Surgical treatment of tumors of the proximal stomach with involvement of the distal esophagus: A 26-year experience with Siewert type III tumors

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Objective: A paucity of outcome data exists regarding patients with proximal stomach cancer involving the distal esophagus (Siewert type III tumors). This is especially true with regard to long-term survival rates after surgical intervention.

Methods: Medical records were reviewed of all patients who underwent total gastrectomy and distal esophagectomy with Roux-en-Y esophagojejunostomy for Siewert type III tumors from January 1975 through December 2000.

Results: There were 116 patients (93 men and 23 women). The median age was 66 years (range, 22-87 years). Pathologic stage was 0 (carcinoma in situ) in 1 patient, IB in 13 patients, II in 17 patients, IIIA in 34 patients, IIIB in 10 patients, and IV in 41 patients. Complete resection was achieved in 69 (59.5%) patients. Eleven (9.5%) patients were treated with neoadjuvant therapy, 49 (42.2%) received adjuvant therapy, and 6 (5.2%) received intraoperative radiation. Follow-up was complete in 114 (98.3%) patients, ranging from 1 to 281 months (median, 14 months). Operative mortality was 5.2%. Complications occurred in 51 (43.9%) patients. Clinically significant anastomotic leaks occurred in 15 (12.9%) patients. Median hospitalization was 13 days (range, 8-70 days). Median follow-up was 14 months (range, 1-281 months). Overall median survival was 434 days, with 1-, 5-, and 10-year survivals of 56.2%, 19.0%, and 13.5%, respectively. The only factor associated with increased hospital mortality was anastomotic leakage ($P = .002$). Incomplete resection, increased tumor stage and grade, and splenic involvement significantly worsened long-term survival.

Conclusions: Total gastrectomy and distal esophagectomy for Siewert type III tumors is associated with reasonable mortality and significant morbidity. Although often palliative, surgical intervention can provide long-term survival, especially in patients with completely resected, early-stage, low-grade tumors.

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The prevalence of gastric carcinoma has been decreasing; however, a sharp increase in the prevalence of adenocarcinoma of the esophagogastric junction (AEG) has occurred.¹ Unfortunately, inconsistencies in defining tumor location have made it difficult to evaluate the results, prognosis, and optimal treatment strategies for patients with carcinoma in the region of the esophagogastric junction. To address those issues, a recent consensus report from the International

Abbreviations and Acronyms

AEG = adenocarcinoma of the esophagogastric junction

UICC = Union Internationale Contre le Cancer

Gastric Cancer Association and the International Society for Diseases of the Esophagus has provided a workable definition of these tumors (Table 1).²

Few comparative data exist for subcardial gastric carcinoma involving the gastroesophageal junction and distal esophagus (Siewert type III). This is especially true concerning morbidity and long-term mortality after surgical resection. Although treatment options for these patients include surgical resection, chemotherapy, and radiotherapy in various types of combinations, the only potentially curative therapy for these cancers remains surgical resection. The purpose of this study is to evaluate the outcomes of our patients with Siewert type III tumors who underwent total gastrectomy with distal esophagectomy to better define the role of surgical intervention in this clinical situation.

Patients and Methods

All patients who underwent total gastrectomy and distal esophagectomy with Roux-en-Y esophagojejunostomy for adenocarcinoma of the proximal stomach involving the distal esophagus (Siewert type III tumors) at our institution between January 1975 and December 2000 were identified from a prospectively maintained surgical database. A dedicated review of pathology, operative and endoscopic reports, and radiologic studies was undertaken to ensure that cases included in this study complied with the definition of a Siewert type III tumor: adenocarcinoma of the stomach that infiltrates the esophagogastric junction and distal esophagus from below with a tumor epicenter within 5 cm of the cardia.

The medical records of these patients were reviewed for patient demographics, presenting signs and symptoms, tumor stage (including T, N, and M status), grade of tumor, surgical approach, completeness of resection, date of surgical intervention, tumor involvement of the spleen or other organs, induction chemotherapy or radiotherapy, adjuvant chemotherapy or radiotherapy, postoperative morbidity and mortality, length of hospitalization, last follow-up visit or date of death, disease status at follow-up or death, and cause of death.

