Lymph node involvement in advanced gastroesophageal junction adenocarcinoma

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Objective: The prognosis of gastroesophageal junction adenocarcinoma is unquestionably related to the extent of nodal involvement; nonetheless, few studies deal with the pattern of lymph node spread and specifically analyze the prognostic value of the site of metastasis. The present study was aimed at evaluating these key aspects in advanced gastroesophageal junction adenocarcinoma.

Methods: Of 219 patients consecutively operated on for gastroesophageal junction adenocarcinoma at the Department of General Surgery and Surgical Oncology, University of Siena, and at the Department of General Surgery, University of Verona, 143 pT2-4 tumors not submitted to prior chemoradiation were analyzed according to the Japanese Gastric Cancer Association pN staging system.

Results: The majority of patients were given diagnoses of nodal metastases (77.6%). The mean number ($P = .076$) and the percentage of patients with pN⁺ disease ($P = .022$) progressively increased from Siewert type I to type III tumors. Abdominal nodes were involved in all but 1 of the patients with pN⁺ disease; conversely, nodal metastases into the chest were 46.2% for type I, 29.5% for type II, and 9.3% for type III tumors. Survival analysis showed virtually no chance of recovery for patients with more than 6 metastatic nodes or lymph nodes located beyond the first tier.

Conclusions: In advanced gastroesophageal junction adenocarcinoma, the high frequency of nodal metastases and the related unfavorable long-term outcome achieved by means of surgical intervention alone are indicative of the need for aggressive multimodal treatment along with surgical intervention to improve long-term results.

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Adenocarcinoma of the gastroesophageal junction (GEJ) remains a neoplasia of great interest in view of the remarkable increase of incidence observed during the last decades^{1,2} and of the unfavorable long-term results achieved by means of surgical intervention alone, even after extended resections.³⁻⁵ The prognosis of GEJ adenocarcinoma is unquestionably related to the extent of nodal involvement,^{6,7} which is complicated by the regional lymphatic drainage of the tumor evenly above and below the diaphragm.^{8,9}

The Japanese literature and some dedicated Western centers extensively investigated the pattern of lymph node spread in stomach cancer to characterize the pattern of dissemination, to define the appropriate extent of nodal dissection, and to evaluate the related prognostic significance.¹⁰⁻¹²

The mode of diffusion of GEJ adenocarcinoma is less known, and the pattern of lymph node spread and its prognostic significance have not yet been investigated in this tumor. The present study was aimed at considering these key aspects in GEJ adenocarcinoma.

Abbreviations and Acronyms

GEJ = gastroesophageal junction

JGCA = Japanese Gastric Cancer Association

Materials and Methods**Inclusion Criteria and Study Population**

GEJ adenocarcinoma was defined according to the Siewert classification.¹³ The most important inclusion criteria were histologic diagnosis of adenocarcinoma; no preoperative chemotherapy, radiotherapy, or both; locally advanced tumor (pT2, pT3, and pT4); macroscopic curative resection (R0-R1); no systemic metastasis; no history of secondary malignancy; and possibility of follow-up with a minimum follow-up period of 18 months. Informed consent was obtained from all the patients, and the study was approved by the local ethics committee.

Two hundred nineteen patients affected by GEJ adenocarcinoma underwent resection at the Department of General Surgery and Surgical Oncology, University of Siena, between January 1995 and June 2004 and at the Department of General Surgery, University of Verona, between January 1988 and June 2004. Among these, 76 patients did not match the inclusion criteria and were hence excluded from the analysis. In particular, 39 patients underwent preoperative chemoradiotherapy (type I, 17 patients; type II, 22 patients),¹⁴ 19 patients underwent macroscopic noncu-

rative (R2) surgical intervention (type II, 10 patients; type III, 9 patients), and a pT1 tumor was diagnosed in 18 patients (type I, 7 patients; type II, 8 patients; type III, 3 patients).

Clinical, histopathologic, and follow-up data of the 143 patients under study were prospectively collected and presented in Table 1. The median age of the cohort was 68 years (range, 27-90 years), with a male/female ratio of 4.5 to 1.

Staging Work-up

Preoperative work-up included a barium swallow, esophagogastros-
troscopy with biopsy, and computed tomography of the chest and abdomen in every case. Endoscopic ultrasonography was performed in 79 patients, whereas neither thoracoscopy nor laparoscopy was used in this series of patients for evaluation of tumor resectability or staging.

