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Original article

Combined resection of invaded organs in patients with T4 gastric carcinoma

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Abstract

Background. **To understand the efficacy of gastrectomy combined with the resection of other organs and to refine the indications for this type of surgery, the records of 156 patients with carcinoma of the stomach directly invading adjacent organs or structures (T4 gastric carcinoma) were analyzed retrospectively.**

Methods. **The patients were divided into three groups, as follows: in group A, curative resection was performed by the combined resection of invaded organs or structures; in group B, although combined resection was performed, curative resection could not be performed because of the extent of lymph node metastasis, liver metastasis, and/or peritoneal metastasis; in group C, combined resection was not performed.**

Results. **In patients with peritoneal or liver metastasis, there was no significant difference in prognosis among the three groups. In patients without peritoneal and liver metastasis, the prognosis of group A was significantly better than that of group B or group C, irrespective of the extent of lymph node metastasis or the number of invaded organs. In these group A patients, the 5-year survival rates of those with localized tumors and no lymph node metastasis, those with localized tumors and lymph node metastasis, those with infiltrating tumors and no lymph node metastasis, and those with infiltrating tumors and lymph node metastasis were 100%, 56.2%, 57.1%, and 13.6%, respectively.**

Conclusions. **Combined resection of involved organs should be carried out with curative intent in patients with localized gastric cancer or infiltrating gastric cancer without lymph node metastasis.**

Key words Gastric carcinoma · Survival · Combined resection

Introduction

Although in the majority of patients with gastric carcinoma the primary lesion is confined to the gastric wall, in approximately 10% to 20% of patients who undergo resection, the tumor has crossesd the serosal layer and extends to adjacent organs [1,2]. In such patients, extensive en-bloc resection of the invaded organs is required [2–5]. However, en-bloc resection has an associated high risk, and such advanced carcinoma is frequently associated with other incurable factors, such as peritoneal, hematogenous, and/or distant lymph node metastasis [6]. It is therefore important to understand the efficacy of gastrectomy combined with the resection of other organs and to refine the indications for this type of surgery. In the current study, we retrospectively analyzed the records of 156 patients with carcinoma of the stomach directly invading adjacent organs or structures, to investigate the efficacy of gastrectomy combined with invaded organ resection.

Patients and methods

Patients

Among 2212 gastric adenocarcinoma patients who underwent gastrectomy at our institution from January 1970 to December 1996, the records of 156 patients with tumors extending to adjacent organs or structures (T4 gastric carcinoma) were examined in this study. For the patients in whom en-bloc resection was performed, diagnosis was made by histological examination. For the patients in whom en-bloc resection was not performed, diagnosis was made based on both macroscopic observation during surgery and histological examination of the abraded margin on the resected specimen. The invaded organs and the number of invaded organs are listed in Table 1. Invasion to the pancreas was observed

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Table 1. Invaded organs in 156 patients with T4 gastric carcinoma

	No. of patients	5-Year survival rate (%)
Invaded organs		
Pancreas	84	6.9**
Mesocolon	54	13.7**
Peritoneum[a]	22	10.0**
Colon	16	12.5
Diaphragm	14	10.0
Liver	14	50.0*
Spleen	6	0**
Portal vein	6	0**
Gallbladder	3	25.0
Adrenal gland	2	0**
Small intestine	1	0
Number of invaded organs		
One	99	16.5
Two	48	7.7
Three	7	14.3
Four	2	0

* vs ** $P < 0.05$

[a] Peritoneum includes that lining the abdominal wall and the retroperitoneum

most frequently (84 patients; 53.8%), followed by the mesocolon (54 patients; 34.6%).

