GENERAL THORACIC SURGERY

ESOPHAGOGASTRECTOMY FOR CARCINOMA OF THE ESOPHAGUS AND CARDIA: A COMPARISON OF FINDINGS AND RESULTS AFTER STANDARD RESECTION IN THREE CONSECUTIVE EIGHT-YEAR INTERVALS WITH IMPROVED STAGING CRITERIA

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Objective: A review of findings and results after standard resection for carcinoma of the esophagus and cardia without neoadjuvant therapy was done to provide a basis for comparison with current reports of radical resection and neoadjuvant therapy. **Methods:** A 24-year experience on one surgical service with 454 operations for carcinoma of the esophagus and cardia was reviewed. A comparison of findings and results in three consecutive 8-year intervals was analyzed, and new staging criteria were developed and compared with those currently favored by the American Joint Committee on Cancer. **Results:** From January 1, 1970, to January 1, 1994, 454 patients with carcinoma of the esophagus or cardia underwent operation, of whom 408 (90%) had esophagogastrectomy with a 30-day mortality rate of 2.5% and an additional hospital mortality rate of 1.2%. Of the 121 complications (30.7%), 71 (18%) were major and 50 (12.7%) were minor. Cardiovascular complications predominated. The overall 5-year survival was 24.7%, with a 33.7% survival after complete resections in the most recent interval under study. Palliation of dysphagia was achieved in nearly 80% of patients who survived the operation. During the three intervals under review, resectability, mortality, and complication rates remained constant. The percentages of left thoracotomies and transhiatal resections increased, and there was a decrease in thoracoabdominal incisions. The percentages of patients with Barrett's esophagus and stage 0 and I tumors increased. The percentage of complete resections (R0) increased, whereas that for resections with residual microscopic tumor (R1) decreased, and there was no change in the percentage of patients with residual gross tumor after resection (R2). Modified WNM staging criteria are proposed that provide better prognostic stratification of the disease than those currently favored by The American Joint Committee on Cancer. **Conclusions:** Standard esophagogastrectomy is applicable in 90% of patients with operable carcinoma of the esophagus or cardia, with consistently low mortality and morbidity rates and satisfactory palliation of dysphagia. The 5-year survival (24.7% overall) remains suboptimal, but the current figure for complete resections (33.7%) is encouraging. There is a need for revision of the current American Joint Committee on Cancer staging criteria. (*J Thorac Cardiovasc Surg* 1997; 113:836-48)

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Results of surgical treatment for patients with carcinoma of the esophagus and cardia remain suboptimal. Efforts to improve results either by enlarging the

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extent of the resection, as in the "en bloc" technique,¹ or by the use of neoadjuvant therapy are currently being pursued aggressively. Enthusiasm for these new approaches prompted us to review our experience with standard techniques of resection, without neoadjuvant therapy, performed by one surgical team in an effort to provide a basis for comparison with the results of other approaches. By comparing the findings and clinical results in three separate consecutive 8-year intervals, we have attempted to determine the changes that may have occurred during the 24 years of the study. In so doing, we encountered limitations with the current staging criteria outlined in the *Manual for Staging of Cancer*,² prepared by the American Joint Committee on Cancer (AJCC), and have developed new staging criteria that provide better prognostic stratification by stage of disease.

Patients and methods

From January 1, 1970, to January 1, 1994, 454 patients with carcinoma of the esophagus or cardia underwent operation, of whom 408 (90%) had an esophagogastrectomy. Carcinomas of the cardia were included because the surgical approach to such lesions is similar to that for carcinomas of the lower esophagus. A recent comparison of staging criteria for esophageal and stomach cancer showed no difference in the staging results.³ Furthermore, current studies suggest that up to 50% of carcinomas of the cardia may arise from tongues or short segments of Barrett's esophagus and thus have their origin from the esophagus rather than from gastric mucosa.⁴⁻⁶ Although it is difficult to determine precisely the limits of the cardia, we continue to adhere to our original definition,⁷ which describes a carcinoma of the cardia as one arising in the upper part of the stomach and involving the esophagogastric junction and part of the lower thoracic esophagus. Carcinomas arising in the gastric corpus and diffuse carcinomas of the linitis plastica variety are excluded, even though they may involve the esophagogastric junction.

Six of the 454 patients had esophageal achalasia, a known precursor of squamous cell carcinoma of the esophagus.⁸ Only 24 patients had neoadjuvant therapy in the form of either radiotherapy or chemotherapy alone or a combination thereof. Only three of these patients lived 5 or more years after operation. Most of these patients came to us after the development of recurrent dysphagia after failure of what had initially been undertaken as definitive therapy for the disease. Follow-up information after discharge from the hospital was based either on direct examination or the response to letters or telephone calls to the patient or the patient's relatives or physician. The 24-year period of the study was divided into three separate 8-year intervals to permit a comparison of the incidence of several variables (see later section) in each of the three periods.

Survival was calculated by the product limit method of Kaplan and Meier.⁹ Tarone-Ware¹⁰ analysis was used to determine the significance of survival distributions among

Fig. 1. Location of the tumor in 454 patients seen between 1970 and 1994 with carcinoma of the esophagus or cardia.

groups. Contingency tables were analyzed with the use of Miettinen's modification of Fisher's exact test¹¹ or χ^2 test where appropriate. Probabilities are two-tailed, with $p < 0.05$ regarded as statistically significant.

