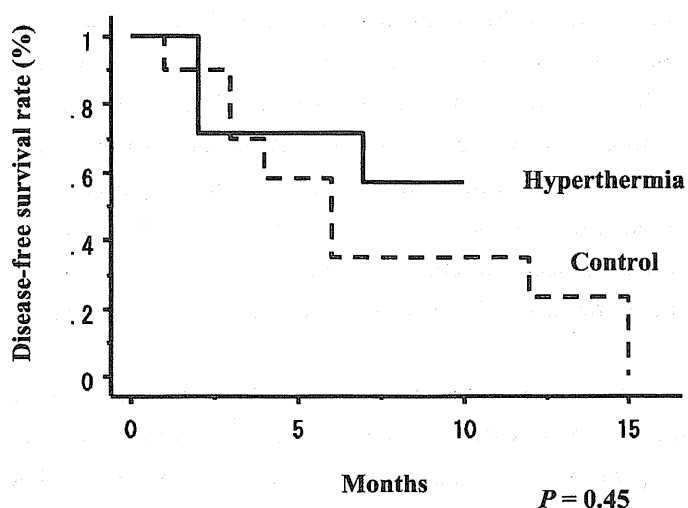


Fig. 3. Disease-free survival curves for patients with peritoneal carcinomatosis. No significant differences was noted in the 10-month disease-free survival rates between the hyperthermia and control groups.

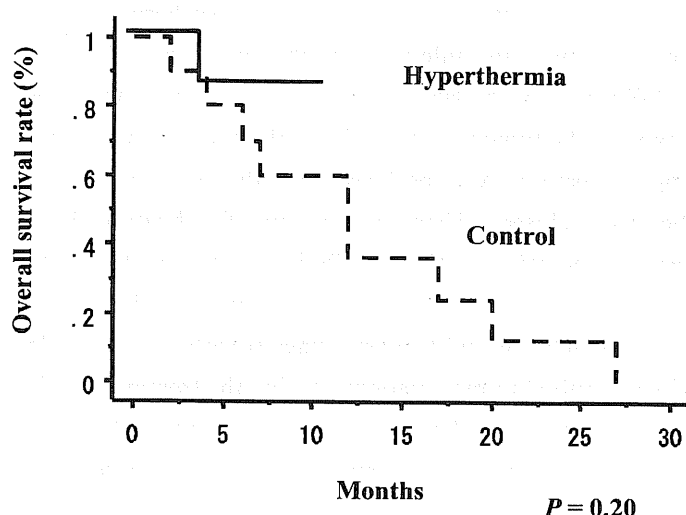


Fig. 4. Overall survival curves for patients with peritoneal carcinomatosis. No significant differences was observed in the 10-month survival rates between the hyperthermia and control groups.

chemohyperthermia and surgery for serosal-invasive gastric cancer had a higher survival rate and better prognosis than the patients who underwent surgery only. However, patients with peritoneal carcinomatosis confirmed by cytological and/or pathological examination were excluded from the study<sup>8)</sup>. In this study, we evaluated the efficacy of chemohyperthermia for gastric cancer patients with peritoneal carcinomatosis. Most patients with peritoneal carcinomatosis die within 6 months of diagnosis<sup>1)</sup>. In our study, the 10-month disease-free and overall survival rates for the hyperthermia were 57.1% and 85.7%, respectively, and were higher than those of the control group. We consider that chemohyperthermia with the removal of the primary tumor can produce a satisfactory therapeutic effect. However, no significant differences were observed in the 10-month survival rates between the two groups because this study was performed with a small number of patients. Therefore, a study that includes a large number of patients will be necessary. Furthermore, in order to prove availability of chemohyperthermia for gastric cancer patients with peritoneal carcinomatosis, we must compare chemohyperthermia with chemotherapy only regarding the overall survival rate.

Although it has been attested that intraoperative chemohyperthermia is an effective procedure, several complications, such as leakage of intestinal anastomosis, intestinal perforation, bone marrow suppression, and renal failure, have been reported<sup>9)</sup>. Therefore, we preformed chemohyperthermia two weeks after surgery, when the general condition of the patients was better. No patient in the hyperthermia group had life-threatening complications. This finding indicates that postoperative chemohyperthermia can be recommended when resection and anastomosis have been performed.

In conclusion, postoperative chemohyperthermia appears to improve the prognosis of gastric cancer

perforation, bone marrow suppression, or renal dysfunction.

#### Discussion

Gastric carcinoma cells were often detected in the abdominal cavity even when it was not demonstrated macroscopically that patients with serosal-invasive gastric cancer had peritoneal dissemination<sup>2)</sup>. Peritoneal carcinomatosis is an important factor that affects the prognosis of patients with serosal-invasive gastric cancer. In recent years, hyperthermia combined with chemotherapeutic agents, such as cisplatin, mitomycin c, and cyclophosphamide, has been employed to prevent peritoneal carcinomatosis<sup>5-7)</sup>. It has been reported that the patients who underwent intraoperative

patients with peritoneal carcinomatosis. This method is feasible, easy to performed, and relatively safe.

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## 腹膜播種を伴った進行胃癌に対する温熱化学療法の有効性

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**要 旨：**胃癌術後の腹膜播種は、予後を脅かす状態であり、大多数の患者は 6 ヶ月以内に死亡すると報告されている。今回、我々は腹膜播種を伴った進行胃癌に対して胃切除後に温熱化学療法を施行し、その効果を比較検討した。1999 年から 2003 年に術中の細胞診または迅速病理組織検査により腹膜播種を確認し、胃切除術を施行した 17 名を対象とし、温熱化学療法併用群 (7 名) と手術単独群 (10 名) の 2 群に分類し無再発率、生存率を比較した。温熱化学療法併用群の術後 10 ヶ月の無再発率と生存率は、57.1%と 85.1%であり、手術単独群より予後良好であった。また、縫合不全、消化管穿孔、骨髄抑制、腎不全などの副作用を認めなかった。結語として、温熱化学療法は、腹膜播種を伴った胃癌患者の予後を改善することが出来る有効な治療法と考えられた。