For the purposes of our analysis, the patients were divided into 2 groups depending on the date of esophagogastrectomy: the initial era (1975-1987) and the latter era (1988-2000). We classified the procedures as either complete resection (R0) or incomplete resection (R1) if microscopic examination of the surgical margins revealed the presence of residual cancer. Operative mortality included patients who died within 30 days after the operation or at any time during their initial postoperative hospitalization. All patients were staged with the Union Internationale Contre le Cancer (UICC) staging system.³ Survival and mortality data were verified with the Social Security Death Index.

TABLE 1. Classification of adenocarcinoma of the esophagogastric junction*

Classification type	Description
I	Adenocarcinoma of the distal esophagus that infiltrates the esophagogastric junction from above
II	Adenocarcinoma of the cardia, "junctional carcinoma"
III	Adenocarcinoma of the stomach that infiltrates the esophagogastric junction and distal esophagus from below

*Siewert and Stein.²

Descriptive statistics are reported by using numbers (percentages) for discrete data and medians (ranges) for continuous data. Survival subsequent to discharge was estimated among the remaining patients who survived hospitalization by using the Kaplan-Meier survival method.⁴ The association between patient survival and risk factors was examined by using the log-rank test.^{4,5} The study was reviewed and approved by the Mayo Clinic Institutional Review Board.

Results

One hundred sixteen patients were identified: 93 (80.2%) men and 23 (19.8%) women. Median age at the time of the operation was 66 years (range, 22-87 years). Signs and symptoms were present at the time of diagnosis in 113 (97.4%) patients. The most common symptoms were dysphagia (60.3%), weight loss (31.0%), pain (15.5%), bleeding (14.7%), and early satiety (12.1%). Thirteen (11.2%) patients had undergone prior gastric surgery for other pathology, most commonly peptic ulcer disease.

The operative approach was laparotomy alone in 63 (54.3%) patients, a left thoracoabdominal approach in 46 (39.7%) patients, and laparotomy with a right thoracotomy in 7 (6.0%) patients. Total or completion gastrectomy and distal esophagectomy with Roux-en-Y esophagojejunostomy was performed in all 116 patients. Sixty-nine (59.5%) patients had complete resections (R0), and 47 (40.5%) had incomplete resections (R1), as evidenced by microscopically positive resection margins. Of the 47 patients with positive margins, 5 (10.6%) had positive margins at the proximal esophageal margin alone. Forty-one (87.2%) had positive margins on the stomach or other organ resected en bloc. One (2.1%) patient had both a positive proximal esophageal margin and distal margin. Positive margins were encountered in 28 (44.4%) of the laparotomy-alone approaches, 16 (34.8%) of the left thoracoabdominal approaches, and 7 (100%) of the laparotomy and right thoracotomy approaches.

The median number of lymph nodes resected in the specimen was 13 (range, 2-46). In patients classified as having N0 disease, 20 (66.7%) had at least 15 lymph nodes

TABLE 2. Patient characteristics and operative details

Characteristic	Median	Range
Age (y)	66	22-87
	n	%
Sex		
Male	93	80.2
Female	23	19.8
Prior gastric surgery		
Billroth I	2	1.7
Billroth II	9	7.8
Other	2	1.7
None	103	88.8
Grade of adenocarcinoma		
2	16	13.8
3	32	27.6
4	68	58.6
Surgical approach		
Laparotomy alone	63	54.3
Left thoracoabdominal	46	39.7
Laparotomy with right thoracotomy	7	6.0
Completeness of resection		
Complete resection, R0	69	59.5
Incomplete resection, R1	47	40.5
Spleen		
Splenectomy	76	65.5
Spleen preserved	40	34.5
Year of operation		
1975-1987	40	34.5
1988-2000	76	65.5
Induction treatment		
Chemotherapy alone	7	6.0
Chemotherapy and Radiotherapy	4	3.5
None	105	90.5
Adjuvant treatment		
Chemotherapy	30	25.9
Radiotherapy	6	5.2
Chemotherapy and radiotherapy	13	11.2
None	67	57.7

resected. In most cases a D1 lymph node dissection was accomplished, often including further dissection of N2 level nodes.