Surgical Intervention

Surgical resection and mode of reconstruction have been previously described in detail.³ Briefly, the standard procedure for type I tumors was a right thoracotomy with a subtotal esophagectomy above the azygos vein with proximal gastric resection. The procedure of choice for type III tumors was a total gastrectomy with transhiatal resection of the distal esophagus. A transthoracic approach was necessary in 2 cases. Type II tumors were treated with subtotal esophagectomy, as in type I cancers, or with total gastrectomy with transhiatal or transthoracic resection of the distal

TABLE 1. Main clinicopathologic characteristics according to Siewert classification for the 143 patients under study*

Variable	Siewert type			P value
	Type I (n = 20)	Type II (n = 62)	Type III (n = 61)	
Age (y)				.937
Median (range)	68 (27–90)	67 (27–90)	68 (36–82)	
Sex				.137
Male (n = 117)	19 (95)	47 (75.8)	51 (83.6)	
Female (n = 26)	1 (5)	15 (24.2)	10 (16.4)	
Lauren type				.117
Intestinal (n = 102)	16 (80)	48 (77.4)	38 (62.3)	
Nonintestinal (n = 41)	4 (20)	14 (22.6)	23 (37.7)	
Depth of invasion (pT)				.007
pT2 (n = 62)	9 (45)	32 (51.6)	21 (34.4)	
pT3 (n = 69)	11 (55)	29 (46.8)	29 (47.5)	
pT4 (n = 12)†	—	1 (1.6)	11 (18)	
Nodal involvement (pN)				.022
pN0 (n = 32)	7 (35)	18 (29)	7 (11.5)	
pN+ (n = 111)	13 (65)	44 (71)	54 (88.5)	
No. of positive nodes				.036
0 (n = 32)	7 (35)	18 (29)	7 (11.5)	
1–6 (n = 53)	9 (45)	21 (33.9)	23 (37.7)	
>6 (n = 58)	4 (20)	23 (37.1)	31 (50.8)	
Mean (± SD) no. of positive nodes	4.2 (7.4)	7.5 (10.3)	10.4 (13.1)	.076
R category				.474
R0 (n = 129)	19 (95)	57 (91.9)	53 (86.9)	
R1 (n = 14)‡	1 (5)	5 (8.1)	8 (13.1)	

SD, Standard deviation. *Numbers in parentheses are percentages. †R0 resection was achieved in 10 (83.3%) of 12 patients with pT4 disease. ‡Microscopic residual disease was at the proximal resection margin in 9 patients, at the distal resection margin in 1 patient, and in peritoneal washing in 4 patients.

esophagus, as in type III tumors; the type of resection was chosen to obtain clear proximal and distal margins and adequate lymphadenectomy. After subtotal esophagectomy, reconstruction was performed with a gastric tube, whereas a jejunal Roux-en-Y reconstruction was performed after total gastrectomy.

Lymph node dissection was classified according to the Japanese Gastric Cancer Association (JGCA) rules: D1 lymphadenectomy (resection of perigastric nodes in positions 1-4s), D2 lymphadenectomy (resection of nodes in positions 1-11), and D3 lymphadenectomy (resection extended to the nodes in positions 12-16).¹⁵ The preferred lymph node dissection was a standard mediastinal (including paraesophageal, tracheal bifurcation, right bronchial, posterior mediastinal, and diaphragmatic nodes) and D2 abdominal lymphadenectomy for type I tumors and D2-D3 abdominal lymphadenectomy added to nodes of the lower posterior mediastinum for type II and III tumors. Lymphadenectomy at the splenic hilum was limited to patients with enlarged nodes or tumors reaching the gastric fundus, and it was achieved by means of pancreas-preserving splenectomy. D1 dissection was reserved for high-risk patients.

Pathologic Staging and Assignment to JGCA

Nodal Station

Considering the depth of tumor invasion (pT), American Joint Committee on Cancer and International Union Against Cancer rules for esophageal cancer were adopted in Siewert type I tumors, whereas those for gastric cancer were used in Siewert type II and III tumors.¹⁶ Regarding nodal staging (pN), both the number and site of nodal metastasis were evaluated in each case. The number-based classification was derived from the American Joint Committee on Cancer and International Union Against Cancer classification for gastric cancer,¹⁶ and 3 classes were considered: no positive nodes, 1 to 6 positive nodes, and greater than 6 positive nodes. The site-based classification adhered to the criteria stated by the JGCA.¹⁵ Perivisceral lymph nodes were dissected from the excised specimen by the surgeon immediately after resection, assigned to the appropriate station according to the JGCA classification, and sent for histologic examination. The second- and third-tier nodes were subdivided by the surgeon himself during lymphadenectomy, as described in a previous study,¹⁷ to avoid errors caused by difficulties in assigning nodes to the correct lymph node station after en bloc resection.

