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## Surgical Treatment of Gastric Cancer with Invasion Into the Contiguous Organs

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### ABSTRACT

Between 1968 and 1983, out of 1,137 gastric cancer patients who underwent laparotomy, 344 patients had cancer invasion into a contiguous organ based on gross findings. The incidences of peritoneal dissemination, metastasis to the liver and extensive lymph node involvement were observed at the rates of 52.9%, 17.2% and 37.8%, respectively. Two hundred and twenty-one patients had gastrectomy with or without combined resection of other organs. The resectability rate was 62.9%. The commonly invaded organs were the pancreas (49.3%), transverse colon (13.1%), liver (10.4%), and diaphragm (5.9%). Combined resection of the stomach and the surrounding organ was performed in 139 patients (62.9%). The operative mortality rate was 4.9%. The crude five-year survival rate for gastrectomy was 10.8%; 27.4% in curative resection and 3.5% in non-curative resection. In contrast, none of the 123 patients in the non-resected group survived 3 years postoperatively.

The results support that aggressive gastrectomy is indicated in selected patients as far as curability can be expected by means of combined resection.

### INTRODUCTION

With the recent advancements in diagnostic techniques and surgical treatment with adjuvant chemo- and immuno-therapy, the survival rates of gastric cancer patients have been improved during the last two decades. However, despite progresses in these medical and surgical fields, the incidence of advanced gastric cancers is still high. Among them,

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simultaneously coexistent macroscopic cancer invasions into the neighboring organs or structures are often found.

Since January 1, 1961, 344 cases of gastric cancer associated with such invasions have been operated on at the First Department of Surgery, Nagasaki University Hospital. This study was aimed to obtain basic clinico-pathologic data of surgical treatment and its results on gastric cancer with a direct and/or indirect cancer invasion, based on gross findings, into the neighboring organs or structures.

## PATIENTS AND METHODS

During the 16-year period between January 1, 1968 and December 31, 1983, a total of 1,137 patients underwent operation for gastric cancers. The diagnosis of gastric cancer was based on radiological and endoscopical findings, and confirmed by histology of endoscopic biopsy specimens and/or surgical specimens. Out of 1,127 patients, 344 (30.3%) were judged to have macroscopic direct or indirect cancer invasion into the surrounding organ and were evaluated in this present study. 'Indirect invasion' here implies cancer invasion into the contiguous organs via metastatic lymph nodes.

These 344 patients had a mean age of  $59.2 \pm 12.5$  years ( $m \pm S.D.$ ), ranging from 24 to 86. There were 213 men and 131 women.

Two-hundred and twenty-one (64.2%) out of 344 patients underwent gastrectomy with or without combined resection of other organs. For the remaining 123 patients (35.8%), exploratory laparotomy or palliative surgery without gastric resection was performed, including anastomosis of the gastrointestinal tract for temporary relief of gastric and bowel obstruction or establishment of intestinal tubing for nutritional support. The severity of cancer invasion to the serosa, degree of lymph node involvement, and staging of the disease are expressed according to 'The general rules for gastric cancer' which has become accepted and popularized worldwide (1). Briefly, on gross findings, the invasion of stomach cancer into the other adjacent organs is referred to as  $S_3$ . In this paper, the term  $S_3$  will be often used. Incidentally,  $S_0$ ,  $S_1$  and  $S_2$  indicate absence of serosal invasion, probably but not definite serosal invasion, and distinct serosal invasion, respectively.

## RESULTS

Among the total number of 1,137 patients who underwent laparotomy for gastric cancer,  $S_3$  cases comprised 30.3% (344 patients). The percentage of  $S_3$  cases has gradually been decreased over the years, however,  $S_0$  cases have increased (Table 1). It seems that this reflects an increased number of early gastric cancer patients, and comparatively earlier diagnosed cases of advanced cancer patients.

As shown in Table 2, most  $S_3$  cases had other critically poor prognostic factors such

as peritoneal dissemination (positive P factor), metastasis to the liver (positive H factor). These incidences were 52.9%, 17.2% and 37.8%, respectively. Extensive lymph node metastasis implies here that the third and/or fourth group lymph nodes are involved macroscopically (N<sub>3</sub>, N<sub>4</sub>).<sup>1)</sup> Eight patients (2.3%) of 344 had metastasis to both the peritoneal cavity and liver. The number of cases of gastric cancer determined as Stage IV only by S factor (namely, cases with S<sub>3</sub>:H<sub>0</sub> P<sub>0</sub> N<sub>0-2</sub>) were 92 (26.7%).

