Selection of Operation for Esophageal Cancer Based on Staging

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The concept of *en bloc* removal of tissue surrounding the esophagus was applied to intrathoracic esophageal cancers, and the first 80 cases were operated on by this technique between 1969 and 1981. Analysis of prognostic factors showed that only penetration through the esophageal wall and lymph node spread influenced survival. Since 1981, a new staging system based on wall penetration (W) and lymph nodes (N), as well as systemic metastases (M), and similar to the modified Dukes' system for colon cancer has been used to select patients before and during surgery for *en bloc* resection if favorable pathology (W1, N0, or N1) could be anticipated. When curative resection was not attainable, based on preoperative and operative staging, a standard esophagectomy was considered for relief of symptoms when necessary. From July 1981 to June 1984, 68 esophageal cancers were referred to us, and 31 were resected by the *en bloc* method, 21 by standard esophagectomy, and 16 were not resected. The success of preoperative staging was confirmed, as only nine of the 31 *en bloc* cases demonstrated both W2 and N2 pathology. The proportion of W2N2 cases subjected to *en bloc* esophagectomy was less ($p < 0.01$) than that in the preceding series. This selection of cases showed a favorable deviation in the survival curve following *en bloc* esophagectomy since 1981 compared to the earlier interval. Patients treated by *en bloc* esophagectomy had a significantly greater survival than they did following standard esophagectomy at all time intervals after 6 months. There was no difference in hospital mortality or complications between the two operations. Further evidence for the value of the new staging system was shown by the significant difference in survival curves between those with favorable *versus* unfavorable staging and treated by *en bloc* esophagectomy. Among all cases resected between 1981 and 1984, 18-month survival in W1 stage was 67% compared to 35% for W2 disease. Survival with N0 disease was 58% *versus* 43% for N1 stage and 21% for N2 stage. The favorable survival rates after *en bloc* resection in those with limited (<W2N2) disease support the concept of selecting patients for curative surgery based on preoperative and operative staging.

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Preoperative radiation therapy caused a significant decline in patient survival at 6 and 12 months and has been abandoned. Adjuvant postoperative irradiation and/or chemotherapy was offered to all patients with W2, N1, N2, or M1 pathology and was accepted by approximately two thirds. There was no difference in the survival curves between those who did and did not accept postoperative therapy. However, in the patients with W2N2 disease, survival between 9 and 15 months was prolonged by approximately 6 months in those receiving postoperative treatment, and the difference approached statistical significance ($0.1 > p > 0.5$). Staging for esophageal cancer based on wall penetration and lymph node spread is valuable in determining prognosis and selection of treatment. For those with favorable staging, the use of *en bloc* resection for attempted cure has an acceptable mortality and an improved survival rate compared to those with the same stage disease treated by standard esophagectomy. *En bloc* resection appears particularly worthwhile in those with limited spread from the primary (W1N1 and W2N0). For those whose staging indicates little hope for prolonged survival, resection may be used for palliation of dysphagia and bleeding. Adjuvant therapy is still not a proven benefit, but trials should continue in patients with unfavorable disease.

ESOPHAGECTOMY, as widely practiced since its introduction[1,2] in the 1930s, consists of removing the muscular tube of esophagus and any obviously enlarged lymph nodes. It is generally considered to be a palliative operation for relief of dysphagia,[3] and long-term survivals are often regarded as happy accidents.[4]

The application of *en bloc* resection principles to carcinoma of the cardia was introduced by Logan in 1963.[5] Extension of this concept to intrathoracic carcinomas as well as those of the abdominal esophagus was described in a series treated from 1969 to July 1981.[6] This analysis of the first 80 consecutive cases treated by *en bloc* esophagectomy established the feasibility of this approach. Although the mortality rates are comparable, *en bloc* eso-

phagectomy is a more extensive procedure than standard esophagectomy. Accordingly, *en bloc* esophagectomy should be selected for those with hope for long-term survival. For those in whom only palliation can be expected, alternative treatment to relieve symptoms is appropriate. This report presents our results with preoperative and operative staging to make these treatment decisions.

Based on a multivariate analysis of factors influencing the prognosis for 2-year survival with no evident disease (NED) in 91 patients undergoing standard or *en bloc* esophagectomy, only the depth of wall penetration and number of lymph node metastases were independent predictors.[7] Tumor size, histologic grade, cell type, and level within the esophagus did not independently predict outcome. These findings required the development and verification of a new staging system based exclusively on wall penetration (W), lymph node involvement (N), and systemic metastases (M). To emphasize that wall penetration alone was critical among the factors describing the primary tumor, the symbol W instead of T was employed. W0 was designated for neoplasms limited to the mucosa, W1 for penetration through the submucosa and into but not through the muscle, and W2 for neoplasms penetrating full thickness. Lymph nodes were classified as N0 when all were negative, N1 when one to four were positive, and N2 when five or more showed metastases. This designation was derived from the initial study in which some patients with one to four lymph nodes survived NED at 2 years, but all with five or more lymph nodes were dead or had recurrent disease. Since July 1981, our policy has emphasized staging to select patients who had disease more favorable than W2N2M0 as candidates for *en bloc* esophagectomy. This study assesses the impact of WNM staging on our complete series during the 3-year interval compared with the earlier series. Effects of both preoperative and postoperative adjuvant radiation and/or chemotherapy are presented based on overall experience with 95 resected cases previously reported from 1969 to 1981 plus 52 resections from 1981 to 1984.

Clinical Material

Of 71 consecutive esophageal cancer patients referred to us (AGL, DBS) from July 1981 through June 1984, three were not included. In one, a W2N0 cancer treated by standard esophagectomy, insufficient records were available. The second excluded patient had a large squamous carcinoma involving both the right lower lobe bronchus and esophagus; the primary site was not definitely esophageal. The third exclusion was a carcinoma-*in-situ* arising in ectopic gastric epithelium in the cervical esophagus treated by local resection without prior knowledge of the cancer. Of the 68 patients analyzed, 31 were treated by *en bloc* esophagectomy, 21 by standard or palliative esophagectomy, and 16 without resection. Follow-up was complete until death or the spring of 1986.

