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ORIGINAL SCIENTIFIC REPORT

Clinicopathological Characteristics and Prognostic Factors of Patients with Siewert Type II Esophagogastric Junction Carcinoma: A Retrospective Multicenter Study

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Abstract

Background The incidence of esophagogastric junction (EGJ) carcinoma is increasing, but its optimal surgical management remains controversial.

Methods We retrospectively reviewed the database of 400 patients with Siewert type II EGJ carcinoma who were treated surgically at 7 institutions between March 1986 and October 2010. We examined the clinicopathological characteristics, prognostic factors, and risk factors associated with each recurrence pattern.

Results The 5-year overall survival rate of all patients with Siewert type II EGJ carcinoma was 58.4 %. Multivariate analysis showed that T and N stages were independent prognostic factors. We also found that the incidence of lower mediastinal lymph node metastasis (17.7 %) and para-aortic lymph node metastasis (16.1 %) was relatively high. In addition, the para-aortic lymph nodes ($N = 39$, 9.8 %) were the most frequent node recurrence site, followed by the mediastinal lymph nodes ($N = 23$, 5.8 %). Lung recurrence was more common than was peritoneal recurrence. Considering each type of recurrence, multivariate analysis showed that the differentiated type was associated with a higher risk of lung recurrence than was the undifferentiated type, and N stage (pN2–3) and positive venous invasion were independent risk factors for liver recurrence.

Conclusions This study is one of the largest retrospective studies to evaluate patients with Siewert type II EGJ carcinoma. Para-aortic and mediastinal lymph node metastasis and recurrence rates were relatively high. During the postoperative follow-up of patients with differentiated Siewert type II EGJ carcinoma, patients should be monitored for lung recurrence more closely than that for peritoneal recurrence.

Tatsuo Matsuda, Yukinori Kurokawa, and Takaki Yoshikawa have contributed equally to this work.

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Introduction

The incidence of adenocarcinoma of the esophagogastric junction (EGJ) is increasing in developed countries [1–3]. The Siewert classification of EGJ adenocarcinoma has been widely accepted [4]. Siewert type II EGJ adenocarcinomas are located along the borderline between the mediastinum and abdomen; they can metastasize to both cavities. Thus, its optimal surgical management, including surgical approach (transthoracic or transhiatal), range of nodal dissection, and type of gastrectomy, remains controversial and has attracted considerable interest [5–9]. Siewert type II EGJ adenocarcinoma is currently treated using a multimodal approach involving surgery with a curative intent; however, outcomes remain unsatisfactory, even after curative resection [5–10].

Further information regarding prognostic factors and recurrence patterns of surgically treated patients with Siewert type II cancer is important for future strategic therapeutic planning. Oncological outcomes of Siewert type II EGJ adenocarcinoma have been reported by many researchers; however, the number of patients analyzed has not been adequate. Therefore, we aimed to clarify the clinicopathological characteristics, prognostic factors, and recurrence patterns of patients with Siewert type II EGJ carcinoma. In addition, we examined the risk factors for recurrence and each type of recurrence. This is the first report to examine the risk factors for each type of recurrence.

To the best of our knowledge, this study is one of the largest multicenter retrospective studies to evaluate patients with Siewert type II EGJ carcinoma.

Materials and methods

Patients

In this study, we retrospectively examined the medical records of 400 patients with Siewert type II EGJ carcinoma who underwent surgical treatment at 7 institutions between March 1986 and October 2010 in Japan. All tumors were histologically diagnosed as adenocarcinoma. Tumor staging was performed according to the International Union against Cancer tumor–node–metastasis (TNM) staging system [11]. Patients who underwent palliative (R2) surgery were excluded. This study (HIK-01) was approved by the Steering Committee of the Young Gastric Surgeons Research Group in Japan and the institutional review board of Keio University Hospital. We examined the overall survival (OS) of patients, distribution of lymph node metastasis, and recurrence patterns. Additionally, we examined the prognostic factors and risk factors associated with each recurrence pattern for 331 patients who underwent R0 surgery without preoperative chemotherapy.

