GENERAL THORACIC SURGERY

TUMORS OF THE ESOPHAGOGASTRIC JUNCTION

Long-term survival in relation to the pattern of lymph node metastasis and a critical analysis of the accuracy or inaccuracy of pTNM classification

From 1983 to 1989, 95 patients with carcinoma of the esophagogastric junction underwent resection. Overall hospital mortality rate was 6.2% (6/95). Actuarial survival analysis showed 5- and 10-year survivals of 33% and 31%, respectively. Five- and 10-year survivals of patients according to TNM stages were as follows: stage I ($n = 13$), 90% at both 5 and 10 years; stage II ($n = 13$), 70% at both intervals; stage III ($n = 28$), 28% at both intervals; and stage IV ($n = 40$), 11% and 8%, respectively. For patients with undiseased nodes ($n = 26$), 5- and 10-year survivals were 72% and 72%, compared with 18% and 16% for patients with diseased nodes ($n = 68$; $p < 0.005$). In patients who had involvement of both the abdominal and thoracic lymph nodes ($n = 28$), 5- and 10-year survivals were 13% and 13%, compared with 26% and 26% if metastases were confined to the abdomen ($n = 37$; $p > 0.05$). Grouping patients with diseased intrathoracic nodes together with patients with N2 abdominal nodes showed survivals of 14% at both 5 and 10 years. When tumors were staged as an esophageal carcinoma, classification of individual patients changed, as did the 5- and 10-year survivals. Five- and 10-year survivals were as follows: stage I ($n = 8$), 100% for both 5 and 10 years; stage II ($n = 18$), 68% for both 5 and 10 years; stage III ($n = 27$), 37% for both 5 and 10 years; and stage IV ($n = 41$), 10% for 5 years and 6% for 10 years. These data indicate that tumors of the esophagogastric junction tend to spread to both abdominal and thoracic nodes. However, reasonably good 5- and 10-year survivals can be obtained even in patients with nodal metastases in both areas. We suggest that N2 labeling be included for thoracic node metastases instead of the actual M+Ly label, because the N2 label better reflects the potential for curative surgery. Finally, staging tumors as gastric or esophageal carcinoma makes no significant difference in survival analysis, which raises the question whether these tumors behave more like esophageal carcinoma than gastric carcinoma. (*J THORAC CARDIOVASC SURG* 1996;111:85-95)

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In sharp contrast to a decreasing occurrence of gastric carcinoma,¹ a dramatic increase of adenocarcinoma of the esophagus and cardia has been

reported by several authors in recent years.²⁻⁵ Even after resection the prognosis for these tumors is poor,⁶ and a recent article has suggested that prognosis for patients with adenocarcinoma of the cardia is so poor that surgical treatment is not justified.⁷ This poor prognosis seems to be related to the particular location of the tumor, positioned on both the stomach and esophagus, and its tendency for lymphatic spread into the lymph nodes of the superior abdominal compartment, as well as into the posterior mediastinum.⁸ As a result, adenocarcinoma of the cardia is often considered to be a

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different entity that should be distinguished from gastric carcinoma and esophageal carcinoma.

Great controversy exists concerning the definition, classification, staging, and surgical access tactics. The effect of the extent of gastric and esophageal resection, lymphadenectomy, and the consequences of these factors on long-term survival is still open for discussion.^{9, 10} However, only a few studies are available analyzing the results of surgical therapy for carcinoma of the esophagogastric junction.¹ The aim of this study is to analyze in a retrospective way results of resectional surgery and especially long-term survival as a function of lymph node metastatic pattern, inasmuch as the latter may be strongly influential in determining surgical strategies and defining proposals or recommendations for classifications and staging.

Patients and methods

Definition. Inasmuch as no strict criterion exists by which to define carcinoma of the esophagogastric junction, we chose to include in the definition all adenocarcinomas with the core of tumor located at the Z line or within an area of 5 cm orally and 5 cm aborally of the anatomic junction between the esophageal and gastric walls.¹¹ Indeed, many tumors completely destroy the cardiac mucosa. In these cases we preferred to rely on muscular wall rather than on the mucosal Z line to define the transition between esophagus and stomach. As a result, adenocarcinomas in Barrett's mucosa located in the above-mentioned area were included, but tumors arising from Barrett's mucosa located in the tubular structure of the esophagus were excluded. Lower esophageal adenocarcinomas and subcardial gastric carcinomas encroaching on the Z line were excluded and considered to be esophageal and gastric carcinoma, respectively.