The 156 patients were divided into three groups, as follows: in group A, curative resection was performed by the combined resection of invaded organs or structures; in group B, although combined resection was performed, curative resection could not be performed because of the extent of lymph node metastasis, liver metastasis, and/or peritoneal metastasis; in group C, combined resection was not performed. The criteria considered for curative resection were the complete removal of a primary gastric tumor, dissection of regional lymph nodes, and no remaining macroscopic tumor. The background of each group is listed in Table 2. The clinicopathologic findings were determined according to the rules set forth by the Japanese Research Society for Gastric Cancer [7]. The macroscopic appearance of gastric carcinoma was classified into two types; localized and infiltrating. The extent of lymph node metastasis was classified as follows: N0/1/2, no lymph node metastasis or metastasis limited to group 1 or group 2 nodes; N3/4, lymph node metastasis had spread to group 3 or group 4 nodes. The extent of lymph node dissection was similarly classified as D0/1/2 and D3/4. Combined resection of the invaded organ was not performed in group C. However, D1 or D2 lymph node dissection was performed in most of the patients. Thus, the patient's nodal status was evaluated based on both the histological findings of the resected lymph nodes and the surgical findings.

A total of 127 patients had recurrence. Peritoneal recurrence was observed in 56 of 127 patients (44.1%), followed by hematogenous recurrence in 30 of 127 patients (23.6%). In the 30 patients with hematogenous recurrence, metastasis to the liver was observed in 28 patients, to the lung in patient 1, and to the bone in 1. Lymph node recurrence, local recurrence, and recurrence in the remnant stomach were observed in 28 of 127 (22.0%), 7 of 127 (5.5%), and 8 of 127 (6.3%), patients, respectively. Thirteen patients presented with recurrent tumors at multiple sites. The sites of recurrence could not be determined in 12 patients.

Statistical analysis

The association of factors was evaluated by the χ^2 test or Fisher's exact test. The significance of differences among means was determined by the Mann-Whitney test. Survival curves were constructed by the Kaplan-Meier method, and differences between survival curves were examined with the log-rank test. Multivariate analysis was performed using the Cox proportional hazards model. The accepted level of significance was $p < 0.05$. A Macintosh personal computer system (Stat View software; Abacus Concepts, Berkeley, CA, USA) was used for all statistical analyses.

Results

Prognosis of entire cohort of patients with T4 gastric carcinoma according to the invaded organ

The 5-year survival rates of patients, according to the invaded organ, are listed in Table 1. The prognosis of patients with invasion to the liver was significantly better than that of the patients with invasion to the pancreas, mesocolon, peritoneum, spleen, portal vein, or adrenal gland.