The spleen was removed in 76 (65.5%) patients and was involved by tumor in 19 (25%) patients. Splenectomy was more frequent in the earlier era of this series (38/40 [95.0%]) compared with in the latter era (38/76 [50.0%]). In addition, 28 (24.1%) patients had concomitant resection of at least one other organ/structure that included the diaphragm, pancreas, gall bladder, liver, adrenal, ureter, pericardium, and kidney. All resections and reconstructions were completed during the same operation. Patient demographics and details of the operative procedure and pathologic staging are included in Tables 2 and 3.

TABLE 3. Pathologic stage of tumor

Stage	n	%
UICC stage		
0 (carcinoma in situ)	1	0.9
IB	13	11.2
II	17	14.7
IIIA	34	29.3
IIIB	10	8.6
IV	41	35.3
T status		
T0	1	0.9
T1	1	0.9
T2	29	25.0
T3	54	46.6
T4	31	26.7
N status		
N0	30	25.9
N1	55	47.4
N2	21	18.1
N3	10	8.6
M status		
M0	101	87.1
M1	15	12.9

UICC, Union Internationale Contre le Cancer; T, tumor metastases; N, lymph node metastases; M, distant metastases.

Hospital Course

There were no intraoperative deaths. Six patients died within 30 days of resection or during the initial postoperative hospitalization (operative mortality, 5.2%). Cause of death was sepsis caused by anastomotic leak in 4 patients and stroke and myocardial infarction with stroke in 1 patient each. Median hospitalization was 13 days (range, 8-70 days). All patients were dismissed on a soft diet and monthly injections of vitamin B₁₂. Complications occurred in 51 (43.9%) patients. The 2 most common complications were anastomotic leak (12.9%) and atrial fibrillation (11.2%). With regard to the anastomotic leaks, the operative approach was laparotomy alone in 7 (11.1%) patients and left thoracoabdominal in 8 (17.4%) patients and was not statistically different. All other complications are listed in Table 4.

The only factor predictive of operative mortality was anastomotic leak ($P = .002$), with an odds ratio of 18.0 (95% CI, 3.0-109.8). Operative mortality was 26.7% in those with an anastomotic leak compared with only 2.0% in those without a leak.

Long-term Survival

Follow-up was complete in 108 (98.1%) operative survivors. Median follow-up was 14 months (range, 1-281 months). Overall median survival was 434 days (range, 9 days-281 months). One-, 5-, 10-, and 15-year survivals were 56.2%, 19.0%, 13.5%, and 12.3%, respectively (Figure 1). Fifty-seven (49.1%) patients had 63 recurrences. Of these

Table 4. Complications of surgery*

Complication	n	%
Anastomotic leak	15	12.9
Atrial fibrillation	13	11.2
Wound infection	9	7.8
Pneumonia	6	5.2
Intra-abdominal abscess	5	4.3
Urinary retention	4	3.4
Enterocutaneous fistula	3	2.6
Myocardial infarction	3	2.6
Empyema	3	2.6
Stroke	2	1.7
Pancreatic leak	2	1.7
Pancreatitis	2	1.7
Respiratory failure	2	1.7
Wound dehiscence	2	1.7
Bleeding requiring reoperation	1	0.9
Deep venous thrombosis	1	0.9
Pulmonary embolism	1	0.9
Atelectasis requiring bronchoscopy	1	0.9
Small bowel obstruction requiring operative intervention	1	0.9
Diaphragmatic dehiscence	1	0.9

*Some patients experienced more than one complication.

63 recurrences, 36 (57.1%) were locoregional, 11 (17.5%) were anastomotic, and 16 (25.4%) were distant.