According to the JGCA, stations 1, 2, 3, and 4s were regarded as first-tier nodes; inversely, other lymph nodes were termed non-first tier. Additionally, paraesophageal nodes of the lower third (station 110) were considered as first-tier nodes in type I tumors.

The histologic classification followed the criteria of Lauren, and mixed-type tumors were considered together with the diffuse type (nonintestinal type).

Follow-up

After discharge from the hospital, all patients were followed up after 4 months and subsequently at 6-month intervals until their death or the time of study (December 2005). None of the patients was lost to follow-up. The median follow-up period for surviving patients was 46.5 months (range, 18.2-208.1 months).

Statistical Analysis

The χ^2 test was used for categorical data and the analysis of variance test for continuous variables was used to evaluate the significance of differences among Siewert types.

Survival curves were estimated by using the Kaplan-Meier method and compared by using the log-rank test. Multivariate analysis was performed with the Cox regression model to evaluate the independent prognostic value of lymph node involvement. Relative risks in relation to the site and number of nodal metastases were considered separately and derived by controlling for age, sex, Siewert type, Lauren type, pT, and R category. Deaths from causes other than GEJ adenocarcinoma were considered censored observations at the time of death. Patients who died during the postoperative period were computed in survival analysis. Analyses were performed with the Statistical Product and Service Solutions (SPSS 12.0 for Windows XP; SPSS, Inc, Chicago, Ill).

Results

In the series of 143 patients, a total of 5357 lymph nodes was retrieved and analyzed, with a mean number $\pm$ SD per patient of 37.5 ± 20.3 . The mean $\pm$ SD number of dissected nodes was 23.4 ± 10.8 for type I, 37.3 ± 19.9 for type II, and 42.3 ± 21.1 for type III tumors ($P < .001$). A mean $\pm$ SD of 18.8 ± 10.1 nodes was removed by means of D1 lymphadenectomy, 35.2 ± 17.1 by means of D2 lymphadenectomy, and 47.8 ± 20.5 by means of D3 lymphadenectomy ($P < .001$).

Incidence of Nodal Metastases

Metastases were diagnosed in 1186 lymph nodes in 111 (77.6%) patients for a mean $\pm$ SD of 8.3 ± 11.4 . The mean $\pm$ SD number ($P = .076$) and the percentage of patients with pN⁺ disease ($P = .022$) progressively increased from type I to type III tumors (Table 1). The incidence of nodal metastases, as well as the mean number of involved nodes ($P = .042$), significantly correlated with the depth of tumor invasion (pT). Lesions with invasion limited to the visceral wall (pT2) had a 61.3% incidence of pN⁺ disease; it was 88.4% for pT3 tumors, whereas all pT4 lesions showed nodal metastases ($P < .001$). More than 6 metastatic nodes were present in 18 (29.0%) patients with pT2 disease, in 31 (44.9%) patients with pT3 disease, and in 9 (75%) patients with pT4 disease ($P < .001$).

Distribution of Nodal Metastases

The conformity and pertinence of lymphadenectomy evaluated according to the total/mean number of retrieved nodes for each JGCA station and to the percentage of patients in which each single JGCA station had been retrieved are reported in Table 2. Figure 1 correlates the distribution of nodal metastases with the location of the tumor according to Siewert classification.

The site and level of nodal metastases for the 3 Siewert types in the 111 node-positive patients is reported in

TABLE 2. Conformity and pertinence of lymphadenectomy according to Siewert classification for the 143 patients under study*

