

Surgery and Clinicopathological Features of Gastric Adenocarcinoma Involving the Esophago-Gastric Junction

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Summary: To clarify the optimal operative procedure for gastric adenocarcinoma involving the esophago-gastric junction (EGJ), we investigated 49 cases with an upper gastric cancer invading the esophagus who underwent surgical treatment in our department during the period from 1991 to 2000. According to Siewert's classification, there were 21 cases with a type II tumor, and 28 cases with a type III tumor. Twenty-five cases underwent surgery through an abdominal approach only. The remaining 24 cases were operated on via a left thoraco-abdominal approach. Eight (33%) of 24 cases who underwent extended lymphadenectomy through a left thoraco-abdominal approach had lower mediastinal lymph node metastasis. Metastasis was observed in cases with cancer invasion more than 2 cm from the EGJ. There were 6 cases with a T1 tumor, 6 with a T2 tumor, 27 with a T3 tumor, and 10 with a T4 tumor. Incidences of lymph node metastasis were 0% for T1, 67% for T2, 81% for T3, and 80% for T4. Proximal gastrectomy was performed in 6 cases at the early stage and in 10 cases at the advanced stage with distant metastasis (M1). Total gastrectomy was done in 33 cases at the advanced stage, and 3 of these 33 cases had metastasis to the parapyloric lymph nodes. We performed combined resection of the body and tail of the pancreas and the spleen in 7 cases. One of these 7 cases had direct invasion to the pancreas and 6 cases had remarkable metastasis to the lymph nodes along the splenic artery. Splenectomy preserving the pancreas was done in 24 cases. The incidences of metastasis of the lymph nodes along the splenic artery and the splenic hilum were 25% and 17%, respectively. We performed partial resection of the diaphragm surrounding the esophageal hiatus in 15 cases through a left thoraco-abdominal approach. Six cases had metastasis to the diaphragm and nine cases had direct invasion to the diaphragm.

Tumors were stage I in 8 cases, II in 5 cases, III in 13 cases and IV in 23 cases, and the curability was categorized as A in 8 cases, B in 20 and C in 21. The overall 5-year-survival rate was 25%, and the rates according to cancer stage were 86% for stage I, 40% for stage II, 21% for stage III and 0% for stage IV. The 5-year survival rates of cases at stage II and III were 33% for cases using the left thoraco-abdominal approach and 28% for cases with the abdominal approach. Based on these results, we recommend distal esophagectomy with total gastrectomy, and occasional combined resection of the spleen and the diaphragm through a left thoraco-abdominal approach for advanced gastric adenocarcinoma involving the EGJ.

Key words gastric adenocarcinoma, esophago-gastric junction, thoracotomy, esophageal invasion, cardia

INTRODUCTION

The operability and resectability rates for gastric

cancer have increased in the past decade. The prognosis for gastric cancer has also improved. However, most cases of gastric adenocarcinoma

involving the esophago-gastric junction (EGJ) are at an advanced stage when they are diagnosed. This fact requires not only improved diagnostic technique, but also improved surgical treatment. Presently there are several questions regarding surgical treatment for gastric adenocarcinomas involving the EGJ that remain controversial.

The first controversy concerns the route of the operation, i.e. whether thoracotomy is required for the dissection of the mediastinal lymph nodes and combined resection of the diaphragm.

The second concerns the extent of resection, i.e. total gastrectomy versus proximal gastrectomy, or total esophagectomy versus lower esophagectomy.

The third concerns combined resection of the body and tail of the pancreas and the spleen.

In the present report, 49 gastric adenocarcinomas involving the EGJ were reviewed with particular attention to the surgical procedure, postoperative complications and prognosis.

