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# Combined Gastrectomy with Adjacent Organs in T4 Gastric Cancer: Therapeutic Results and Indication

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The postoperative morbidity, mortality and survival of 244 T4 gastric cancer patients were examined to assess the therapeutic results and to clarify the indication for combined gastrectomy with adjacent (T4) organs. A total of 190 combined and 54 simple gastrectomies were performed during the 25-year period between 1969 and 1994. Fourteen (7.4%) and 7 (13.0%) patients died of the complications after combined and simple gastrectomies respectively. No statistical significant difference was found in the mortality rates between the gastrectomies. The histological examination of 190 resected specimens by the combined gastrectomy with T4 organs revealed that gastric resections with conclusive curability A, B and C were performed in 33 (17.4%), 84 (44.2%) and 73 (38.4%) cases respectively. Significant differences ($P < 0.01$) among 3 survival curves of the patients with curability A, B and C were found, and the 5-year survival rates were 65.5%, 35.4% and 9.2% respectively. The survival curve of 176 patients with combined gastrectomy was significantly ($P < 0.01$) higher than that of 47 patients with simple gastrectomy, and the 5-year survival rates were 31.3% and 4.3%. However, the survival curve and the 5-year survival rate of the patients with simple gastrectomy were not statistically different from those of the patients with curability C. These results suggest that combined gastrectomy with T4 organs in T4 gastric cancer may be indicated for the patients with surgical curability B, but not surgical curability C.

Key Words: T4 gastric carcinoma, Combined gastrectomy, Survival, Postoperative morbidity.

## Introduction

Accurate diagnosis of the invasive depth of the gastric wall and adjacent (T4) organs is essential for the determination of therapeutic design in the gastric cancer patients. It has been reported that the diagnosis becomes considerably accurate by the recently available diagnostic methods such as computed tomography (CT), magnetic resonance imaging (MRI) and endoscopic ultrasonography (EUS).[1-9] However, the discrepancy is often found between the pre- or intra-operative and histological diagnoses.[1-11]

T4 gastric cancer patients have been often found, even though the propor-

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tion of early gastric cancer in Japan increases for the advances in diagnostic methods and mass screening programs. Some physicians, particularly in most Western countries, still consider T4 gastric cancer as a sign of incurable disease.[12-15] However, many surgical oncologists have often experienced that curative and relative non-curative resections[16] which are almost same as conclusive curability A and B[17] have been able to be performed in the patients, who are pre- and intraoperatively estimated to be T4 gastric cancer.[18-21] As a result, some of these patients have a long disease-free period and are cured of the disease.

In this study, the postoperative morbidity, mortality and survival of T4 gastric cancer patients were retrospectively examined, to assess the therapeutic results and to clarify the indication for combined gastrectomy with T4 organs. Furthermore, the specimens resected by combined gastrectomy with T4 organs were histologically examined, to study the accuracy of the pre- and intraoperative diagnoses of T4 gastric cancer.

## Materials and Methods

A total of 244 T4 gastric cancer patients who underwent gastrectomy during the 25-year period between 1969 and 1994 at the Department of Surgery, Kobe University Hospital (Kobe, Japan), were included in this study. These patients corresponded to 11.5% (244/2116) of the patients treated with gastrectomy. Of these patients, combined gastrectomy with T4 organs and simple gastrectomy were carried out in 190 and 54 patients respectively. Simple gastrectomy was performed due to the apparent residual tumors mainly consisting of n3～4, P2～3 or H1～3.

The resected specimens were fixed in 10% neutral formalin solution and then embedded in paraffin. The histological examination was routinely carried out using hematoxylin-eosin stain and elastica van Gieson's stain. The macroscopical (surgical) and histological (conclusive) findings were described according to the "Japanese research classification of gastric carcinoma (first English edition)"[17] authorized by the Japanese Research Society for Gastric Cancer. In this classification, capital and small letters imply macroscopical and histological findings. The cases with tumor invasion into the serosa, the proper muscle or subserosal layers and into the mucosa or submucosal layer were determined to be t3, t2 and t1 respectively according to the classification,[17] even though the lesions accompanied by severe fibrous adhesion to the adjacent organs. The cases with histological tumor invasion into the adjacent organs and/or structures were estimated to be t4.[17] The surgical and conclusive curability A, B and C were also estimated according to the classification. In brief, the cases with P0, H0, M0, T1～2 (t1～2), N0 (n0) > D1 or N1 (n1) > D2 and without tumor invasion within 10 mm from the oral and distal gastrectomy margins were evaluated to be curability A (no residual tumors with high probability of cure). The cases with definite residual tumors were determined as curability C. The cases without residual tumors but not valuable as "curability A" were evaluated to be curability B.[17]