Factors found to be significantly associated with long-term survival were complete resection ($P < .0001$), early UICC stage ($P < .0001$), early-stage T status ($P = .0001$), low N status ($P < .002$), low tumor grade ($P < .02$), and lack of splenic involvement by tumor ($P < 0.007$). These results are summarized in [Figures 2 through 4](#) and [Figures E1 through E3](#). Factors not affecting survival included age, sex, induction therapy, prior gastric surgery, surgical approach, splenectomy, era of operation, anastomotic leak or other postoperative complications, adjuvant therapy, and M1 status.

Discussion

Opinions differ regarding the definition and optimal treatment of AEG.^{6,7} The classification system proposed initially by Siewert and Stein is useful because it differentiates the cancers in a way that assists in planning the appropriate surgical resection.^{2,8} Type I tumors (see [Table 1](#)) are seemingly the least controversial and are most commonly treated by means of esophagectomy with en bloc resection of the proximal stomach and reconstruction with the stomach as the replacement conduit. Type II tumors are less well defined in terms of optimal surgical resection, and the optimal type of resection depends on whether the tumor extends proximally, distally, or in both directions.⁹ If subcardial gastric involvement is minimal, we prefer to treat these

Figure 1. Overall survival (death from any cause). Zero time on the abscissa represents the date of surgical resection.

tumors by means of esophagectomy with proximal gastrectomy. The goals of treatment are a complete resection with adequate (5 cm) margins, similar to type I cancers.¹⁰ Type III tumors, despite having a distinct anatomic localization in the region below the gastric cardia, have not been approached in a consistent fashion.¹¹ Because these cancers have the bulk of their tumor in the proximal stomach, the most common procedure has been total gastrectomy with resection of the distal esophagus and reconstruction with Roux-en-Y esophagojejunostomy to obtain adequate margins.⁹ This has been the preferred approach for these tumors at our institution for the last 30 years.

In our earlier experience (1975-1987), en bloc splenectomy was also performed in 95% of our patients. It was not until the 1990s that randomized studies demonstrated the decreased survival of patients undergoing concomitant splenectomy.^{12,13} More recently, concomitant splenectomy has also been associated with an increase in infectious complications.¹⁴ As a result, splenectomy was not only done less frequently (50%) in our later experience but also more selectively, with 40% of these being performed for direct splenic involvement by tumor. Today, it is now our practice to avoid splenectomy in these cases unless it is directly involved by tumor.

Our operative approach varied, with 40% of cases being done from a left thoracoabdominal incision, whereas the remaining cases were approached with a laparotomy alone (54%) or a laparotomy and subsequent right thoracotomy (6%). Surgeon preference was the most common determining factor. The surgical approach was not associated with differences in operative mortality, morbidity, or long-term survival.

Anastomotic leaks were the most ominous complication seen in our series, with an operative mortality rate of 26.7%.

Figure 2. Survival (death from any cause) by completeness of resection. R0 and R1 denote complete resection and incomplete resection, respectively. Zero time on the abscissa represents the date of surgical resection ($P < .0001$).

They were the only independent factor predictive of operative mortality with an odds ratio of 18.0. The management of these unfortunate events is clearly an important aspect of the overall care of patients undergoing this operation. Avoidance of anastomotic leaks by means of meticulous surgical technique is paramount. Furthermore, a high index of suspicion for the early detection and treatment of this complication might also play a significant role in mitigating the ultimate severity of this injury. As a practice, we have generally been very liberal in placing drains at the site of our esophagojejunostomy at the time of the initial operation. If an anastomotic leak is identified, adequate drainage is essential, with early primary repair being accomplished if possible. The placement of a downstream feeding jejunos-

Figure 3. Survival (death from any cause) by Union Internationale Contre le Cancer (UICC) stage. Zero time on the abscissa represents the date of surgical resection ($P < .0001$).

Figure 4. Survival (death from any cause) by T status. Zero time on the abscissa represents the date of surgical resection ($P < .0002$).

tomy tube at the time of the initial operation is also helpful in managing these complications, if they occur.