Table 2. Background of each group of patients with T4 gastric carcinoma

	Group A ($n = 55$)	Group B ($n = 27$)	Group C ($n = 74$)
Age (years) (mean ± SD)	60.6 ± 9.7	59.1 ± 12.9	62.6 ± 11.8
Sex			
Male ($n = 101$) (%)	35 (63.6)	17 (63.0)	49 (66.2)
Female ($n = 55$) (%)	20 (36.4)	10 (37.0)	25 (33.8)
Tumor size	9.6 ± 3.6	11.4 ± 4.1	10.3 ± 4.2
Tumor location			
Upper 1/3 ($n = 34$) (%)	16 (29.1)	6 (22.2)	12 (16.2)
Middle 1/3 ($n = 25$) (%)	9 (16.4)	7 (25.9)	9 (12.2)
Lower 1/3 ($n = 56$) (%)	21 (38.2)	5 (18.5)	30 (40.5)
Whole ($n = 41$) (%)	9 (16.3)	9 (33.4)	23 (31.1)
Histology			
Differentiated ($n = 43$) (%)	18 (32.7)	5 (18.5)	20 (27.0)
Undifferentiated ($n = 113$) (%)	37 (67.3)	22 (81.5)	54 (73.0)
Macroscopic appearance			
Localized type ($n = 39$) (%)	22 (40.0)*	3 (11.1)**	14 (18.9)**
Infiltrative type ($n = 117$) (%)	33 (60.0)	24 (88.9)	60 (81.1)
Lymph node metastasis			
Absent ($n = 18$) (%)	14 (25.5)*	1 (3.7)	3 (4.1)***
Present ($n = 138$) (%)	41 (74.5)	26 (96.3)	71 (95.9)
Lymphatic vessel invasion			
Absent ($n = 22$) (%)	12 (21.8)	2 (7.4)	8 (10.8)
Present ($n = 134$) (%)	43 (78.2)	25 (92.6)	66 (89.2)
Blood vessel invasion			
Absent ($n = 70$) (%)	27 (49.1)	7 (25.9)	36 (48.6)
Present ($n = 86$) (%)	28 (50.9)	20 (74.1)	38 (51.4)
Peritoneal metastasis			
Absent ($n = 116$) (%)	49 (89.1)*	19 (70.4)	48 (64.9)***
Present ($n = 40$) (%)	6 (10.9)	8 (29.6)	26 (35.1)
Liver metastasis			
Absent ($n = 143$) (%)	55 (100)*	24 (88.9)**	64 (86.5)***
Present ($n = 13$) (%)	0 (0)	3 (11.1)	10 (13.5)
Operation procedure			
Partial ($n = 70$) (%)	25 (45.5)	5 (18.5)*	40 (54.1)**
Total ($n = 77$) (%)	26 (47.3)	18 (66.7)	33 (44.6)
Other ($n = 9$)[a] (%)	4 (7.2)	4 (14.8)	1 (1.3)
Lymph node dissection			
D0/1/2 ($n = 114$) (%)	26 (47.3)*	19 (70.4)*	69 (93.2)***
D3/4 ($n = 42$) (%)	29 (52.7)	8 (29.6)	5 (6.8)
Number of invaded organs			
One ($n = 99$) (%)	41 (74.5)	15 (55.6)	43 (58.1)
More than two ($n = 57$) (%)	14 (25.5)	12 (44.4)	31 (41.9)

* vs ** $P < 0.05$; * vs *** $P < 0.01$

[a] These patients were excluded from statistical analysis

Prognosis of the entire cohort of patients with T4 gastric carcinoma according to groups

The correlations between each group and prognosis are shown in Fig. 1. The prognosis of group A was significantly better than that of group B or group C. There was no significant difference in survival between groups B and C. As shown in Table 2, however, patients in groups B and C generally had a higher frequency of lymph node metastases, peritoneal metastases, and liver metastases, as well as a larger number of invaded organs, than patients in group A.

Prognosis of patients with peritoneal and liver metastasis

Of the 40 patients with peritoneal metastasis, 6 were in group A, 8 in group B, and 26 in group C. All these patients died within 26 months after surgery. There was no significant difference in prognosis among these three groups. Of the 13 patients with liver metastasis, there were no patients in group A; 3 were in group B and 10 in group C. All these patients died within 18 months after surgery. In these patients, there was no significant difference in prognosis between group B and

group C. Thus, combined resection seemed to be of no value in patients with peritoneal metastasis and/or liver metastasis.

Prognosis of patients without peritoneal or liver metastasis

Of the 105 patients without peritoneal and liver metastasis, 50 were in group A, 17 in group B, and 38 in group C. The prognostic significance of surgery was evaluated in each group in terms of extent of lymph node metastasis. The prognosis of group A patients was significantly better than that of group B and group C, both in patients with N0/1/2 (Fig. 2a) and in those with N3/4 lymph node metastasis (Fig. 2b). Analysis with regard to the number of invaded organs revealed that the prognosis of group A was significantly better than that of group B and group C when there was one invaded organ (Fig. 3a). The prognosis of group A was also significantly better than that of group B and group C when more than two organs were invaded (Fig. 3b).