The data were analyzed by Student's *t* test and either the chi-square or Fisher's exact probability calculation

tests. The survival curves and rates of the patients with curability A, B and C after combined gastrectomy and with simple gastrectomy were estimated by the Kaplan-Meier method, and the statistical difference of the survival curves was determined by the generalized Wilcoxon test. *P* values of less than 0.05 were estimated to be significant.

## Results

### Postoperative Morbidity and Mortality

The postoperative complications occurred in 42 (22.1%) and 13 (24.1%) patients after combined and simple gastrectomies respectively, as shown in Table 1. Of these complications, broncho-pneumonia was oftenest and then peritonitis or sepsis primarily due to the anastomotic failure and leakage of the pancreatic juice after combined and also simple gastrectomies. Intra-abdominal bleeding, heart failure and intracranial bleeding were found in 5, 3 and 2 patients after combined gastrectomy and in 2, 1 and 1 patients after simple gastrectomy. The morbidity rates were not significantly different between the gastrectomies (Table 1).

Fourteen (14/190, 7.4%) and 7 (7/54, 13.0%) patients died of the postoperative complications within 3 months after combined and simple gastrectomies respectively. No significant difference was found between the mortality rates as well as the morbidity rates (Table 1). The main causes of postoperative death were peritonitis or sepsis and followed by bronchopneumonia after combined gastrectomy. Bronchopneumonia was the main cause of postoperative death after simple gastrectomy (Table 1). One (3.0%), 5 (5.0%) and 8 (11.1%) patients with curability A, B and C died of the postoperative complications after combined gastrectomy respectively. No significant difference was found among the mortality rates.

### Histological Depth of Tumor Invasion

A total of 190 specimens resected by combined gastrectomy were examined histologically, according to the criteria described in Materials and Methods. The examination revealed that the lesions with t1 ~ 2, t3 and t4 were 21 (11.1%), 82 (43.2%) and 87 (45.8%)

**Table 1.** Postoperative morbidity and mortality of 190 gastric cancer patients with combined gastrectomy and 54 gastric cancer patients with simple gastrectomy.

| Gastrectomy | Postoperative morbidity and mortality | | | | | Total† |
|---|---|---|---|---|---|---|
| | Peritonitis or sepsis | Pneumonia | Abdominal bleeding | Heart failure | Intracranial bleeding | |
| Combined | 15, 7.9% (7, 3.7%) | 17, 8.9% (4, 2.1%) | 5, 2.6% (1, 0.5%) | 3, 1.6% (1, 0.5%) | 2, 1.1% (1, 0.5%) | 42, 22.1% (14, 7.4%) |
| Simple | 3, 5.6% (1, 1.9%) | 6,11.1% (3, 5.6%) | 2, 3.7% (1, 1.9%) | 1, 1.9% (1, 1.9%) | 1, 1.9% (1, 1.9%) | 13, 24.1% ( 7, 13.0%) |

Parenthesis indicates the number of mortality cases.
† No significant difference was found in the morbidity and mortality rates between the patients with combined and simple gastrectomies.

cases respectively. Accordingly, true tumor invasion into the adjacent organs was found to be less than half of the cases, even though they were diagnosed to be T4 cancer pre- and intra-operatively. The examination disclosed also that gastric resections with curability A, B and C were performed in 33 (17.4%), 84 (44.2%) and 73 (38.4%) of the patients respectively.

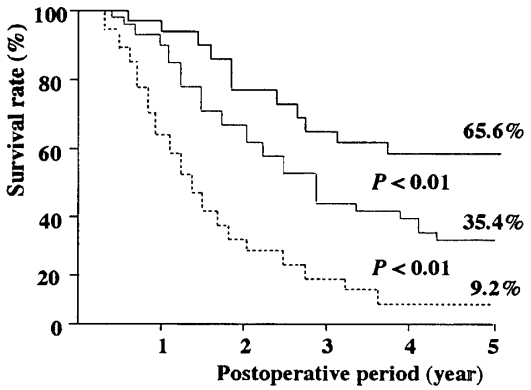



**Figure 1.** Survival curves and the 5-year survival rates of gastric cancer patients with conclusive curability A, B and C after combined gastrectomy with T4 organs Thick and thin solid lines and dotted line indicate the survival curves of 32, 79 and 65 patients with curability A, B and C except 1, 5 and 8 patients died of the postoperative complications respectively.