SUBJECTS AND METHODS

During the 10-year period from 1991 to 2000 a total of 1270 cases of gastric adenocarcinoma were resected in our department. Of these, 49 (3.9%) were gastric adenocarcinoma involving the EGJ. According to Siewert's classification [1], there were 21 cases with a type II tumor, and 28 cases with a type III tumor (Fig.1). There were 34 men and 15 women. The mean age was 66 years old (range, 41-83 years). The macroscopic types and histological

types are shown in Table 1. The most frequent macroscopic and histological type were the type-3 and poorly differentiated adenocarcinoma, respectively. There were 6 T1 tumors, 6 T2 tumors, 27 T3 tumors, and 10 T4 tumors. Of the latter, 9 infiltrated the diaphragm and one infiltrated the pancreas and liver. Mean tumor length was 79 mm and the mean length of esophageal invasion was 25 mm. Thirty-four cases (69%) had lymph node metastasis. According to the N factors, N0 was found in 15 cases, N1 in 8, N2 in 14, N3 in 9, and M1 (Virchow metastasis) in 3. Seven cases had liver metastasis and 3 cases had peritoneal dissemination. The curability was classified as A in 8 cases, B in 20 cases and C in 21 cases.

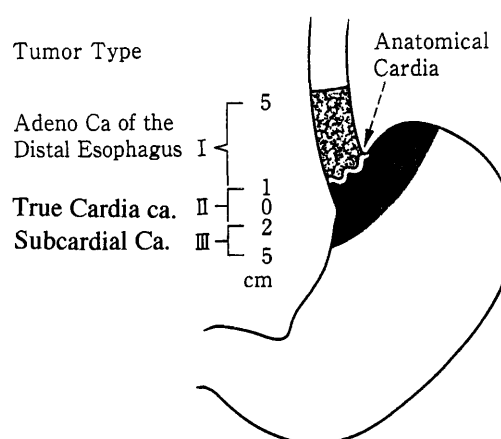


Fig. 1. Siewert's classification of adenocarcinoma at the esophago-gastric junction.

TABLE 1.
Macroscopic types and histological types
(Classification by Japanese Research Society)

Macroscopic type	Cases	Histological type	Cases
Type-0 (superficial, flat tumor)	6	papillary adenocarcinoma	4
Type-1 (polypoid tumor)	2	well differentiated adenocarcinoma	15
Type-2 (ulcerated carcinoma with demarcated and raised tumor)	14	moderately differentiated adenocarcinoma	9
Type-3 (ulcerated carcinoma without definitive limits)	26	poorly differentiated adenocarcinoma (solid type)	8
Type-5 (un-classifiable carcinoma)	1	poorly differentiated adenocarcinoma (non-solid type)	12
		adenosquamous carcinoma	1

Based on the clinicopathological features of these tumors, we discussed the most reasonable operative procedure for gastric adenocarcinoma involving the EGJ. Clinicopathological factors were classified in accordance with the Japanese Classification of Gastric Carcinoma [2].

Survival curves for patients were plotted using the Kaplan-Meier method, and the differences between the survival curves were assessed using the log-rank test.

RESULTS

Surgical approach

Twenty-five cases were resected through an abdominal approach only. The remaining 24 cases were resected through a left thoraco-abdominal approach. When invasion to the esophagus was 2 cm or more, thoracotomy was done in curative cases. Five of 24 cases who underwent resection of the tumor through the left thoraco-abdominal approach had cancer at the proximal margin of the resected specimen. In two of these cases there was intramural

metastasis to the esophagus (Fig. 2) and in the other three cases there were distant metastasis (M1). Eight (33%) of 24 cases who underwent extended lymphadenectomy through a left thoraco-abdominal approach had metastasis in the lower mediastinal lymph nodes. Of these, 7 cases had metastasis to the para-esophageal lymph nodes in the lower thorax, 4 had metastasis to the supra-diaphragmatic lymph nodes and 2 had metastasis to the posterior mediastinal lymph nodes (Fig. 3). One patient with metastasis to the para-esophageal lymph nodes in the lower thorax survived (has survived??) for more than 5 years. The relationship between the positive rates of lower mediastinal lymph node metastasis and the extent of esophageal invasion of the tumor is shown in Table 2. Metastasis was observed in cases with esophageal invasion more than 2 cm from the EGJ, and increased in proportion to the length of esophageal invasion.