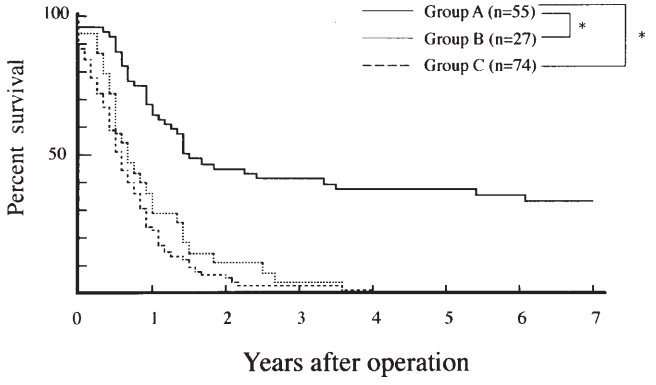
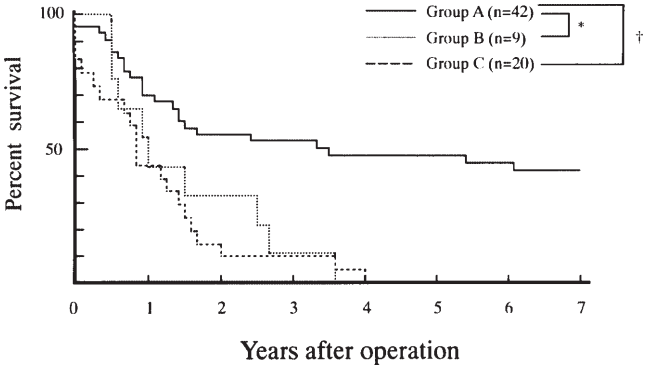


Fig. 1. Entire cohort of 156 patients with T4 gastric carcer. Correlations between each group and prognosis. The prognosis of group A was significantly better than that of group B and group C. $*P < 0.001$

Prognosis of patients who underwent curative surgery

As indicated above, combined resection was useful in group A patients without peritoneal or liver metastasis. To determine whether any variable had affected the prognosis in these patients, we carried out multivariate analysis, using the Cox proportional hazards model and a stepwise procedure. The covariates included were age, sex, tumor size, histologic classification, macroscopic appearance, lymph node metastasis, lymphatic vessel invasion, blood vessel invasion, lymph node dissection, surgical procedure, and the number of invaded organs. Age and tumor size were regarded as continuous variables in this analysis. The multivariate analysis indicated that macroscopic appearance and lymph node metastasis were independent prognostic factors (Table 3).

With regard to both macroscopic appearance and the extent of lymph node metastasis, we found that the 5-year survival rates of patients without peritoneal or liver metastasis with localized tumors and no lymph node metastasis; those who had localized tumors and lymph node metastasis; those who had infiltrating tumors and no lymph node metastasis; and those who had infiltrating tumors and lymph node metastasis were 100%, 56.2%, 57.1%, and 13.6%, respectively. The prognosis of patients who had localized tumors and no lymph node metastasis and those who had localized tumors and lymph node metastasis was significantly better than that of the patients who had infiltrating tumors and lymph node metastasis (Fig. 4). The prognosis of patients who had infiltrating tumors and no lymph node



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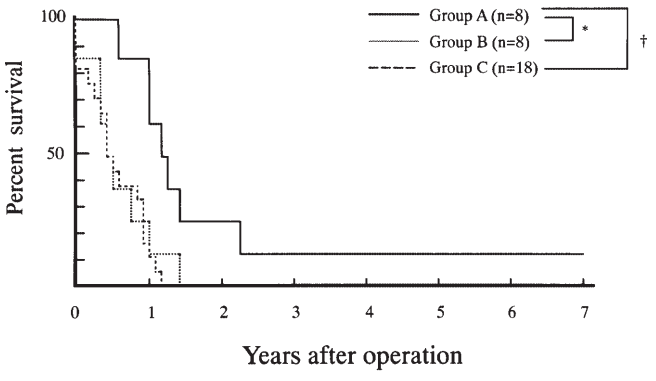

b

Fig. 2a,b. Patients without peritoneal or liver metastasis. Correlations between each group and prognosis with respect to the extent of lymph node metastasis. In patients with N0/1/2 lymph node metastasis, the prognosis of group A was significantly better than that of group B and group C (**a**). In patients with N3/4 lymph node metastasis, the prognosis of group A was also significantly better than that of group B and group C (**b**). **a** and **b** $*P < 0.05$; $^{\dagger}P < 0.001$. See text for explanation of node metastasis