Pathology. The locations of the 454 tumors are illustrated in Fig. 1: 213 (47%) involved the esophagogastric junction, 103 (23%) the lower thoracic esophagus, 128 (28%) the upper thoracic esophagus, and 10 (2%) the cervical esophagus. Of these tumors, 303 were adenocarcinomas, with 208 of these being carcinomas of the cardia whereas 94 arose in Barrett's esophagus. Only one primary adenocarcinoma of the thoracic esophagus was found. Squamous cell carcinoma was the next most common tumor and was present in 139 patients. Twelve miscellaneous malignant tumors included five adenoacanthomas, two small cell carcinomas, two histiocytic lymphomas, two mucoepidermoid carcinomas, and one carcinosarcoma. Postresection staging according to the criteria of the AJCC, as published in the fourth edition of the *Manual for Staging of Cancer*,² revealed that 16 patients had stage 0, 22 had stage I, 80 had stage IIA, 39 had stage IIb, 218 had stage III, and 33 had stage IV disease (Table I). Patients with stage IV disease had one or more small metastatic deposits at operation, undetected before operation, and underwent palliative resection for relief of dysphagia.

Surgical technique. Our surgical technique for the management of carcinoma of the esophagus and cardia has been described in detail elsewhere^{12,13} and, for the

Table I. *Histologic type of tumors and stage of the resected specimens*

	No.
Adenocarcinoma	303
Cardia	208
Barrett's esophagus	94
Esophageal adenocarcinoma	1
Squamous cell carcinoma	139
Miscellaneous	12
Adenoacanthoma	5
Small cell carcinoma	2
Histiocytic lymphoma	2
Mucoepidermoid carcinoma	2
Carcinosarcoma	1
Total	454
Stage	
0	16
I	22
IIA	80
IIB	39
III	218
IV	33

most part, was dependent on the location of the lesion.¹⁴ Thus for tumors of the distal esophagus and cardia, a left thoracotomy through the bed of the nonresected eighth rib was the most common procedure done (162). An Ivor Lewis approach was preferred for lesions at a higher level (118) and a transhiatal approach for selected patients in whom the computed tomographic scans suggested the absence of extrasophageal extension or massive mediastinal nodal involvement preferably for tumors located caudad to the trachea (96). This approach was particularly appropriate for patients with adenocarcinoma in Barrett's esophagus in whom all of the benign Barrett's mucosa must be removed to prevent later development of a second carcinoma in this abnormal epithelium. A thoracoabdominal incision, used early in the series in only 12 patients, is no longer favored. Miscellaneous approaches were used in 4 patients, and those who required colon interposition (16) underwent esophagectomy and a sub-sternal colon interposition as a second-stage procedure. Exclusive of the 4 miscellaneous procedures, 279 of the anastomoses were done within the thorax, whereas 125 were done in the neck, 13 after a preliminary thoracic incision proved inadequate to remove all the involved tissue, thus necessitating a separate cervical incision for completion of the procedure. The stomach was the preferred esophageal substitute, with the distal colon being used most often in the early years of the study. All of the anastomoses were done manually with an inner layer of running catgut and an outer layer of interrupted silk or polyglactin 910 (Vicryl) sutures.

Results

Operative results. Ten patients (2.5%) died within 30 days of operation and an additional five patients (1.2%) were not able to leave the hospital

Table II. *Causes of hospital mortality after esophagogastrectomy for carcinoma of the esophagus and cardia in 408 patients*

Cause	No. of patients
Cardiovascular	7
Myocardial infarction	3
Pulmonary embolus	2
Mesenteric artery thrombosis	1
Cardiac arrest	1
Respiratory	3
Pneumonia	1
Respiratory failure	1
Empyema	1
Gastrointestinal tract	1
Gastric infarction	1
Miscellaneous	4
Hepatorenal failure	2
Thoracic duct fistula	1
Hemorrhage	1
Total	15 (3.7%)

and died later, for an overall mortality rate of 3.7%. The causes of death are listed in Table II: the most common causes were cardiovascular in nature, three patients dying of myocardial infarction, two of a pulmonary embolus, one of mesenteric artery thrombosis, and one of cardiac arrest during attempted computed tomographic-guided needle aspiration of a posterior mediastinal abscess. Three patients died of respiratory problems, including pneumonia, respiratory failure, and thoracic empyema (one each). Another died after excision of an area of infarcted stomach. Two patients died of hepatorenal failure. Another patient died of unrecognized hemorrhage the night after a transhiatal resection, and another died of a persistent thoracic duct leak, despite multiple surgical attempts to control the leakage.

We recorded 121 complications (30.7%) in 110 patients: 71 (18%) were major in that they prolonged the hospitalization time and 50 (12.7%) were considered minor in that they did not do so. Because several patients had more than one complication, a total of 27.9% had complications. The major and minor complications according to general categories are listed in Table III. Anastomotic leakage predominated among the major complications. Of the three intrathoracic leaks, one was successfully resutured, another was a contained leak successfully managed conservatively, and the third necessitated open drainage, and this patient eventually died of a pulmonary embolus. The cervical anastomotic leaks,

Fig. 2. Adjusted actuarial survival for all patients who survived esophagogastrectomy exclusive of noncancer deaths. *n*, Number of patients remaining at risk.

