

World Journal of *Gastroenterology*

World J Gastroenterol 2017 April 21; 23(15): 2635-2818



**EDITORIAL**

- 2635 Dietary compliance in celiac disease

Freeman HJ

- 2640 Is there still a role for the hepatic locoregional treatment of metastatic neuroendocrine tumors in the era of systemic targeted therapies?

Cavalcoli F, Rausa E, Conte D, Nicolini AF, Massironi S

REVIEW

- 2651 Hepatitis B virus infection and alcohol consumption

Iida-Ueno A, Enomoto M, Tamori A, Kawada N

- 2660 Endoscopic management of pancreatic fluid collections-revisited

Nabi Z, Basha J, Reddy DN

ORIGINAL ARTICLE**Basic Study**

- 2673 Overexpression of fibrinogen-like protein 2 protects against T cell-induced colitis

Bartczak A, Zhang J, Adeyi O, Amir A, Grant D, Gorczynski R, Selzner N, Chruscinski A, Levy GA

- 2685 Changes in human hepatic metabolism in steatosis and cirrhosis

Schofield Z, Reed MAC, Newsome PN, Adams DH, Günther UL, Lalor PF

- 2696 Effect of *Lactobacillus rhamnosus* HN001 and *Bifidobacterium longum* BB536 on the healthy gut microbiota composition at phyla and species level: A preliminary study

Toscano M, De Grandi R, Stronati L, De Vecchi E, Drago L

- 2705 Effects of Hwangryunhaedok-tang on gastrointestinal motility function in mice

Kim H, Kim I, Lee MC, Kim HJ, Lee GS, Kim H, Kim BJ

- 2716 Role of $\Delta 133p53$ isoform in NF- κ B inhibitor PDTC-mediated growth inhibition of MKN45 gastric cancer cells

Zhang HM, Sang XG, Wang YZ, Cui C, Zhang L, Ji WS

Retrospective Cohort Study

- 2723 Optimal treatment for Siewert type II and III adenocarcinoma of the esophagogastric junction: A retrospective cohort study with long-term follow-up

Hosoda K, Yamashita K, Moriya H, Mieno H, Watanabe M

Retrospective Study

- 2731 Colorectal and interval cancers of the Colorectal Cancer Screening Program in the Basque Country (Spain)

Portillo I, Arana-Arri E, Idigoras I, Bilbao I, Martínez-Indart L, Bujanda L, Gutierrez-Ibarluzea I

- 2743 Performance of 18-fluoro-2-deoxyglucose positron emission tomography for esophageal cancer screening

Sekiguchi M, Terauchi T, Kakugawa Y, Shimada N, Saito Y, Matsuda T

- 2750 Association of obesity with
- Helicobacter pylori*
- infection: A retrospective study

Xu MY, Liu L, Yuan BS, Yin J, Lu QB

- 2757 Outcomes and prognostic factors of patients with stage IB and II A pancreatic cancer according to the 8
- th
- edition American Joint Committee on Cancer criteria

Li Y, Tang CG, Zhao Y, Cao WY, Qu GF

Clinical Trials Study

- 2763 Patients with non-viral liver disease have a greater tumor burden and less curative treatment options when diagnosed with hepatocellular carcinoma

Mohsen W, Rodov M, Prakoso E, Charlton B, Bowen DG, Koorey DJ, Shackel NA, McCaughan GW, Strasser SI

- 2771 Urinary metabolomics analysis identifies key biomarkers of different stages of nonalcoholic fatty liver disease

Dong S, Zhan ZY, Cao HY, Wu C, Bian YQ, Li JY, Cheng GH, Liu P, Sun MY

Observational Study

- 2785 Age-related impairment of esophagogastric junction relaxation and bolus flow time

Cock C, Besanko LK, Burgstad CM, Thompson A, Kritas S, Heddle R, Fraser RJL, Omari TI

- 2795 Endoscopic ultrasound-guided cutting of holes and deep biopsy for diagnosis of gastric infiltrative tumors and gastrointestinal submucosal tumors using a novel vertical diathermic loop

Liu YM, Yang XJ

- 2802 Non-ALT biomarkers for markedly abnormal liver histology among Chinese persistently normal alanine aminotransferase-chronic hepatitis B patients

Cheng JL, Wang XL, Yang SG, Zhao H, Wu JJ, Li LJ

CASE REPORT

- 2811 One step minilaparotomy-assisted transmesenteric portal vein recanalization combined with transjugular intrahepatic portosystemic shunt placement: A novel surgical proposal in pediatrics

Pelizzo G, Quaretti P, Moramarco LP, Corti R, Maestri M, Iacob G, Calcaterra V

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Retrospective Cohort Study

Optimal treatment for Siewert type II and III adenocarcinoma of the esophagogastric junction: A retrospective cohort study with long-term follow-up

Kei Hosoda, Keishi Yamashita, Hiromitsu Moriya, Hiroaki Mieno, Masahiko Watanabe

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Abstract

AIM

To determine the optimal treatment strategy for Siewert type II and III adenocarcinoma of the esophagogastric junction.