Age, Sex, and Race

The age range for the 68 patients was from 31 to 78 years with a mean age of 58.5 and median of 59 years. Fifty-two were male and 16 female. Patients were equally distributed by age and sex among the three treatment groups. Sixty patients were white and eight were black. All eight black patients had squamous cell carcinomas, and their average age was 54.5, with a median of 52 years.

Cell Type and Location

One half or 34 carcinomas were squamous cell, and 34 were adenocarcinoma of the esophagus, defined as a cancer with its center and presumed site or origin within the muscular tube of esophagus. Cancers in which the center was within the stomach but encroaching on the cardia were classified as gastric and were not included in this report. Among the 34 adenocarcinomas, 14 arose in metaplastic glandular epithelium (Barrett's esophagus), extending for 3 cm or more within the distal tubular esophagus.[8] Approximately one half of the squamous (16) and Barrett's (8) carcinomas were treated by *en bloc* esophagectomy, but only one third (7) of the other adenocarcinomas were suitable for attempted curative surgery. The more advanced state of adenocarcinomas in the distal esophagus when diagnosed has been noted previously.[7]

Thirty-three cancers were in the distal one third of esophagus, 31 in the midesophagus, and four in the upper or cervical esophagus. Approximately one half of those in the upper (2) and midesophagus (16) were suitable for *en bloc* esophagectomy but fewer (13/33) distal cancers were potentially curable, again reflecting their more advanced state at presentation.

Classification by Wall Penetration and Lymph Node Involvement Versus *Conventional Staging*

Based on pathologic analysis of resected specimens, the 52 resected cases were assigned to W, N, and M categories (Table 1). Six showed neither full thickness wall penetration nor involved lymph nodes (W1N0). By American Joint Commission (AJC) staging,[9] three were classified as stage I, with negative lymph nodes and a primary tumor less than 5 cm that was not obstructing or circumferential. Three were stage II, as the primary tumor was 6 × 8 cm in one instance, and the other two were circumferential and obstructing when diagnosed. By AJC staging, all 46 remaining cases were stage III, based on penetration outside the wall of the esophagus or positive intrathoracic or abdominal lymph nodes.

Among the 31 cases selected for *en bloc* esophagectomy, only nine (29%) had both full thickness wall penetration

TABLE 1. *WNM Staging in Resections (All M0 Unless Noted)*

		Stage					
	Resections	W1N0	W1N1	W2N0	W2N1	W1, 2N2	Total
1981–1984	*En bloc*	3	3	3	13	9	31
	Standard	3	0	3	5 (2M1)	10 (3M1)	21
1969–1981	*En bloc*	18	8	11	19	24	80
	Standard	0	0	2 (1M1)	7	6 (4M1)	15

% W2N2 + M1 *en bloc vs.* standard 1981–1984, $p < 0.05$.

% W2N2 *en bloc* 1981–1984 *vs.* 1969–1981, $p < 0.01$.

and five or more lymph nodes positive. Among those undergoing palliative resection, 12 (57%) had either W2N2 or known M1 disease at the time. The proportion of favorable cases selected for *en bloc* resection was significantly greater ($p < 0.05$) than for standard esophagectomy, indicating the relative accuracy of the preoperative and intraoperative staging.

Of the 11 patients with W1, N0, or N1 disease treated by standard resection who might have been candidates for *en bloc* esophagectomy, the reasons for choosing the lesser resection varied. In one the preresection diagnosis was benign stricture. Two patients had been treated recently for other primary cancers and were not certain to be disease free. In three patients the lesser resection was chosen for medical reasons: marked obesity in an elderly patient, severely restricted pulmonary function in a second, and pneumonitis after preoperative radiation in the third. In five patients the final decision to perform a standard esophagectomy for palliation was based on operative findings that lymph nodes were positive at the planned resection margins or that the tumor was attached to adjacent vital structures or that liver metastases were found. In these five incurable cases, the final pathology staging was W2N1.

Among the 16 unresected cases, four had malignant tracheoesophageal fistula. Six had systemic metastases. Five were unresectable at exploration. One patient was deemed inoperable because of advanced atherosclerosis and died from a stroke 5 months later.

Investigations

Prior to a treatment decision, an extensive evaluation was carried out to assess the patient's suitability for major surgery and to stage the extent of tumor. Chest x-ray, barium swallow, and esophagoscopy with biopsy were obtained routinely for confirmation of the esophageal neoplasm but contributed little to WNM staging. Chest radiography showed pulmonary nodules in four patients, but two were benign and two metastatic, emphasizing the need for a tissue diagnosis of solitary pulmonary nodules. In two patients pneumonitis was seen before operation, and both died after operation from pneumonia. An upper gastrointestinal radiographic study and barium enema were obtained to determine the suitability of stomach or colon for esophageal replacement.

Preoperative Staging

In AJC staging, a circumferential or obstructive tumor is a criterion for stage II disease. A stricture was reported on 19 barium swallow examinations, but three proved to have less than full thickness wall penetration. A circumferential or obstructing tumor was seen at esophagoscopy in 26 examinations, but four of these tumors proved to be W1. Accordingly, circumferential or obstructing tumor did not always indicate a more advanced neoplasm. The finding of axis deviation or angulation on full length biplane barium swallow has been proposed by Akiyama as an indicator of mediastinal penetration.[10] Although these views were not obtained consistently, a deviated axis was found in eight patients, and all demonstrated mediastinal spread.

Azygos venography was done in 55 patients. The study was normal in six with W1 disease. Thirteen of 36 studies were positive in W2 resected patients demonstrating compression or displacement of the azygos vein, and in four of 13 unresectable patients. When the azygos vein was compressed, obstructed, or deviated, this was a strong indication of full thickness wall penetration of the tumor, but the test was not very sensitive.

