Selection of Operative Procedure for Adenocarcinoma of the Midstomach

Twenty Years' Experience with Implications for Future Treatment Strategy

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Pathoanatomic studies of the regional spread of adenocarcinoma of the middle one-third of the stomach suggested the need for extensive gastric and lymphatic resection. To seek evidence of improved results, a retrospective study was made of 213 patients curatively treated by three commonly used procedures: 1) radical high subtotal gastrectomy (SG, n = 39), 2) radical total gastrectomy (TG, n = 48), and 3) extended total gastrectomy (ETG, n = 126). The overall five-year survival rates were SG:10%, TG:16%, and ETG:19%. Advanced stage tumors (N2, N3, or M1) were highly lethal, irrespective of the type of resection. However, patients with early stage tumors (T1–4, N0 or N1) showed higher survival rates after more extensive resections (ETG:42% and TG: six of eight patients, versus SG:17%). The highest survival rate (93%) was observed in a subset of patients with early stage tumors electively treated by ETG; this was achieved despite the presence of metastasis to the juxtagastric (N1) lymph nodes or direct invasion of an adjacent organ in most of these patients. These observations confirm the merit of extensive resection for carcinoma of the midstomach.

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UNLIKE TUMORS OF THE prepyloric or cardiac regions of the stomach, which tend to cause obstructive symptoms early in the disease process, adenocarcinomas of the midstomach are often not diagnosed until the tumor has become bulky and metastases to the regional lymph nodes have occurred. The surgeon confronted with such a neoplasm, which is mobile and apparently resectable, must decide on an appropriate type of resection which will encompass all gross and microscopic areas of disease in the stomach and its lymphatic drainage field. The three types of commonly performed gastric resections for such a tumor are 1) high radical subtotal gastrectomy, 2) radical total gastrectomy, and 3) extended total gastrectomy with en bloc distal pancreatectomy and splenectomy (Fig. 1). Most surgeons favor the use of high subtotal gastrectomy because of its technical simplicity, reserving the other procedures for lesions of the proximal stomach.[2–6,8,15] Others advocate extended total gastrectomy for most tumors of the midstomach, regardless of its size or anatomic extent.[7,11,12,13,14] An extended version of high distal subtotal gastrectomy with en bloc distal pancreatectomy and splenectomy is feasible but seldom practiced.[16]

Although these surgical procedures have been performed for many years, little information is available in the literature with which one can compare, in a meaningful way, the efficacy of each procedure in terms of the extent of the disease. This constitutes one of the many problems in the treatment of gastric cancer which may require solution by conducting a prospective, randomized, clinical trial.[18] There is, however, considerable theoretical basis for believing that the extended total gastrectomy can better satisfy the basic tenets of a curative cancer operation, namely, resection of the primary lesion with a wide margin, and *en bloc* removal of those lymph nodes and lymphatic channels most likely to harbor metastatic deposits. Thus for the typical tumor of the midstomach, which is large and infiltrative, total gastrectomy is the best assurance of adequate proximal and distal margins of resection. Also, pathoanatomic studies[13,19] have demonstrated that carcinomas of the midstomach may metastasize to all of the regional lymph node basins of the stomach—including those of the juxtapyloric area, along the superior border of the pancreas, and at the hilum of the spleen (Fig. 2). These