METHODS

We retrospectively reviewed the medical records of 83 patients with Siewert type II and III adenocarcinoma of the esophagogastric junction and calculated both an index of estimated benefit from lymph node dissection for each lymph node (LN) station and a lymph node ratio (LNR: ratio of number of positive lymph nodes to the total number of dissected lymph nodes). We used Cox proportional hazard models to clarify independent poor prognostic factors. The median duration of observation was 73 mo.

RESULTS

Indices of estimated benefit from LN dissection were as follows, in descending order: lymph nodes (LN) along the lesser curvature, 26.5; right paracardial LN, 22.8; left paracardial LN, 11.6; LN along the left gastric artery, 10.6. The 5-year overall survival (OS) rate was 58%. Cox regression analysis revealed that vigorous venous invasion (v2, v3) (HR = 5.99; 95%CI: 1.71-24.90) and LNR of > 0.16 (HR = 4.29, 95%CI: 1.79-10.89) were independent poor prognostic factors for OS.

CONCLUSION

LN along the lesser curvature, right and left paracardial LN, and LN along the left gastric artery should be dissected in patients with Siewert type II or III adenocarcinoma of the esophagogastric junction. Patients with vigorous venous invasion and LNR of > 0.16 should be treated with aggressive adjuvant chemotherapy to improve survival outcomes.

Key words: Adenocarcinoma of the esophagogastric junction; Lymph node ratio; Venous invasion; Lymph node dissection; Prognostic factor

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Core tip: We reviewed the medical records of 83 patients with Siewert type II and III adenocarcinoma of the esophagogastric junction. The median duration of observation was 73 mo. Lymph nodes along the lesser curvature, right and left paracardial lymph nodes, and lymph nodes along the left gastric artery should be dissected in patients with Siewert type II or III adenocarcinoma of the esophagogastric junction. Patients with vigorous venous invasion and lymph node ratio of > 0.16 should be treated with aggressive adjuvant chemotherapy to improve survival outcomes.

Hosoda K, Yamashita K, Moriya H, Mieno H, Watanabe M. Optimal treatment for Siewert type II and III adenocarcinoma of the esophagogastric junction: A retrospective cohort study with long-term follow-up. *World J Gastroenterol* 2017; 23(15): 2723-2730 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v23/i15/2723.htm> DOI: <http://dx.doi.org/10.3748/wjg.v23.i15.2723>

INTRODUCTION

The incidence of adenocarcinoma of the esophagogastric junction (AEG) is increasing in both Western^[1,2] and Eastern^[3-5] countries. Rüdiger Siewert *et al*^[6] have proposed a classification system for AEG and discussed its characteristics and treatment according to disease types.

Siewert types II and III are more common than Siewert type I AEG in Japan^[7,8]. The JCOG-9502 trial demonstrated that a left thoracoabdominal approach, which enables thorough lower mediastinal LN dissection, does not improve survival and leads to increased morbidity in patients with Siewert type II or III AEG with esophageal invasion of ≤ 3 cm. The JCOG0110 trial showed that spleen preservation does not impair survival in patients with proximal gastric cancer without invasion of the greater curvature, which includes Siewert type II and III AEG with esophageal invasion of ≤ 3 cm^[9]; the authors therefore concluded that spleen preservation is indicated for reasons of both operative safety and survival benefit. However, that trial was

not solely for Siewert type II and III AEG and did not include AEG with invasion of the greater curvature. Several reports have addressed the optimal extent of LN dissection in patients with AEG^[10-14]. The right and left paracardial, lesser curvature, and left gastric artery LNs should be dissected because of their high rate of metastatic involvement and the associated benefit from dissection. However, the above-cited reports focused on various types of cancers; none have evaluated the benefit of LN dissection for Siewert type II and III AEG independently.