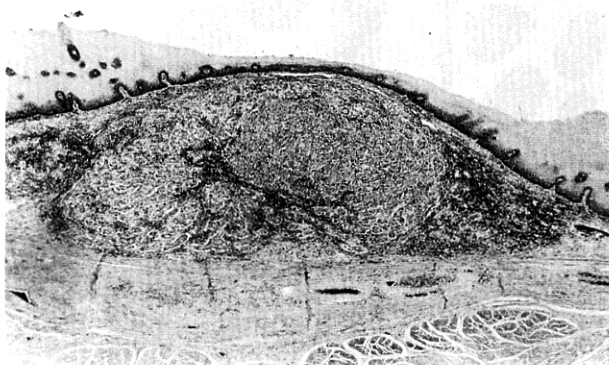


Fig. 2. Intramural metastasis to the distal esophagus. magnification, 200X, hematoxylin and eosin stain.

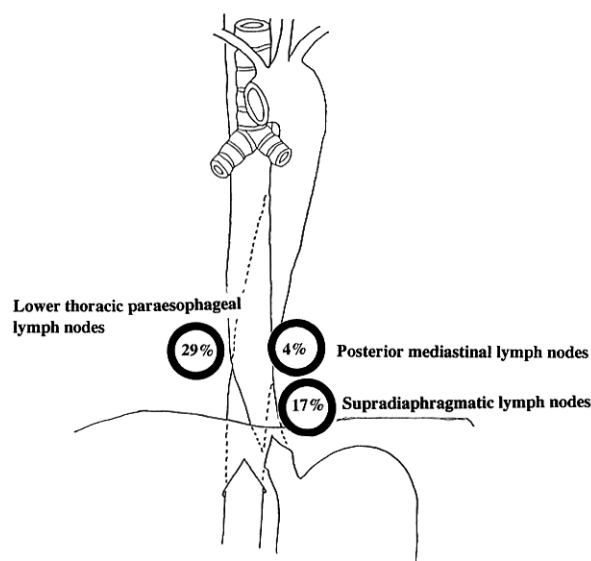


Fig. 3. Metastatic rates in the lower mediastinal lymph nodes.

TABLE 2.
Relationship between mediastinal lymph node metastasis and the extent of esophageal invasion

	Extent of esophageal invasion			
	-1.9 cm n=25	2.0-2.9 cm n=12	3.0-3.9 cm n=9	4.0 cm- n=3
Metastasis-Positive rate	0%	8%	44%	100%

Extent of resection

We performed total gastrectomy in 33 cases and proximal gastrectomy in 16 cases. Proximal gastrectomy was done in 6 cases with early cancer and in 10 cases of advanced cancer with distant metastasis (M1). Incidence of lymph node metastasis was 0% in T1, 67% in T2, 81% in T3, and 80% in T4. Peri-gastric lymph node metastasis was frequently observed in the right paracardial lymph nodes (61%), the lymph nodes along the lesser curvature (55%), the left paracardial node (52%), those along the left gastric artery (42%), and those around the celiac artery (27%) (Fig. 4). Three of 33 cases who underwent total gastrectomy had metastasis to the infra-pyloric lymph nodes.

Combined resection

We performed combined resection of the body and tail of the pancreas and the spleen in 7 cases. In one case the tumor had directly invaded the pancreas and in 6 cases, remarkable metastasis to lymph nodes along the splenic artery was observed. Splenectomy preserving the pancreas was done in 24 cases without macroscopically remarkable metastasis to lymph

nodes along the splenic artery. The incidence of metastasis to lymph nodes along the splenic artery and the splenic hilum was 25% and 17%, respectively. Metastasis in those lymph nodes was found only in T3 or T4 cases. We performed partial resection of the diaphragm surrounding the esophageal hiatus during the left thoraco-abdominal approach in 6 cases with metastasis to the diaphragm and in 9 cases with direct invasion to the diaphragm. Although in those six cases metastasis to the diaphragm was not observed macroscopically, histologic metastasis was found, as shown in Fig. 5. In all cases without lymph node metastasis, there was no metastasis to the diaphragm.