Patients. From 1983 until 1993, 259 patients with carcinoma of the esophagogastric junction as defined herein were operated on in our institution. So that a minimum follow-up of 5 years could be obtained, the cohort of 95 patients treated from 1983 to 1989 was studied retrospectively. Files and follow-up were available for all except one patient.

Preoperative staging was performed in all patients. The methods included chest roentgenography, barium swallow, endoscopy with biopsy, bronchoscopy, computed tomography of the chest and upper abdominal compartment, ultrasonography of the liver, and echoendoscopy, the latter in the more recent group of patients. Resected specimens were staged according to criteria of the revised TNM classification of 1992.¹²

Statistical analysis. Survival curves were calculated according to the Kaplan-Meier method. The curves express the percentage of survivors. Statistical significance between slopes of curves was tested by the nonparametric log-rank score for censored values.

Surgical technique. The standard access consisted of an extended left thoracotomy through the sixth intercostal

space. This incision provides excellent exposure of the thorax and upper abdominal compartment through an incision in the left part of the diaphragm at its periphery. This approach was used in 93.6% of the patients.

In the remaining six patients the following techniques were used: A right thoracotomy and laparotomy were performed in two patients because of a previous operation on the left side in one and a left-sided tuberculous pachypleura in the other. In four patients judged to be in poor condition for a thoracotomy, we decided to perform a transhiatal stripping of the esophagus.

Inasmuch as this is a retrospective study spanning 12 years, the surgical techniques were modified to some degree. In the initial period the operation consisted of a wide resection of the tumor, with lymph node resection being restricted to sampling of suspected lymph nodes in the upper abdominal compartment and posterior mediastinum. From 1985 on, however, resection and lymphadenectomy became much more radical.

Radical resection consisted in a subtotal esophagectomy with wide peritumoral resection including the thoracic duct and all peritumoral fatty and lymphatic tissue together with resection of the lesser curvature of the stomach. The aim of this more aggressive approach was to obtain a complete resection (R0 situation according to the TNM classification). Extensive lymphadenectomy included the following nodal groups: subcarinal, aortopulmonary window, paraesophageal, mediastinal, parahiatal, left gastric, hepatic, splenic, and celiac nodes.

As a rule, stomach was used to restore continuity, but again the oral and aboral extent of the operation changed over the years. During our initial experience, resection of the lesser curvature down to the junction of the gastric antrum and corpus and a safety margin of at least 5 cm distally from the lower pole of the tumor was judged to be sufficient. Along with the decision to perform extended two-field lymphadenectomies, we also decided to extend the safety margin on the gastric site by extending the resection of the lesser curvature to a level just proximal to the pylorus and taking away more of the fundus and corpus of the stomach laterally, thereby leaving a gastric tubulus along the greater curvature to be used for reconstruction.

On the esophageal side, initially a partial esophagectomy was the standard procedure. Anastomosis was performed at the level of the aortic arch, guaranteeing a margin of macroscopically healthy tissue above the proximal pole of the tumor of at least 5 cm and usually about 10 cm. For oncologic reasons, but even more because of the prevalence of reflux esophagitis after an intrathoracic anastomosis,¹³ we decided to perform a subtotal esophagectomy with cervical esophagogastrostomy whenever possible. This resulted in 45 intrathoracic and 37 cervical esophagogastrostomies.

Finally, in the 13 remaining patients a total gastrectomy was performed: by necessity in four, and because of oncologic reasons (gross lymph node involvement along the lesser or greater curvature, or metastatic deposits on the gastric wall) in nine. In those patients continuity was restored with a jejunal Roux-en-Y loop with an intrathoracic esophagojejunostomy.

Table I. Demographic data

	No.	%
Male	81	82.3
Female	14	14.7
Age (yr)		
Mean: 63		
Range: 35-89		
Age distribution		
<70 yr	48	50.5
>70 yr	27	28.5
>75 yr	16	16.8
>80 yr	4	4.2

Results

Mortality and morbidity. The study group consisted of 95 patients with a mean age of 63 years (range 35 to 89 years). The demographic data are presented in Table I. Hospital mortality was 6.2% (6/95). In the first half of the study period, before 1986, mortality was 13% (3/23 patients). Mortality decreased in the second half (from 1986 on) to 4.1% (3/72 patients), reflecting the increasing experience of the team as a whole.

Forty-six patients (48.5%) had a completely uneventful postoperative course with a mean hospital stay of 16 days (10 to 43 days), and 43 patients had a total of 53 nonfatal complications. Their mean hospital stay was 24.3 days (10 to 90 days). Pulmonary infection with subsequent respiratory failure was the most frequent complication.