Computed Tomography (CT)

A CT scan of the chest and upper abdomen was performed in 63 cases. Full thickness wall penetration was suggested by irregular or indistinct esophageal borders in 36 resected cases, and 35 had W2 disease. Ten of 15 unresectable cases showed CT evidence suggestive of wall penetration. There was only one false-positive assessment of wall penetration by this technique. Lymph nodes >2 cm in diameter were noted in ten CT scans of resected cases, and each patient had positive lymph nodes. Further detailed analyses of CT scan findings in resected specimens are necessary to validate this technique, but it appears the most promising method for staging.

Radionuclide Scanning

Gallium 67 scintigraphic tomography was done in 49 patients. The gallium scan imaged the primary tumor in 20 instances including five unresectable and 15 resectable cases. Among the latter, 14 had full thickness wall penetration indicating a high likelihood of W2 disease when gallium is taken up in the primary tumor. Metastatic disease was detected in three patients by the gallium scan.

A liver spleen scan was done in 28 patients but contributed little, as only two scans were positive for metastases, one of which was also shown by CT scan. In the sole instance in which the liver spleen scan detected an adenocarcinoma, metastasis was confirmed at surgery, but a palliative resection was still performed.

Bone scan was obtained in 59 patients and was abnormal in five out of 15 with unresectable disease, including two in whom it was the only indicator of systemic metastases. Among 44 bone scans in resected cases, there were three false-positives from arthritis identified by appropriate bone radiographs and one true-positive in a patient who received a palliative resection to relieve dysphagia. The bone scan had a limited but important role by detecting unsuspected systemic metastases in 5% of studies.

General Health Status

The cardiovascular and respiratory systems were investigated prior to a decision about major surgery. Fifteen of the 68 patients had evidence of cardiovascular disease, and six had restricted pulmonary function. There were no significant differences in cardiopulmonary risk factors among the three groups. Based on nutritional evaluation, preoperative parenteral nutrition or tube feedings were given for 7–10 days before operation to 11 patients. After operation, 12 patients received nutritional support using needle catheter jejunostomies. Preoperative hospitalization for investigations and preparation averaged 8 days (2–24) for patients undergoing resection and 10 days (5–18) for unresectable patients.

Choice of Treatment and Operative Staging

When preoperative staging unequivocally showed extensive disease, *e.g.*, metastases (M1) or both neoplasm extending beyond the esophagus and multiple nodal metastases (W2N2), the treatment decision was based solely on providing palliation. A standard esophagectomy or nonoperative therapy was chosen, depending on the degree of dysphagia bleeding or other symptoms. When preoperative staging suggested that curative resection might be possible, operative staging was used to determine the type of esophagectomy to be done, *en bloc* or standard. When confirmed by biopsies and frozen sections, metastases, spread of the tumor beyond the limits of *en bloc* resection, or involved lymph nodes 10 cm beyond the tumor were used as determinants of surgical incurability and indications for standard or palliative esophagectomy.

Surgical Treatment

En Bloc *Esophagectomy*

The technique for *en bloc* esophagectomy is described in detail elsewhere.[6] The operation is more extensive than standard esophagectomy in that it includes the right and left parietal pleura and the pericardium where these natural anatomical barriers abut on the esophageal muscle. All tissues between the esophagus and aorta or vertebral bodies are resected in continuity with the esophagus, including removal of the thoracic duct, azygos vein, segments of the right intercostal arteries, and right and left intercostal vein segments on the anterior vertebral bodies. This dissection provides an envelope of tissue surrounding the esophagus, which itself is not seen except at the upper and lower limits of the dissection. Based on pathology studies demonstrating the potential for submucosal spread for up to 10 cm,[11] the dissection is carried 10 cm, or whatever lesser amount is available proximally, and 10 cm distally. Recognizing the multifocal nature of squamous carcinoma, a subtotal esophagectomy with cervical anastomosis is routinely performed.

For carcinomas arising at least 10 cm caudal to the aortic pulsation on endoscopy, the resection is performed through a left thoracotomy. The diaphragm is detached peripherally; the omentum, spleen, retroperitoneal lymph nodes from the celiac axis into the hiatus, and a cuff of diaphragm muscle surrounding the hiatus are resected. Ten centimeter margins from the tumor on the lesser and greater curvature of the stomach are obtained. If the tumor extends for any distance down the lesser curvature into the stomach, a total gastrectomy may be included (2 cases). If the 10 cm proximal margin can be achieved comfortably below the aortic arch in cases of adenocarcinoma, and all of the Barrett's epithelium is encompassed, an intrathoracic anastomosis may be made just below the aortic arch. Otherwise, the esophagus is dissected up to the neck for a cervical anastomosis.

For tumors closer than 10 cm to the aortic arch, the resection is performed through a right thoracotomy and carried to the neck. A cervical anastomosis is made through a separate incision. An abdominal incision is made in addition to the right thoracotomy when necessary to mobilize the colon or stomach for replacement. In three instances advancement of the stomach through the hiatus without laparotomy was performed, as described by Belsey and Hiebert.[4]

In this series, 14 *en bloc* resections were done through a left thoracotomy and 16 through a right thoracotomy.

In one thin patient with a small carcinoma of the abdominal esophagus, the 10 cm *en bloc* dissection was achieved through the hiatus *via* an abdominal incision, and the rest of the esophagus was removed without thoracotomy. Reconstruction was achieved by advancing the stomach in 24 cases and isoperistaltic left and transverse colon in seven cases. The anastomosis was made in the neck in 25 procedures, including all cases of squamous carcinoma.

Standard Esophagectomy

A palliative esophagectomy was carried out by dissecting on the esophagus and removing any obviously enlarged lymph nodes. No effort was made to remove pleura, pericardium, thoracic duct, dorsal mesoesophagus, or azygos venous system. The choice of left or right thoracotomy was based on the location of the tumor. In nine instances (4 W2N1, 5W2N2), we started the procedure with the intent of performing *en bloc* esophagectomy, but operative staging led to recognition that the operation could only be palliative; thus, the more limited resection was done. A standard esophagectomy was the initial intent in six patients with potentially favorable disease who had the limited resection for reasons mentioned previously, and in six for relief of severe dysphagia. Standard esophagectomies were done through a left thoracotomy in 15 patients and right thoracotomy in six (3 without laparotomy). Stomach was used by preference for reconstruction in these instances, as it was faster and involved fewer anastomoses. Colon was used in only one instance. A cervical anastomosis was made in 11 of the 21 cases.