Although AEG tumors have recently been acknowledged as a unique clinical entity, few studies have examined type III tumors as a distinct group; instead, most studies group all 3 types together.^{6,15,16} This might be inappropriate, however, because type III tumors appear to have a poorer long-term survival, with overall 5-year survival of approximately 20% to 25%.^{8,9,17} Siewert and colleagues⁹ have reported a 10-year survival of 17%. Our series with a 1-, 5-, 10-, and 15-year survival of 56%, 19%, 13%, and 12%, respectively, suggests that despite a rapid decrease in survival during the first 5 years, a small subset of patients survive long term.

Predictors of long-term survival in our series included UICC stage, T status, N status, and tumor grade. These results are relevant in the context of the existing debate over whether the current staging system provides adequate prognostic information for AEG tumors.^{2,6,15,16,18} For patients with Siewert type III tumors, the UICC staging system for gastric adenocarcinoma would appear to provide useful and prognostic information. Stage I tumors showed relatively favorable 1-, 5-, 10-, and 15-year survival rates of 92.3%, 53.8%, 29.9%, and 15.0%, respectively.

Achieving a complete resection was associated with significantly improved long-term survival. There was no 5-year survival for patients with positive margins. Clearly, to avoid a purely palliative yet potentially morbid operation, approaches and strategies that improve the ability to achieve negative surgical margins (R0 resection) are needed and might include neoadjuvant therapies.

We identified tumor grade as a prognostic factor for long-term survival. Although no other investigators have specifically looked at the influence of grade on survival in

Siewert type III cancers, this factor has been found to be important in other studies of early gastric cancer and of AEG tumors that are grouped together.¹⁹⁻²¹

Prior gastric surgery, induction therapy (including chemotherapy and radiotherapy), and adjuvant treatments did not influence operative mortality or long-term survival in our series. Because our series was retrospective and reports on a relatively small number of patients treated with induction or adjuvant therapy, we cannot comment on the role of either of these treatment adjuncts for Siewert type III tumors. Nevertheless, for locally advanced gastric cancers, combined adjuvant chemotherapy and radiotherapy have become a routine consideration at our institution.^{22,23}

In summary, total gastrectomy and esophagectomy with Roux-en-Y reconstruction for Siewert type III cancers is associated with significant morbidity. Nonetheless, long-term survival can be achieved with surgical intervention in a small subset of selected patients.