Nine patients (9.5%) had an anastomotic leak (being fatal in two patients). Anastomotic leak was defined as any clinical or radiologic evidence of extravasation. There was no significant difference in the prevalence of anastomotic leaks between cervical (16%) and intrathoracic anastomoses (6.6%) ($p > 0.05$). Specific data on mortality and morbidity are listed in Table II.

Staging and survival analysis. In all patients the disease was staged on the basis of the findings on the resected specimen according to TNM classification of malignant tumors (fourth edition, second revision, 1992); staging is shown in Table III. Inasmuch as insufficient data were available in one patient, the rest of the study comprises 94 patients. Seventy-two percent of all resected lesions were classified as advanced stage III or IV.

Twelve patients had histologic evidence of adenocarcinoma in Barrett's metaplastic mucosa. Seven of these patients had stage I disease, two stage III, and three stage IV.

Overall survivals including all causes of death

Table II. Hospital mortality and morbidity after resection of tumors of the esophagogastric junction

Mortality	6/92 (6.2%)
Fatal anastomotic leak	2
ARDS-pulmonary sepsis	1
Abdominal sepsis	1
Catheter sepsis	1
Cardiac failure	1
≤70 yr	3/48 (6.2%)
≥70 yr	3/47 (6.4%)
Morbidity: 53 complications in 43 patients	
Pneumonia	16
Wound infection	8
Nonfatal anastomotic leak	7
Sepsis	4
Pancreatic fistula	2
Prolonged lymph leak	3
Ileus	1
Cardiac	6
Transient ischemic attack	1
Recurrent nerve paralysis	2
Deep venous thrombosis	3

ARDS, Adult respiratory distress syndrome.

Table III. Staging of resected tumors of the esophagogastric junction

Stage	pTMN classification	No. of patients	%
Stage Ia	T1 N0 M0: 8	13	14
Stage Ib	T2 N0 M0: 5		
Stage II	T2 N1 M0: 1	13	14
	T3 N0 M0: 12		
Stage IIIa	T2 N2 M0: 2	28	30
	T3 N1 M0: 15		
Stage IIIb	T3 N2 M0: 7		
	T4 N1 M0: 4		
Stage IV	T4 N2 M0: 7	40	42
	Any T Any N M1: 33		

were 51% at 1 year, 35% at 2 years, 28% at 5 years, and 16% at 10 years. The specific aim of this study, however, was to evaluate the impact of cancer-related mortality at the very long-term follow-up beyond 5 years. For this reason 11 patients who died of causes known to be unrelated to cancer were censored to death. Overall survival at 1 year was 54%, at 2 years 39%, at 5 years 33%, and at 10 years 31% (Fig. 1). All subsequent survival analyses were performed by excluding causes of death unrelated to cancer. As expected, TNM stage at the time of resection significantly influences survival. Fig. 2 shows 5- and 10-year survivals stage by stage. In patients not having lymph node disease ($n = 26$), 5- and 10-year survivals were both 72%, compared with

Fig. 1. Overall survival in years after resection for tumors of the esophagogastric junction.

18% and 16%, respectively, for patients having diseased lymph nodes ($n = 68$) ($p < 0.005$) (Fig. 3).

Twenty-eight patients had diseased lymph nodes in both the abdomen and mediastinum, whereas 37 patients had lymph node invasion confined only to the abdomen. Five- and 10-year survivals were clearly lower in the first subgroup (13%) than in the second subgroup (26%), but the difference did not reach statistical difference ($p > 0.05$) (Fig. 4). Only three patients had lymph node metastasis strictly confined to the mediastinum.

In view of the persistent controversy whether carcinoma of the esophagogastric junction is to be considered as behaving like gastric or esophageal carcinoma, the patients' tumors were restaged according to the TNM classification for esophageal carcinoma. Although the numbers of patients with each stage of disease are practically identical, staging of disease in individual patients changed (N2, i.e., extension of lymph nodes beyond the left gastric artery in gastric staging, becomes $M+Ly$ in esophageal staging, and $M+Ly$, i.e., lymph nodes in the mediastinum in gastric staging, becomes $N1$ in esophageal staging) (Table IV). Fig. 5 shows the 5- and 10-year survivals stage by stage. The main difference with the staging as gastric carcinoma is a

better outcome for stage III (37% versus 28%), but this difference is not statistically significant ($p > 0.2$).