The pathologic depth of invasion and number of LN metastases are recognized as independent prognostic factors for gastric and esophagogastric junction (EGJ) cancer. According to some studies, metastasis to mediastinal LNs is an independent risk factor for Siewert type II and III AEG^[11,15]. Others have determined that the number of examined LNs and the ratio of LNs (LNR) with metastases are significant prognostic factors for gastrointestinal cancer^[16,17]. However, because these studies were retrospective and had various biases, additional studies are needed to strengthen these findings.

We aimed to determine the optimal treatment strategy for Siewert type II and III AEG by clarifying the benefit of dissecting specific LN stations and identifying poor prognostic factors.

MATERIALS AND METHODS

AEG definition and classification

AEG is defined as adenocarcinoma that has invaded the EGJ. Siewert type II and III AEGs are defined, respectively, as having epicenters located 1 cm above to 2 cm below, and 2 cm below to 5 cm below, the EGJ. The location of the epicenter and proximal extent of the tumor are evaluated based on findings from resected specimens.

Patients

The medical records of 83 patients with Siewert type II or III AEG who had undergone R0 or R1 resection at Kitasato University between January 1998 and December 2010 were retrospectively reviewed. Patients who had received preoperative chemotherapy or chemoradiotherapy, or who had pT1a tumors, were excluded. The median duration of observation was 73 mo.

Tumor stage was classified according to the International Union Against Cancer TNM staging system, 7th edition^[18]. LN stations were classified according to the Japanese Classification of Gastric Carcinoma^[19]. The upper thoracic paraesophageal nodes and thoracic paratracheal nodes were classified as upper mediastinal LNs; the subcarinal nodes, middle thoracic paraesophageal nodes, and main bronchus nodes were classified as middle mediastinal LNs; and the lower thoracic paraesophageal nodes, supradiaphragmatic nodes, and posterior mediastinal

nodes were classified as lower mediastinal LNs. Lymph node ratio (LNR) was defined as the ratio of the number of positive LNs to the total number of dissected LNs. Log-rank plot analysis was performed to determine the threshold value of LNR for prediction of overall survival (OS). Relative risks and *P* values were calculated by prognostic analysis using the log-rank method, classifying LNR at 0.01 intervals. The highest relative risk was considered the critical point in this analysis. The degrees of lymphatic and venous invasion were defined according to the Japanese Classification of Gastric Carcinoma. Venous invasion was evaluated by histopathological examination of hematoxylin-, eosin-, and Elastica-van-Gieson-stained operative specimens; lymphatic invasion was evaluated on hematoxylin- and eosin-stained specimens. In our hospital, the following definitions apply: v0, no venous invasion found on any slide examined; v1, one or two sites of venous invasion found throughout all slides examined; v2, intermediate between v1 and v3; v3, one or more sites of venous invasions found on every slide examined. Lymphatic invasion levels of ly0, ly1, ly2, and ly3 are defined in the same way.

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of Kitasato University School of Medicine. All study participants or their legal guardians provided informed written consent for personal and medical data collection prior to study enrollment.

Surgical procedures

Surgical procedures were determined on the basis of tumor location and length of esophageal invasion. A right thoracic approach was used to perform subtotal esophagectomy and mediastinal LN dissection through a right thoracotomy, and gastric conduit reconstruction was performed through a laparotomy. A left thoracic approach through a left thoracotomy and laparotomy, and a transhiatal approach after wide splitting of the esophageal hiatus were used to perform total gastrectomy, distal esophagectomy, D2 LN dissection including splenectomy, and lower-mediastinal LN dissection. For cT1 cancer, proximal gastrectomy with either jejunal interposition or esophagogastric anastomosis was performed if possible.

Chemotherapy

Postoperative adjuvant chemotherapy was given to 29 patients. The most commonly used regimen was S-1 monotherapy (17 out of 29 patients) followed by UFT monotherapy (6 out of 29 patients).

Statistical analysis

Student's *t*-test was used to analyze continuous variables, and the χ^2 or Fisher's exact test to analyze categorical variables. Survival was calculated by the Kaplan-Meier method. Univariate analyses of prognostic factors for OS were performed using log-

rank tests. Factors with *P* < 0.10 on univariate analysis were subjected to multivariate analysis using a Cox's proportional-hazards model to identify independent prognostic factors. All calculations were performed using JMP® Pro 11.2.0 (SAS Institute, Cary, NC, United States). Values of *P* < 0.05 were considered to indicate statistical significance.