Table III. Complications in 393 survivors of esophagogastrectomy for carcinoma of the esophagus and cardia

Major	No.	Minor	No.
Anastomotic leak	25	Arrhythmia	23
Cervical	22	Respiratory	18
Thoracic	3	Wound infection	4
Gastrointestinal tract	14	Urinary tract infection	4
Respiratory	8	Phlebitis	1
Recurrent nerve injury	5		
Subphrenic abscess	5		
Cardiovascular	4		
Chylothorax	3		
Diaphragmatic hernia	2		
Miscellaneous	5		
Total	71 (18.0%)		50 (12.7%)

with one exception, healed spontaneously within a few days to 2 weeks by discontinuation of oral feedings and initiation of antibiotic therapy and hyperalimentation. One patient required surgical closure of the fistula. Gastrointestinal tract complications comprised the next most common major complication, and these usually involved outlet obstruction of the stomach. Six of these complications necessitated operation. Three patients needed pyloroplasty. Two patients with obstruction at the level of the hiatus required surgical relief. One patient with torsion of the stomach also required surgical correction. The other four patients had prolonged gastric stasis, which eventually resolved under conservative management. Other surgical corrections

necessitated by gastrointestinal tract complications were cholecystectomy for acute cholecystitis (1), resection of the right colon because of infarction (1), surgical relief of small bowel obstruction (1), and closure of a gastric leak from the staple line of the lesser gastric curvature closure (1). Seven of the eight respiratory complications were the result of pneumonia, which responded to appropriate antibiotics. One patient with thoracic empyema was treated successfully by tube drainage.

Among the five patients who had recurrent nerve injury, the nerve was purposely sacrificed because of involvement by the tumor in one patient. Another patient is still alive and has hoarseness and presumably permanent nerve damage. Two others died of

Fig. 3. Adjusted actuarial survival for patients with R0 (no residual tumor), R1 (microscopic residual tumor), and R2 (obvious residual tumor) conditions after resection. *n*, Number of patients remaining at risk.

metastatic disease within 2.5 and 3 years, and the status of the vocal cord function was unknown. A fifth patient is still alive and recovered vocal cord function a few months after operation. Of the five patients with subphrenic abscesses, two required open drainage, whereas the other three were treated successfully by catheter drainage. The cardiovascular complications included two strokes, one myocardial infarction, and one case of congestive heart failure. In three patients, a postoperative chylothorax developed that required surgical ligation of the thoracic duct, and two patients had postoperative herniation of the stomach through the widened hiatus, which necessitated surgical reduction. Three of the miscellaneous complications necessitated splenectomy after operative injury to the spleen. One patient died of multiple system failure, and another patient died of renal failure.

The majority of minor complications were related to cardiac arrhythmias (23), which were controlled for the most part by antiarrhythmic medications. Respiratory complications (18) included excessive retained secretions necessitating bronchoscopy. Wound infections (4), urinary tract infections (4), and phlebitis (1) accounted for the rest of the minor complications.

Because palliation of dysphagia is one of the main goals of esophagogastrectomy, information on this point is important. Worthwhile information was

available for 356 patients, 277 (78%) of whom had partial or complete relief of swallowing difficulties. Because many patients died at home without a postmortem examination, whether stenosis of the anastomotic site was benign or malignant is not known with assurance. There were, however, 32 known anastomotic recurrences among the 393 survivors of resection (8%).

Survival. Actuarial survival curves for all patients, adjusted for hospital and noncancer deaths, are depicted in Figs. 2 through 5. The overall 5-year survival was 24.7%, with a median survival of 18 months (Fig. 2). In Fig. 3, survival curves related to the completeness of the resection are depicted. Patients who had a complete resection (R0) had a 29.2% 5-year survival, with a median survival of 21.5 months. No patient with residual microscopic evidence of tumor (R1) survived for 5 years, and the median survival for these patients was 10 $\frac{2}{3}$ months. Patients with gross evidence of residual tumor after resection (R2) also did not survive for 5 years. The median survival in this latter group was 7.5 months. The survival curves according to the histologic type of the resected tumor are shown in Fig. 4. The 5-year survival of patients with Barrett's esophagus was 32.6%, with a median survival of 23 $\frac{2}{3}$ months. Patients with adenocarcinoma of the cardia had a 25.3% 5-year survival, with a median survival of 18 months, whereas patients with squamous cell carci-

Fig. 4. Adjusted actuarial survival curves according to histologic types. *n*, Number of patients remaining at risk; *CA*, carcinoma; *Adeno*, adenocarcinoma; *SCE*, squamous cell carcinoma.

noma had a 20.7% 5-year survival, also with a median survival of 18 months. These survival data were not significantly different statistically. The stage of the tumor, however, as illustrated in Fig. 5, had a profound impact on survival. Of patients with stage 0 tumors, 100% survived for 5 years, with a median survival of 20.5 years; 78.9% of patients with stage I disease survived 5 years, with a median survival of 16 $\frac{2}{3}$ years; 37.9% of patients with stage IIA disease survived 5 years, with a median survival of 2 $\frac{1}{2}$ years; 27.3% of patients with stage IIB lesions survived 5 years, with a median survival of 1 $\frac{3}{4}$ years; and 13.7% of patients with stage III lesions survived 5 years, with a median survival of 1 $\frac{1}{4}$ years. No patient with stage IV disease survived for 5 years, and the median survival in this group was only 6 months.