In both staging systems, however, it became clear that a small but distinct percentage of patients with stage IV disease survived for 5 years or more. This becomes even more prominent when excluding patients with stage IV disease because of organ metastasis ($n = 12$) and including only patients whose disease is classified as stage IV because of distant lymph node metastasis ($M+Ly$). Indeed, 5- and 10-year survivals were 16% and 11%, respectively, for patients whose disease was staged as gastric carcinoma and 15% and 9%, respectively, when staged as esophageal carcinoma.

From these figures the assumption was made that patients with diseased lymph nodes beyond the gastric artery and patients with diseased lymph nodes in the posterior mediastinum could be grouped as a separate entity.

To exclude a negative impact from the T factor, we excluded all patients who simultaneously had a T4 staging. As a result, seven patients originally considered to have stage IIIb disease because of N2 classification and 17 patients originally considered to have stage IV disease because of intrathoracic

Fig. 2. Survival curves according to pTNM staging after resection for tumors of the esophagogastric junction.

diseased lymph nodes were grouped together ($n = 24$). In this setup, 5- and 10-year survivals were both 14%, as shown in Fig. 6. This figure is comparable with the 17% survival of the seven patients originally classified as having stage IIIb disease. Moreover, once the 17 patients with diseased intrathoracic lymph nodes were eliminated from stage IV, none of the patients remaining in stage IV survived more than 5 years.

Discussion

Carcinoma of the cardia or esophagogastric junction may be defined as an adenocarcinoma arising in the proximal 1 or 2 cm of the stomach. Ideally, to prove its origin, the residual cardiac mucosa should have in situ adenocarcinoma to distinguish gastric carcinoma, esophageal carcinoma, and Barrett's adenocarcinoma from each other. Because many tumors completely destroy the cardiac mucosa, however, separation of these different cancers is impossible. In the literature the debate continues.

According to Kalish and associates,¹⁴ carcinoma of the esophagogastric junction can be defined as an adenocarcinoma arising within or immediately be-

low the esophagogastric junction with replacement of all or a significant part of the cardiac mucosa and sparing of the more distal gastric tissue, but also including Barrett's carcinomas occurring in the limited zone of the gastroesophageal junction. From the macroscopic point of view, we accepted a 5 cm oral or aboral extension from the anatomic esophagogastric junction as proposed by Hölscher, Schüller, and Siewert.¹¹ Tumors mainly located in the stomach (even if encroaching on the esophagus), Barrett's adenocarcinoma mainly located in the tubular esophagus, and squamous cell carcinomas were excluded.

This approach seems to be more practical than the recommendation from the International Union Against Cancer (UICC) TNM supplement 1993. The UICC suggests classifying adenocarcinoma involving more than 50% of the esophagus as esophageal carcinoma and those involving more than 50% of the stomach,¹⁵ including those equally distributed over the esophagus and stomach, as gastric carcinoma.

Moreover, in our opinion, this UICC TNM approach ignores one of the essential questions—

Fig. 3. Survival curves according to absence or presence of lymph node involvement after resection for tumors of the esophagogastric junction.

whether carcinoma of the esophagogastric junction, because of its particular anatomic location, behaves differently from carcinoma of the esophagus or stomach. In this respect it is worthwhile to note that 12 of our patients had a histologically proved adenocarcinoma in Barrett's metaplasia. It can be assumed that this fraction is probably higher, for in a number of T3 and T4 tumors all mucosal tissue has been destroyed by the tumor, so that further proof of the presence of Barrett's origin is impossible.

Recent data from the literature showed Barrett's metaplasia as the source of adenocarcinoma of the cardia in up to 50% of adenocarcinomas of the esophagogastric junction. These data suggest a common origin of adenocarcinoma of the esophagus and adenocarcinomas located at the esophagogastric junction^{16,17} and a behavior similar to that of an esophageal carcinoma.

Further evidence from Japanese studies and some Western studies suggests that carcinomas of the esophagogastric junction and carcinoma of the esophagus largely share patterns of age, sex distribution, and morphologic characteristics.¹⁸⁻²⁰ When compared with infracardiac gastric carcinoma, there seem to be highly significant differences in age

distribution and macroscopic and microscopic appearance between esophagogastric junction tumors and gastric carcinoma. These differences suggest that the esophagogastric junction tumors must be more closely related to the esophagus than to the stomach.^{19,20}

In this study, carcinomas of the esophagogastric junction were restaged as esophageal carcinomas according to the TNM staging system. No major difference was seen between the two staging modalities either in overall survival or in survival stage by stage. Moreover, our results after resection for esophagogastric junction carcinoma are similar to those obtained after resection for esophageal carcinoma in a series of patients treated in a similar period in our institution.²¹ Five-year survival in that series was 30% as compared with the 33% overall 5-year survival in the present series. As expected, the strongest prognostic indices are provided by the absence or presence of lymph node involvement, with 5-year survivals of 72% and 18%, respectively. Again, these figures are similar to those obtained in our series of esophageal carcinoma, with 63% 5-year survival for patients without lymph node involvement and 12% for those with lymph node involvement.