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References

- Devesa SS, Blot WJ, Fraumeni JF Jr. Changing patterns in the incidence of esophageal and gastric carcinoma in the United States. *Cancer*. 1998;83:2049-53.
- Siewert JR, Stein HJ. Classification of adenocarcinoma of the oesophagogastric junction. *Br J Surg*. 1998;85:1457-9.
- Sobin LH, Wittekind C. Digestive system tumours. In: Sobin LH, Wittekind C, editors. TNM classification of malignant tumours. 6th ed. Hoboken, NJ: John Wiley & Sons; 2002.
- Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc*. 1958;53:457-81.
- Peto R, Peto J. Asymptotically efficient rank invariant procedures. *J Am Stat Assoc*. 1972;135:185-207.
- Driessen A, Van Raemdonck D, De Leyn P, et al. Are carcinomas of the cardia oesophageal or gastric adenocarcinomas? *Eur J Cancer*. 2003;39:2487-94.
- von Rahden BHA, Feith M, Stein HJ. Carcinoma of the cardia: classification as esophageal or gastric cancer? *Int J Colorectal Dis*. 2005;20:89-93.
- de Manzoni G, Pedrazzani C, Pasini F, et al. Results of surgical treatment of adenocarcinoma of the gastric cardia. *Ann Thorac Surg*. 2002;73:1035-40.
- Siewert JR, Feith M, Werner M, Stein HJ. Adenocarcinoma of the esophagogastric junction: results of surgical therapy based on anatomical/topographic classification in 1,002 consecutive patients. *Ann Surg*. 2000;232:353-61.
- Visbal AL, Allen MS, Miller DL, Deschamps C, Trastek VF, Pairolero PC. Ivor Lewis esophagogastric resection for esophageal cancer. *Ann Thorac Surg*. 2001;71:1803-8.
- Siewert JR, Stein HJ. Adenocarcinoma of the gastroesophageal junction: classification, pathology and extent of resection. *Dis Esophagus*. 1996;9:173-82.
- Cuschieri A, Fayers P, Fielding J, et al. Postoperative morbidity and mortality after D1 and D2 resections for gastric cancer: preliminary results of the MRC randomised controlled surgical trial. The Surgical Cooperative Group. *Lancet*. 1996;347:995-9.
- Bonenkamp JJ, Songun I, Hermans J, et al. Randomised comparison of morbidity after D1 and D2 dissection for gastric cancer in 996 Dutch patients. *Lancet*. 1995;345:745-8.
- Weitz J, Jaques DP, Brennan M, Karpeh M. Association of splenectomy with postoperative complications in patients with proximal gastric and gastroesophageal junction cancer. *Ann Surg Oncol*. 2004;11:682-9.
- de Manzoni G, Pedrazzani C, Verlato G, et al. Comparison of old and new TNM systems for nodal staging in adenocarcinoma of the gastroesophageal junction. *Br J Surg*. 2004;91:296-303.
- von Rahden BH, Stein HJ, Feith M, Becker K, Siewert JR. Lymphatic vessel invasion as a prognostic factor in patients with primary resected adenocarcinomas of the esophagogastric junction. *J Clin Oncol*. 2005;23:874-9.
- Ito H, Clancy TE, Osteen RT, et al. Adenocarcinoma of the gastric cardia: what is the optimal surgical approach? *J Am Coll Surg*. 2004;199:880-6.
- Stein HJ, Feith M, Siewert JR. Cancer of the esophagogastric junction. *Surg Oncol*. 2000;9:35-41.
- Sanchez-Bueno F, Garcia-Marcilla JA, Perez-Flores D, et al. Prognostic factors in a series of 297 patients with gastric adenocarcinoma undergoing surgical resection. *Br J Surg*. 1998;85:255-60.
- Erturk MS, Cicek Y, Ersan Y, Saribeyoglu K, Dogusoy G, Erginoz E. Analysis of clinicopathological prognostic parameters in adenocarcinoma of the gastric cardia. *Acta Chir Belg*. 2003;103:611-5.
- Pelz J, Merkel S, Horbach T, Papadopoulos T, Hohenberger W. Determination of nodal status and treatment in early gastric cancer. *Eur J Surg Oncol*. 2004;30:935-41.
- Macdonald JS. Adjuvant therapy for gastric cancer. *Semin Oncol*. 2003;30(suppl 11):19-25.
- Macdonald JS. Clinical overview: adjuvant therapy of gastrointestinal cancer. *Cancer Chemother Pharmacol*. 2004;54:S4-11.

Discussion

Dr Nasser K. Altorki (New York, NY). This retrospective review by the Mayo Clinic group probably is one of the largest reported series on the surgical treatment of a difficult and largely forgotten group of patients, namely those with subcardial cancers invading the gastroesophageal junction. I say "largely forgotten" because this particular subset of patients accounted for only 10% of patients in the Dutch randomized trial for gastric cancer surgery and for less than 15% of patients in the intergroup gastric cancer adjuvant therapy trial. This is truly an orphan disease. Nobody wants to claim it. It is not hard to see why that is, having seen the data we just saw. Nearly 60% of the patients had transmural disease; 27% of the patients had disease that encroached on and invaded adjacent organs, requiring complex multiorgan resections; and 75% of the patients had nodal metastases. Not surprisingly, R0 resections were accomplished in less than 60% of patients, and the overall survival at 5 years is merely 19%.

We have once again learned from the Mayo Clinic that there are several factors significantly associated with improved survival, namely the completeness of the resection and earlier UICC stage and earlier T and N status and lower-grade tumor. This series will be a valuable reference for those of us who continue to treat these patients from time to time.

I have the following questions for you,

Dr Shen, what criteria were used in this retrospective review to identify Siewert type III tumors and distinguish them from massive midgastric tumors that have extended proximally to engulf the gastroesophageal junction? I am particularly concerned about those tumors that required multiorgan resection, such as the kidney, the adrenal, and the ureters, organs that are characteristically present low down in the gastric bed.