Comparison of findings and results in three consecutive eight-year intervals. In an effort to identify measurable trends either in the nature of the disease or in its treatment over the 24 years of the study that might be helpful in the treatment of patients with carcinoma of the esophagus and cardia, we divided our data into three consecutive 8-year intervals as depicted in Table IV. A number of variables were analyzed statistically, and the findings can be summarized briefly as follows: the number of patients in each 8-year interval increased during the 24 years of the study. In the first period (1970 to 1978), there were 64 patients; from 1978 to

1986, 187 patients; and between 1986 and 1994, 203 patients. Resectability, hospital mortality, and post-operative complication rates remained constant. The percentages of left thoracic and transhiatal surgical approaches increased ($p = 0.0177$ and $p < 0.0001$, respectively), and there was a decline in thoracoabdominal incisions ($p < 0.0001$). The percentage of patients with adenocarcinoma in Barrett's esophagus increased ($p = 0.0001$) as did the percentage of stage 0 tumors ($p = 0.0078$). Although there was no change in the percentage of stage I tumors, the combined group of patients with stage 0 and those with stage I tumors exhibited a pronounced increase at the $p = 0.0177$ level. The percentage of patients who had R0 resections increased ($p = 0.0455$), whereas the percentage of R1 resections decreased ($p = 0.015$) and there was no change in the percentage of R2 resections. The overall 5-year survival was higher during the most recent interval than that during the previous one (28.8% vs 20.3%), but the overall trend of mortality rates was not significantly different statistically. The percentage of patients who had partial or complete relief of dysphagia decreased slightly in the most recent interval compared with that in the earliest 8-year period of the study.

Proposal for improved staging criteria. In a previous publication,³ we questioned the validity of the staging criteria proposed in the revised *Manual for*

Fig. 5. Adjusted actuarial survival curves by stage using AJCC criteria. *n*, Number of patients remaining at risk.

Cancer Staging for prognostic stratification of cases of carcinoma of the esophagus and cardia because it provided no better stratification than the earlier edition.¹⁵ This prompted us to propose a revised staging system based on a modification of the WNM system of Skinner and associates.¹⁶ We expanded our patient base by including all of the patients presented in this report and compared the AJCC staging criteria with those of the modified WNM version previously presented by us. The only change in our original proposal is the transfer of the W2 (T3, T4) N1 condition from stage II to stage III (Fig. 6). The comparison is presented in Table V. With use of the new staging criteria, not only is the number of patients more evenly divided among the four stages but also the comparison between stages of 5-year survivals is highly significant statistically, with almost a 50% reduction in survival rates for each increasing stage. With the current AJCC criteria for staging, only two of the comparative analyses between stages are significantly different, and the remaining three show no statistically significant difference in the 5-year survivals.

The major difference in the staging criteria of the proposed new system is the recognition that the number of lymph nodes involved has a profound effect on prognosis: N0 (no nodes involved), N1 (1 to 4 nodes involved), and N2 (5 or more nodes involved). The T categories and their corresponding

W numbers are T0, Tis, and T1 = W0; T2 = W1; and T3 and T4 = W2.

Discussion

The experience with standard resection for carcinoma of the esophagus and cardia that we have reported herein is similar to that of other recent reports from major centers in the United States, with hospital mortality rates of 5% or less and postoperative complication rates of about 30%.¹⁷⁻¹⁹ Higher complication rates, from 60% to 70%, however, have been reported both from this country and from Europe.²⁰⁻²² Respiratory complications and anastomotic leaks, which in earlier years predominated,²³ are no longer the major complications of esophagogastrectomy in our hands; rather, cardiovascular complications predominate. Other reports, however, still indicate the predominance of respiratory problems after operation.²⁴⁻²⁶ Although the number of cervical anastomotic leaks appears high, 22 (17.6%) of 125, this is not out of line with the 10% to 30% incidence of cervical anastomotic leaks reported in the literature.^{27, 28} It should be emphasized that none of our cervical leaks proved life threatening and all but one healed with conservative management. Our resectability rate of 90% is also higher than that usually reported, which could easily be a reflection of patient population differences among hospitals. In contrast to an-