Lymph node station (JGCA)		Total/mean no. of retrieved nodes		
		Type I	Type II	Type III
1	Right paracardial	49/2.6 (95)	257/4.4 (95.2)	190/3.7 (85.2)
2	Left paracardial	37/2 (95)	158/2.7 (93.5)	83/1.8 (77)
3	Lesser curvature	101/5.1 (100)	413/6.8 (98.4)	533/8.7 (100)
4s	Greater curvature	10/0.8 (60)	101/1.9 (83.9)	155/3.4 (75.4)
4d	Right gastroepiploic artery	2/1 (10)	123/2.9 (67.7)	168/3.7 (75.4)
5	Suprapyloric	—	44/1.1 (67.7)	26/0.6 (72.1)
6	Infrapyloric	—	148/3.7 (64.5)	168/3.6 (77)
7	Left gastric artery	30/2 (75)	160/3.0 (87.1)	136/2.8 (80.3)
8	Common hepatic artery	23/2.1 (55)	180/4.0 (72.1)	144/4.2 (55.7)
9	Celiac trunk	29/2.4 (60)	117/2.9 (64.5)	129/3.7 (57.4)
10	Splenic hilum	2 (5)	37/1.8 (33.9)	78/2.8 (45.9)
11	Splenic artery	21/1.9 (55)	72/2.0 (58.1)	69/2.3 (49.2)
12	Hepatoduodenal ligament	8/2 (20)	66/2.8 (38.7)	93/3.9 (39.3)
16	Para-aortic	—	140/5.4 (41.9)	174/6.4 (44.3)
107	Subcarinal	32/2.3 (70)	38/2.1 (29)	8/4 (3.3)
108	Paraesophageal middle third	22/1.5 (75)	22/1.7 (21)	4/2 (3.3)
110	Paraesophageal lower third	39/2.3 (85)	65/1.9 (54.8)	40/2.1 (31.1)
111	Supradiaphragmatic	22/1.6 (70)	40/1.6 (40.3)	40/1.8 (35.5)
112	Posterior mediastinal	34/2.1 (80)	62/2.2 (45.1)	46/2.1 (35.5)

JGCA, Japanese Gastric Cancer Association. *Numbers in parentheses represent the percentage of patients in which each single Japanese Gastric Cancer Association station has been retrieved.

Table 3. All but 1 of the patients with pN⁺ disease showed an involvement of abdominal nodes (99.1%); conversely, nodal metastases into the chest were diagnosed in 6 (46.2%) type I, 13 (29.5%) type II, and 5 (9.3%) type III tumors.

Survival Analysis

Table 4 reports survivals according to the main clinicopathologic characteristics of the cohort under study. It is noteworthy that virtually no chance of recovery was observed for patients with more than 6 metastatic nodes ($P < .001$).

Survival according to the presence of nodal metastasis is reported for each JGCA nodal station in **Table 5**. Remarkably, among patients with pN⁺ disease, long-term survival was restricted to a small proportion of patients with involvement limited to the first-tier perigastric nodes. One patient with deposits in a single lymph node located at the left gastric artery (station 7) survived beyond 60 months.

Multivariate analysis confirmed the independent prognostic value of nodal involvement, both considering the number (relative risk with respect to pN0, 2.20 [95% CI, 1.10–4.39 with 1–6 nodes] and 5.00 [95% CI, 2.47–10.12 with >6 nodes]; $P < .001$) and site (relative risk with respect to pN0, 1.86 [95% CI, 0.90–3.84 with first-tier nodes] and 4.13 [95% CI, 2.11–8.12 with non-first-tier nodes]; $P < .001$) of nodal metastases.

Discussion

The major findings of the present study are as follows: (1) nodal involvement is confirmed as a common event in advanced GEJ adenocarcinoma; (2) the pattern of lymph node spread herein observed was somewhat different among the 3 Siewert types; (3) abdominal nodes were involved in almost all patients with pN⁺ disease; and (4) long-term survival was mostly limited to patients with pN0 disease and to patients with fewer than 7 metastatic nodes located within the first tier.

Reported data about the nodal spread of GEJ adenocarcinoma are scanty and hard to compare because of a lack of an overall consensus on the definition, staging, and treatment of this tumor.^{9,13,18,19}

Surgical treatment is considered the mainstay of therapy, and its founding oncologic principle is focused on the completeness of tumor removal (R0 resection), which has proved to be essential for achieving long-term survival.^{3,20,21} Prognosis of GEJ adenocarcinoma is poor because advanced depth of invasion of the visceral wall and lymph node involvement are usually present at onset^{3,18,22}; accordingly, more than three fourths of our patients were diagnosed with nodal deposits. As is well established, lymph node involvement proved to be a significant predictor of survival^{6,7,23} and a major determinant of locoregional recurrence.^{24,25} For these reasons, lymphadenectomy is considered key in the surgical

Figure 1. Percentage of nodal involvement to each Japanese Gastric Cancer Association (JGCA) lymph node station according to the tumor location (Siewert type I, type II, and type III) for the 143 patients under study.