Postoperative complications and mortality rates

Major complications occurred in 11 patients (22%). These were anastomotic leakage in 3 cases, abdominal abscess in 3 cases, pneumonia in 3 cases, and pancreatic fistula in 2 cases who underwent combined resection of the pancreas. The relationship between surgical approaches and postoperative complications is shown in Table 3. Two patients (4%) died during the hospitalization. One case who was operated on through a left thoraco-abdominal

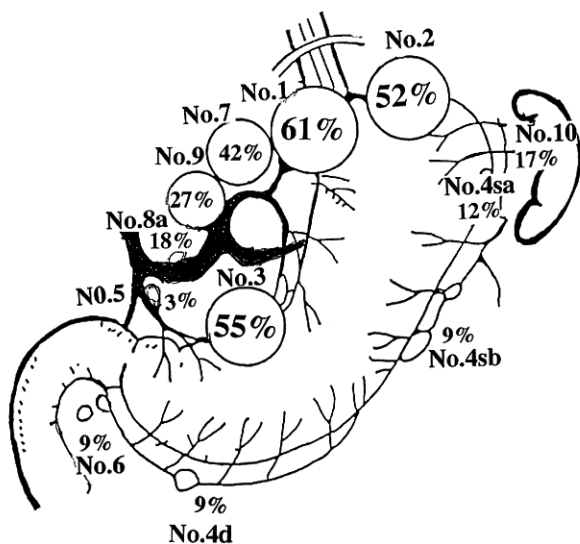


Fig. 4. Metastatic rates in the peri-gastric lymph nodes.

No. 1: Right paracardial LN, No. 2: Left paracardial LN, No. 3: LN along the lesser curvature, No. 4sa: LN along the short gastric vessels, No. 4sb: LN along the left gastroepiploic vessels, No. 4d: LN along the right gastroepiploic vessels, No. 5: Suprapyloric LN, No. 6: Infrapyloric LN, No. 7: LN along the left gastric artery, No. 8a: LN along the common hepatic artery, No. 9: LN along the celiac artery LN; lymph nodes

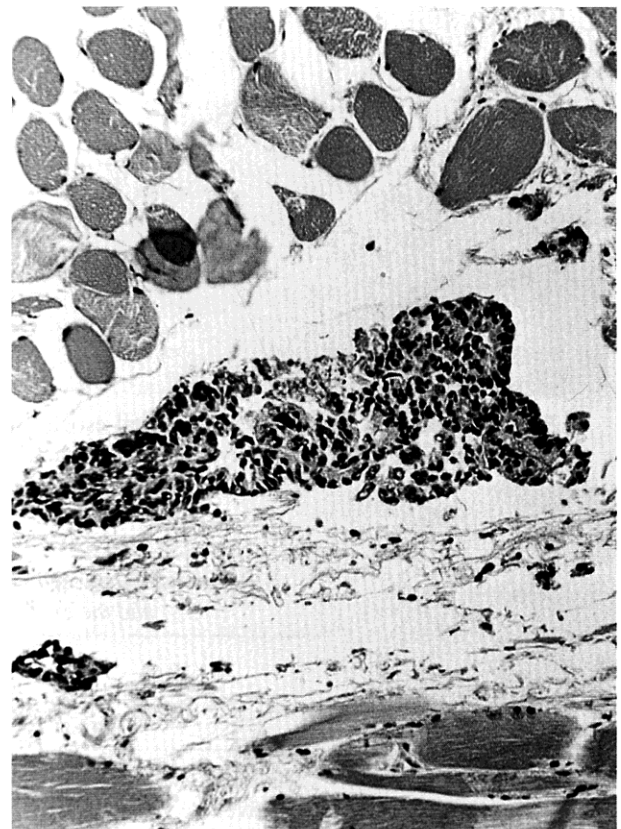


Fig. 5. Microscopic metastasis to the diaphragm.

approach died of anastomotic leakage and another who was operated on through an abdominal approach died of acute myocardial infarction.

Stage and prognosis

Tumor staging showed Type I A in 6 cases, I B in 2 cases, II in 5 cases, III A in 6 cases, III B in 6 cases and IV in 23 cases. The overall 5-year-survival rate was 25% for all the 49 cases, and those rates according to the cancer stage were 86% for Stage I (I A+I

B), 40% for Stage II, 21% for Stage III (III A+III B) and 0% for Stage IV (Fig. 6). The survival of curative cases was significantly better than that of palliative cases ($p < 0.01$) (Fig. 7). The relationship between surgical approaches and stages was shown in Table 4. The 5-year survival rates in cases at stage II and III were 33% for those receiving the left thoraco-abdominal approach, and 28% for those who received the abdominal approach (Fig. 8).