Table IV. Comparison of findings and results in three separate 8-year intervals

	1970-1978 (64 patients)		1978-1986 (187 patients)		1986-1994 (203 patients)		<i>p</i> Value
	No. of patients	%	No. of patients	%	No. of patients	%	
Resectability	54/64	84.3	168/187	89.8	186/203	91.6	NS
Mortality	3/54	5.6	5/168	3.0	7/186	3.7	NS
30-day	2/54	3.7	2/168	1.2	6/186	3.2	NS
Hospital	1/54	1.9	3/168	1.8	1/186	0.5	NS
Complications	20/51	39.2	40/163	24.5	61/179	34.0	NS
Major	10/51	19.6	22/163	13.5	39/179	21.8	NS
Minor	10/51	19.6	18/163	11.0	22/179	12.3	NS
Operations							
Left thoracic	16/54	29.6	80/168	47.6	66/186	35.5	0.0177
Ivor Lewis	22/54	40.7	47/168	27.9	49/186	26.3	NS
Transhiatal	0/54	0	31/168	18.5	65/186	34.9	<0.0001
Thoracoabdominal	10/54	18.5	1/168	0.6	1/186	0.5	<0.0001
Colon	4/54	7.5	8/168	4.8	4/186	2.3	NS
Miscellaneous	2/54	3.7	1/168	0.6	1/186	0.5	NS
Pathologic findings							
Adenocarcinoma of cardia	32/64	50.0	91/187	48.7	81/203	40.0	NS
Squamous cell carcinoma of esophagus	25/64	39.0	58/187	31.0	62/203	30.5	NS
Adenocarcinoma of Barrett's esophagus	4/64	6.3	31/187	16.6	58/203	28.5	0.0001
Miscellaneous	3/64	4.7	7/187	3.7	2/203	1.0	NS
R0	39/54	72.2	144/168	85.7	159/186	85.5	0.0455
R1	6/54	11.1	3/168	1.8	10/186	5.4	0.0150
R2	9/54	16.7	21/168	12.5	17/186	9.1	NS
Stage							
0	1/54	1.9	2/168	1.2	14/186	7.5	0.0078
I	1/54	1.9	6/168	3.6	14/186	7.5	NS
IIA	11/54	20.3	38/168	22.6	27/186	14.5	NS
IIB	10/54	18.5	18/168	10.7	16/186	8.6	NS
III	24/54	44.4	93/168	55.4	100/186	53.8	NS
IV	7/54	13.0	11/168	6.5	15/186	8.1	NS
5-Year survival		27.2		20.3		28.8	NS
Palliation	44/50	88.0	108/151	71.5	125/155	80.6	0.0264

NS, Not significant; R0, complete resection; R1, residual microscopic evidence of tumor after resection; R2, obvious residual tumor after resection.

other report that compared findings in different consecutive time frames,²² our mortality, resectability, and complication rates have remained stable, presumably because our earlier figures were low in terms of mortality and complications and relatively high in terms of resectability. However, we too noted an increasing number of cases of Barrett's carcinoma and, presumably as a result of surveillance programs for patients with benign Barrett's disease, an increased number of patients in the early stages of the disease in the most recent interval studied. Although it was not surprising that the percentage of patients undergoing transhiatal resections increased and the percentage of those undergoing thoracoabdominal approaches decreased, the increase in left thoracotomy approaches was not anticipated in view of the wide-

spread enthusiasm for the Ivor Lewis approach in this country.

The 5-year survival of 28.8% (33.7% for patients having R0 resections) in the most recent 8-year interval is higher than that most commonly reported in the Western world but lower than that reported from Japan, particularly in series in which a "three-field" resection was done.^{29, 30} Although these differences may be stage related, rather than the result of the extent of resection, they raise the question of whether standard resection techniques provide the patient with the best chance for cure. More radical resection would seem unlikely to benefit patients with early-stage disease in view of the excellent survival being reported here after standard resection in such cases. Comparisons with reports from the United States by those using radical resection are

Fig. 6. Adjusted actuarial survival curves using modified WNM criteria. *n*, Number of patients remaining at risk.

Table V. Comparison of two staging systems

AJCC				Modified WNM criteria				
Stage	No. of patients	5-yr survival (%)	p Value	Stage	No. of patients	5-yr survival (%)	p Value	
0	16	100	NS	0	T0, is, 1 (W0) N0	39	88.2	0.0002
I	22	78.9		I	T1 (W0) N1 T2 (W1) N0	59	50.3	
IIA	80	37.9	NS	II	T2 (W1) N1	95	22.5	0.0213
IIB	39	27.3				T3, 4 (W2) N0		
III	218	13.7	<0.0001	III	T3, 4 (W2) N1 Any T N2	182	10.7	<0.0001
IV	33	0		IV	M1	33	0	

NS, Not significant.

hard to interpret because of the highly selective use of these procedures.³¹ One report, that from the service of the originator of the "en bloc" procedure,³² is worth analyzing. It involved 251 patients of whom only 111 (44.2%) had the radical procedure, with an 11% hospital mortality rate and an overall 5-year survival of 19%. When we translated our data into their WNM criteria, their 5-year survival compared with ours is as follows: W1 N0 (55% vs 50%), W1 N1 (29% vs 27%), W2 N0 (15% vs 22%), and W1/W2 N2 (8% vs 11%). A comparison of these two series, although admittedly based on shaky grounds, if anything, favors standard resection over the "en bloc" technique.

Equally as important as survival is the ability of the operation to provide palliation of dysphagia. This was achieved in nearly 80% of the patients for whom information was available, which is a figure comparable to that in our earlier reported experience.^{33, 34} Some failures of palliation were the result of anastomotic recurrences (8%), an identical figure to that reported from Hong Kong where experience with esophagogastrrectomy for carcinoma is far greater than in the Western world.³⁵ Anastomotic recurrences might have been minimized by a more radical esophagectomy, but because the vast majority of the patients have distant metastatic disease at the time local recurrence is diagnosed, it is debat-

able whether the increased morbidity of such a procedure is justified.