Dr Shen. Thank you, Dr Altorki.

The criteria that were used as inclusion in this patient dataset was identification of the center of the tumor or the tumor mass within the parameters we discussed for identification of Siewert type III tumors. Patients who had linitis plastica or tumors that involved the entire stomach were excluded.

Dr Altorki. How do you distinguish, then, clinically before the operation between the Siewert type II and type III tumors, and how does that influence your operative approach, if at all?

Dr Shen. The preoperative evaluation for almost all of these patients involves a combination of upper endoscopy, contrast radiography, and, in the more recent group of patients, endoscopic ultrasonography and computed tomographic scanning. I think the operative management for patients with linitis plastica or massive involvement of a tumor in the stomach would be identical; the approach would be a total gastrectomy with Roux-en-Y esophageojejunostomy.

Dr Altorki. I would just caution you that sometimes the distinction between a type II and a type III tumor would not be immediately apparent using standard preoperative diagnostic criteria, and one thing that you might consider in the distinction between them is the use of laparoscopy.

Would you just comment a little bit on the extent of lymph node dissection currently advocated for this tumor at the Mayo Clinic and your recommendation with respect to adjuvant therapy. Some have suggested that the value of adjuvant therapy shown in the intergroup trial is merely correction for a subpar lymph node dissection associated with those operations.

Dr Shen. The median number of lymph nodes that were examined in the pathologic specimens was 13, with a range of 2 to 46. The median number of positive lymph nodes was 4. A total of 45% of all patients had 15 or more lymph nodes, which is the current recommendation under UICC guidelines for adequate lymph node dissection.

The practice during this study period at the Mayo Clinic was not to formally perform extended lymph node dissection. Nevertheless, I would point out that over the 26-year period analyzed in this study, the practice did change, in particular with regard to whether a splenectomy was routinely performed. As you might imagine, with the increase in the incidence of this type of tumor, there were more patients who underwent surgical intervention during the latter 13 years than the first 13 years of the study. Of the 116 patients, 40 were operated on in the first 13 years, and of those, 38 (95%) of 40 had a splenectomy. Conversely, a splenectomy was only performed in 50% of the 76 patients in the later group. It was the practice at Mayo Clinic in the earlier period to routinely perform a splenectomy as part of the lymphadenectomy, and in those patients more lymph nodes were harvested.

Dr Altorki. I have noticed that the 1-year mortality for incompletely resected patients was 75%. I wanted to know what your current recommendation is regarding the role of “palliative” resection if an R0 resection cannot be reasonably expected and regarding the merits of palliative resection in patients with stage IV disease.

Thank you.

Dr Shen. Whether an R0 or R1 resection could be obtained was, in general, not the determining factor of whether surgical resection was undertaken. We observed that the vast majority of

these patients had important and severe symptoms at the time of diagnosis. Consequently, a significant proportion, although I cannot in retrospect determine the exact proportion, underwent surgical intervention with an a priori palliative objective.

I think one other question that you had asked previously that I have not yet addressed was the recommendation for adjuvant therapy in this group of patients. It is the current feeling of our group at Mayo Clinic, as well as most groups in North America, that because these patients usually present with such an advanced stage of disease and long-term survival with surgical resection is as of yet rather unsatisfying, there might be some evidence that adjuvant therapy provides some long-term survival advantage. The Dutch Gastric Cancer Trial Group recently published their prospective, randomized trial investigating extended lymph node dissection in 1000 patients. One of the subgroup analyses evaluated whether adjuvant therapy was of any benefit. They concluded that adjuvant therapy in this disease is not of any benefit. Nevertheless, I believe that most centers in North America would still recommend giving adjuvant therapy.

Dr Altorki. Congratulations on a great presentation.

Dr Shen. Thank you.

Dr Richard Finley (*Vancouver, British Columbia, Canada*). Again, that was a wonderful presentation.

I have 3 questions for you. Did you look at complications and survival in relationship to the approach? I notice some of the patients had a laparotomy and some had a thoracotomy. Was there any difference in complications and in survival? Did you also look at the surgeon as a risk factor in your multivariate analysis?