Among 344 patients who underwent laparotomy, 221 (64.2%) had curative or non-curative (palliative) resection of the stomach with or without surrounding node dissection or organ resection. Table 3 shows the location of the lesion in S<sub>3</sub> gastric cancer. In 83 patients (37.6%) of 221 S<sub>3</sub> resected cases, the main location of the lesion was in the lower third portion (A), followed by the upper third portion in 55 patients (24.9%), and in the middle third portion in 39 patients (17.6%). In 44 patients (19.9%) the tumor occupied all three regions of the stomach. The cancer extended circumferentially in 86 patients (38.9%). The lesser curvature area was the most common site (26.7%) and the anterior wall was at

**Table 1** Frequency of S<sub>3</sub> cases in gastric cancer according to the severity of serosal invasion and years (Jan. 1, 1968-Dec.31, 1983)

serosal invasion years	S <sub>0</sub>	S <sub>1</sub>	S <sub>2</sub>	S <sub>3</sub>	total
	1968-1972	86 (28.2%)	26 (8.5%)	93 (30.5%)	100 (32.8%)
1973-1977	113 (31.5%)	19 (5.3%)	113 (31.5%)	114 (31.8%)	359 (100%)
1978-1983	170 (35.9%)	32 (6.8%)	141 (29.8%)	130 (27.4%)	473 (100%)
total	369 (32.5%)	77 (6.8%)	347 (30.5%)	344 (30.3%)	1,137 (100%)

**Table 2** The incidence of positive P, H, Extensive N factor in S<sub>3</sub> gastric cancer.

		Stomach resected cases(221 cases)	Stomach non-resected cases(123 cases)	total (344 cases)
P factor	(-)	127	34	161
	(+)	94 (42.5%)	88 (71.5%)	182 (52.9%)
	ND	0	1	1
H factor	(-)	196	87	283
	(+)	25 (11.3%)	34 (27.6%)	59 (17.2%)
	ND	0	2	2
N factor	0-2	157	45	202
	3-4	64 (29.0%)	66 (53.7%)	130 (37.8%)
	ND	0	12	12

ND: not described

the nadir of frequency. Table 4 shows gross and histologic types of gastric cancer in 221 resected cases. Borrmann 3 was the most common type in S<sub>3</sub> cases, comprising 43.3%, followed by Borrmann 2 in 28.1% and Borrmann 4 in 25.3%. Early gastric cancer was seen in one patient, and an advanced cancer invaded the propria muscle layer in another patient. Both of them showed indirect cancer invasion into the pancreas via the metastatic nodes around the common hepatic artery, splenic artery and/or celiac axis. The histologic types of cancer in 221 S<sub>3</sub> resected cases were papillary adenocarcinoma in eight patients (3.6%), well differentiated adenocarcinoma in 10 (4.5%), moderately differentiated adenocarcinoma in 82 (37.1%), poorly differentiated adenocarcinoma in 94 (42.5%), and signet ring cell carcinoma in seven (3.2%). In the remaining 20 patients, mucinous adenocarcinoma was seen in 17 (7.7%), squamous cell carcinoma in two and adenosquamous cell carcinoma in one.

Table 5 shows the histologic depth of cancer invasion, being subserosal in 25 patients (11.3%) and extraserosal or positive exposure of cancer cells outside serosa (se) in 101 patients (45.7%). Ninety-three (42.1%) cases of microscopically confirmed cancer invasion into the neighboring organs were accounted for. Therefore, there was a discrepancy as to the presence of cancer infiltration between macroscopic and microscopic findings. As shown in

**Table 3** Main location of the lesion in S<sub>3</sub> gastric cancer

	A	M	C	three regions	total
Min	12	14	23	10	59( 26.7%)
Maj	17	7	3	2	29( 13.1%)
Ant	4	2	2	3	11( 5.0%)
Post	10	11	13	2	36( 16.3%)
Circ	40	5	14	17	86( 38.9%)
total	83 (37.6%)	39 (17.6%)	55 (24.9%)	44 (19.9%)	221(100.0%)

**Table 4** Gross and histologic types of gastric cancer in 221 resected cases

histologic types	pap	tub <sub>1</sub>	tub <sub>2</sub>	por	sig	muc	others	total
gross types								
Early gastric cancer			1					1( 0.5%)
Borrmann type 1	1		2	2		1		6( 2.7%)
2	3	5	26	19	2	5	2	62(28.1%)
3	4	5	45	32	2	7	1	96(43.4%)
4			8	41	3	4		56(25.3%)
total	8 (3.6%)	10 (4.5%)	82 (37.1%)	94 (42.5%)	7 (3.2%)	17 (7.7%)	3 (1.4%)	221( 100%)

Table 6, in the resected group including 221 patients, the invaded contiguous organs on gross findings were the pancreas in 109 patients (49.3%), transverse mesocolon in 91 (41.1%), transverse colon in 29 (13.1%), retroperitoneal structures in 29 (13.1%), liver in 23 (10.4%), diaphragm in 13 (5.9%) and spleen in 8 (3.6%). While in the non-resected group, although the pancreas was the most frequently affected organ, the incidences of cancer invasion to the liver and retroperitoneal tissue were higher than those in the resected group.