Fig. 4. Survival curves according to lymph node involvement of abdominal and abdominal plus thoracic lymph nodes after resection for tumors of the esophagogastric junction. *LN*, Lymph node; +, positive (diseased); –, negative (normal).

All these data from the literature and from our own experience, as well, seem to support the thesis that esophagogastric junction tumors should be classified as esophageal carcinomas in the TNM system. In such an eventuality lymph node staging, however, should be done according to the recommendations of the UICC TNM supplement 1993 in that lymph node metastases at or beyond the celiac axis are considered as a special subgroup to be separated from other distant metastases. However, this study is only a one-center experience. Confirmation by other groups must be obtained before esophagogastric junction tumors can be classified and staged as esophageal carcinomas.

The other main goal of this study was to critically analyze the value of the actual TNM staging system for carcinoma of the esophagogastric junction, especially in relation to lymph node status. In this respect, a most striking observation was the fact that in stage IV, which is to be considered as noncurable disease, distinct 5- and 10-year survivals of 11% and 8%, respectively, were obtained.

We suspected that surgical resection might indeed result in cure in patients with lymph node involve-

Table IV. Staging of resected tumors of the esophagogastric junction as esophageal carcinoma

Stage	pTMN classifications	No. of patients	%
Stage I	T1 N0 M0	8	8.5
Stage IIa	T2 N0 M0: 5	18	19
	T3 N0 M0: 12		
Stage IIb	T2 N1 M0: 1	27	29
Stage III	T3 N1 M0: 23		
	T4 N1 M0: 4		
Stage IV	Any T Any N M1	41	43.5

ment at the celiac axis and especially at the level of the posterior mediastinum. This theory was confirmed by the findings that even in patients with both abdominal and thoracic involvement of lymph nodes, a 5- and 10-year survival of 13% was achieved. Grouping patients with abdominal N2 and thoracic M+Ly disease together into one group (to be considered as a stage IIb group) again resulted in a cure rate of 14%, not significantly different from the 17% survival of the patients who originally had been classified as having stage IIb disease.

Because mediastinal lymph nodes are frequently

Fig. 5. Survival curves according to pTNM staging after resection for tumors of the esophagogastric junction that were classified as esophageal carcinomas.

involved (up to 38% in our series) in adenocarcinoma of the esophagogastric junction, the consequences of these findings are clear. First, a careful lymph node dissection of the posterior mediastinum up to the carina is necessary to obtain a correct pathologic stage. This of course favors a transthoracic approach. The thoracoabdominal approach not only allows adequate esophagogastric resection but, more important, allows better and more complete removal of mediastinal lymph nodes²²⁻²⁴ than any other approach, although an extended transhiatal approach by incising the diaphragm also may allow correct exposure and lymph node dissection.

Furthermore, the detection of diseased intrathoracic lymph nodes by different staging methods, either noninvasive (endoscopic ultrasonography) or invasive (thoracoscopy),²⁵ should not exclude such patients from treatment modalities aimed at cure, in particular, surgery.

For these reasons we suggest that diseased intrathoracic lymph nodes should no longer be considered as stage IV but should be classified as N2

nodes and added to the N2 group in the actual classification as one stage IIIB, reflecting better the potential for curative surgery in this subgroup.

Conclusion

Resection of carcinoma of the esophagogastric junction offers chances for cure in approximately one of three patients. Stage and especially lymph node involvement are the most important prognostic factors. However, in case of lymph node involvement surgical treatment may cure a distinct percentage of patients. Inasmuch as this is also the case for patients with diseased intrathoracic lymph nodes, these patients should not be considered to have M+L disease. We propose to include them in the N2 classification. Survival curves for patients with esophagogastric junction carcinoma in our experience are similar to those obtained for patients with esophageal carcinoma. These observations endorse data from the literature indicating that esophagogastric junction tumors behave like esophageal carcinoma. This raises the question whether esophago-

Fig. 6. Survival curves after regrouping of patients originally classified as having IIIb or M+Ly intrathoracic disease. Patients with T4 tumors are excluded. Staging is classified as gastric carcinoma.

gastric junction tumors should be classified like esophageal carcinoma rather than gastric carcinoma. Further confirmation from other groups will be required before such a proposal can be made.