The question of the role of neoadjuvant therapy for carcinoma of the esophagus and cardia remains unsettled, although the results of multiple phase II trials have been reported. In general, they show that up to 30% of patients exhibit a complete histologic response to chemoradiation at the expense of considerable toxicity in terms of myelosuppression.³⁶ Survival of patients with a complete response is increased over that of historical controls. Although few phase III studies have been reported, the preliminary results of the University of Michigan's study involving 100 patients are discouraging.³⁷ The median survival was 18 months in both arms of the study, and the 2-year survival was 36% for patients having operation alone and 41% for patients undergoing combined therapy. Neoadjuvant therapy for the treatment of carcinoma of the esophagus and cardia remains investigational. Although continued prospective randomized studies in centers participating in research protocols are justified, operation remains the standard treatment for this disease.

The importance of staging in predicting the long-term survival of patients after resection for carcinoma of the esophagus and cardia is reemphasized by the findings we report herein. Unfortunately, the current staging criteria as proposed by the AJCC fail to prognostically stratify the disease conditions adequately. The modified WNM staging criteria that we are proposing provide improved prognostic stratification, as clearly depicted in Table V. Missing from this proposal is the recent recommendation of the TNM committee of the Union Internationale Contre le Cancer (UICC) that stage T1 be divided into T1a (tumor invades lamina propria) and T1b (tumor invades submucosa).³⁸ Sabik and associates³⁹ reported that T1s and intramucosal carcinomas are associated with a significantly better prognosis than those with submucosal involvement. We are currently reviewing our data to see whether they confirm these observations. Also proposed by the TNM committee is a change in the N classification, with three categories of involved nodes, depending on the number. Because the 5-year survivals associated with two of these categories were identical (0%) in the committee's report, the N1, N2 proposal of ours is simpler and just as accurate. The committee has also altered the M classification into two separate categories, depending on the location of the nodal metastases. However, we have always considered metastases from lower thoracic esopha-

geal carcinomas to the celiac nodes as N1 or N2 rather than M1 disease, as have Ide and associates⁴⁰ from Japan. Much work remains to be done if universally acceptable staging criteria for carcinoma of the esophagus and cardia that provide satisfactory prognostic stratification of disease conditions are to be achieved.

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Discussion

Dr. John R. Benfield (*Sacramento, Calif.*). This thoughtful report from the dean of United States surgery is remarkably successful in meeting its goal. The authors have indeed been successful in providing us with a baseline as to what one can and cannot expect from resection as the treatment of esophageal cancer. I would like to highlight a number of points.

Achalasia is indeed associated with esophageal cancer, but in the authors' experience the coincidence of achalasia and esophageal cancer was low, about 2%. Barrett's dysplasia with esophageal cancer is common, greater than 20%, and this coincidence continues to increase for reasons that we do not fully understand.

In skilled experienced hands, the incidence of intrathoracic anastomotic disruption is now remarkably small. However, the patients who need esophageal resection to treat cancer are so ill that a postoperative complication rate, at least in the United States, of about 30% is about the best one can expect. The bright side includes a median survival greater than 16 years in patients with stage 0 cancers. In stark contrast are the median survivals of 6 months to 2½ years whenever the cancers have shown any evidence of spread into lymphatics or when there is microscopic evidence of postresection residual cancer. This finding suggests that the principles of staging an esophageal cancer are no different from the principles of staging in cancer of the lung or cancer of the breast or cancer of the colon. When cure cannot be achieved it is abundantly clear that complete resection gives about 80% of patients the best available palliation. These are the standards that need to be exceeded if induction or neoadjuvant therapy is to have a lasting therapeutic role.

We participated in a multiinstitutional cooperative intergroup-administered clinical trial by the Radiation Oncology Group wherein induction therapy before resection is being compared with proceeding directly to esophagectomy. The results are not yet available, but it will not surprise me if induction or neoadjuvant therapy fails to be of lasting benefit. In a preliminary report given by Dr. Robert Ginsburg to the General Thoracic Surgical Club last March, it was noteworthy that the incidence of anastomotic disruptions and complications has been strikingly low; that is, in the range of today's report by Dr. Ellis. From this, one can conclude that thoracic surgeons who do a significant number of esophagectomies can accomplish them safely even in patients in debilitated condition. It would be of interest to compare results like those of Dr. Ellis and the intergroup thoracic surgeons with the results of surgeons who occasionally perform esophageal operations. I suspect that the findings would make a compelling argument in favor of restricting esophageal surgical practice to centers of excellence, and I hope

that there will be an opportunity to evaluate this hypothesis.

One of Dr. Ellis' major points is his group's proposal for refined, precise staging nomenclature. I certainly agree with the idea that staging is crucially important and, therefore, on a daily basis I insist that my residents and students always include TNM and staging descriptions when discussing the cases of patients with cancer. Dr. Ellis' specific proposal for modification of nomenclature is worthy and thoughtful, but it really cannot be effective until there is another international agreement as to the nomenclature that will be used. I support proposals for change such as the one we have heard today, but I emphasize that consensus and agreement are required. The generally accepted standards for staging nomenclature should not be abandoned until there is something generally accepted to take its place.