The relationship between involved organs and microscopical curability is also shown in Table 6. The microscopical curability was obtained with low percentages; 26.6% in the pancreas, 33.0% in the transverse mesocolon, 24.1% in the transverse colon, 17.4% in the liver, and 30.8% in the diaphragm. It should be noted, however, that these percentages do not always indicate the practical curability because many cases of S<sub>3</sub> were associated with positive P factor, H factor and/or extensive N factors that reduced the curability rates.

Out of 221 cases where gastrectomy was done, combined resection of the neighboring

**Table 5** Gross types and histologic depth of gastric cancer in 221 resected cases

depth of cancer gross types	sm	pm	ss	se	si, sei	total
Early cancer	1					1 ( 0.5%)
Borrmann						
1	1		1	3	2	6 ( 2.7%)
2			11	28	23	62 (28.1%)
3		1	12	42	41	96 (43.4%)
4			1	28	27	56 (25.3%)
total	1 (0.5%)	1 (0.5%)	25 (11.3%)	101 (45.7%)	93 (42.1%)	221 ( 100%)

**Table 6** Involved organs on gross findings and microscopic curability rates

involved organs	stomach resected cases (n=221)			stomach nonresected cases (n=123)	total (n=344)
	curative	noncurative	total		
pancreas	29	80	109 (49.3%)	78 (63.4%)	187 (54.4%)
T. mesocolon	30	61	91 (41.1%)	9 ( 7.3%)	100 (29.1%)
T. colon	7	22	29 (13.1%)	4 ( 3.3%)	33 ( 9.6%)
retroperitoneum	8	21	29 (13.1%)	22 (17.9%)	51 (14.8%)
liver	4	19	23 (10.4%)	27 (22.0%)	50 (14.5%)
diaphragm	3	7	13 ( 5.9%)	5 ( 4.1%)	18 ( 5.2%)
spleen	3	5	8 ( 3.6%)	10 ( 8.1%)	18 ( 5.2%)
gallbladder	1	2	3 ( 1.4%)	1 ( 0.8%)	4 ( 1.2%)
small intestine	1	2	3 ( 1.4%)	1 ( 0.8%)	4 ( 1.2%)
abdominal wall	0	2	2 ( 0.9%)	0	2 ( 0.6%)
kidney	0	0	0	1 ( 0.8%)	1 ( 0.3%)
others	1	4	5 ( 4.1%)	4 ( 3.3%)	9 ( 7.3%)

**Table 7** Contiguous organs resected in combination with gastrectomy

resected organs	No. of cases (%)
spleen	48 (21.7)
spleen & pancreas	37 (16.7)
pancreas	9 (4.5)
liver	12 (5.4)
T. mesocolon	21 (9.5)
T. colon	18 (8.1)
gallbladder	1 (0.5)
others	9 (4.5)
no combined resection	82 (37.2)

T. mesocolon: transverse mesocolon

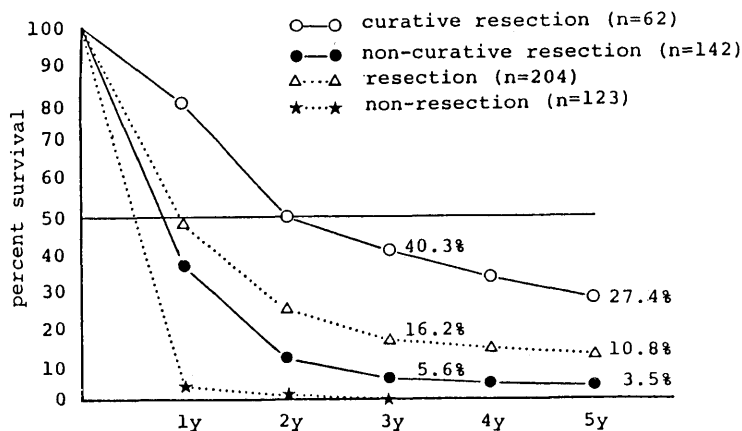
T. colon: transverse colon

organs was performed in 139 cases (62.9%). Resected contiguous organs included the spleen in 48 patients (21.7%), pancreas in 9 (4.5%), both pancreas and spleen in 44 (19.9%), transverse mesocolon in 22 (10.0%), transverse colon in 20 (9.0%) and liver in 12 (5.4%).