Measurement of the distance from the EGJ to the distal end of the tumor

After resection, a fresh specimen was opened longitudinally, and lymph nodes were removed for pathological examination. The resected specimens were stretched and pinned to a board. The distance from the center of the tumor to the EGJ was measured and recorded by the surgeon. Siewert type II EGJ carcinoma was defined as a case where the center of the tumor was located 1 cm above and 2 cm below the EGJ. The EGJ was defined as the region where the tubular esophagus anatomically joins the stomach, based on macroscopic findings of the resected specimens.

Statistical analysis

OS was defined as the time from surgery to death from any cause. Survival curves were estimated using the Kaplan–Meier method. A Cox proportional hazards model was used for the univariate and multivariate survival analyses. The impact of clinicopathological factors on recurrence was investigated using univariate and multivariate logistic regression analyses. P values of <0.05 were considered statistically significant, and multivariate analysis was performed for variables whose P value was <0.10. SPSS Statistics software, version 22 (IBM Corp., Armonk, NY, USA) was used for all statistical analyses.

Results

Clinical parameters and pathological findings

The clinical parameters and pathological findings of the 400 patients with Siewert type II EGJ carcinoma are shown in Table 1. There was a predominance of male patients (79.0 %) in our study. The median tumor length was 50 mm, and the median esophageal invasion length was 7.5 mm. The transhiatal approach was used more often (62.7 %) than the right thoracotomy (10.0 %) and left thoracoabdominal approaches (27.3 %). Of the 370 patients who underwent lower esophagectomy, the transhiatal approach was used in 251 patients (67.8 %) and the transthoracic approach in 119 patients (32.2 %).

Survival rate

The 5-year OS rate of all patients with Siewert Type II EGJ adenocarcinoma in this study was 58.4 %. The median

Table 1 Clinicopathological characteristics of the 400 patients with Siewert Type II esophagogastric junction carcinoma

Age (years)		Tumor length (mm)	
Median (range)	63.0 (18–88)	Median (range)	50.0 (8.0–180.0)
Sex		Center of the tumor from EGJ (mm)	
Male	316 (79.0 %)	Median (range)	7.5 (−10.0– +20.0)
Female	84 (21.0 %)	Esophageal invasion (mm)	
Histological type		Median (range)	15.0 (0–63)
Differentiated	268 (67.0 %)	Surgical approach	
Undifferentiated	127 (31.8 %)	Transhiatal	251 (62.7 %)
Unknown	5 (1.3 %)	Right thoracotomy	40 (10.0 %)
Pathological T stage		Left thoracoabdominal	109 (27.3 %)
T1	77 (19.3 %)	Type of esophagectomy	
T2	55 (13.8 %)	Lower	370 (92.5 %)
T3	146 (36.5 %)	Subtotal	30 (7.5 %)
T4	122 (30.5 %)	Type of gastrectomy	
Pathological N stage		Total	278 (69.5 %)
N0	136 (34.0 %)	Proximal	122 (30.5 %)
N1	78 (19.5 %)	Splenectomy	
N2	93 (23.3 %)	Yes	232 (58.0 %)
N3	93 (23.3 %)	No	168 (42.0 %)
Stage		Preoperative chemotherapy	
I A	64 (16.0 %)	Yes	44 (11.0 %)
I B	26 (6.5 %)	No	356 (89.0 %)
II A	30 (7.5 %)	Postoperative chemotherapy	
II B	24 (6.0 %)	Yes	133 (33.3 %)
IIIA	62 (15.5 %)	No	267 (66.7 %)
IIIB	42 (10.5 %)	Residual tumor stage	
IIIC	115 (28.8 %)	R0 resection	371 (92.8 %)
IV	37 (9.3 %)	R1 resection	29 (7.3 %)

EGJ esophagogastric junction carcinoma

follow-up duration was 5.2 years (range, 1.0–20.6 years) for patients who survived.