treatment of this tumor. Nonetheless, great controversy continues over the optimal extent of lymph node dissection in the absence of prospective randomized trials demonstrating a clear benefit of extended versus limited lymphadenecto-

TABLE 3. Location of nodal metastases according to Siewert classification for the 111 patients with pN⁺ disease*

	Siewert type		
	Type I (n = 13)	Type II (n = 44)	Type III (n = 54)
Level of nodal metastasis			
First tier (n = 43)	6 (46.2)	15 (34.1)	22 (40.7)
Non-first tier (n = 68)	7 (53.8)	29 (65.9)	32 (59.3)
Site of nodal metastasis			
Abdomen (n = 87)	7 (53.8)	31 (70.5)	49 (90.7)
Abdomen and chest (n = 23)	6 (46.2)	13 (29.5)	4 (7.4)
Chest (n = 1)	—	—	1 (1.9)

*Numbers in parentheses are percentages.

mies.²⁶⁻²⁸ In addition, understanding the mode in which GEJ adenocarcinoma spreads to lymph nodes and the related prognostic significance is helpful in defining the appropriate extent of nodal dissection and in tailoring the most appropriate treatment for this tumor.

As already seen in radioisotope lymphography²⁹ and reported in clinical studies,^{8,9,30,31} lymphatic pathways are mainly directed toward the abdomen. In fact, abdominal tiers were involved in virtually all patients with pN⁺ disease, and metastases confined to abdominal nodes were 90.7%, 70.5%, and 53.8% in type III, type II, and type I tumors, respectively. Conversely, the overall rate of nodal metastases into the chest were 46.2% for type I, 29.5% for type II, and 9.3% for type III tumors, and isolated metastases to mediastinal nodes were rarely observed (1 patient).

In Siewert type I tumors paraesophageal nodes of the lower third (station 110) were infiltrated in 1 of 4 patients, whereas metastases were less frequently diagnosed in type II (12.9%) and type III (3.3%) tumors. Dresner and colleagues⁸ reported double that rate of paraesophageal node

TABLE 4. Survival according to main clinicopathologic characteristics for the 143 patients under study

Lymph node station (JGCA)	No. of patients (no. alive)	Median survival*	5-y survival†	P value‡
Age				.200
<Median	71 (25)	21.4	27.7	
≥Median	72 (18)	19.0	22.2	
Sex				.643
Male	117 (34)	19.0	22.6	
Female	26 (9)	19.3	33.5	
Siewert type				.401
Type I	20 (5)	15.5	18.7	
Type II	62 (22)	23.5	27.1	
Type III	61 (16)	17.4	24.5	
Lauren type				<.001
Intestinal	102 (36)	23.5	30.4	
Nonintestinal	41 (7)	12.9	10.4	
Depth of invasion (pT)				<.001
pT2	62 (26)	36.3	35.2	
pT3	69 (15)	16.9	18.4	
pT4	12 (2)	7.4	0	
No. of positive nodes				<.001
0	32 (20)	—	53.9	
1-6	53 (15)	20.0	25.9	
>6	50 (8)	12.7	3.9	
Level of positive nodes				<.001
pN0	32 (20)	—	53.9	
First tier	43 (13)	19.5	28.7	
Non-first tier	68 (10)	14.7	5.5	
R category				<.001
R0	129 (43)	22.3	27.8	
R1	14 (0)	6.9	0	

JGCA, Japanese Gastric Cancer Association. *For pN0, median survival was beyond the observation period. †Five-year survival was calculated by using the Kaplan–Meier method. ‡P value was computed by using the log-rank test.

involvement in 104 cases of type I cancers and a percentage of about 5% in 48 cases of type II tumors. On the other hand, the incidence of metastases to supradiaphragmatic (station 111) and lower mediastinal nodes are comparable (station 112), with data reported by Dresner and colleagues⁸ and Yuasa and associates.³² As reported in Table 2, only about one third of patients with Siewert type III tumors had mediastinal lymph nodes retrieved. This is due to the fact that two thirds of tumors reached the GEJ with a marginal invasion of the esophagus, and hence the involvement of mediastinal stations was considered unusual. Certainly, this statement cannot be regarded as definitive without a complete clearing of chest nodes in each case.