Microscopical curative operations could be performed in 67 patients out of 221 who underwent gastrectomy indicating that the curability rate was raised to 30.3% among the resected patients. Operative procedures included distal gastrectomy in 119 cases (53.8%) proximal gastrectomy in 13 cases (5.9%), and total gastrectomy in 89 cases (40.3%). Left-sided thoracotomy and midsternotomy were added to laparotomy in 18 patients and 4 patients, respectively.

The overall 30-day mortality rate was 4.9% (26 patients).

Figure 1 shows crude survival rates. The five-year survival rate of gastrectomy with or without combined resection was 10.8%; 27.4% in curative resection and 3.5% in

**Fig. 1.** Survival rates of  $S_3$  operation cases

non-curative resection. In contrast to these results, none of the cases survived 3 years postoperatively in the non-resected group; 80.5% died within 5 months, and 95.9% within one year.

## DISCUSSION

It is widely held that the serosal factor (S factor) is one of the most important factors that affects the prognosis in gastric cancer patients. However, many authors have pointed out the presence of a discrepancy between intraoperative macroscopic judgement of the severity of serosal invasion and the histologic diagnosis of the depth of cancer infiltration.<sup>2)3)4)5)</sup> A substantial number of cases exist where macroscopic invasion into the contiguous organs judged to be positive was diagnosed histologically to be only fibrous adhesion without cancer infiltration. The accuracy of macroscopic judgement of cancer infiltration varies in Japanese literature, ranging from approximately 28% to 65%.<sup>2)3)4)5)</sup> It is plausible that, among cases with macroscopical positive serosal exposure, there are some cases where cancer invasion is limited to the subserosa but may be overdiagnosed, or where there is cancer invasion into the other organs but could be underdiagnosed. The present study showed that macroscopic invasion S<sub>3</sub> was compatible with histologic invasion only in 42% of resected cases.

There is a wide variety in resectability rates in S<sub>3</sub> gastric cancer reported in Japan, varying from about 40% to 85%<sup>6)</sup>. In our present study, the resectability rate was 64% (221 patients). Out of these resected cases, 62.9% (139 patients) underwent combined resection of adjacent organs. This figure seems comparatively high in view of high incidences of other positive factors such as P factor in 52%, H factor in 17%, and extensive N factors in 38%.

Can combined resection make a significant contribution to improve the survival rate? Combine resection, including several different kinds of procedures, has become popularized widely in Japan in recent years.<sup>7)8)9)</sup> TABUCHI *et al.*<sup>4)</sup> emphasized significances in combined resection based on the following two points of view. One is that five-year survival rates in combined resection and non-combined resection showed 19% and 0%, respectively, and there was no difference in the mortality rate between the two groups. The second point is that it is often hard to determine an accurate depth of cancer invasion from gross findings. KOYAMA *et al.*<sup>5)</sup> described an implication of combined resection for patients who could undergo such a curative operation, considering the five year survival rate of 34.2% compared to no survivors in non-curative combined resection. TAKAGI *et al.*<sup>7)</sup> justified pancreatoduodenectomy as a pertinent operation for selected patients with gastric cancer which invades or adheres to the pancreas, coexists with extensive lymph node metastases around the head of the pancreas, or is associated with marked invasion into the duodenum.



They showed a 5.6% five-year survival rate.

For our patients with S<sub>3</sub> gastric cancer who underwent gastric resection, the five-year survival rate was 10.8%. These are results comparable to those previously reported.<sup>6)</sup> To our knowledge, KOYAMA *et al.*<sup>5)</sup> have reported the best survival rate, 19%. In the present study, the five year survival rates in curative resection and in non-curative resection were 27.4% and 3.5%, respectively, these results being also comparable to those shown by others.<sup>6)</sup>

The results shown in previous studies and that obtained from our present study support that aggressive surgery, if conditions are acceptable, is indicated for selected cases when curability can be expected by means of combined resection. It should be emphasized that practically no five-year survivors existed within the non-resected group.

However, since the five-year survival rate is still low even in curative resection, there seems to be a limit to the improvement of surgical results. More active multidisciplinary treatment including chemotherapy, immunotherapy, thermotherapy and radiotherapy must be taken into consideration to ameliorate the surgical outcome of advanced gastric cancer.

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