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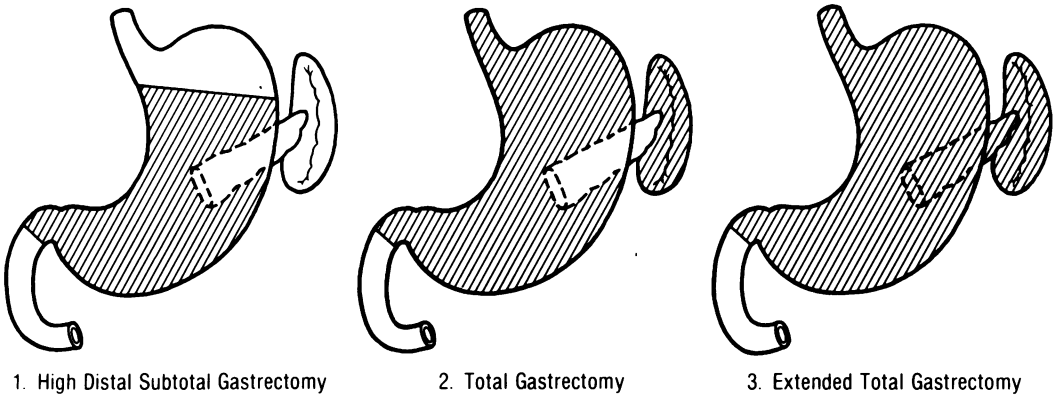

FIG. 1. The three types of gastric resection commonly performed for carcinoma of the midstomach: (1) radical high distal subtotal gastrectomy, (2) radical total gastrectomy, with splenectomy, and (3) extended total gastrectomy, with en bloc distal pancreatectomy and splenectomy.

nodal areas are conveniently encompassed by en bloc distal pancreatectomy with splenectomy, but are partly omitted in the standard high distal, subtotal, or total gastrectomy procedures. Despite the theoretical merit of the extended total gastrectomy, convincing data in the form of better survival rates are lacking, so that most surgeons continue to offer the lesser procedures, which carry lower morbidity rates, to patients who have resectable tumors of the midstomach.

The purpose of this study is to retrospectively examine and compare the curative efficacies of the three types of gastric resections performed for adenocarcinoma of the midstomach at our institution over a 20-year period. The surgical procedures varied according to the operative findings, according to the preference of the individual surgeons, and according to changes in the prevailing policy or surgical philosophy during the long period of study. In order to minimize bias intrinsic to retrospective nonrandomized studies, comparisons were made according to the extent of disease as indicated by tumor node metastasis (TNM) stage, tumor size, and the presence or absence of tumor invasion of adjacent organs. Based on the observations made in this study, a proposal is made for future treatment strategy and prospective clinical trials in the management of resectable cancer of the midstomach.

Materials and Method

Clinical Material

The medical records of patients who underwent surgical resection for adenocarcinoma of the middle one-third of the stomach from 1955 to 1975 at Memorial Sloan-Kettering Cancer Center were reviewed. The criteria for acceptance into the study were as follows: 1) that gastric resection was performed with curative intent, and 2) that adjuvant chemotherapy, radiation therapy, or immunotherapy was not used. 3) Patients who developed gastric cancer after previous gastrectomy or gastrojejunostomy for benign conditions were excluded from the study. Two hundred thirteen cases satisfied these criteria and formed the subject of this study.

Surgical Technique

Details of the three surgical procedures used in this study have been presented previously.[10,13,14] High distal subtotal gastrectomy (performed on 39 patients) entailed transection of the stomach near the cardia, removal of the organ except for a cuff of fundus, excision of the first part of the duodenum and both omenta, as well as en bloc removal of the lymph nodes in the hepatoduodenal ligament (around the hepatic artery and left gastric artery) with ligation of the latter at its origin.[13] Total gastrectomy (performed on 48 patients) included removal of the entire stomach, abdominal esophagus, first part of duodenum, both omenta, and spleen, and the dissection of the lymph nodes along the hepatic and left gastric arteries. Extended total gastrectomy (performed on 126 patients) meant that in addition to the structures resected at