To evaluate the therapeutic value of LN dissection, we used a previously described method to circumvent the stage migration phenomenon^[20]. In brief, the frequency of metastasis to each station was determined by dividing the number of patients with metastases to that station by the number of patients in whom the station had been dissected. The 5-year OS rates of patients with metastases at each nodal station were calculated irrespective of the presence or absence of metastases at other nodal stations. An index of estimated benefit from LN dissection (IEBLD) for each station was calculated by multiplying the frequency of metastasis to the station by the 5-year survival rate of patients with metastases to that station.

RESULTS

Patient characteristics

Tumor size was significantly larger and esophageal invasion significantly shorter in type III than in type II tumors (Table 1). Pathological classifications did not differ significantly between the groups (Table 2).

Seven patients with Siewert type II AEG had R1 resection: four of them had positive abdominal lavage cytology (CY1), one had positive pleural effusion cytology, one had positive proximal and one had positive circumferential margins. Two patients with Siewert type III AEG and R1 resection had positive abdominal lavage cytology.

Estimated benefit from lymphadenectomy

Table 3 shows the number of patients with dissection and the number of patients with metastases for each LN station and the resultant IEBLDs, which in descending order were as follows (# denotes LN station): LNs along the lesser curvature (#3), 26.5; right paracardial (#1), 22.8; left paracardial (#2), 11.6; along the left gastric artery (#7), 10.6; along the distal splenic artery (#11d), 8.6; around the celiac artery (#9), 6.5; lower mediastinal LN, 6.3; and splenic hilum (#10), 5.0. No metastases were found in the lower mediastinal LNs in patients with Siewert type III AEG; such metastases were found only in patients with Siewert type II AEG.

Patients with lower mediastinal LN metastases who survived over 5 years all had Siewert type II tumors with esophageal invasion of more than 30 mm. Additionally, patients with splenic hilar LN metastases who survived over 5 years all had Siewert type II tumors with invasion of the greater curvature

Survival analysis

All patients were followed up for more than 5 years,

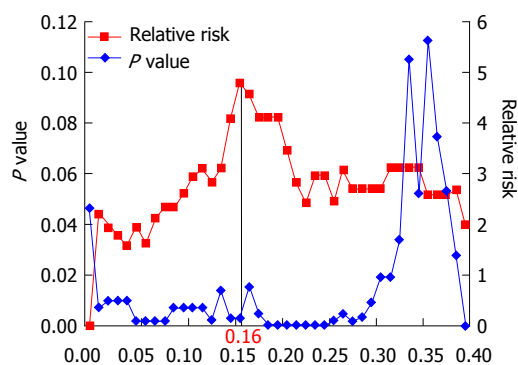


Figure 1 Optimal threshold value for lymph node ratio was determined to be 0.16 by log-rank plot analysis.

Table 1 Baseline characteristics of patients and therapeutic approaches ($n = 83$) n (%)

	Type II ($n = 62$)	Type III ($n = 21$)	<i>P</i> value
Age (yr)			0.72
Median (range)	68.5 (33-87)	69 (54-80)	
Sex			0.78
Male	49 (79)	16 (76)	
Female	13 (21)	5 (24)	
Tumor size (mm)	50 (10-168)	70 (12-120)	0.016
Esophageal invasion (mm)	9 (0-85)	5 (0-15)	0.024
Total number of examined lymph nodes	36.5 (5-96)	51 (22-80)	0.016
Approach			
Right thoracic	8 (13)	0 (0)	
Left thoracic	8 (13)	1 (5)	
Transhiatal	46 (74)	20 (95)	
Resection method			
Subtotal esophagectomy	8 (13)	0 (0)	
Total gastrectomy with distal esophagectomy	37 (60)	21 (100)	
Proximal gastrectomy with distal esophagectomy	17 (27)	0 (0)	
Adjuvant chemotherapy			0.24
Yes	19 (31)	9 (43)	
No	43 (69)	12 (57)	

Type II: Siewert type II adenocarcinoma of the esophagogastric junction;
Type III: Siewert type III adenocarcinoma of the esophagogastric junction.