Unresectable Cases

Among the 16 unresectable carcinomas, substernal bypass was created in six, using colon in four and stomach in two. The reason for the bypass was tracheoesophageal fistula in four patients and relief of dysphagia in two patients with unresectable tumors. The esophageal anastomoses were all made in the neck. Thoracotomy was done in hopes of resecting the tumor in three patients, but this could not be achieved. Since they did not have severe dysphagia, no bypass was done. In the remaining seven patients the extent of the disease was established by node biopsies, cervical exploration, bone biopsies, limited laparotomy, or lung nodule biopsies.

Operative Outcomes

All anastomoses employed a single layer running suture technique using 5-0 monofilament wire in 50 and 4-0 Prolene® in eight. There were three anastomotic leaks (5%) in the 58 esophageal anastomoses, one each in the *en bloc,* palliative, and bypass groups. One leak was asymptomatic and a radiographic finding only. The other two resulted in fistulas. All three leaks were in the neck and involved the stomach twice and colon once.

En Bloc *Esophagectomy*

Three patients (9.7%) died during the postoperative hospitalization, including two within the standard 30-day reporting interval (6.5% 30-day hospital mortality). Hospital deaths were due to leakage plus pneumonia and sepsis in one; a second patient died following shock and reoperation for postoperative bleeding; and a third who had pneumonitis before operation died from pneumonia during the second month of hospitalization. Five other patients were initially discharged after operation but died within 6 months (26% 6-month mortality), three from recurrent cancer, one from a massively bleeding gastric ulcer, and one from pneumonia.

Among the 28 initial hospital survivors, 16 had an uncomplicated course, and one or more complications occurred in 12 patients (43%). These included pneumonia in six, which led to respiratory insufficiency requiring tracheostomy in two. Four had significant atelectasis. Five patients had arrhythmias requiring treatment. Three patients had persisting pleural effusion requiring prolonged or reinstituted chest tube drainage. One patient had a wound dehiscence requiring reoperation. One had late postoperative bleeding requiring re-exploration on the third day, and another developed an infection around a feeding jejunostomy tube.

Palliative Resections

There was one death (5%) during initial hospitalization after palliative resection in a patient with preoperative chronic pneumonitis following radiation and chemotherapy. Six other patients died within 6 months (33% 6-month mortality), including four from metastatic cancer, one from suicide, and one from hemorrhage during postoperative radiotherapy.

Ten of 20 patients had no complications. Four had persistent pleural effusions requiring reintubation, and in one a chylothorax required reoperation for thoracic duct ligation. Three patients had arrhythmias requiring treatment, one had severe pneumonia, and two had significant atelectasis. Two patients had vocal chord palsies. One developed a deep wound abscess requiring reoperation, and a leak was found from the sutured gastric stump.

Bypass Procedures and Unresectable Cases

There were no hospital deaths from the bypass procedures or operations in unresectable cases. The 6-month mortality rate was 63% (10/16). Two of the six patients with substernal bypasses had no complications. One developed an anastomotic fistula. One had a persistent lym-

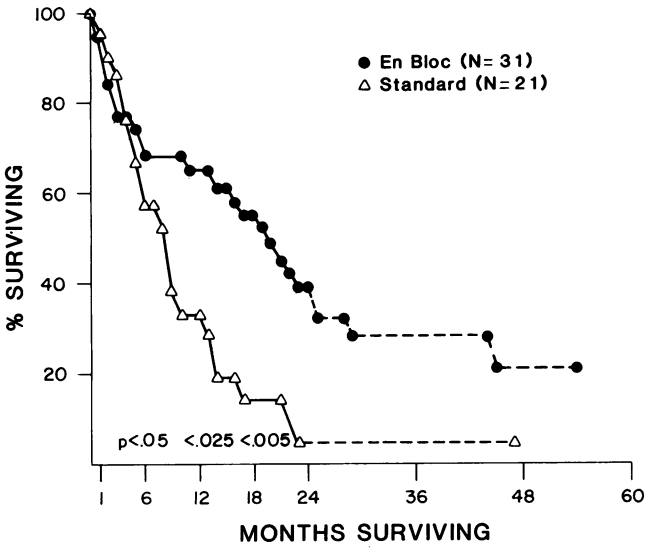

FIG. 1. Comparison of survival after *en bloc versus* standard esophagectomy during 1981–1984. Survival curves are determined by actual survival for 24 months and by actuarial method thereafter. The curves diverge significantly by 9 months.

phatic leak and required surgical ligation of the thoracic duct. One had severe pneumonia requiring tracheostomy and respiratory support, and one had a subcutaneous wound infection. Fourteen of 16 were treated by radiation and/or chemotherapy. Two have survived for 2 and 3 years after diagnosis.

Final Pathology and Correlation of Preoperative and Operative Staging

All specimens were examined for size of the primary tumor, cell type, degree of differentiation, wall penetration, margins, and numbers of involved lymph nodes. (See Table 1 for WNM classification.) Preoperative and operative staging combined was 75% (39/52) accurate for presence or absence of wall penetration, and there were no instances of overstaging. Twelve cases with negative lymph nodes were correctly staged before and during operation. Combined preoperative and operative staging predicted the lymph nodes' status accurately in 27 of 52 cases (52%). In 22 cases the lymph nodes were understaged before resection, and the three overstaged (N1) cases were still judged to be incurable.