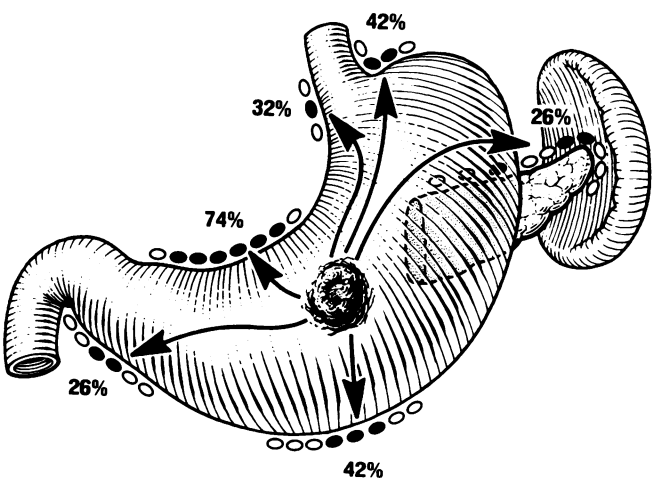

FIG. 2. The frequencies of metastases in the various regional lymph node groups from adenocarcinoma of the midstomach (modified after McNeer and Pack 13).

TABLE 1. *TNM Classification of Stomach Neoplasms by the American Joint Committee, 1978*

Primary tumor (T)
- T1: tumor limited to mucosa or mucosa and submucosa
- T2: tumor involves mucosa, submucosa, muscle, and extends to or into serosa, but does not penetrate serosa
- T3: tumor penetrates through the serosa without invading contiguous structures.
- T4: tumor invades adjacent contiguous structures

Nodal involvement (N)
- N0: no metastases to regional lymph nodes
- N1: involvement of perigastric lymph nodes within 3 cm of primary tumor along the lesser or greater curvature
- N2: involvement of regional lymph nodes more than 3 cm from primary tumor which are removable at operation, including those along the left gastric, splenic, celiac, and common hepatic arteries
- N3: involvement of other intra-abdominal lymph nodes such as the para-aortic, hepatoduodenal, retropancreatic and mesenteric nodes.

Distant metastasis (M)
- MO: No known distant metastasis
- M1: distant metastasis present.

total gastrectomy, the body and tail of the pancreas were removed en bloc, the splenic and left gastric arteries were ligated at their origins, and the celiac lymph nodes were completely dissected.

The two more extensive procedures, total and extended total gastrectomy, were also retrospectively categorized as either elective or obligatory. An obligatory procedure was performed when the surgeon had no choice but to resort to the more extensive procedure (for example, high extension of disease near the cardia which necessitated total gastrectomy, or fixation of tumor to the pancreas which required its removal by the extended radical procedure). The procedure was categorized as elective when the surgeon could have chosen a procedure of lesser magnitude, but a more extensive operation was performed for better margins or lymphatic clearance.

Evaluation of Extent of Disease

The extent of the primary neoplasm in the stomach wall and the presence and absence of metastases in the regional lymph nodes were determined in each case by review of the operative and pathology reports. This information was used to classify the neoplasms according to the TNM Staging System (Table 1) adopted by the American Joint Committee on Tumor Staging and End Results Reporting.[1]

Statistical Analysis

Survival curves were plotted by means of the Kaplan-Meier Method.[9] Deaths that occurred within the first month after operation or while the patient was in the hospital were regarded as deaths from the disease. The log rank test[17] was used to compute the statistical significance of differences in the survival rates of various groups of patients. The chi square test was employed in analyzing the statistical significance of other observations.

Results

Of the 213 patients studied, 39 patients underwent high distal subtotal gastrectomy, 48 patients underwent total gastrectomy, and 126 patients underwent extended total gastrectomy.

TNM Stage

The TNM Staging scheme is summarized in Table 1. For purposes of comparison, the patients were separated into an early-stage group (consisting of those patients in whom the disease was limited to the primary tumor [T1–4 N0M0], or primary tumor with metastases to the immediately adjacent lymph nodes [T1–4 N1 M0]) and an advanced-stage group (comprising patients in whom tumors had metastasized to remote lymph node basins [T1–4 N2–3 M0] or distant sites [T1–4 N0–3 M1]). The latter subset of M1 tumors were those in patients in whom the presence of minimal distant metastatic disease was not recognized until after resection with curative intent had been performed. The frequencies of early- and advanced-stage tumors in this