Subcarinal node (station 107) involvement was identified in 5% of type I and 1.6% of type II tumors. Nigro and coworkers⁹ reported slightly higher percentages in 8 (13%) cases of distal esophageal and in 36 (8.3%) cases of GEJ

adenocarcinoma in patients who underwent en bloc esophagectomy for tumors with transmural growth. Dresner and colleagues,⁸ in the above-mentioned study, recorded a percentage of about 10% in type I and 0% in type II cancers.

Taking into account abdominal lymphatic spread, lesser curvature (station 3) and right paracardial nodes (station 1) were the most frequently involved. Less common was the involvement of stations along the left side of the stomach (stations 2, 4, and 6).

Altogether, the 3 Siewert types often spread to second-tier abdominal nodes. Above all, left gastric artery nodes (station 7) were affected in 20% of type I (14%–60%), 30.6% of type II (18%–65%), and 18% in type III (10%–42%) tumors.^{8,9,31-33} Likewise, the percentage of metastases to the common hepatic artery (station 8) and celiac trunk nodes (station 9) cannot be considered negligible (10%–17.7%).

Interestingly enough, para-aortic node metastases (station 16) were an extremely common event when considering type III cancers. Nodal diffusion to para-aortic stations was present in 13.1% of all resected patients and in the 29.6% of patients who underwent D3 lymphadenectomy (data not shown). Consistently, a rate of 30% was reported by Hsu and associates.³⁴

Considering the data reported here, it should be taken into account that in this clinical study, the extent of lymph node dissection was tailored according to tumor location, and lymph node dissection differed in the 3 Siewert types. As a consequence, an underestimation of the real frequency of involvement of some nodal stations is possible. As a fact, the above-mentioned data prove the regular involvement of second-tier (and third-tier) nodes in GEJ adenocarcinoma and support the use of extended lymphadenectomy to achieve complete removal of the tumor. Transthoracic subtotal esophagectomy with standard 2-field lymphadenectomy is regarded as the treatment of choice for type I and type II tumors with significant esophageal involvement,³⁵ even though some authors, taking into account the possibility of metastases to upper mediastinal³⁶ and cervical^{19,37} nodes, advocate the use of more extensive lymph node dissection (extended 2-field and 3-field lymphadenectomy). In view of the high rate of second-tier abdominal node involvement, the use of D2 lymphadenectomy seems to be advisable in type I and II tumors, whereas a lymph node dissection extended to para-aortic nodes (D3 lymphadenectomy) would be justified in type III and type II tumors with major gastric involvement.^{34,38}

Conversely, one could argue that the poor long-term results reported in the present, as in previous experiences after adequate lymph node clearing,^{9,18,30,39} do not justify the use of an extended lymphadenectomy.⁴⁰ As a matter of fact, in our study little chance of survival was observed for patients with involvement of second-tier (and third-tier) lymph nodes,^{5,18,30} as well as for patients with more than 6 metastatic nodes, which confirms the findings reported by

TABLE 5. Survival according to the presence of nodal metastasis in each JGCA nodal station for the 111 patients with pN⁺ disease

	Lymph node station (JGCA)	No. of patients (no. alive)	Median survival	5-y survival*
1	Right paracardial	55 (11)	17.1	11.7
2	Left paracardial	35 (8)	17.1	0
3	Lesser curvature	87 (16)	14.1	15.5
4s	Greater curvature	7 (0)	14.1	14.3
4d	Right gastroepiploic artery	10 (1)	13.4	0
5, 6	Suprapyloric/infrapyloric	7 (0)	5.0	0
7	Left gastric artery	34 (7)	13.6	6.4
8, 9, 11	Celiac trunk arteries	34 (4)	13.6	0
16	Para-aortic	10 (0)	7.2	0
107, 108	Subcarinal/paraesophageal middle third	3 (1)	13.8	33.3†
110	Paraesophageal lower third	15 (3)	13.8	0
111, 112	Supradiaphragmatic/posterior mediastinal	14 (3)	14.2	0

JGCA, Japanese Gastric Cancer Association. *Five-year survival was calculated by using the Kaplan-Meier method. †Survival was computed at 25.8 months.

other authors.^{8,36,41} However, because this is a retrospective study with no control group, the role of extended lymph node dissection in improving survival cannot be assessed. In light of these results, we can affirm that the high frequency of nodal metastases and the related unfavorable long-term outcome achieved by means of surgical intervention alone are indicative of the need for aggressive multimodal treatment along with surgical intervention to improve the survival possibilities of these patients.^{14,42} Accordingly, some attention should be provided to thoracoscopy or laparoscopy as staging tools useful in guiding the choice of treatment.⁴³

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