Histological grading of tumors did not correlate with wall penetration, lymph node metastases, or survival. Among eight specimens evaluated to be W1 disease and in which histological grading was reported, four were poorly differentiated, and only one was well differentiated. Eleven of 12 well-differentiated cases demonstrated full thickness wall penetration. Grading did not correlate with lymph node metastases. In 11 N0 cases in whom grading was reported, four were poorly differentiated, three were moderately differentiated, and four were well differentiated tumors. In the 12 patients with well differentiated tumors, six were N2.

Similarly, tumor size did not predict the W and N classifications. Of four tumors less than 2 cm in greatest diameter, three penetrated completely through the esophageal wall. Three of these small primary tumors had from two to ten positive lymph nodes in the *en bloc* resected specimens. On the other hand, two W1 tumors were greater than 5 cm in diameter, and four tumors greater than 5 cm had negative lymph nodes. These findings confirmed observations from our earlier series that tumor histology and size did not correlate well with wall penetration, positive lymph nodes, or survival.[7]

Lymph node staging was not affected by the total number of nodes examined in the specimens. For those classified as N0, an average of 31 (4–78) nodes were inspected. N1 cases had an average of 24 (4–60) nodes, and those with N2 disease had a mean of 34 (18–61) nodes examined microscopically. Among *en bloc* esophagectomy specimens, an average of 32 (9–78) nodes were identified compared to 24 (4–53) in palliative resections.

Survival Data

Absolute survival curves for patients treated by *en bloc* esophagectomy compared to standard esophagectomy during the 1981–1984 interval are shown in Figure 1. By 9 months after operation, the curves diverge ($p < 0.05$). One-year survival after *en bloc* resection is 65% (20/31), significantly greater ($p < 0.025$) than the 33% (7/21) survival after standard resection. At 18 months the differences are 55% *versus* 14% ($p < 0.005$).

Among patients with W1, N0, or N1 disease, survival after *en bloc* resection was 64% (14/22) at 12 months compared to 45% (5/11) for palliative resection. At 2 years the difference was 41% *versus* 9%. Of nine W2N2 cases treated by *en bloc* esophagectomy, three were living at 2 years compared to none of ten for palliative resection.

The effect of wall penetration is demonstrated by 67% (6/9) survival at 18 months for all W1 resected cases compared to 35% (15/43) in W2 stage. For *en bloc* esophagectomy 18-month survival was 83% for W1 *versus* 52% for W2. The effect of positive lymph nodes is illustrated in the whole group of 52 resections by 58% (7/12) 18-month survival in those with negative lymph nodes compared to 43% (9/21) in N1 and 21% (4/19) for N2 disease. Among *en bloc* esophagectomies, 18-month survival was 83% for N0, 53% for N1, and 43% for N2.

Comparison of 1981–1984 Series to 1969–1981 Series

As previously reported,[6] 80 patients out of 181 referred between 1969 and July 1981 were treated by *en bloc* esophagectomy and 15 by palliative resection. Forty-five per

cent of patients in both series were treated by *en bloc* esophagectomy, but the percentage of palliative resections increased from 8 to 31%, and the total resectability increased from 53 to 77%. Recent emphasis on preoperative separation of potentially curable *versus* incurable cases permitted selection of appropriate palliation, which was often surgical resection. In past years, surgery was avoided if a patient appeared to have advanced disease, but the value of resection to relieve obstruction and bleeding in incurable cases is now accepted.

Influence of staging on the results of *en bloc* esophagectomy is illustrated in Figure 2. Thus far, no patient without evident recurrence at 3 years has subsequently developed a recurrence or died of cancer. The difference in survival curves between *en bloc* esophagectomy during 1981–1984 *versus* 1969–1981 approaches statistical significance at 18 months, at which time 55% (17/31) were alive in the recent series compared to 36% (29/80) in the earlier experience ($0.10 > p > 0.05$). Several reasons might be offered for this improvement, but it is most likely that this is attributable to the increased accuracy in selecting potentially curable cases. Could more favorable cases be included in the recent experience? The reverse is true and accounts for the higher proportion of palliative resections in recent years. Comparing the percentage of W1N0, W1N1, and W2N0 cases among total resections, there are fewer favorable cases in each category during 1981–1984, 15 of 52 (29%) compared to 40 of 95 (42%). Since the proportion of unfavorable cases is higher in the recent series, the impact of better survival for *en bloc* esophagectomies is diluted. Nevertheless, the overall survival curves in the two series are almost identical, although fewer cases were resected in the earlier series (53% *vs.* 77%).

Another variable could be adjuvant therapy. Early in the 1969–1981 series, patients were entered into a trial of preoperative radiation therapy. The 30-day hospital mortality was not increased, but, since survival at 1 year was significantly less for those receiving radiation, the trial was terminated. However, patients continued to be referred for possible resection after having received radiotherapy. Among the 147 resections done during the 15-year span, 18 patients had preoperative irradiation and 129 did not. The proportion surviving the first 30 days was identical at 89% *versus* 90%, but by 6 months only 39% of irradiated patients were alive compared to 74% resected without preoperative radiation ($p < 0.001$). By 12 months survival was 22% *versus* 54% ($p < 0.001$), and at 18 months only two of 18 (11%) treated by radiotherapy before resection were alive compared to 49 of 129 (38%). Ironically, a greater proportion of favorable, *i.e.*, W1N0, W2N0, and W1N1, cases were included in the preoperative irradiation group. The greater use of preoperative irradiation with its adverse effects in the earlier series might have had some bearing on the more favorable results obtained during 1981–1984 when preoperative irradiation was used in only three individuals.