except for 11 excluded patients who were lost to follow-up within the 5-year period. The 5-year OS rate was 58%. The threshold point for LNR was determined to be 0.16 (Figure 1). Univariate analysis revealed that pT, pN, mediastinal LN metastasis, LNR, lymphatic invasion, venous invasion, and residual tumor were potential prognostic factors for OS. According to Cox's regression analysis, vigorous venous invasion (v2 or v3) (HR = 5.99, 95%CI: 1.71-24.90, $P = 0.004$) and LNR of > 0.16 (HR = 4.29, 95%CI: 1.79-10.89, $P = 0.001$) were independent prognostic factors for poor OS (Table 4). The 5-year survival rate of patients with v2 or v3 was 46% and of patients with LNR of > 0.16 was 23% (Figure 2A and B); whereas that of patients without either of the independent predictors of poor prognosis (v0 or v1 and LNR of < 0.16) was 85% and

Table 2 Pathological characteristics of patients ($n = 83$) n (%)

	Type II ($n = 62$)	Type III ($n = 21$)	<i>P</i> value
T category			0.06
T1b	11 (18)	0 (0)	
T2	11 (18)	2 (10)	
T3	40 (64)	19 (90)	
N category			0.41
N0	21 (34)	4 (19)	
N1	12 (19)	6 (29)	
N2	13 (21)	3 (14)	
N3	14 (23)	6 (29)	
LNR	0.063 (0-1)	0.047 (0-0.41)	0.74
M category			0.64
M0	58 (94)	19 (90)	
M1	4 (6)	2 (10)	
TNM stage			0.30
I A	10 (16)	0 (0)	
I B	5 (8)	0 (0)	
II A	6 (10)	4 (19)	
II B	5 (8)	1 (5)	
III A	8 (13)	5 (24)	
III B	11 (18)	3 (14)	
III C	12 (19)	6 (29)	
IV	5 (8)	2 (10)	
ly category			0.35
ly0	8 (13)	0 (0)	
ly1	16 (26)	5 (24)	
ly2	22 (35)	9 (43)	
ly3	16 (26)	7 (33)	
v category			0.55
v0	7 (11)	3 (14)	
v1	13 (21)	4 (19)	
v2	24 (39)	5 (24)	
v3	18 (29)	9 (43)	
Histopathological grade			0.56
G1 + G2	37 (60)	11 (52)	
G3 + G4	25 (40)	10 (48)	

Type II: Siewert type II adenocarcinoma of the esophagogastric junction;
Type III: Siewert type III adenocarcinoma of the esophagogastric junction;
LNR: Lymph node ratio; ly: Lymphatic invasion; v: Venous invasion.

of patients with both of these predictors (v2 or v3, and LNR of > 0.16), 13% (Figure 2C).

Recurrence occurred in 30 of the study patients. In all six patients with CY1 the first recurrence site was peritoneal. The initial recurrence sites of the other patients were as follows: peritoneum, 8; liver, 6; lung, 3; bone, 1; adrenal, 1; abdominal LNs, 8; upper or middle mediastinal LNs, 3; and local, 3. Of the eight patients with first recurrence in abdominal LNs, three developed recurrence only in para-aortic LNs. All three patients with mediastinal LN recurrence had simultaneous liver, generalized LN, and para-aortic LN recurrence.

DISCUSSION

This study had two major findings. First, LNs in stations 1, 2, 3, and 7 had high IEBLDs, as previously reported^[10-12] and should therefore be dissected