TABLE 2. *Distribution of Tumors According to TNM Stage and Type of Resection*

	Early-stage Tumors		Advanced-stage Tumors		
	T1–4 N0	T1–4 N1	T1–4 N2–3	All M1 Cases	Total
High distal subtotal gastrectomy	6	6	15	12	39
Total gastrectomy	6	2	25	15	48
(elective cases only)	(2)	(1)	(8)	(4)	(15)
Extended total gastrectomy	15	21	77	13	126
(elective cases only)	(5)	(8)	(20)	(2)	(35)
All cases	27	29	117	40	213
	(27%)		(73%)		(100%)

TABLE 3. *Median Size of Tumors (Maximum Diameter in Centimeters) According to TNM Stage and Type of Resection*

	Early Stage Tumors		Advanced Stage Tumors		
	T1–4 N0	T1–4 N1	T1–4 N2–3	All M1 Cases	All Stages
High distal subtotal gastrectomy	5†	6†	6.5	8	6.5*
Total gastrectomy	5.5	11	8	9	8
Extended total gastrectomy	10	9	10	8	9.5*
(elective cases only)	(8.5)†	(10)†	(9.5)	(8)	(9.5)
All cases	7.5	8.5	8	8	8

* $p < 0.05$. † $p < 0.05$.

study are recorded in Table 2 according to the type of operative procedure performed. The advanced-stage tumors (73%) more than doubled the number of early-stage tumors (27%). The distributions of the three types of resection were quite similar within the two groups. Thus the ratio of subtotal gastrectomy to extended total gastrectomy was approximately 1:3 for both early- and advanced-stage tumors.

Tumor Size

The median size of the tumors, as measured by the maximum diameter in centimeters is listed in Table 3 according to the TNM stage groups and the type of surgical resection. The median size of the tumors showed little difference among the TNM stage groups, but showed a remarkable difference according to the type of operation performed. The smaller tumors (median size: 6.5 cm) tended to be managed by high distal subtotal gastrectomy, while the larger tumors (median size: 9.5 cm) were managed by extended total gastrectomy ($p < 0.05$). This tendency toward a lesser procedure for smaller neoplasms and a more extensive procedure for larger neoplasms was most noticeable in the early-stage group, in which the median tumor sizes were 5–6 cm for high subtotal gastrectomy as compared with 9–10 cm for extended total gastrectomy or 8.5–10 cm for elective extended total gastrectomy. As will be seen later, this has an important bearing on the interpretation of the curative efficacies of the various operative procedures. No statistically significant differences were found in tumor sizes between total and extended total gastrectomy, or between any of the procedures when only advanced-stage tumors were compared.

Invasion of Adjacent Organs

In 49 of the 213 patients studied (23%) the primary tumor had invaded organs adjacent to the stomach (Table 4). En bloc removal of portions of these organs, such as liver, intestine or kidney, was performed with gastric resection, and subsequent microscopic examination of the resected specimen confirmed the presence of direct carcinoma invasion. Such invasions were more commonly encountered in patients who underwent extended total (24% of the patients) or total gastrectomy (27% of the patients) than in those managed with high distal subtotal gastrectomy (15% of the patients), but the difference was not statistically significant. The preponderance of tumors showing adjacent organ invasion was even more discernible with elective extended total gastrectomy (3/13, or 23% of the patients) performed for early-stage lesions, as compared with distal subtotal gastrectomy (1/12, or 8% of the patients), even though the difference did not achieve statistical significance because of the small number of patients.

Survival after Resection

The five-year survival rates (Kaplan-Meier) for all TNM stages were 10% after high distal subtotal gastrectomy, 16% after total gastrectomy, and 19% after extended total gastrectomy. Figure 3 shows the respective

TABLE 4. *Frequency of Direct Invasion of Adjacent Organs According to TNM Stage and Type of Resection*

	Early-stage Tumors*	Advanced-stage Tumors*	Total All Stages
High distal subtotal gastrectomy	1/12 (8%)	5/27 (18%)	6/39 (15%)
Total gastrectomy	4/8 (50%)	9/40 (24%)	13/48 (27%)
Extended total gastrectomy	5/36 (14%)	25/90 (28%)	30/126 (24%)
(elective cases only)	(3/13, 23%)	(5/22, 23%)	(8/35, 23%)
All cases	10/56 (18%)	39/157 (25%)	49/213 (23%)

* See Table 2 for explanation.