Surgical results from experienced centers, especially results obtained after extended resection and lymphadenectomy, remain the gold standard to which other therapeutic modalities (i.e., induction therapy)^{5, 26} should be compared.

REFERENCES

1. Antonioli DA, Cady B. Changing aspects of gastric adenocarcinoma [Letter]. *N Engl J Med* 1984;310:1538.
2. Hölscher AH, Siewert JR. Surgical treatment of adenocarcinoma of the gastroesophageal junction. *Dig Surg* 1985;2:1-6.
3. Clark GWB, Peters JH, Ireland AP, et al. Nodal metastasis and sites of recurrence after en bloc esophagectomy for adenocarcinoma. *Ann Thorac Surg* 1994;58:646-54.
4. Pera M, Cameron AJ, Trastek VF, Carpenter HA, Zinsmeister AR. Increasing incidence of adenocarcinoma of the esophagus and esophagogastric junction. *Gastroenterology* 1993;104:510-3.
5. Wright CD, Mathisen DJ, Wain JC, et al. Evolution of treatment strategies for adenocarcinoma of the esophagus and gastroesophageal junction. *Ann Thorac Surg* 1994;58:1574-9.
6. Mathisen DJ, Grillo H, Wilkins EW, Monciere AC, Hilgenburg AD. Transthoracic esophagectomy: a safe approach to carcinoma of the esophagus. *Ann Thorac Surg* 1988;45:137-43.
7. Wilson NV, Geall A, Killermaster R, Bentley PG. Thoracoabdominal total gastrectomy in the management of carcinoma of the cardia. Is it worth it? *Ann R Coll Surg Engl* 1990;72:329-34.
8. Castrini G, Pappalardo G. Carcinoma of the cardia. *J THORAC CARDIOVASC SURG* 1981;82:190-3.
9. Launois B, Bourdonnec P, Bardaxoglou E, et al. The influence of the extent of the gastrectomy on survival in adenocarcinoma of the cardia. *Dis Esophagus* 1993;6:41-6.
10. Papachristou DN, Former JG. Adenocarcinoma of the gastric cardia. *Ann Surg* 1980;192:58-64.
11. Hölscher AH, Schüller M, Siewert R. Surgical treatment of adenocarcinomas of the gastroesophageal junction. *Dis Esophagus* 1988;1:35-49.
12. Hermanek P, Sobin LH. International Union Against Cancer (UICC). TNM classification of malignant tumours. 4th ed. Berlin: Springer, 1992.

13. De Leyn P, Coosemans W, Lerut T. Early and late functional results in patients after esophagectomy for carcinoma. *Eur J Cardiothorac Surg* 1992;79-85.
14. Kalish RJ, Clancy PE, Orringer MB, Appelman HD. Clinical, epidemiologic, and morphologic comparison between adenocarcinomas arising in Barrett's esophageal mucosa and in the gastric cardia. *Gastroenterology* 1984;86:461-7.
15. Hermanek P, Henson DE, Hutter RVP, Sobin LH. International Union Against Cancer. TNM Supplement 1993: a commentary on uniform use. Berlin: Springer, 1993:29.
16. Clark GWB, Smyrk TC, Burdiles P, et al. Is Barrett's metaplasia the source of adenocarcinomas of the cardia? *Arch Surg* 1994;129:609-14.
17. Duhaylongsod FG, Wolfe WG. Barrett's esophagus and adenocarcinoma of the esophagus and gastroesophageal junction. *J THORAC CARDIOVASC SURG* 1991;102:36-42.
18. Nakane Y, Okamura S, Boku T, Okusa T, Tanaka K, Hioki K. Prognostic differences of adenocarcinoma arising from the cardia and the upper third of the stomach. *Am Surg* 1993;59:423-9.
19. Heidl G, Langhans P, Mellin W, Bunte H, Grundmann E. Adenocarcinomas of esophagus and cardia in comparison with gastric carcinoma. *J Cancer Res Clin Oncol* 1993;120:95-9.
20. Pensioen CY, Welvaart K, Hermans J. Significance of tumor invasion and lymph node involvement on the prognosis and selection for surgery of adenocarcinoma of the cardia. *Eur J Surg Oncol* 1989;15:301-6.
21. Lerut T, De Leyn P, Coosemans W, Van Raemdonck D, Scheys I, Le Saffre E. Surgical strategies in esophageal carcinoma with emphasis on radical lymphadenectomy. *Ann Surg* 1992;216:583-90.
22. Skinner DB. En bloc resection for neoplasms of the esophagus and cardia. *J THORAC CARDIOVASC SURG* 1983;85:59-71.
23. Akijama H. Esophageal cancer: toward improved results. Tokyo: Nakayama Institute of Cancer Research, 1993:50-1.
24. Hagen JA, Peters JH, DeMeester TR. Superiority of extended en bloc esophagogastrrectomy for carcinoma of the lower esophagus and cardia. *J THORAC CARDIOVASC SURG* 1993;106:850-9.
25. Krasna MJ, McLaughlin JS. Thoracoscopic lymph node staging for esophageal cancer. *Ann Thorac Surg* 1993;56:671-4.
26. Aikou T, Shimazu H, Takao T, Baba M, Natsugoe S, Simada M. Significance of lymph nodal metastases in treatment of esophagogastric adenocarcinoma. *Lymphology* 1992;25:31-3.