We evaluated the 5-year OS rate according to tumor depth, N stage, TNM stage, and residual tumor stage (Fig. 1a–d). Patients with pT1 and pT2 carcinoma showed good outcomes (5-year OS rate of 90.6 and 81.3 %, respectively). The 5-year OS rate of patients with pT3 and pT4 carcinoma was low at 46.6 and 41.8 %, respectively. The 5-year OS rate for pN0 and pN1 patients was 77.4 and 73.2 %, respectively, and it decreased to 54.7 and 22.0 % for pN2 and pN3 patients, respectively. The 5-year OS rate according to the stage was as follows: stage I, 87.4 %; stage II, 70.9 %; stage III, 51.4 %; and stage IV, 12.6 %. The 5-year OS rate for patients who underwent R0 resection was 60.8 %, compared with the rate of 25.9 % for those who underwent R1 resection.

The results of the univariate and multivariate Cox regression analyses for OS are shown in Table 2. Univariate analysis showed that T and N stages, lymphatic invasion, venous invasion, >30 mm gastric invasion, postoperative chemotherapy use, and tumor length >50 mm were significant predictors of survival. Multivariate analysis showed that T and N stages were independent prognostic factors. The hazard ratio for early death was 3.120 (95 % confidence interval 1.761–5.527) for pT3–T4 versus pT1–T2 and 2.013 (95 % confidence interval 1.347–3.006) for pN2–N3 versus pN0–N1.

Distribution of lymph node metastasis

The distribution of lymph node metastases is shown in Table 3. Most lymph node metastases were located in the lesser curvature area and right paracardiac area. Lower mediastinal lymph node metastasis was observed in 37 of 208 patients (17.7 %) who underwent lower mediastinal lymph node dissection. Sixty-seven of 208 patients