**Survival Curves and the 5-year Survival Rates**

Survival curves and the 5-year survival rates after combined gastrectomy were examined except 14 patients died of the postoperative complications. Significant differences were found among 3 survival curves of the patients with conclusive curability A, B and C. The 5-year survival rates were 65.6%, 35.4% and 9.2% respectively (Fig. 1). As shown in Table 2, P1, n2 = D2 and/or resection of H1 were the main causes of conclusive curability B. Of these variables, P1 was the commonest cause and was found in 44 (52.4%) patients, and then n2 = D2 was shown in 35 (41.7%) patients. The resection of H1 was the cause of conclusive curability B only in 3 (3.6%) patients. As for the conclusive curability C, invasion into the major arteries and/or veins often accompanied by invasion into the retroperitoneum was found in 37 (50.6 %) patients, and n3 > D2 or n4 > D3 were shown in 36 (49.3%) patients (Table 2).

A significant difference ($P < 0.01$) was found between the survival curves of the patients with combined and sim-

**Table 2.** Causal variables of conclusive curability B and C in 157 T4 gastric cancer patients with combined gastrectomy.

| Curability | Causal variable | | | | | Total |
|---|---|---|---|---|---|---|
| | P1 | n2 = D2 | H1† | n3 > D2 or n4 > D2~3 | others‡ | |
| B | 44, 52.4% | 35, 41.7% | 3, 3.6% | | | 84, 100% |
| C | | | | 36, 49.3% | 37, 50.6% | 73, 100% |

† Resection of H1.

‡ Invasion into the major arteries and/or veins often accompanied by the invasion into the retroperitoneum.

ple gastrectomies, and the 5-year survival rates were 31.3% and 4.3% respectively. However, the survival curve and 5-year survival rate of the patients with simple gastrectomy were not significantly different from those of the patients with conclusive curability C (Fig. 2). Regarding the coexistent variables with T4 organs in the simple gastrectomy, P2～3 was the commonest variable and found in 18 (34.0%) patients, and then double or triple variables consisting of n3～4, P2～3 and/or H1～3 were confirmed in 17 (31.5%) patients. In a small number of the cases, simple gastrectomy was performed due to n3～4 or H1～3 (Table 3).

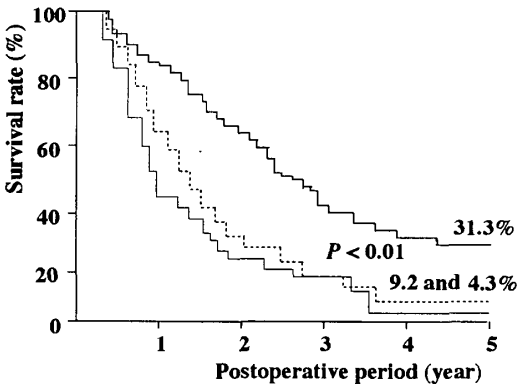



**Figure 2.** Survival curves and the 5-year survival rates of gastric cancer patients with combined and simple gastrectomies Thick and thin lines and dotted line indicate the survival curves of 176, 47 and 65 patients with combined gastrectomy, simple gastrectomy and conclusive curability C respectively Fourteen, 7 and 8 patients died of the postoperative complications are excluded in the curves respectively.

## Discussion

The proportion of early gastric cancer in Japan increases gradually and has amounted approximately to 50～60% of gastric cancer in the 1990's,[15,24] although the proportion has been reported to be less than 10% in Europe and the United States.[12-15,18] However, advanced gastric cancer including T4 cancer has been often found also in Japan. In this study, T4 gastric cancer corresponded to 11.5% of all the patients who underwent gastrectomy during the 25-year period. By the way, the combined gastrectomy of T4 organs in T4 gastric cancer patients seems to be performed in many Japanese medical facilities, and the aggressive combined gastrectomy with T4 organs may be of benefit to the patients with these Stages (stages) III and IVa.[17] However, the "Japanese research classification of gastric carcinoma" has been recently revised,[22] and T4 cancer with P1 and/or