Discussion

Dr. Jeffrey A. Hagen (*Los Angeles, Calif.*). I thank Dr. Lerut and his coworkers for the opportunity to focus on

the problems being faced with the current staging system of cancers in the region of the esophagogastric junction.

Their article draws attention to two of the most important aspects of the difficulties encountered staging these tumors. The first involves the issue of whether these tumors are of gastric or esophageal origin and how they should be classified. We agree that the clinical behavior, patient demographics, and morphologic characteristics of these tumors more closely resemble esophageal cancers. In addition, our experience documenting intestinal metaplasia in about half the patients with adenocarcinomas of the cardia suggests a common pathophysiology with Barrett's adenocarcinomas arising higher in the tubular esophagus.

Dr. Lerut, you propose adding the involved mediastinal nodes to N2 disease in the gastric staging system, implying that you propose staging these as gastric tumors. Is this your preference or do you believe, as we do, that these tumors are distinct from the usual gastric cancers and thus should be staged instead as esophageal tumors?

My second question deals with the larger issue of the need for revising the staging system of esophageal cancer. We, too, have encountered problems with the current system, mostly with regard to patients with limited nodal disease. This has led to our adopting a modification of the staging system originally proposed by Dr. Skinner and recently endorsed by Dr. Ellis and his coworkers. This system stratifies patients on the basis of the degrees of lymph node involvement, using the number of involved nodes rather than their location. Have you considered this type of staging system? Has your experience been similar to ours in Los Angeles and that of Dr. Ellis in Boston?

This study has evolved over the years with respect to the extent of resection. In your current practice the gastric resection is carried distally along the lesser curvature to lower the prevalence of recurrence, and you have taken the anastomosis up into the neck for similar reasons.

My final question is this: Why not resect the stomach at the level of the antrum and use the colon to establish continuity, maximizing the potential for complete resection?

Dr. Lerut. In answer to your first question, we have not done the same study that you did, evaluating the relation with intestinal metaplasia. This was out of the scope of our study. However, if we evaluate the results of your group, our work, and the results obtained by some other groups, I believe we will discover that it is better to distinguish them from gastric carcinoma and to classify them as esophageal carcinoma.

With regard to use of the Skinner classification rather than the TNM classification, we have not made a count of the lymph nodes. We have begun doing that only recently. As a result, we are not in a position to use number of involved lymph nodes as a prognostic parameter; therefore we restricted ourselves to evaluating whether this classification is accurate enough within the TNM classification. It is commonly accepted now that the number of the lymph nodes that are involved and also the location of the lymph nodes in respect to the primary tumor play an important role.

As to the last question, we routinely use the stomach if possible. We have had one local recurrence in the neck

and two recurrences within the operative field in those patients in whom we could make a complete analysis of the pattern of recurrence. However, the recurrence rate is less than 10%, which is similar to the rates reported in most published series. Moreover, using the colon may add to the mortality risk, and that is the primary reason that we have been using the stomach instead of the colon. But I fully agree. If the operation can be done with the same rate of morbidity and mortality, the colon certainly can be used.

Dr. David B. Skinner (*New York, N.Y.*). It was 33 years ago at this meeting that Andrew Logan first presented the concept of a mediastinal and upper abdominal node dissection for carcinoma of the cardia and introduced the term "en bloc resection." Since 1969 we have been using an en bloc resection for these tumors. We have extended the indications to include all types of thoracic esophageal cancer and presented our results here initially in 1983.