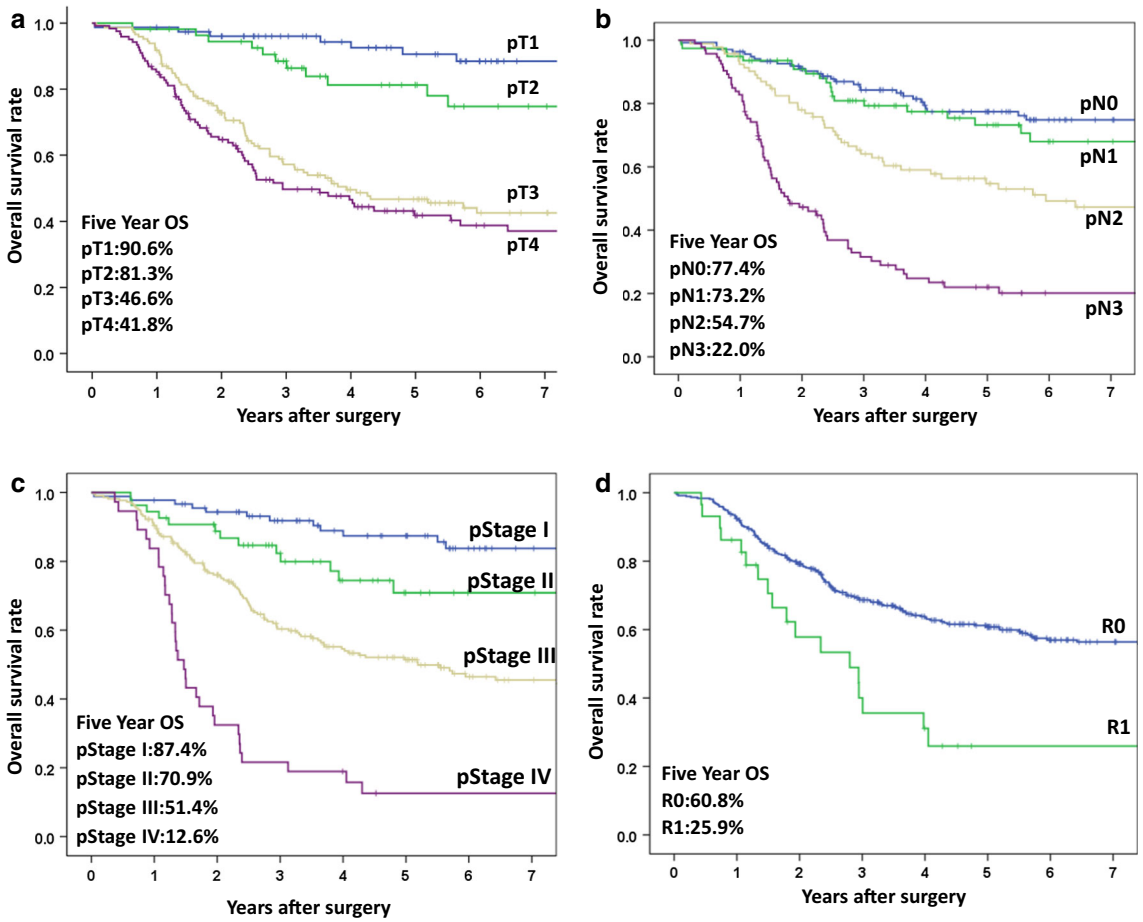

Fig. 1 **a** Overall survival *curves* in patients with Siewert type II esophagogastric junction carcinoma according to tumor depth stage. **b** Overall survival *curves* in patients with Siewert type II esophagogastric junction carcinoma according to N stage. **c** Overall survival *curves* in patients with Siewert type II esophagogastric junction carcinoma according to TNM stage. **d** Overall survival *curves* in patients with Siewert type II esophagogastric junction carcinoma according to residual tumor stage

Table 2 Univariate and multivariate Cox regression analyses for overall survival

Variables	Unfavorable/Favorable	Univariate		Multivariate	
		HR (95 % CI)	*P*	HR (95 % CI)	*P*
Age (years)	≥65/<65	1.362 (0.977–1.898)	0.069	1.183 (0.839–1.668)	0.337
Gender	Female/male	0.980 (0.654–1.468)	0.922		
Postoperative chemotherapy	±	**1.653 (1.167–2.342)**	**0.005**	1.071 (0.736–1.558))	0.722
Tumor length (mm)	>50/≤50	**1.828 (1.311–2.551)**	**0.000**	0.949 (0.617-–1.459)	0.810
Histology	Undifferentiated/differentiated	1.260 (0.884–1.793)	0.201		
Lymphatic invasion	±	**2.238 (1.440–3.478)**	**0.000**	1.010 (0.612–1.666)	0.969
Venous invasion	±	**2.054 (1.409–2.995)**	**0.000**	1.152 (0.772–1.718)	0.488
Esophageal invasion (mm)	>30/≤30	1.542 (0.915–2.598)	0.104		
Gastric invasion (mm)	>30/≤30	**1.813 (1.299–2.532)**	**0.000**	1.020 (0.670–1.551)	0.928
Tumor depth	pT3–4/pT1–2	**4.647 (2.918–7.399)**	**0.000**	**3.120 (1.761–5.527)**	**0.000**
Lymph node metastasis	pN2–3/pN0–1	**3.069 (2.162–4.356)**	**0.000**	**2.013 (1.347–3.006)**	**0.001**