Table 3. Multivariate analysis by the Cox proportional hazards model and a stepwise procedure in group A patients who had no peritoneal or liver metastases

Variables	*P* value	Hazard ratio	95% CI
Macroscopic appearance	0.0311	1.617	1.045–2.503
Lymph node metastasis	0.0097	1.621	1.124–2.338

CI, Confidence interral

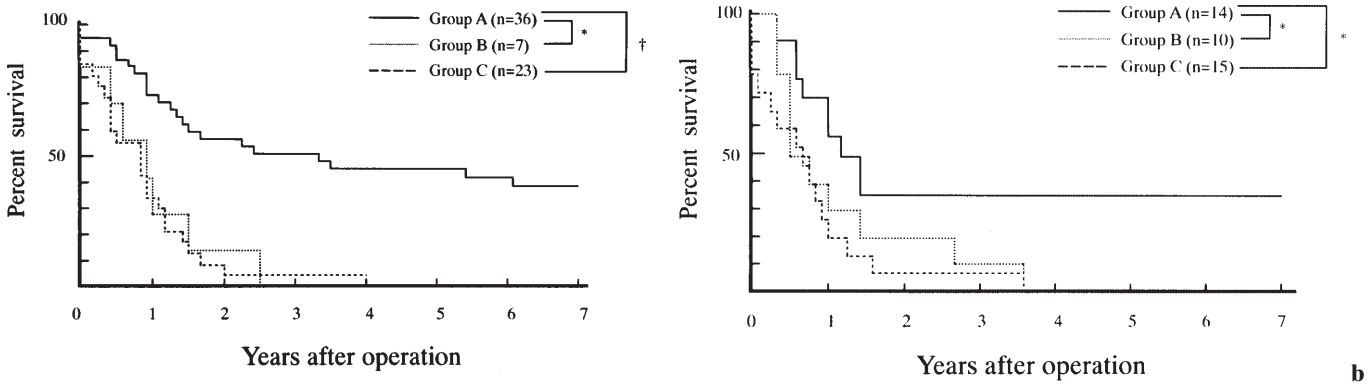

Fig. 3a,b. Patients without peritoneal or liver metastasis. Correlation between each group and prognosis with regard to the number of invaded organs. The prognosis of group A was significantly better than that of group B and group C when one organ was invaded (**a**). The prognosis of group A was also significantly better than that of group B and group C when more than two organs were invaded (**b**). **a** $*P < 0.01$; $^{\dagger}P < 0.001$; **b** $*P < 0.05$

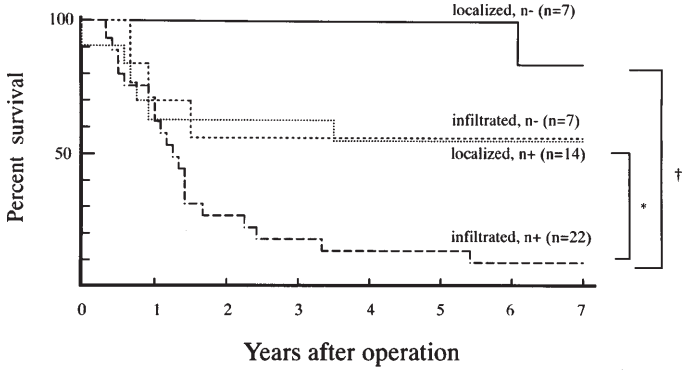

Fig. 4. Correlations between macroscopic appearance, lymph node metastasis, and prognosis. The prognosis of patients who had localized tumors and no lymph node metastasis and those who had localized tumors and lymph node metastasis was significantly better than that of patients who had infiltrating tumors and lymph node metastasis. $*P < 0.05$; $^{\dagger}P < 0.001$

metastasis was better than that of the patients who had infiltrating tumors and lymph node metastasis, although the difference was not significant.