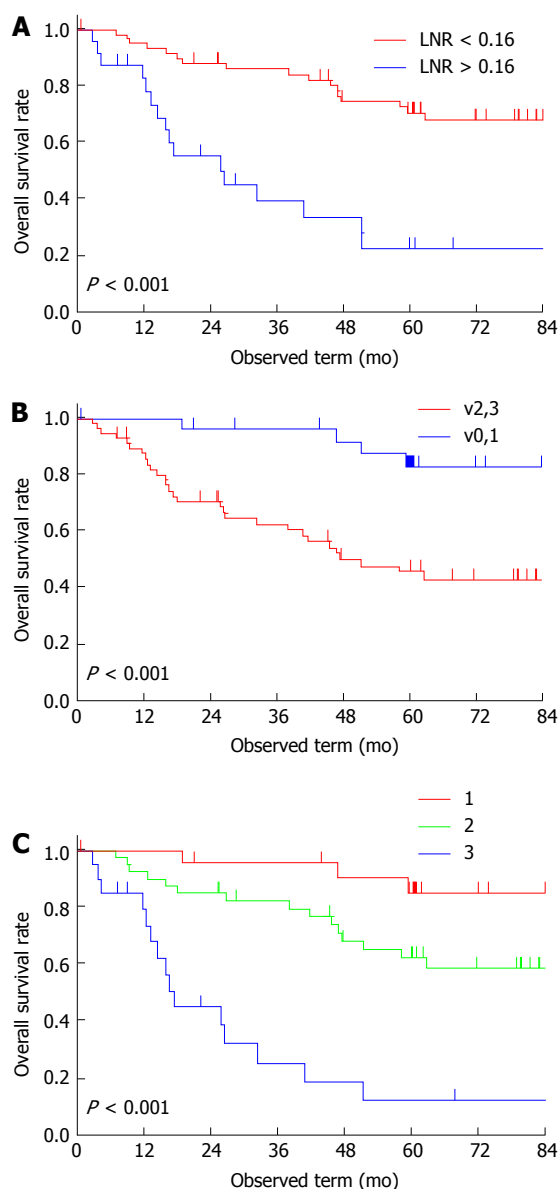


Figure 2 Kaplan-Meier curves for overall survival stratified by lymph node ratio of > 0.16 or < 0.16 (A), by v0/v1 or v2/v3 (B), and by the number of these independent prognostic factors.

in patients with Siewert type II or III AEG. Second, vigorous venous invasion (v2 or v3) and LNR of > 0.16 are independent predictors of poor OS.

Regarding splenic hilar LN dissection, the JCOG0110 study reported that splenectomy had little impact on survival of patients with proximal gastric cancer that did not invade the greater curvature^[9]. Goto *et al.*^[21] concluded that splenectomy could be omitted from the treatment of AEG because of its high complication rate and minor impact on survival. However, the JCOG0110 study excluded patients with tumors that did invade the greater curvature. In addition, our current study revealed that splenic hilar LNs had a small, but not negligible, IEBLD. We therefore believe that splenectomy should not necessarily be omitted for patients with AEG who have extensive invasion of the greater curvature.

The JCOG9502 study reported no benefit for lower mediastinal LN dissection through a left thoracoabdominal approach in patients with ≤ 3 cm esophageal invasion^[22]. Our current study confirmed that patients with tumors affecting ≤ 3 cm of the esophagus achieved no benefit from lower mediastinal LN dissection. In addition, a transthoracic approach was proven to increase pulmonary complications^[22,23]. Therefore, thorough lower-mediastinal LN dissection through a right or left thoracic approach would be unnecessary for these patients. If we changed our approach to include only a laparotomy (laparoscopy) in patients with tumors affecting ≤ 3 cm of the esophagus, it appears that it would not impair survival outcomes and would reduce postoperative complications. However, Siewert type II AEG with ≥ 2 cm esophageal invasion is associated with metastasis to lower mediastinal LNs^[24]. No standard surgical approach has been defined for AEG with esophageal invasion of > 3 cm. In the current study, patients who benefitted from lower mediastinal LN dissection had tumors with > 3 cm esophageal invasion. We therefore consider lower mediastinal LN dissection is likely important for patients with > 3 cm of esophageal invasion. We recommend a left or right thoracic approach for patients with esophageal invasion of > 3 cm because with a transhiatal approach, lower mediastinal LN dissection may be inadequate and the proximal margin may not be cancer-free. Relatively few patients underwent upper or middle mediastinal LN dissection; however, the IEBLDs for these LNs were zero. Additionally, patients whose first recurrence site was upper or lower mediastinal LNs had simultaneous distant metastases. Upper or middle mediastinal LN dissection needs to be performed cautiously in patients with Siewert type II or III AEG.

In the current study, v2 or v3 and LNR of > 0.16 were identified as independent predictors of poor OS. Because both v2 or v3 and LNR of > 0.16 cannot be diagnosed preoperatively, postoperative adjuvant chemotherapy would likely improve prognoses of such high-risk patients. Either v2 or v3 is reportedly an independent prognostic factor for Stage IB node-negative gastric cancer^[25]. Venous invasion theoretically predicts hematological metastases, and lymphatic invasion, LN metastases. Therefore, it is unsurprising that v2 and v3 were identified as independent prognostic factors for Siewert type II and III AEG, which tend to metastasize hematologically.