HR hazard ratio, *CI* confidence intervals

Bold values indicate statistical significance

Table 3 The incidence of node metastasis

Lymph node station	Metastatic incidence (%)
Cervical lymph node	18.1 (2/11)
Mediastinal lymph node	
Upper mediastinal	17.3 (4/23)
Middle mediastinal	25.0 (12/48)
Lower mediastinal	17.7 (37/208)
No. 110	16.1 (30/186)
No. 111	5.5 (8/144)
No. 112	15.3 (8/52)
Abdominal lymph node	
No. 1	40.8 (159/389)
No. 2	31.7 (122/384)
No. 3	43.2 (172/398)
No. 4sa	4.5 (15/337)
No. 4sb	3.2 (10/308)
No. 4d	3.1 (9/295)
No. 5	2.0 (5/251)
No. 6	0.7 (2/273)
No. 7	27.6 (107/387)
No. 8a	5.5 (19/344)
No. 9	13.0 (41/316)
No. 10	9.7 (23/236)
No. 11p	1.8 (60/325)
No. 11d	6.0 (11/184)
No. 12a	2.5 (2/81)
No. 19	5.6 (8/144)
No. 20	1.4 (2/141)
Para-aortic lymph node	16.1 (22/136)
No. 16a2	13.6 (18/132)
No. 16b1	20.0 (7/35)

Thoracic lymph node (LN) station numbers: 110, Lower thoracic para-esophageal LNs; 111, Supradiaphragmatic LNs; 112, Posterior mediastinal LNs

Abdominal LN station numbers: 1, right cardiac LNs; 2, left cardiac LNs; 3, LNs along the lesser curvature; 4sa, left greater curvature LNs along the short gastric arteries; 4sb, left greater curvature LNs along the left gastroepiploic artery; 4d, Rt. greater curvature LNs along the 2nd branch and distal part of the right gastroepiploic artery; 5, Suprapyloric LNs along the 1st branch and proximal part of the right gastric artery; 6, Infrapyloric LNs along the first branch and proximal part of the right gastroepiploic artery down to the confluence of the right gastroepiploic vein and the anterior superior pancreatoduodenal vein; 7, LNs along the trunk of left gastric artery between its root and the origin of its ascending branch; 8a, LNs along the common hepatic artery anterosuperior group; 9, LNs along the celiac artery; 10, LNs at the splenic hilum; 11p, LNs along the proximal splenic artery; 11d, LNs along the distal splenic artery; 12a, Hepatoduodenal ligament LNs along the proper hepatic artery; 19, Infradiaphragmatic LNs predominantly along the subphrenic artery; 20, Para-esophageal LNs in the diaphragmatic esophageal hiatus; 16a2, Para-aortic LNs between the upper margin of the origin of the celiac artery and the lower border of the left renal vein; 16b1, Para-aortic LNs between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery

Table 4 Number of patients for each site of first recurrence

Recurrence site	$N = 151$ (%)
Lymphatic	63 (15.8)
Para-aortic	39 (9.8)
Mediastinal	23 (5.8)
Upper	9 (2.3)
Middle	12 (3)
Lower	9 (2.3)
Cervical	9 (2.3)
Gastric regional	6 (1.5)
Others	6 (1.5)
Lung	29 (7.3)
Liver	44 (11.0)
Peritoneal	27 (6.8)
Esophagus	4 (1.0)
Others	20 (5.0)

(32.2 %) underwent lower mediastinal dissection by the transhiatal approach. Para-aortic lymph node metastasis was observed in 22 of 136 patients (16.1 %) who underwent para-aortic lymph node dissection.

Recurrence patterns

The initial recurrence patterns are shown in Table 4. One hundred fifty-one (37.7 %) of the 400 patients experienced relapse, and 207 recurrence sites were considered to be the initial recurrence sites. Sixty-three (15.8 %) of the 400 patients showed lymph node recurrences in $\geq$1 region. The para-aortic lymph nodes ($N = 39$, 9.8 %) were the most frequent lymph node recurrence site, followed by the mediastinal lymph nodes ($N = 23$, 5.8 %).

With regard to hematogenous recurrence, 44 patients experienced liver recurrence and 29 patients experienced lung recurrence. Peritoneal recurrence was observed in 27 patients.