**Table 3.** Coexistent variables with T4 organs in 54 gastric cancer patients with simple gastrectomy.

| Variable | Main T4 organ | | | | Total |
|---|---|---|---|---|---|
| | Diaphragm | Liver | Pancreas | Colon | |
| n3~4 | 1, 1.9% | 4, 7.4% | 3, 5.6% | 1, 12.9% | 9, 16.1% |
| P2~3 | 2, 3.7% | 1, 1.9% | 12, 22.2% | 3, 5.6% | 18, 34.0% |
| H1~3 | 2, 3.7% | | 6, 11.1% | 2, 3.7% | 10, 18.9% |
| n3~4, P2~3 and/or H1~3 | 3, 5.6% | 2, 3.7% | 7,13.0% | 5, 9.3% | 17, 31.5% |

H1 is inclusively classified as Stage (stage) IV cancer,[23] even though surgical curability B can be performed and the survival of the patients with the curability B will be different from that of the patients with the curability C. Regarding the diagnosis of tumor invasive depth of the gastric wall and the adjacent organs, it has been reported that the diagnosis becomes considerably accurate by the recently available diagnostic methods.[1-9] However, the discrepancy is often found between the pre- or intra-operative and histological diagnoses.[1-11] To clarify the aforementioned controversial phenomena, this study was carried out.

The histological examination of 190 T4 gastric tumor lesions resected by combined gastrectomy with T4 organs revealed that the cases with t1 ~ 2, t3 and t4 were 11.1%, 43.2% and 45.8% of the patients respectively. The examination disclosed also that gastric resections with curability A, B and C were performed in 17.4%, 44.2% and 38.4% of the patients respectively. Accordingly, true tumor invasion (t4) into the adjacent organs was found to be less than half of the cases in this study, as already reported by some investigators.[9-11] The result suggests that gastric resections with conclusive curability A and B may be performed by the combined gastrectomy in about 50 ~ 60% of the T4 gastric cancer patients.[9-11]

In this study, the postoperative complications occurred in 22.1% and 24.1% of patients after combined and simple gastrectomies respectively. The morbidity rates were not significantly different from each other. The postoperative mortality rates were 7.4% and 13.0% after combined and simple gastrectomies and 3.0%, 6.0% and 11.0% after gastric resections with conclusive curability A, B and C respectively. No significant difference was found in the mortality and morbidity rates between the gastrectomies and among the gastric resections. The rates are not so different from the recently reported results[18,25,28], although the higher[26,27,29] and lower rates[19] than the present results have been also reported. Therefore, it could not be estimated on the basis of the morbidity and mortality rates whether or not combined gastrectomy is performed in T4 gastric cancer patients.

A significant difference was found between the survival curves of the patients with combined and simple gastrectomies in this study, and the 5-year survival rates were 31.3% and 4.3% respectively. The survival curves of the patients with conclusive curability A, B and C were significantly different from each another, and the 5-year survival rates were 65.6%, 35.4% and 9.2% respectively. The survival curve and the 5-year survival rate (4.3%) of the patients with simple gastrectomy meaning palliative resection were not significantly different from those of the patients with conclusive curability C. Since the survival curves and the 5-year survival rates analyzed by the conclusive curability have not yet been found through our review of the literature, it is difficult to compare with the already published results. However, the 5-year survival rate (31.3%) of the whole patients with combined gastrectomy including curability A, B and C was not so different from the published data.[18-21,24,25] These results suggest that combined gastrectomy with T4 organs is indicated for the patients in whom sur-

gical curability B can be carried out[17], because a significant survival benefit has been achieved for the gastrectomy.[18-21,24,25] Although the gastrectomy with definite residual tumors may be necessary for the alleviation or elimination of suffering symptoms, the combined gastrectomy will not be indicated for the patients with surgical curability C accompanied by residual tumors.[17] From this viewpoint, the first English edition of "Japanese research classification of gastric carcinoma";[17] in which Stage (stage) IV is subdivided into 2 groups, IVa and IVb, may be reasonable rather than the second one.[22]

In conclusion, the combined gastrectomy with adjacent organs in T4 gastric cancer patients may be indicated for the patients with surgical curability B, but not for the patients with surgical curability C, based on the results obtained by the retrospective study of 244 T4 gastric cancer patients. T4 gastric cancer should not be considered to be unresectable or incurable disease, because the cancer patients with Stages III and IVa[17] benefit from the combined gastrectomy.

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