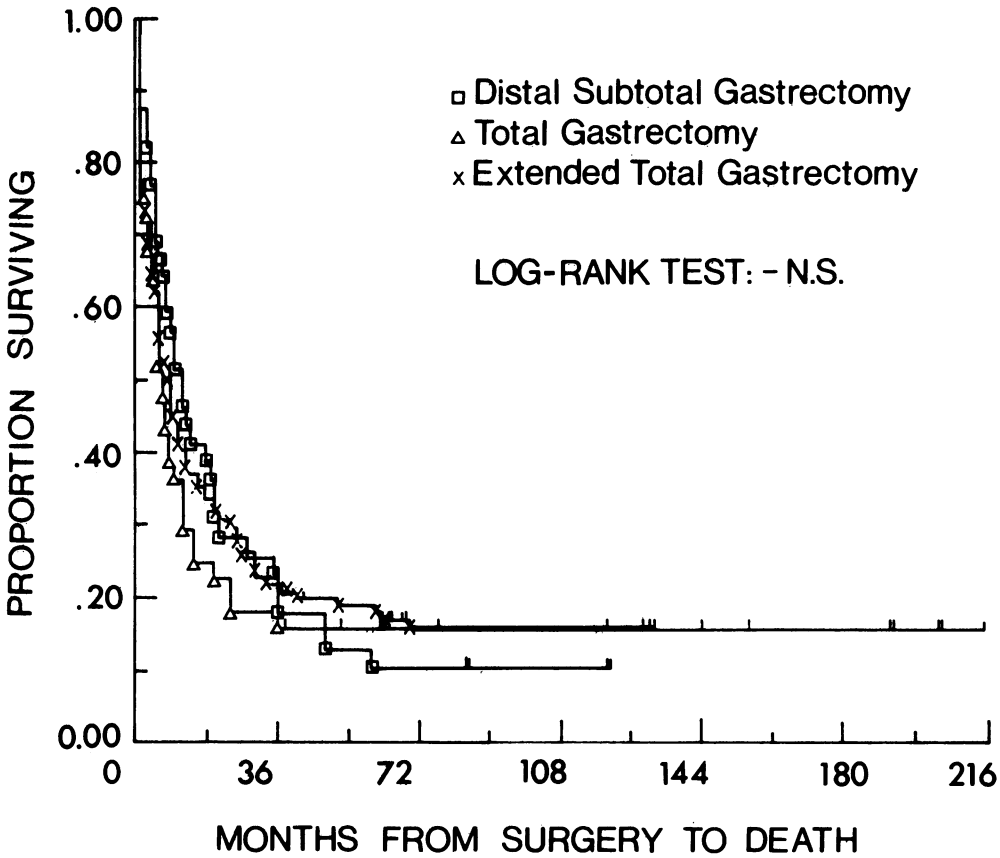

FIG. 3. Survival curves of patients after treatment by the three types of gastric resection: all TNM groups combined.

survival curves, which overlap considerably, and in which no statistically significant difference could be discerned. Examination of the survival data by the TNM classification indicated, however, that almost all of the patients who had advanced-stage tumors died; only six of the 157 patients survived for five years or more (three patients died after extended total gastrectomies, two patients died after distal subtotal gastrectomies, and one patient died after total gastrectomy). The large number of advanced-stage tumors with unfavorable outcomes suggested that the behavior of the smaller number of early stage tumors may have been overshadowed. A separate analysis of these cases was therefore peformed.