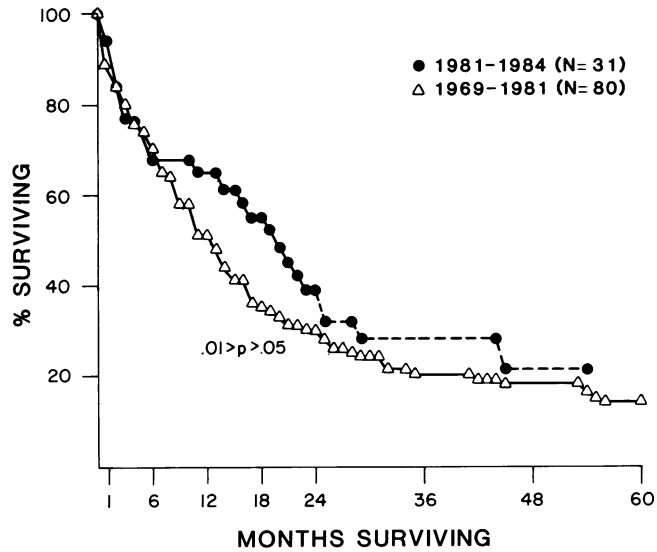

FIG. 2. Comparison of survival after *en bloc* esophagectomy during 1969–1981 to survival after the same operation during 1981–1984 when staging was used to select patients. The separation of the curves at 18 months approaches significance ($0.01 > p > 0.05$). Survival date is complete and actual for the 1969–1981 curve and for the first 24 months of the 1981–1984 curve.

Using the combined series, the validity of the WN staging system can be demonstrated more convincingly (Fig. 3). Since operative mortality was scattered randomly among the stages, and since preoperative radiation had an adverse effect and was used proportionately more in

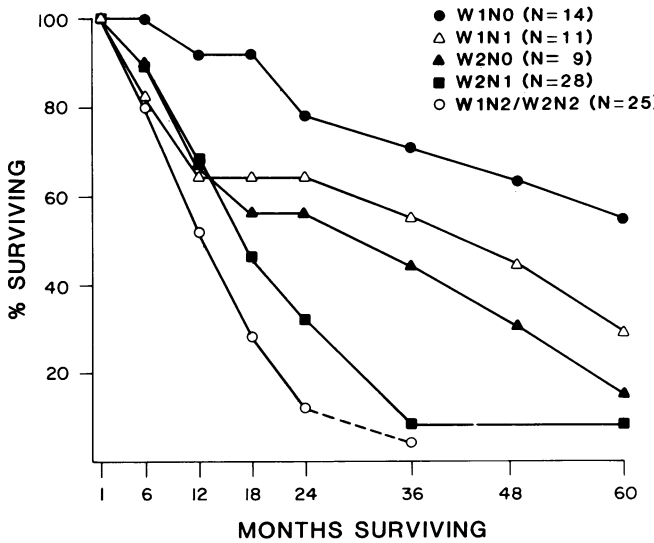

FIG. 3. Survival data illustrating the effects of WN staging in *en bloc* esophagectomy cases (1969–1984). Because postoperative deaths and the high mortality following preoperative irradiation are not related to staging, they are excluded. All cases are M0.

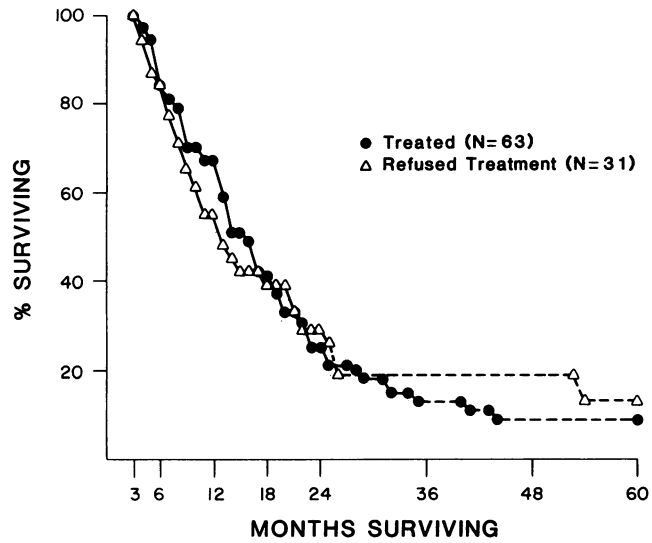

FIG. 4. Comparison of survival in patients who did or did not accept recommendations for postoperative chemotherapy and/or radiotherapy after either *en bloc* or standard resections (1969–1984). Excludes W1N0, 3-month mortality, and preoperative radiotherapy cases. Eligibility for postoperative therapy is discussed in the text.

favorable stages, the analysis was done excluding operative mortality and preoperative irradiation cases. Following *en bloc* esophagectomy, actuarial 3-year survival was W1N0 (71%), W1N1 (55%), W2N0 (44%), W2N1 (8%), and W1N2/W2N2 (4%). (W1N0, W1N1, W2N0 *vs.* W2N1, W1N2, W2N2; $p < 0.001$.) At 5 years the comparable percentages were 55, 29, 15, 8, and 0%.

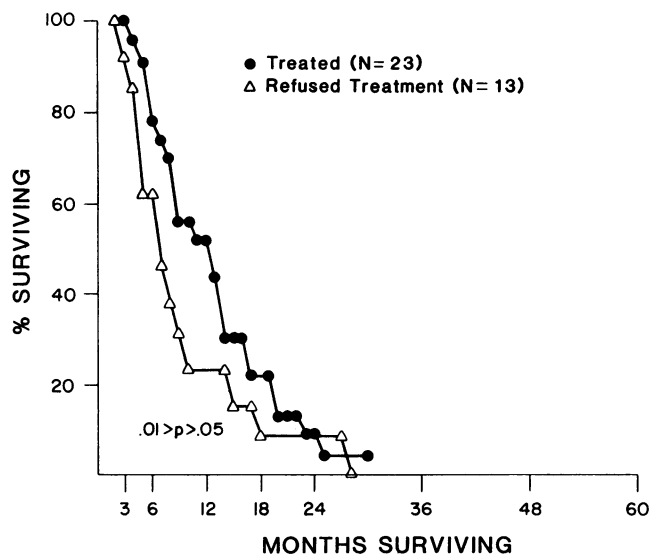

FIG. 5. Survival in patients with W2N2 stage disease who met eligibility for recommended postoperative chemotherapy and/or radiotherapy, comparing those who did with those who did not accept treatment (1969–1984). At 10 months the divergence approaches significance ($0.01 > p > 0.05$). In the interval between approximately 9 to 15 months, those treated survived approximately 6 months longer, but nearly all were dead by 2 years.