In my own practice, despite routine pyloroplasty or pyloromyotomy, transient and sometimes prolonged postoperative gastric stasis remains a problem. Clearly a pyloroplasty is not always a sufficient solution and therefore there are excellent esophageal surgeons in the United Kingdom and elsewhere who do not routinely use pyloroplasty or pyloromyotomy. Thus I close by asking Dr. Ellis to enlighten us as to how best to avoid and to treat gastric stasis in conjunction with esophagectomies.

Dr. Ellis. I would like to first make a comment or two about some of the things that Dr. Benfield has said. I agree that, in all likelihood, early diagnosis is going to be the only way we can improve long-term postresection survival, because the results of superradical procedures and neoadjuvant therapy have not been encouraging.

Preliminary optimistic results of phase II neoadjuvant studies were not supported by the initial results of a prospective randomized study from the University of Michigan, which was published only in abstract form. The median survival was 18 months in both arms of that study and the 2-year survival was 36% for patients undergoing operation alone and 41% for those undergoing combined therapy. Although the data at 5 years will be interesting, it is doubtful that there will be any statistically evident advantage of the neoadjuvant approach over standard approaches.

The comments regarding the results of operation by surgeons who occasionally perform esophageal operations are pertinent, and, in fact, Dr. Matthews from the United Kingdom has made such a comparison and found a major difference in hospital mortality rates for the "occasional" surgeon as compared with the rates for those who perform many esophagectomies.

Gastric emptying is always a potential postoperative problem after bilateral vagotomy, and it is surprising to me that it is not a more common occurrence. Of the 14 gastrointestinal tract complications of esophagogastrectomy we reported, 7 could be related to gastric stasis, and 3 of these patients required pyloroplasties. The other cases resolved under conservative management. Approximately 10% of patients in whom the left thoracic approach is used, in which a gastric drainage procedure is not done, will have problems with gastric emptying. It is my custom, however, to do a pyloromyotomy when either an Ivor Lewis or a transhiatal resection is done, despite which some patients have problems with gastric emptying.

As Dr. Benfield indicated, the British, for the most part, advise against performance of a gastric drainage procedure because of the problem of bile reflux and have treated those patients with troublesome gastric stasis by per oral dilation of the pyloric sphincter muscle. However, the use of prokinetic drugs such as bethanechol chloride (Urecholine), metoclopramide hydrochloride (Reglan), and cisapride (Propulsid) usually controls the symptoms, though they may take considerable time to resolve.

Dr. Tom R. DeMeester (*Los Angeles, Calif.*). I have been privileged to have the unique opportunity to review two manuscripts summarizing the life work on esophageal carcinoma by two surgeons. Like Dr. Akiyama, Dr. Ellis has invested a major portion of his life to studying this disease. Their two manuscripts summarize their personal work on the subject and reflect the commitment each has had to further our understanding of a disease that is slow to yield its secrets. The prevalence of esophageal carcinoma is such that it is common enough to be a menace but uncommon enough that a lifetime is required to understand the disease in its details. All of this may change if the current prevalence of adenocarcinoma of the esophagus and cardia continues to increase. If its rise remains on the current course, it will become one of Western man's most common cancers.

Dr. Ellis, 65% of the patients in this series had adenocarcinoma, whereas this histologic type was rarely seen by Dr. Akiyama. Do you have any thoughts as to why there is such a difference in histologic type of the tumor between the East and the West?

Dr. Ellis. The Japanese rarely have gastroesophageal reflux disease so they do not get Barrett's esophagus and hence they do not get adenocarcinoma as often as occurs in the Western world.

Dr. DeMeester. Do you have any reason why the Japanese do not get reflux?

Dr. Ellis. The Japanese are rarely as fat as are many Americans. Other than that, I have no real explanation. Maybe Hiroshi could answer that question, but gastroesophageal reflux disease is not common in Japan.

Dr. DeMeester. Because of the opportunity afforded me in reviewing both manuscripts, I noticed that Dr. Ellis' survival for patients with seemingly similar stages of disease, that is, tumors that penetrate the submucosa and muscular propria, is about half that of Dr. Akiyama. As a consequence, Dr. Ellis, are these results moving your group toward a more extensive resection for patients with an intermediate stage of disease, that is, disease beyond the muscularis mucosa but not advanced to the point of penetration into the adventitia and involving multiple lymph nodes?

Dr. Ellis. No, because Dr. Akiyama's 5-year survival before he began doing three-field resections was far better than any reported from the Western world. It makes one wonder whether there is a difference in the biologic makeup of the tumor in Japan. Also, the selection of a radical approach not only by Dr. Akiyama but also by Dr. Skinner and his group is highly selective. The most favorable cases are selected for the radical approach. In such cases, our 5-year survival is 75%. Those are the ones selected for total gastrectomy, whereas the ones in which resection is done have a much higher risk and the results

are similar. The same applies to Dr. Skinner's data. Long-term results of Skinner's "en bloc" resection are reported in a chapter in a textbook and involve 100 patients, who incidentally make up only 44% of all the cases this group saw. The mortality rate was 11%; ours is 3%. Skinner's 5-year survival was 19%; ours is 24.7%.