Risk factors associated with each recurrence pattern

We examined the risk factors for recurrence and each type of recurrence (para-aortic lymph node, mediastinal lymph node, lung, liver, and peritoneal recurrence) by logistic regression analysis. The results of univariate and multivariate logistic regression analyses are shown in Table 5. With regard to each type of recurrence, multivariate analysis showed that T stage (pT3–4) was an independent risk factor for para-aortic lymph node and lung recurrence. N stage (pN2–3) and positive venous invasion were independent risk factors for liver recurrence. Being less than 65 years old was independent risk factor for mediastinal recurrence. The undifferentiated type had at lower risk of lung recurrence than did the differentiated type.

Table 5 Logistic regression analyses

Variables	Unfavorable/Favorable	Univariate		Multivariate	
		HR (95 % CI)	*p*	HR (95 % CI)	*p*
Para-aortic lymph node recurrence					
Age (years)	≥65/< 65	0.930 (0.422–2.054)	0.858		
Gender	Female/male	2.167 (0.633–7.421)	0.218		
Postoperative chemotherapy	±	1.428 (0.629–3.239)	0.394		
Tumor length (mm)	>50/≤50	1.551 (0.705–3.412)	0.276		
Histology	Undifferentiated/differentiated	1.364 (0.601–3.093)	0.458		
Lymphatic invasion	±	1.768 (0.649–4.820)	0.265		
Venous invasion	±	1.831 (0.751–4.467)	0.184		
Esophageal invasion (mm)	>30/≤30	1.400 (0.394–4.975)	0.603		
Gastric invasion (mm)	>30/≤30	**2.319 (1.028–5.232)**	**0.043**	1.278 (0.542–3.012)	0.575
Tumor depth	pT3–4/pT1–2	**8.333 (1.923–35.825)**	**0.004**	**6.711(1.395 –32.278)**	**0.018**
Lymph node metastasis	pN2–3/pN0–1	**2.288 (1.015–5.162)**	**0.046**	1.227 (0.519–2.900)	0.640
Para-aortic lymph node dissection	±	1.389 (0.622–3.102)	0.423		
Mediastinal lymph node recurrence					
Age (years)	≥65/<65	**0.255 (0.071–0.914)**	**0.036**	**0.217 (0.060–0.787)**	**0.020**
Gender	Female/male	1.848 (0.410–8.334)	0.424		
Postoperative chemotherapy	±	1.074 (0.363–3.175)	0.898		
Tumor length (mm)	>50/≤50	1.840 (0.668–5.065)	0.238		
Histology	Undifferentiated/differentiated	1.377 (0.486–3.897)	0.547		
Lymphatic invasion	±	2.806 (0.625–12.600)	0.178		
Venous invasion	±	1.366 (0.463–4.031)	0.572		
Esophageal invasion (mm)	>30/≤30	2.686 (0.717–10.057)	0.142		
Gastric invasion (mm)	>30/≤ 30	1.290 (0.472–3.523)	0.620		
Tumor depth	pT3–4/pT1–2	4.402 (0.983–19.705)	0.053	3.593 (0.721–17.906)	0.119
Lymph node metastasis	pN2–3/pN0–1	2.912 (0.989–8.577)	0.053	2.064(0.643–6.632)	0.217
Mediastinal lymph node dissection	±	1.731(0.614–4.878)	0.299		
Lung recurrence					
Age (years)	≥65/<65	1.273 (0.524–3.095)	0.594		
Gender	Female/male	0.622 (0.232–1.670)	0.346		
Postoperative chemotherapy	±	1.488 (0.596–3.711)	0.394		
Tumor length (mm)	>50/≤50	1.573 (0.649–3.813)	0.316		
Histology	Undifferentiated/differentiated	0.357 (0.101–1.239)	0.095	**0.209 (0.058–0.759)**	**0.017**
Lymphatic invasion	±	3.896 (0.889–17.078)	0.071	2.343 (0.480–11.446)	0.293
Venous invasion	±	2.749 (0.903–8.368)	0.075	1.143 (0.344–3.799)	0.828
Esophageal invasion(mm)	>30/≤30	2.814 (0.877–9.030)	0.082	2.018 (0.586–6.950)	0.266
Gastric invasion (mm)	>30/≤30	1.170 (0.483–2.835)	0.728	0.466 (0.178–1.218)	0.119
Tumor depth	pT3–4/pT1–2	**13.085 (1.734–98.757)**	**0.013**	**12.764 (1.437–113.335)**	**0.022**
Lymph node metastasis	pN2–3/pN0–1	**2.677 (1.051–6.816)**	**0.039**	1.438 (0.516–4.009)	0.487
Liver recurrence					
Age (years)	≥65/<65	0.583 (0.272–1.251)	0.166		
Gender	Female/male	1.898 (0.642–5.609)	0.246		
Postoperative chemotherapy	±	1.262 (0.584–2.727)	0.554		
Tumor length (mm)	>50/≤50	1.252 (0.603–2.602)	0.546		
Histology	Undifferentiated/differentiated	1.205 (0.558–2.603)	0.636		
Lymphatic invasion	±	1.754 (0.697–4.413)	0.233		
Venous invasion	±	**4.814 (1.646–14.085)**	**0.004**	**3.522 (1.150–10.798)**	**0.028**
Esophageal invasion (mm)	>30/≤30	1.138 (0.324–4.001)	0.840		