Postoperative Adjuvant Therapy

After termination of the preoperative radiotherapy trial, postoperative irradiation, usually 4500 rads, was recommended for patients with positive lymph nodes or full thickness wall penetration. Beginning in 1976, adjuvant postoperative chemotherapy was added to radiotherapy for this group. This was not accepted by all patients, but participation has increased such that 34 of 39 eligible patients during 1981–1984 began the treatment program. Patients were excluded because of W1N0 staging or early death within 3 months of surgery before any effect of therapy could be expected. Those having preoperative irradiation were not included in the analysis.

In the complete series, 94 patients were regarded as eligible, and 63 actually began the postoperative treatment. Details of treatment and the patient's ability to complete therapy are discussed elsewhere.[12] In general, a three-drug protocol of 5-fluorouracil, Adriamycin®, and mitomycin C or methyl-CCNU was used for adenocarcinoma. Bleomycin with methotrexate or cisplatinum was the common protocol for squamous carcinoma. Postoperative irradiation was generally given prior to chemotherapy. Comparisons of survival between the 63 who received postoperative treatment and the 31 that did not are shown in Figure 4. The widest separation is at 12 months when 67% of treated patients survived compared to 55% without treatment (not significant). Among those treated by *en bloc* esophagectomy, 49% are surviving at 18 months in the treated group compared to 46% in the untreated group. The use of postoperative adjuvant chemotherapy did not explain the improvement in survival following *en bloc* esophagectomy in the recent series.

The only encouraging indicator for some effect of postoperative adjuvant therapy was seen in the 36 W2N2 patients treated by either type of resection. Among 23 in whom adjuvant therapy was given after surgery, 12 (52%) were alive at 1 year compared to 23% (3/13) who did not receive adjuvant therapy. Median survival was prolonged from 7 to 13 months (Fig. 5). Although the numbers were too small to be significant, this difference suggested the potential for postoperative treatment to shift survival curves in favor of prolongation of life. However, by 2 years nearly all patients in both groups were dead.

Discussion

Experience with the WNM method of analyzing esophageal carcinoma demonstrates the merits of this staging system compared to conventional AJC staging, which places more emphasis on tumor size and clinical presentation. As in our previous analysis, this study confirms that only wall penetration (W) and lymph node status (N) independently influence survival. Tumor size, histologic grading, level within the esophagus, and cell

type do not influence prognosis. To allow comparison of results for different types of preoperative, operative, and postoperative therapy, we urge that others adopt this staging system. Similarities of this staging system to the Astler–Coller modification of the Dukes' staging system for colorectal cancer are obvious. The results are attempted curative resection of esophageal cancer can be presented in comparison with the results of colorectal resections (Table 2). In this comparison, data reported by Copeland et al.[12] are used as an example of colorectal cancer results.

The value of *en bloc* resections for potentially curable esophageal cancer is confirmed by this experience. Survival is significantly greater in patients treated by *en bloc* compared to standard esophagectomy. The 44% and 50% 3-year survival rates and 15% and 27% 5-year survival rates achieved in patients with W2N0 or W1N1 disease are unlikely to be obtained by an esophageal resection limited to the esophagus and obviously involved lymph nodes. It is difficult to construct a satisfactory randomized trial among *en bloc* esophagectomy, standard esophagectomy, or esophagectomy without thoracotomy, as the greater extent of tissue removed in the *en bloc* resection inevitably results in more accurate staging.

Another observation favoring the more complete regional extirpation of the disease in selected patients is the low incidence of mediastinal or anastomotic recurrences. In the earlier series, only three of 71 patients surviving *en bloc* esophagectomy had a localized recurrence in the anastomosis or dissected mediastinum. Among the more recent series, two of 29 patients had a mediastinal or trachea wall recurrence in the region of the *en bloc* esophagectomy, giving an overall regional recurrence rate of only 5% (5/100).

The low long-term survival following any esophagectomy in patients with W2N2 disease argues for selecting patients for either curative or palliative treatment by preoperative and operative staging. This approach results in a selection of favorable cases for *en bloc* esophagectomy, and influences survival rates favorably. For staging the CT scan is likely to emerge as the single most important method, but more experience is required in its interpretation and comparison of CT findings with operative and pathology findings. Azygos venography and gallium scan offer confirmatory evidence for W2 disease but lack the sensitivity that may be achieved by the CT scan.

Although mortality from *en bloc* resection is not increased compared to the mortality for standard esophagectomy in this series or other reported results, the more extensive curative operation should be restricted to patients who can benefit from it. Some assessment of the relative magnitude of standard *versus en bloc* esophagectomy can be offered. Median blood loss for the two operations is identical in this series, but the risk of major hemorrhage is greater during *en bloc* esophagectomy, as reflected in an average blood loss of 2.4 L compared to 1.5 L for standard esophagectomy. The median transfusion requirement was 4 units for the more extensive operation compared to 3 for standard esophagectomy. Operating time averaged 1 hour and 10 minutes longer for *en bloc* resection. The median duration of intensive care following standard esophagectomy was 3 days compared to 5 days for *en bloc* esophagectomy, and the median postoperative hospitalization for standard esophagectomy was 13 days compared to 17 days. In this era of medical cost accounting, the need to reserve the more costly but potentially curative operation for appropriate patients is evident. Since much of the preoperative staging can be done prior to hospitalization, staging to achieve cost effective case selection is warranted.