Dr. DeMeester. I compliment Dr. Ellis on his attempt to improve our staging of esophageal cancer. His modifications have clearly separated the stages of disease to the point where they have prognostic significance. Further, because his group has focused on tumor removal and not on an exclusive lymph node dissection, these data provide an excellent baseline for what can be accomplished by minimal dissection. What we need is for Dr. Akiyama to arrange his data into Dr. Ellis' proposed staging classification. If this were done, I am sure we would learn more from the two men collectively than we have from each separately. I would encourage the two of them to get together and with use of the staging system proposed by Dr. Ellis publish a letter comparing the results achieved by an advocate for a limited dissection with those of an advocate for an extensive dissection.

It is a tribute to the Society to have these two classic papers presented at its meeting, and I thank both Dr. Akiyama and Dr. Ellis for their contributions.

Dr. Arthur Thomas (*San Francisco, Calif.*). We have noticed a similar increase in Barrett's esophagus over the same time frame and a question I wanted to ask is whether the patients in whom Barrett's esophagus malignant degeneration is developing are being overtreated by the gastroenterologist. It seems to me that referral for hiatal hernia repair occurs after complications have developed, because gastroenterologists can relieve the symptoms so well with the H₂ blockers and it is not until after many years of treatment that discovery of a complication is made. Even the patients with Barrett's esophagus are not ordinarily referred and they are included in a surveillance program. We recently treated a patient who one year had negative findings for malignancy and the next year had positive findings, and he had one lymph node that was positive, which according to the findings in the current report would make him half as likely to survive 5 years. I would be interested in the authors' thoughts in this area.

Dr. Ellis. There is no question that Barrett's esophagus is a premalignant lesion. People with benign Barrett's esophagus have a 75-fold increased risk for the development of cancer compared with that of an age- and sex-adjusted population; thus anyone with Barrett's esophagus needs at least yearly endoscopic surveillance. We have determined that such an approach is cost effective. If there is any evidence of what some call high-grade dysplasia, which is synonymous with in situ carcinoma, such patients should have resection because a third to a half will have invasive cancer in the resected specimen. When we followed that approach, the 5-year survival of patients in whom cancer was detected during surveillance was in the neighborhood of 60% to 70%, as compared with that of patients with adenocarcinoma in Barrett's esophagus when we first see them with cancer, in whom the survival is about 20% to 25%. In my opinion close surveillance is the answer to better long-term survival,

because it permits resection at an early stage of the disease. One final word about this matter is that performance of an antireflux operation does not protect such patients from subsequent malignant transformation of benign Barrett's mucosa.

Dr. Thomas. I was thinking of patients before Barrett's esophagus develops. The thing that I find worrisome is the sampling error in patients with Barrett's esophagus, and I think that the risk for the patient undergoing biopsy as concerns the true status of the Barrett's esophagus is not really known.

Dr. Ellis. Sampling errors certainly occur with conventional endoscopic techniques. The group from the University of Washington has advocated taking giant biopsy bites at many levels, and they say that by doing so they can eliminate the sampling error and decrease the need for resection. I think the techniques that are being looked into now, such as the use of laser obliteration of the abnormal mucosa followed by antireflux maneuvers, may stimulate regrowth of squamous epithelium and minimize the chance of later malignant transformation.

Dr. Robert Mitchell (*Mountain View, Calif.*). I have followed Dr. Ellis' work and believe that his work is the gold standard, with one caveat, however. I noticed that his group continues to do a left thoracotomy for gastroesophageal junction cancers. I performed a few left thoracotomies in the early days in the 1970s but concluded that proximal margins could be a problem and thereafter have used the Lewis approach routinely. Previous papers from this group quoted an 11% anastomotic recurrence rate with gastroesophageal junction adenocarcinomas. I would consider that a rather high percentage. Would the authors not consider that these results might be a result of an anastomosis this is not proximal enough with the left thoracotomy as opposed to a right thoracotomy, with which I routinely put the anastomosis above the azygos or sometimes in the neck?

Dr. Ellis. We always obtain frozen sections at the time of the operation, and it is true that adenocarcinomas of the cardia tend to spread proximally submucosally, but they do not have skip areas like some squamous cancers do. Most of the left thoracotomies were done for cancers of the cardia, and some of them had to be converted into a more extensive resection with a cervical anastomosis. It is difficult to do this through a left thoracotomy, but it can be done. In some patients we had to convert the procedure into an Ivor Lewis operation. As indicated in the manuscript, our local recurrence rate remains about 8% to 10%. Unfortunately, most of the patients have metastatic disease when they get the local recurrence. Whether the performance of a superradical procedure with its attendant morbidity and mortality is worthwhile just to get a few more centimeters of tissue when the cause of death is not the local recurrence but the metastatic disease remains debatable.

Dr. Mitchell. At least in my experience, I would not think that an Ivor Lewis approach increases the mortality or morbidity.

Dr. Ellis. I am referring to the superradical operations that some of the physicians in this room advocate.