What has become apparent over the past 15 years or so is that the extended resection does yield a high survival, such as Professor Lerut has described, for patients with stage I or stage II disease. It is not so clear that it improves survival for patients with stage III or IV disease. However, when there is any question, the patient should receive the benefit of the doubt.

The issue of the staging system here is important. Those who view the cardia as part of the stomach use the stomach staging system. Those of us who view it as part of the esophagus use the esophageal staging system. For the benefit of the patients, though, we probably should consider both, because a diseased left gastric or celiac node from an esophageal cancer does not necessarily indicate stage IV disease, nor does a diseased mediastinal node for gastric cancer at the cardia necessarily indicate stage IV disease. I would urge against overstaging in these patients.

You reported that the prognosis is poor for patients who have involvement of both thoracic and abdominal nodes. In our series we have identified some adenocarcinomas with involvement of the mediastinal nodes but no involvement of the abdominal nodes. Have you encountered that situation and, if so, did that make any difference in the outcome?

We agree with your left thoracotomy approach because it gives excellent exposure for both the abdominal dissection and the mediastinal dissection. Those who advocate mainly an abdominal approach tend to cut corners on a mediastinal dissection. A few surgeons can do a good clean-out of the lower mediastinum through the hiatus, but not many use that procedure and thereby deny patients the advantages of the mediastinal dissection.

We tend to use colon for the reconstruction as well, mainly because we have had several patients in whom further Barrett's epithelium has developed above an esophagogastric anastomosis. That does not happen if we use the colon.

Finally, I would like to ask why you are excluding squamous carcinoma of the cardia. In the last month I have done two of these resections for identical gross tumors growing down the lesser curvature of the stomach from the cardia. One was squamous cell and one was adenocarcinoma, but grossly they looked the same. The metastatic pattern was interesting. The squamous cell

tumor actually metastasized to the left gastric artery and not to the mediastinum. We would lump any tumor in this category, regardless of cell type, and treat both the mediastinum and the gastric dissection. Have you any comments on that?

Dr. Lerut. Only three patients in our series had only thoracic lymph nodes involved, too small a group to allow any conclusions to be drawn. I certainly agree that these tumors should not be considered to be usual gastric carcinomas, and therefore a thorough mediastinal lymph node dissection is required. We favor the transthoracic approach.

We excluded squamous cell carcinoma specifically because we wanted to have a homogeneous cohort of patients. For this reason we excluded all Barrett's carcinomas located in the tubular esophagus and all squamous cell carcinomas. Your comment adds to the arguments that these tumors are behaving much more like esophageal carcinomas and should be considered as such, but only for practical reasons.

I can recall no experience in dealing with squamous cell carcinomas of the cardia growing down on the lesser curvature.

Dr. Zwi Steiger (*Detroit, Mich.*). At Wayne State University we usually use combined chemotherapy to treat patients with adenocarcinomas of the distal esophagus: two courses of cisplatin 75 mg/m² and 5-fluorouracil 1000 mg/m² per day every day for 96 hours. The chemotherapy is separated by 4 weeks and is given concurrently with radiotherapy. An additional two courses of the same chemotherapy 3 weeks apart are given after radiation treatment. The radiotherapy consists of 5500 to 6000 cGy given over 6 weeks, starting at day 1 together with the first chemotherapy cycle. Patients will have computed tomographic scans of the chest and abdomen, esophagograms, esophagoscopy, and possible biopsy at the end of the radiotherapy and again on completion of chemotherapy. This is repeated 3 months later if the results of the initial evaluation are negative. Patients with persistent disease are offered surgical treatment. The complete response rate confirmed by biopsy is about 60%, and 30% of the patients are alive and well at 3 years.

The question in our institution is not how much to resect but whether to resect at all. The nonsurgical options need to be compared with surgical treatment in these patients in a natural prospective phase III trial.

Dr. Lerut. Most of us are involved with programs dealing with chemotherapy, radiotherapy, or the combination in a neoadjuvant setting, and indeed for adenocarcinomas complete remissions have been reported. According to the literature, it appears that without subsequent surgery the risk for local recurrence and further metastasis is much higher than if this induction treatment is followed by surgery. Certainly the risk of surgery is not as high as it used to be; we can keep the mortality rate below let's say 5%. So that is not really an argument not to perform a resection after induction therapy. We do have to wait for the results of a number of ongoing trials to see whether the combination of induction therapy and surgery will give better 5-year survival results than no subsequent surgery or than primary surgery.