LNR is reportedly an independent prognostic factor for esophagogastric cancer^[16,26]. In Western countries, extended LN dissection is seldom performed for gastric or esophagogastric cancer; thus, an average of about 15 LNs are dissected, resulting in under-diagnosis of the number of LNs with metastases^[17]. Therefore, LNR rather than the number of LNs with metastases is thought to be a more useful prognostic indicator. In the current study, though the total number of examined LNs was relatively large (median 36.5, range 5-96 for Siewert type II; median 51, range 22-80 for Siewert

Table 3 Incidence, 5-year survival rate, and index of estimated benefit from lymph node dissection

Lymph node station	Type II		Type III		Total		5-yr survival rate	IEBLD
	Number of patients with dissection	Number of patients with metastasis	Number of patients with dissection	Number of patients with metastasis	Number of patients with dissection	Number of patients with metastasis		
1	62	27	21	11	83	38	49.70%	22.8
2	62	14	21	5	83	19	50.70%	11.6
3	62	27	21	14	83	41	53.70%	26.5
4sa	42	1	18	0	60	1	0	0.0
4sb	43	1	19	1	62	2	100%	3.2
4d	39	0	20	0	59	0	NA	0.0
5	25	0	14	1	39	1	0	0.0
6	31	0	21	0	52	0	NA	0.0
7	58	17	21	6	79	23	36.30%	10.6
8	42	4	21	2	63	6	20.80%	2.0
9	32	5	14	2	46	7	42.90%	6.5
10	28	3	12	0	40	3	66.70%	5.0
11p	33	4	19	0	52	4	33.30%	2.6
11d	24	4	11	1	35	5	60%	8.6
12	2	0	1	0	3	0	NA	0.0
16	2	0	0	0	2	0	NA	0.0
LMLN	13	5	3	0	16	5	20%	6.3
MMLN	8	1	0	0	8	1	0	0.0
UMLN	7	1	0	0	7	1	0	0.0

IEBLD: Index of the estimated benefit of lymph-node dissection; Type II: Siewert type II adenocarcinoma of the esophagogastric junction; Type III: Siewert type III adenocarcinoma of the esophagogastric junction; LMLN: Lower mediastinal lymph-node; MMLN: Middle mediastinal lymph-node; UMLN: Upper mediastinal lymph-node.

Table 4 Prognostic analysis in patients with adenocarcinoma of the esophagogastric junction

Category	Classification	Univariate analysis				Multivariate analysis				
		<i>n</i>	Proportion	5 yr-OS	<i>P</i> value	HR	95%CI	<i>P</i> value		
Age (yr)	< 65	29	35%	67%	0.084	4.29	1.79-10.89	0.47		
	≥ 65	54	65%	52%						
Sex	Male	65	78%	56%	0.57					
	Female	18	22%	67%						
Siewert type	II	62	75%	58%	0.88					
	III	21	25%	57%						
Esophageal invasion	≤ 3 cm	73	88%	60%	0.21					
	> 3 cm	10	12%	40%						
Tumor size	< 6 cm	45	54%	58%	0.86					
	≥ 6 cm	38	46%	58%						
pT	pT1-2	24	29%	77%	0.01 ^a			0.001 ^a		
	pT3	59	71%	50%						
pN	pN0	25	30%	78%	0.028 ^a				0.30	
	pN1-3	58	70%	49%						
Mediastinal LN meta	No	78	94%	60%	0.007 ^a				0.17	
	Yes	5	6%	20%						
LNR	< 0.16	59	71%	71%	< 0.001 ^a					
	> 0.16	24	29%	23%						
ly	ly0, 1	29	35%	69%	0.059				0.13	
	ly2, 3	54	65%	52%						
v	v0, 1	27	33%	83%	< 0.001 ^a				0.004 ^a	
	v2, 3	56	67%	46%						
Histopathological Grade	G1 + G2	48	58%	60%	0.28				5.99	1.71-24.90
	G3 + G4	35	42%	55%						
Adjuvant chemotherapy	No	54	65%	56%	0.52					
	Yes	29	35%	61%						
Residual tumor	R0	74	89%	62%	< 0.001 ^a				2.61	0.97-6.59
	R1	9	11%	22%						

AEG: Adenocarcinoma of the esophagogastric junction; OS: Overall survival; HR: Hazard ratio; LNR: Lymph node ratio; ly: Lymphatic invasion; v: Venous invasion. ^a*P* < 0.05.

type III), the same was shown to be true. Where the extent of LN dissection is not standardized, LNR may be a more relevant prognostic indicator than the number of LNs with metastases in Siewert type II and III AEG.