Discussion

Carcinoma of the stomach that invades adjacent organs or structures involves potentially incurable factors such as distant lymph node metastasis, peritoneal metastasis, or hematogenous metastasis. Treating such advanced carcinoma of the stomach involves serious considerations, especially the technical difficulty of a gastrectomy combined with the resection of other organ(s), the potentially serious morbidity after such operations, and the poor correlation of combined resection with survival. Thus, the decision or whether to perform combined resection of invaded organs during a gastrectomy must be weighed seriously by the surgeon. The aim of the current study was to clarify the efficacy of en-bloc combined resection and to indicate which patients might benefit from en-bloc resection.

With regard to the invaded organ, the most frequent sites of invasion in the current study were the pancreas, followed by the mesocolon, the peritoneum, colon, diaphragm, and liver. Shirakabe et al. [8] have reported on a very large number of patients with invasion and similarly found the pancreas to be the most frequent site of invasion, followed by the mesocolon, colon, liver, and diaphragm.

In the current study, the patients were divided into three groups, as described in "patients and methods." The prognosis of group A was significantly better than that of groups B and C. As shown in Table 2, the frequency of lymph node metastasis, peritoneal metastasis, and liver metastasis was higher, and the number of invaded organs was greater in groups B and C than in

group A. Thus, the combined resection was reevaluated precisely. There was no significant difference in prognosis among the groups in those patients with peritoneal or liver metastasis. Combined resection was not effective in patients with peritoneal or liver metastasis, even when curative surgery was performed. In contrast, in patients without peritoneal and liver metastasis, the prognosis of group A was better than that of group B or group C, irrespective of the extent of lymph node metastasis and the number of invaded organs. These findings suggest that the effectiveness of complete excision is related not so much to multiple organ involvement and the presence of lymph node metastasis as it is to the presence of incurable factors such as peritoneal metastasis and liver metastasis. Korenaga et al. [2] have also recommended complete excision of invaded organs, irrespective of the number of organs or the site of organs involved, provided that there is no evidence of incurable factors.

To refine the indications for combined resection of invaded organs in more detail, we examined prognostic factors in group A patients who had no peritoneal or liver metastasis. Multivariate analysis indicated that macroscopic appearance and lymph node metastasis were independent prognostic factors. Based on this result, these patients were divided into four groups: (a) patients with localized tumors and no lymph node metastasis, (b) patients with localized tumors and lymph node metastasis, (c) patients with infiltrating tumors and no lymph node metastasis, and (d) patients with infiltrating tumors and lymph node metastasis. The prognosis of patients who had localized tumors and no lymph node metastasis and those who had localized tumors and lymph node metastasis was significantly better than that of patients who had infiltrating tumors and lymph node metastasis. The prognosis of patients who had infiltrating tumors and no lymph node metastasis was better than that of patients who had infiltrating tumors and lymph node metastasis, although the difference was not significant. Thus, the best indication for combined resection was for those patients without peritoneal and liver metastasis who had localized or infiltrating tumors without lymph node metastasis, irrespective of the extent of the lymph node metastases and the number of invaded organs, and specifically, in those patients in whom curative resection was possible.

In conclusion, combined resection is not effective in patients with peritoneal or liver metastasis, even when curative surgery is performed. On the other hand, combined resection is effective in patients without peritoneal or liver metastasis when curative surgery is performed. Of these patients, those with the best indications for combined resection are those with localized tumors, irrespective of the extent of lymph node metastasis and the number of invaded organs. In patients with infiltrating tumors with lymph node metastasis, combined resection does not seem to be effective even when curative resection is performed.

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