TABLE 3.
Relationship between the incidence of complications and the surgical approach

Complications	Approach	
	Thoraco-abdominal (n=24)	Abdominal (n=25)
Anastomotic leakage (esophago-jejunostomy)	2 (8%)	1 (4%)
Abscess in the abdominal cavity	2 (8%)	1 (4%)
Pneumonia	2 (8%)	1 (4%)
Fistula of pancreas	2 (8%)	0

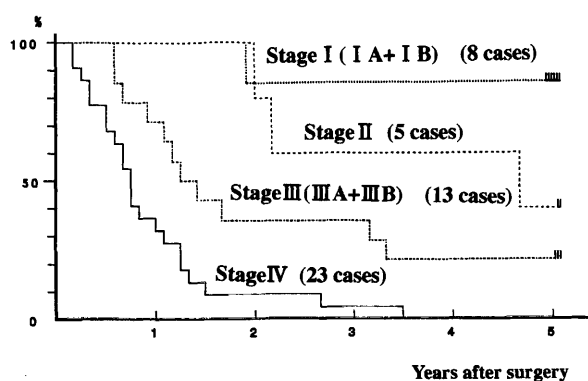


Fig. 6. Survival curves according to the tumor stage.

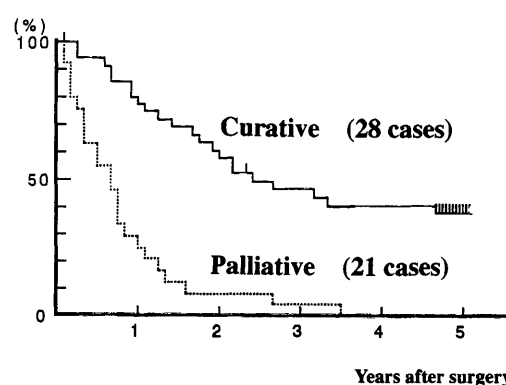


Fig. 7. Survival curves according to curability.

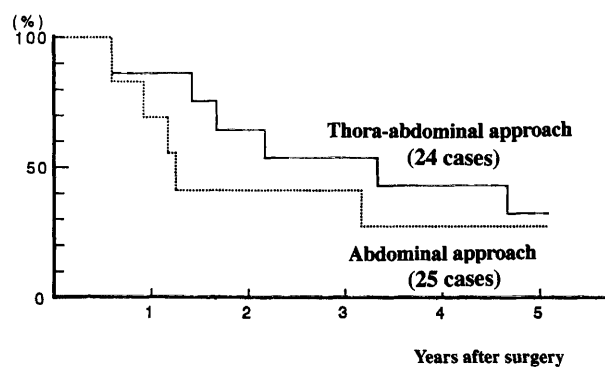


Fig. 8. Survival curves of patients at Stage II and III according to surgical approach.

TABLE 4.
Relationship between Stages and surgical approach

Stage	Approach	
	Thoraco-abdominal (n=24)	Abdominal (n=25)
I A	0 cases	6 cases
I B	0 cases	2 cases
II	4 cases	1 cases
III A	4 cases	2 cases
III B	2 cases	4 cases
IV	14 cases	10 cases

DISCUSSION

Tumor location is described by the Classification of the Japanese Research Association for Gastric Cancer (1999) [2] as U (upper third of the stomach), M (middle stomach), L (lower stomach), D (duodenum) and E (esophagus). The location of an upper gastric cancer invading the distal esophagus is described as UE or EU. The definition of the cardia commonly employed in Japan is the area within 2 cm above and below the EGJ [4] and tumors whose center is situated in this area are considered to be cancer of the cardia; such cancers are distinguished from upper gastric cancers. When this definition is employed, a few squamous cell carcinomas of esophageal origin are included in the category, but the majority are adenocarcinomas of gastric origin. On the other hand, in 1987, Siewert et al. [1] reported that adenocarcinomas in the E-G junction were divided into three types; 1) type I: Adenocarcinoma of the distal esophagus (Barrett's adenocarcinoma), 2) type II: Adenocarcinoma in the cardia, 3) type III: Subcardial carcinoma in the stomach infiltrating the distal esophagus. Reasonable surgery for type I tumors can be achieved by a radical two-field trans-mediastinal esophagectomy and proximal gastrectomy with en bloc removal of the lymphatic drainage in the lower posterior mediastinum and along the celiac axis. On the other hand, the adequate treatment for type II or type III is total gastrectomy with trans-hiatal resection of the distal esophagus and en block lymph node dissection in the posterior lower mediastinum and along the celiac axis [3].