TABLE 2. *Five-year Survival after Resection*

Colon Cancer Dukes–Astler–Coller[13]		Esophageal Cancer WNM System–*En Bloc* Resection	
Category	%	Category	%
A	74	W0N0	
B1	65	W1N0	55
B2	43	W2N0	15
C1	53	W1N1	27
		W1N2	
C2	15	W2N1	8
		W2N2	?4

Another benefit of careful preoperative staging is the identification of patients who are not candidates for cure. This focuses the clinical decision making on the most appropriate means to palliate symptoms and emphasizes the importance of symptoms in this analysis. For patients who have little dysphagia but systemic disease, a resection has little to offer, and primary radiation or chemotherapy can be started after the metastases are confirmed. On the other hand, since a patient with severe obstruction is likely to continue to have dysphagia, palliative resection is justified. For institutions participating in trials of preoperative or "neoadjuvant" therapy, the selection of patients who may be curable by surgery alone is important. Those who have a chance at cure should not be subjected to the risks, discomfort, and costs of preoperative therapy that is unlikely to improve results in the more favorable categories. Trials of experimental treatment should be restricted and are justifiable only in those in whom staging indicates no likelihood of cure by conventional therapy.

Although this experience does not prove the benefits of postoperative adjuvant radiation and chemotherapy, it does suggest a trend in favor of treating patients with unfavorable W2N2 esophageal cancer. More detailed analyses, revised protocols, and randomized trials are indicated.

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Discussion

Dr. Tom R. DeMeester (Omaha, Nebraska): I appreciate the opportunity to discuss this paper and wish to congratulate Dr. Skinner for a clear presentation on the staging and application of radical esophagectomy for carcinoma of the esophagus.

Back in 1982 Dr. Dowlatshahi, Dr. Skinner, and I published the paper in *Cancer* that he alluded to, in which we evaluated the prognostic factors important in survival from carcinoma of the esophagus (Cancer 50:2571). Two independent factors emerged as being predominantly important: penetration of the esophageal wall by the tumor and the presence of lymph node metastasis. Today Dr. Skinner has refined these observations by showing that there is a difference in survival between patients with no lymph node metastasis, with less than five metastatic nodes, and with more than five.

(Slide) Since 1981 he has performed a radical resection in 31 patients who before operation were thought to have good prognostic factors and has shown the relative success of preoperative staging, in that only seven of the 31 patients had poor prognostic factors, that is, both wall penetration and the presence of more than five metastatic nodes. During the same period, I performed a radical resection on ten patients similarly suspected of having good prognostic factors. Only two of the patients subsequently were shown to have poor prognostic factors with wall penetration and more than five lymph nodes positive. This compares favorably with the seven of 31 patients he has observed. Both patients are alive and free of disease 21 and 37 months following surgery; this supports the principle of a radical resection. Among the ten patients there have been two deaths, one from recurrent tumor and one from a cerebrovascular accident. The remainder are alive and free of disease, four of whom have survived more than 3 years. This experience is supportive of Dr. Skinner's concept that *en bloc* radical resection is worthwhile in patients with limited disease.

(Slide) I have two thoughts I would like him to comment on. First, since there is a high probability of cure in these patients, the surgical therapy should not be compromised by inadequate resection of the stomach, and the problems associated with long-term esophagogastrectomy should be avoided. For this reason we have used the left colon to re-establish gastrointestinal continuity between the remaining antrium after an 80% gastric resection and the cervical esophagus. I would like to hear his comments concerning why he retains the stomach to establish gastrointestinal continuity.

Second, since the operation is of considerable magnitude, we have limited its use to patients under the age of 75 and prefer only palliative resection, regardless of the stage of disease in patients over that age. I would appreciate his comments on this as well.

Dr. Jerome J. DeCosse (New York, New York): I would like to thank the authors for the opportunity to read the manuscript and thank them for an outstanding contribution. I want to make two points, which can be derived from the presentation.

They have highlighted a larger issue in the treatment of gut cancer, namely, the significance of full-thickness penetration. They have illustrated the consequences of full-thickness penetration in the esophagus in decreasing survival. That is equally true in the stomach, where serosal penetration sharply reduces survival, and it is certainly true in the large bowel where Basil Morson has demonstrated solidly that full-thickness penetration increases fivefold the likelihood of lymph node metastases. It is probably also true in the oral pharynx.

Secondly, the authors have raised the interesting, difficult, challenging, and generic issue that an attempt to individualize treatment requires accurate pretreatment clinical staging in areas in the gut where our traditional staging depends on a specimen and perforce an operation.

It is of interest in the author's data that tumor size does not predict in the esophagus, and this is also true in the large bowel, that histology does not predict in the esophagus but seems to in the large bowel, and that the CT scan appears very useful in the esophagus but seems to be less so in the large bowel. Progress is necessary in this area if you wish to consider individualization in terms of surgery or in terms of adjuvant treatments.

Dr. Walter Lawrence, Jr. (Richmond, Virginia): I, too, very much enjoyed reading this paper. Also, I was particularly impressed by Dr. Skinner's presentation, in which he covered so many fascinating concepts regarding the approach to selecting a patient for a palliative *versus* a curative operation. Since I am not an esophageal surgeon *per se,* I would like to concentrate my remarks on the concepts of staging that he has discussed.

When I read the abstract, and when I had the pleasure of reading the paper, I felt very confused at first about this staging system. I think his presentation has reduced my confusion somewhat, but I have some concerns.

First of all, when we look at Oliver Beahrs' AJCC Manual on Staging, the bible for everybody who works with cancer, there are a number of things we are trying to do. First, we wish to have a common language. Second, we want to be able to use staging to pick the best treatment for the individual patients. Third, we want to have some prognostic indices.

For those of us who treat breast cancer, head and neck cancer, anal and cervical cancer, the TNM system is great. Ahead of time, we can tell a lot of things about the individual cancers because they are accessible. The trouble with all the visceral cancers, colon, stomach, and esophagus, is that it is difficult to define T or N for these lesions. The practical fact is that it is hard to tell, ahead of the operation and before the treatment, what the stage is and what the treatment ought to be. The way I see this is that if we can end up with a preoperative staging approach that does not require surgery, such as using CT more effectively, then possibly we can select nonoperative palliative treatments for the appropriate clinical situations. I think that would be the optimum.

I find some difficulty suddenly accepting WNM, this new staging nomenclature. If a common language is what we want out of staging, we