Value of splenectomy in patients with Siewert type II adenocarcinoma of the esophagogastric junction

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Abstract

Background The incidence of adenocarcinoma of the esophagogastric junction (AEG) has been increasing recently in both Western and Eastern countries. However, an optimal treatment strategy for Siewert type II AEG is still unclear. The aim of this study was to clarify the value of splenectomy in patients with Siewert type II AEG.

Methods From September 2002 to November 2011, 42 patients underwent total gastrectomy with D2 lymph node dissection for Siewert type II AEG and were included in this study. We used the index of estimated benefit from lymph node dissection (IEBLD) to assess the efficacy of lymph node dissection of each station. Surgical complications were graded by the Clavien–Dindo classification.

Results The overall 5-year survival rate of the 42 patients was 57.5 %. The incidence of splenic hilar lymph node metastasis was 4.8 % and the 5-year survival rate of patients with splenic hilar lymph node involvement was zero. Consequently, the IEBLD of splenic hilar lymph nodes was zero. Postoperative morbidities occurred in 25 patients (59.5 %). Pancreas-related complications were the most frequently observed (28.5 %), followed by intraabdominal abscess (14.3 %) and anastomotic leakage (9.5 %).

Conclusions Splenic hilar lymph node dissection may be omitted without decreasing curability in patients with

Siewert type II AEG, although a prospective study is necessary for more conclusive results.

Keywords Gastric cancer · Adenocarcinoma of esophagogastric junction · Siewert type II · Splenectomy

Introduction

The incidence of adenocarcinoma of the esophagogastric junction (AEG) has been increasing recently in both Western and Eastern countries [1]. In the East, the westernized lifestyle habit and the increased incidence of gastroesophageal reflux disease are thought to be possible reasons, with the incidence of AEG likely to increase further [2]. Siewert et al. [3] classified AEG into three subgroups according to the location of the tumor epicenter. Siewert type I AEG, which is frequently observed in Western countries, is generally treated as an esophageal cancer. Siewert type III AEG, which is frequently observed in Eastern countries, is mostly treated as a gastric cancer. An optimal treatment strategy for Siewert type II AEG is still unclear, and it is under debate whether Siewert type II AEG should be regarded and treated as an esophageal cancer or a gastric cancer [4, 5].

The latest European Society for Medical Oncology clinical practice guideline recommends D2 gastrectomy for curable gastric cancer. However, splenectomy is not recommended unless the tumor is directly infiltrating the spleen [6, 7]. In contrast, Japanese guidelines include splenectomy in D2 total gastrectomy. Consequently, splenectomy is mandatory in patients with type II AEG undergoing total gastrectomy in Japan [8, 9]. However, recent reports from the East have raised the question of whether splenectomy is valuable in these patients [10, 11].

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Reported are an increased incidence of pancreas-related complications following splenectomy and a low incidence of splenic hilar nodal involvement in patients with AEG [10–12]. However, these reports included a variety of patients, such as those with Siewert type I or III AEG and patients undergoing noncurative surgery [10, 11]; thus, the therapeutic value of splenectomy in patients with Siewert type II AEG undergoing curative gastrectomy remains unclear.

The aim of this study was to clarify the value of splenectomy in patients with Siewert type II AEG. We investigated the clinicopathological characteristics and long-term outcome of patients with Siewert type II AEG who underwent total gastrectomy with D2 lymph node dissection.

Materials and methods

Patients

From September 2002 to November 2011, 2,995 patients with gastric cancer underwent gastrectomy at the Shizuoka Cancer Center, Japan. Of these, 64 patients underwent total gastrectomy with D2 lymph node dissection for Siewert type II AEG. Patients with early gastric cancer (13 patients), those who received neoadjuvant chemotherapy (3 patients), and those who underwent noncurative gastrectomy (R1 or R2, 6 patients) were excluded, and the remaining 42 patients were included in the present study.

The International Union Against Cancer (UICC) TNM staging system for esophageal cancer was used for tumor staging [4]. The lymph node stations were numbered according to the definition of the Japanese Gastric Cancer Association (JGCA) [13].

Tumor histology was evaluated according to the JGCA classification [13]. Well- and moderately differentiated tubular adenocarcinoma and papillary adenocarcinoma were classified as differentiated-type carcinomas. Poorly differentiated adenocarcinoma, signet-ring cell carcinoma, and mucinous carcinoma were classified as undifferentiated-type carcinomas.

Patient characteristics and pathological and surgical findings were collected from our database records and individual patient electronic medical records. The data collection and analysis were approved by the institutional review board of the Shizuoka Cancer Center.

Surgery

Total gastrectomy with D2 lymphadenectomy was carried out in all patients included in the present study. All perigastric nodes and extraperigastric nodes, defined as second-compartment lymph nodes according to the JGCA

classification, were retrieved (2nd English edition of JGCA). To completely remove the splenic hilar lymph nodes, all patients underwent splenectomy. The surgical complications were assessed by the Clavien–Dindo classification [14]. We defined any complication categorized as grade II or higher as a postoperative morbidity.