For cancer of the gastric cardia that has invaded the distal esophagus, an abdominal approach, an abdominal approach plus sternotomy, an abdominal and trans-hiatal esophagectomy without thoracotomy, a left thoraco-abdominal approach, and a right thoraco-abdominal approach have each been reported [5-12]. Eight (33%) of 24 cases who underwent extended lymphadenectomy through a left thoraco-abdominal approach had lower mediastinal lymph node metastasis, and metastasis was observed in cases which had esophageal invasion more than 2 cm from the EGJ. Furthermore, five cases had metastasis to the diaphragm and 9 cases had direct invasion to the diaphragm. The technique of partial resection of the diaphragm around the esophageal hiatus was difficult when thoracotomy is not done. Our department has adopted the policy of performing thoracotomy in cases of gastric cancer invading the esophagus more

than 2 cm from the EGJ. Five cases who underwent esophago-gastrectomy through a left thoraco-abdominal approach had intramural metastasis to the esophagus and two of these five cases unfortunately had cancer at the proximal margin of the resected specimen. Our results indicated that the distance between the resection line and the tumor border needed to be over 3 cm from the macroscopically-recognized border of invasive tumors.

One of the factors which should be considered when deciding whether to perform proximal gastrectomy or total gastrectomy is metastasis to the parapyloric lymph nodes. There were no cases of early cancers with metastasis to the parapyloric lymph nodes. Proximal gastrectomy can be indicated also for cases undergoing palliative resection and who are at a high risk. On the other hand, for patients with an advanced cancer in the upper gastric portion, total gastrectomy may provide higher survival rates compared to proximal gastrectomy. Papachristou and Fortner [13] reported that extended total gastrectomy resulted in a significantly higher survival rate than proximal gastrectomy and that the cancer-positivity in the resection margin and local recurrence were less frequently observed after total gastrectomy.

Gastric adenocarcinoma involving the EGJ frequently directly extended to adjacent organs, including the spleen, pancreas, diaphragm and the liver. In such cases combined resection is the best treatment when possible. We performed partial resection of the diaphragm around the esophageal hiatus in 15 cases through a left thoraco-abdominal approach. Takeda et al. [14] reported that in cases at stage II, III or IV without hepatic metastasis and peritoneal dissemination, the 2-year survival rate was 64% for those who underwent a combined resection of the diaphragm and 42% for those who did not.

For complete dissection of the retroperitoneal lymph nodes, resection of the body and tail of the pancreas was frequently performed in addition to splenectomy. In this report, a pancreatic fistula after resection of the pancreas was found in two cases. Siewert et al. [3] reported that the morbidity associated with left pancreatic resection can be avoided by means of a pancreas preserving splenectomy without compromising the extent of lymphadenectomy. We performed combined resection of the tail of the pancreas in 7 cases and pancreas preserving splenectomy to resect the lymph nodes along the splenic artery and the splenic hilum in 24 cases. Combined resection of the body and tail of the pancreas can be indicated for cases with direct invasion of the pan-

creas and those with remarkable lymph node metastasis along the splenic artery.

Among 24 cases who underwent surgery through a left thoraco-abdominal approach, one case died of anastomotic leakage and the overall mortality rate was 4%. The 5-year survival rate at stage II and III was 33% for the left thoraco-abdominal approach and 28% for the abdominal approach. This difference was not significant. The standard operative procedure we employ for advanced gastric adenocarcinoma involving the EGJ is total gastrectomy with combined resection of the spleen and diaphragm around the esophageal hiatus through a left thoraco-abdominal approach. This approach provides a large operative field that facilitates resection of the entire stomach and the lower esophagus, as well as the more complete resection of both the lower mediastinal and the abdominal lymph nodes.

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