Table 5 continued

Variables	Unfavorable/Favorable	Univariate		Multivariate	
		HR (95 % CI)	*p*	HR (95 % CI)	*p*
Gastric invasion (mm)	>30/≤30	0.990 (0.475–2.064)	0.978		
Tumor depth	pT3–4/pT1–2	**2.810 (1.123–7.032)**	**0.027**	1.194 (0.425–3.352)	0.737
Lymph node metastasis	pN2–3/pN0–1	**3.627 (1.623–8.106)**	**0.002**	**2.531 (1.048–6.112)**	**0.039**
Peritoneal recurrence					
Age (years)	≥65/<65	0.431 (0.150–1.239)	0.118		
Gender	Female/male	0.492 (0.178–1.363)	0.172		
Postoperative chemotherapy	±	**4.036 (1.516–10.743)**	**0.005**	2.744 (0.989–7.615)	0.053
Tumor length (mm)	>50/≤50	1.793 (0.689–4.665)	0.232		
Histology	Undifferentiated/differentiated	1.875 (0.717–4.902)	0.200		
Lymphatic invasion	±	3.236 (0.729–14.367)	0.122		
Venous invasion	±	0.959 (0.362–2.544)	0.934		
Esophageal invasion (mm)	>30/≤30	2.312 (0.627–8.528)	0.208		
Gastric invasion (mm)	>30/≤30	2.687 (0.983–7.341)	0.054	1.699 (0.582–4.956)	0.332
Tumor depth	pT3–4/pT1–2	**5.083 (1.149–22.496)**	**0.032**	2.116 (0.398–11.246)	0.379
Lymph node metastasis	pN2–3/pN0–1	**3.493 (1.216–10.034)**	**0.020**	1.891 (0.604–5.916)	0.274

HR hazard ratio, *CI* confidence intervals

Bold values indicate statistical significance

Discussion

We retrospectively examined the clinicopathological characteristics, prognostic factors, recurrence patterns, and risk factors associated with each recurrence pattern of Siewert type II EGJ carcinoma. This study is one of the largest multicenter, retrospective studies to evaluate patients with Siewert type II EGJ carcinoma and is the first report to examine the risk factors for each type of recurrence.