Evaluation of the therapeutic value of intraabdominal lymph node dissection

In the present study, we adopted the index of estimated benefit from lymph node dissection (IEBLD), a concept proposed by Sasako et al. [15] to assess the efficacy of lymph node dissection of each station. This index is calculated by multiplying the frequency of lymph node metastasis to each station by the 5-year survival rate of patients with positive lymph nodes at each station. The incidence of metastasis and the 5-year survival rate of patients with positive nodes were calculated independently for each lymph node, without any reference to the overall pathological nodal stage.

Statistics

Statistical analysis was carried out using SPSS version 19 for Windows. The Kaplan–Meier method was used to estimate survival curves. All continuous variables are presented as the median (range).

Results

Patient characteristics

The characteristics of the patients are described in Table 1. There were 26 male patients (62 %) and 16 female patients (38 %). Type 3 tumor was the most frequently observed macroscopic type (17 patients, 40.5 %). The transabdominal approach was the most preferred surgical approach used in this study (37 patients, 88.1 %). The reconstruction was performed by Roux-en-Y in all cases, and esophagojejunostomy was performed using a circular stapler. Lymph node metastases were observed in 32 patients (76.2 %: N1, 11 patients; N2, 7 patients; N3, 14 patients). Consequently, tumor stage was determined as IB in 6 patients, IIA in 4, IIB in 2, IIIA in 8, IIIB in 3, and IIIC in the remaining 19 patients. Adjuvant chemotherapy by S-1 was given to 15 patients.

Postoperative morbidities

The details of postoperative morbidities are described in Table 2. Grade II or higher postoperative complications

Table 1 Demographics of 42 patients with Siewert type II adenocarcinoma of the esophagogastric junction

Parameters	N
Age median (range), years	67 (30–79)
Sex	
Male	26
Female	16
Tumor size median (range), mm	57 (20–145)
Macroscopic type	
Type 0	9
Type 1	5
Type 2	11
Type 3	17
Circumferential distribution	
Lesser curvature	20
Greater curvature	1
Anterior wall	4
Posterior wall	8
Circular	9
Histological type	
Differentiated	21
Undifferentiated	21
Type of surgery	
TG + S	40
TG + PS	2
Approach	
Abdominal	37
Left thoracoabdominal	5
Tumor depth (histological)	
MP(T2)	8
SS(T3)	22
SE(T4)	12
Node stage (histological)	
N0	10
N1	11
N2	7
N3	14
Stage	
IA	0
IB	6
IIA	4
IIB	2
IIIA	8
IIIB	3
IIIC	19
IV	0
Adjuvant chemotherapy (S-1)	
+	15
–	27

PS pancreaticosplenectomy, S splenectomy, TG total gastrectomy, MP muscularis propria, SS subserosa, SE exposed beyond the serosa

Table 2 Postoperative complications in 42 patients after total gastrectomy with D2 lymphadenectomy

Complications	n	%
Complication, grade II or higher ^a	25	59.5
Pancreas-related complication	12	28.5
Intraabdominal abscess	6	14.3
Anastomotic leakage	4	9.5
Pneumonia	4	9.5
Pleural fluid	4	9.5
Bleeding	2	4.8
Cholecystitis	1	2.4
Wound complication	1	2.4

^a Based on the Clavien–Dindo classification [14]

occurred in 25 patients (59.5 %). Pancreas-related complications were the most frequently observed morbidity (28.5 %), followed by intraabdominal abscess (14.3 %) and anastomotic leakage (9.5 %).

Survival outcomes

The 5-year survival rate of the 42 patients in this study was 57.5 %. Table 3 presents the frequency of metastasis of each regional lymph node, the 5-year survival rate of patients with nodal involvement, and the IEBLD for each station.

Lymph node involvement was observed in more than 10 % of patients (range 16.7–59.5 %) in stations 1, 2, 3, 7, 9, and 11p, and the IEBLDs of these stations ranged from 5.6 to 30.3. The incidence of metastasis was lower than 10 % (range 0–9.5 %) in the other stations, and the IEBLD was low (0–4.8). Lymph node metastasis was not found in stations 4d and 12a. In addition, the 5-year survival rate was zero if station 4sa, 4d, 6, 8a, 10, 11d, or 12a was involved.

Consequently, the IEBLDs of stations that were located far from the esophagogastric junction, such as stations 4d, 6 (along the right gastroepiploic artery), 8a (along the common hepatic artery), and 12a (along the proper hepatic artery), were zero. In addition, the IEBLDs of stations 10 and 11d, where splenectomy is necessary for complete retrieval of these nodes, were also zero (Fig. 1).

Discussion

The present study shows the IEBLD of regional lymph nodes in patients with Siewert type II AEG ranged from 0 to 30.3. It is plausible that dissection of some of these stations could be omitted even in advanced cases.