In Japan, the standard treatment for resectable gastric adenocarcinoma, including AEG, is gastrectomy with D2 LN dissection followed by adjuvant chemotherapy using S1^[27]. However, adjuvant chemotherapy with S1 reportedly has inadequate power to prevent hematological metastases and improve OS of patients with pStage IIIB gastric cancer^[28]. In the CLASSIC trial, capecitabine plus oxaliplatin improved recurrence-free survival even in patients with pStage IIIB gastric cancer and well-controlled distant metastases^[29]. Considering that hematological metastasis occurs relatively frequently in Siewert type II and III AEG, patients with AEG, and with mild or marked venous invasion and/or LNR of > 0.16, should receive aggressive adjuvant chemotherapy using a platinum-containing regimen such as capecitabine plus oxaliplatin.

This study has several limitations. First, it was a single-center, retrospective, observational study with various biases. Second, during the lengthy accrual period various regimens of adjuvant chemotherapy were used. Third, various surgical procedures, including subtotal esophagectomy, proximal gastrectomy with lower esophagectomy, and total gastrectomy with lower esophagectomy were performed, and the extent of LN dissection was not standardized, which may have resulted in bias in the IEBLD. Almost no patients underwent dissection of para-aortic LNs. The incidence of metastases in para-aortic LNs around the left renal vein is reportedly 17% and the 5-year survival rate of node-positive patients is 19%^[30]. In the current study, para-aortic LNs were the first recurrence site in three patients. In Japan, a multicenter clinical study is evaluating the efficacy of mediastinal and para-aortic LN dissection in EGJ cancer (UMIN000013205). This study will provide useful information about the optimal extent of LN dissection for EGJ cancer.

In conclusion, based on our findings we recommend the following: LNs in stations 1, 2, 3, and 7 should be dissected in Siewert type II and III AEG because of their high IEBLDs. Patients with vigorous venous invasion or LNR of > 0.16 should receive aggressive adjuvant chemotherapy to improve survival outcomes. Patients with esophageal invasion of > 3 cm should undergo dissection of inferior mediastinal LNs, and those with invasion of the greater curvature should undergo dissection of splenic hilar LNs.

COMMENTS

Background

The incidence of adenocarcinoma of the esophagogastric junction (AEG) is increasing in both Western and Eastern countries. Siewert *et al.* have proposed a classification system for AEG and discussed its characteristics and treatment according to disease types.

Research frontiers

In patients with Siewert type II or III AEG, a left thoracoabdominal approach, which enables thorough lower mediastinal lymph node (LN) dissection, was demonstrated not to improve survival and to lead to increased morbidity. The right and left paracardial, lesser curvature, and left gastric artery LNs should reportedly be dissected because of their high indices of estimated benefit of lymph node dissections (IEBLDs). The ratio of the number of positive LNs to the total number of dissected LNs (LNR) has been reported to be a significant prognostic factor for gastrointestinal cancer including AEG. However, these claims are based on clinical studies of various types of esophagogastric junction cancer and additional studies are needed to strengthen these findings specifically for Siewert type II or III AEG, which is a prevalent form in Eastern countries including Japan.

Innovations and breakthroughs

This study included only Siewert type II or III AEG. IEBLDs were again higher in the right and left paracardial, lesser curvature, and left gastric artery LNs. Vigorous venous invasion (v2 or v3) and LNR of > 0.16 were independent predictors of poor OS. IEBLDs of splenic hilar and lower mediastinal LN were 5.0 and 6.3, respectively. Patients who survived more than 5 years with splenic hilar LN and lower mediastinal LN involvement had tumors with esophageal invasion of more than 30 mm and with invasion of the greater curvature, respectively.

Applications

The right and left paracardial, lesser curvature, and left gastric artery LNs should be dissected in Siewert type II and III AEG because of their high IEBLDs. Patients with vigorous venous invasion or LNR of > 0.16 should receive aggressive adjuvant chemotherapy to improve survival outcomes. Patients with esophageal invasion of > 3 cm should undergo dissection of inferior mediastinal LNs, and those with invasion of the greater curvature should undergo dissection of splenic hilar LNs.

Terminology

The LNR was the ratio of the number of positive LNs to the total number of dissected LNs. An IEBLD was calculated by multiplying the frequency of metastasis to a specified station by the 5-year OS rate of patients with metastases to that station.

Peer-review

Hosoda *et al* present a retrospective case series of esophagogastric junction tumors to show the prognostic of lymph node dissection. The manuscript is interesting with a significant number of patients and a long follow-up.

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