We examined prognostic factors in patients who underwent R0 surgery without preoperative chemotherapy. Multivariate analysis showed that pT and pN stages were independent prognostic factors. These results are also in line with those reported previously [5, 10, 12, 13]. With regard to gastric cancer, pT and pN stages were also reported as independent prognostic factors by another group [14]. We found that the para-aortic lymph nodes ($N = 39$, 9.8 %) were the most frequent lymph node recurrence site, followed by the mediastinal lymph nodes ($N = 23$, 5.8 %). We also found that the incidence of lower mediastinal lymph node metastasis (17.7 %) and para-aortic lymph node metastasis (16.1 %) was relatively high.

According to the results of a multicenter randomized controlled trial in Japan (Japan Clinical Oncology Group [JCOG] 9501), para-aortic nodal dissection is no longer performed for Siewert type II EGJ carcinoma in several institutions [15]. In this study, only 137 patients (33.1 %) underwent para-aortic lymph node dissection. However, the target of JCOG 9501 was gastric cancer and not EGJ carcinoma. Anatomically, EGJ is proximal to the para-aortic region, which is why lymph node metastasis and recurrence are often observed. Thus, the necessity of para-aortic nodal dissection for Siewert type II EGJ carcinoma remains controversial. In addition, the benefit of mediastinal lymph node dissection remains controversial. Omloo et al. [8] reported that patients with adenocarcinoma of the mid/distal esophagus and 1–8 metastatic lymph nodes appear to benefit from extended transthoracic esophagectomy. On the other hand, Sasako et al. reported that the left thoracoabdominal approach does not improve survival rates after applying the transhiatal approach and that it can lead to higher morbidity rates in patients with Siewert type II or III EGJ carcinomas with esophageal invasion of ≤3 cm [9]. As far as we know, prospective studies have not been conducted to clarify the benefit of para-aortic and mediastinal lymph node dissection in patients with Siewert type II EGJ carcinomas. From our results and those of previous reports, a prospective study (UMIN000013205) is ongoing to determine the true incidence and benefit of para-aortic and mediastinal lymph node dissection among such patients.

In this study, we examined the recurrence patterns and risk factors for each recurrence pattern. These results highlight the recurrence types that should be closely monitored during follow-up. Some authors reported the recurrence patterns of a small number of patients with Siewert type II EGJ carcinoma [12, 13, 16]. However, they could not examine the risk factors for each recurrence pattern owing to the small number of patients. We found that lung recurrence was more common than was peritoneal

recurrence. However, in gastric cancer, lung recurrence is rare, and peritoneal recurrence is the most frequent recurrence pattern [17, 18]. Siewert type II EGJ carcinoma is located along the borderline between the abdominal and thoracic cavities, with venous return to the azygos and portal venous system. Thus, Siewert type II EGJ carcinoma is associated with a lower risk of peritoneal recurrence and a higher risk of lung recurrence than is gastric cancer. Interestingly, patients with differentiated adenocarcinoma were at a significantly higher risk of lung recurrence as an initial recurrence than were patients with the undifferentiated type. Differentiated-type gastric cancer is known to have a higher risk of hematogenous recurrence than does the undifferentiated type of gastric cancer [17, 18]. N stage (pN2–3) and positive venous invasion were independent risk factors for liver recurrence.

This study had some limitations. First, this was a retrospective study. Second, preoperative chemotherapy was also chosen according to the preference of the surgeons in this study. Third, the surgical strategy was determined by the surgeon; thus, various surgical procedures were included in this study.

This study is one of the largest retrospective studies aimed at evaluating patients with Siewert type II EGJ carcinoma. We found that the N stage was an independent prognostic factor. Moreover, we found that para-aortic and mediastinal lymph node metastasis and recurrence rates were relatively high. With regard to each type of recurrence, the differentiated type was an independent risk factor for lung recurrence, and N stage (pN2–3) and positive venous invasion were independent risk factors for liver recurrence.

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Compliance with ethical standards

Conflict of interest The authors declare no conflicts of interest.

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