Dr Shen. We did look at survival by the surgical approaches that were used. There were 3 approaches: (1) laparotomy only, (2) combined thoracoabdominal, and (3) laparotomy followed by thoracotomy. There was no difference in terms of long-term survival on the basis of the approach that was used. We did not look at specific complication rates of each surgical approach.

Your second question referred to variation in results by specific surgeon. We did examine this. As you might imagine, over a 26-year period at Mayo Clinic, there were quite a number of surgeons involved. Of the 116 patients, there were 24 different surgeons, although the 3 surgeons with the highest volume accounted for 53% of the total cases. There was no association or relationship between surgeon volume in our study and long-term survival.

Dr Finley. Second, do you do a frozen section on the esophageal margin? If it is positive, what do you do?

Dr Shen. Yes, frozen sections are done routinely on all resected specimens at Mayo Clinic. If the esophageal margin is positive, attempts are made to obtain a clear margin. In some cases in which a clear esophageal margin was not obtained, either intraoperative radiation therapy was given or the patients received adjuvant radiation or chemoradiation.

Dr Finley. Finally, do you use jejunostomies? How do you support your patients nutritionally?

Dr Shen. There was also a change in the use of jejunostomy tubes. Overall, 33 (28%) of the 116 patients had a jejunostomy tube placed. This was dependent on the era in which the operation was performed. We bisected the dataset, and in the first 13 years, only 1 (2.5%) of the 40 patients had a jejunostomy tube placed, whereas in the latter half, the more contemporary era, 32 (42%) of

76 had a jejunostomy tube placed. It is the current standard at Mayo Clinic that all patients undergoing this operation undergo jejunostomy tube placement at the time of the surgical resection and receive tube-feed supplementation postoperatively.

Dr Finley. Congratulations on your paper.

Dr Shen. Thank you.

Dr Douglas Mathisen (*Boston, Mass*). Rob, that was an excellent presentation.

I believe I saw that there was a 13% incidence of anastomotic leaks, with a significant contribution to the operative mortality. Do you have any sense from looking at these patients how the anastomotic leak was handled in this group of patients after a total gastrectomy?

Dr Shen. Yes. The majority of patients who had an anastomotic leak were initially managed conservatively. I do not know the exact number, but in at least a third to a fourth, the patients became quite ill and required reoperation.

Dr Tony Lerut (*Leuven, Belgium*). This is a very nice study on a very complex and difficult group.

I noticed that you had about 50% strictly transabdominal approaches versus 50% transthoracic approaches. On what criteria did you decide to do the approach using laparotomy versus a transthoracic access route?

Dr Shen. It really was the surgeon's preference as far as which approach was used. I think an important factor that went into that decision was obviously the preoperative evaluation of how much of the distal esophagus was involved with tumor in terms of length. There were other significant preoperative factors that for reasons of time I did not mention in the presentation but that we discuss in the manuscript. Eleven percent of all of the 116 patients had prior gastric surgery, most for peptic ulcer disease. There has been an association in prior studies with patients who have had prior gastric surgery, usually for benign conditions, predisposing them to gastric cancer. Therefore it was not surprising that 11% of these patients had prior partial gastrectomies. Therefore that also played into the decision of which surgical approach was used.

Dr Lerut. I can imagine that through an abdominal approach it is more difficult to obtain a sufficient safety margin toward the proximal extension of the tumor. Was there any difference in the incidence of positive margins either at frozen section or final examination between the 2 groups (ie, transabdominal vs transthoracic)?

Dr Shen. I do not have any data regarding that question. I am sorry.

Dr Lerut. Thank you.

Figure E1. Survival (death from any cause) by N status. Zero time on the abscissa represents the date of surgical resection ($P < .002$).

Figure E2. Survival (death from any cause) by tumor grade. Zero time on the abscissa represents the date of surgical resection. ($P < .02$).

Figure E3. Survival (death from any cause) by splenic involvement by tumor. Zero time on the abscissa represents the date of surgical resection. ($P < .008$).