In the present study, the IEBLD of stations 1, 2, 3, 7, 9, and 11p were higher than the other stations. Previous

Table 3 Frequency of lymph node metastasis and 5-year survival for each lymph node station

Lymph node station	Number of patients with metastatic nodes	Number of patients in whom the station was dissected	Incidence of lymph node metastasis (%)	Five-year survival rate of patients with metastatic nodes (%)	IEBLD
1	25	42	59.5	50.3	29.9
2	8	42	19.0	46.9	8.9
3	24	42	57.1	53.0	30.3
4sa	1	42	2.4	0	0
4sb	2	42	4.8	50.0	2.4
4d	0	42	0	0	0
5	1	42	2.4	100	2.4
6	1	42	2.4	0	0
7	13	42	30.9	58.4	18.1
8a	1	42	2.4	0	0
9	10	42	23.8	30.0	7.1
10	2	42	4.8	0	0
11p	7	42	16.7	33.3	5.6
11d	2	42	4.8	0	0
12a	0	14	0	0	0
19	4	42	9.5	50.0	4.8
20	2	42	4.8	50.0	2.4

IEBLD index of estimated benefit from lymph node dissection

studies also reported a high IEBLD in these stations in patients with AEG [10, 11]. Investigation of lymphatic flow showed that these stations were sentinel nodes for the upper part of the stomach [16]. We consider complete retrieval of these stations would be of value and should not be omitted during curative surgery for Siewert type II AEG.

The IEBLDs of the remaining stations were lower than that of station 1, 2, 3, 7, 9, and 11p, and was zero in stations 4sa, 4d, 6, 8a, 10, and 11d; thus, lymph node dissection of some of these stations could be omitted. If we omit the supra- and infrapyloric lymph nodes, then the distal part of the stomach might be preserved [17]. In addition, the spleen could be preserved if the station 10 lymph node dissection was omitted, even in cases with advanced disease.

Previously, the therapeutic value of removing station 10 lymph nodes in AEG was investigated, and similar results, a low IEBLD for station 10 (0–2.2), were reported [5, 10, 11]. Yamashita et al. investigated IEBLD of 225 patients with Siewert type II AEG, and reported that of station 10 was 0.7. In addition, Hosokawa et al. reported IEBLD for station 10 in patients with AEG was 2.2. However, these previous studies included patients underwent non-curative gastrectomy or those with Siewert type I or III AEG. Therefore, to the best of our knowledge, our study is the first study to investigate the IEBLD of station 10 in patients with Siewert type II AEG underwent curative surgery.

The circumferential distribution is a possible reason why IEBLD of station 10 was zero in this study. Of 42 patients

with circumferentially localized AEGs, the AEG was located along the lesser curvature in 20 patients. In contrast, it was located along the greater curvature in only one patient, the resulting tumor location being far away from the spleen, and there was a low incidence of station 10 lymph node involvement in this series. The same trend was also reported by Suh et al. [5] previously.

It would be advantageous to avoid splenectomy, a procedure necessary for the complete removal of the splenic hilar lymph node, as it has been reported that splenectomy increases pancreas-related complications and disturbs immune functions [12, 18, 19]. In fact, pancreas-related complications were the most frequently observed complication (28.5 %) in our study, and it was higher than that after spleen-preserving total gastrectomy in our institute (2.5 %; data not shown). Even in Japan, where splenectomy is mandatory for D2 gastrectomy, some studies have reported a lack of survival benefit and increased postoperative morbidities in patients undergoing splenectomy [12, 20–22]. In the West, although the current standard treatment for curable gastric cancer is a D2 gastrectomy, splenectomy is not a mandatory procedure, presumably because of increased postoperative pancreas-related complications and a lack of evidence that supports the feasibility of splenectomy [23–26]. Thus, splenectomy itself increases postoperative morbidities. Therefore, it would be of value if we could avoid splenectomy without worsening the long-term outcome of patients.

Fig. 1 Index of estimated benefit from lymph node dissection (IEBLD) for each lymph node station. Circles, IEBLD greater than 5; triangles, IEBLD less than 5

The present retrospective study has limitations, which include the small number of patients investigated in the study. Even though the number of patients with Siewert type II AEG has been increasing in Japan, the number of patients at each institute is still limited. Second, mediastinal lymph node dissection was not performed routinely, particularly in the early period of this study. Consequently, the value of mediastinal lymph node dissection cannot be assessed. The latest JGCA guidelines recommend mediastinal lymph node dissection for patients with AEG; thus, we currently perform lower mediastinal lymph node dissection for these patients (14th JGCA guidelines). We will be able to assess the value of lower mediastinal lymph node dissection in the near future.

In conclusion, the IEBLD of the splenic hilar lymph nodes was zero in the present study. Splenic hilar lymph node dissection may be omitted without decreasing curability in patients with Siewert type II AEG, although a prospective study is necessary for more conclusive results.

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