Figure 4 depicts the survival curves of the patients with early-stage tumors (T1–4 N0 M0 and T1–4 N1 M0) according to the type of resection performed. Remarkable differences in survival rates were noted. Patients treated by distal subtotal gastrectomy had a very low five-year survival rate (2/12, or 17% of the patients) as compared with those treated by total gastrectomy (six of eight patients) and the much higher survival rate after extended total gastrectomy (15/36, or 42% of the patients). The superior curative potential of a more extensive resection became even more evident when patients who underwent elective extended total gastrectomy for early-stage tumors were compared with similarly staged patients treated by subtotal gastrectomy (Fig. 5). As indicated earlier, these patients' tumors could, according to retrospective review of the pathology and operative records, have been managed by high distal subtotal gastrectomy, but the attending surgeons elected to apply the extended radical procedure. Also, as recorded above, the proportion of these patients' tumors that manifested unfavorable characteristics, such as the large size and invasion of adjacent organs, far exceeded that of patients with similarly staged tumors treated by high subtotal gastrectomy. Nonetheless, the patients treated by extended total gastrectomy showed a remarkably higher survival rate of 93% (11/13 patients) at five years, as compared with a 17% (2/12 patients) survival rate for the patients treated by high subtotal gastrectomy. This difference in survival distribution is statistically significant ($p < 0.01$).

Local Tumor Recurrence

Recurrence of the stomach tumor was confirmed by barium roentgenograms, reoperation, or autopsy in 39 of the 169 patients (23%) who survived the surgical procedure. The recurrence rates for the three types of resections were: high distal subtotal gastrec-

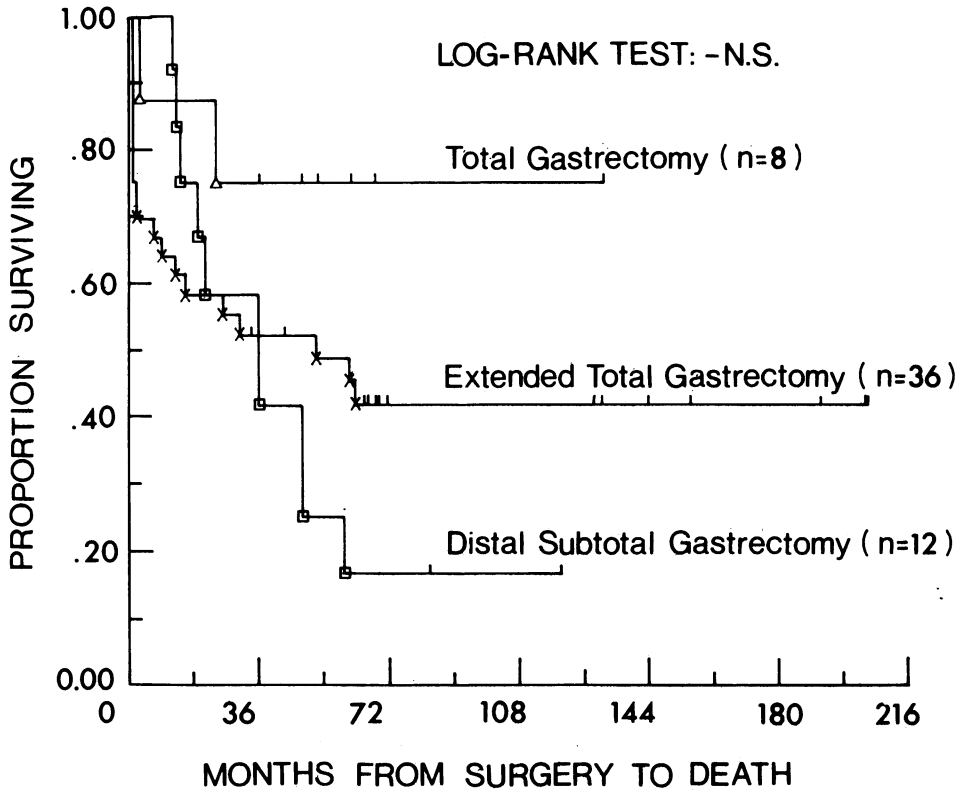

FIG. 4. Survival curves of patients after treatment by the three types of gastric resection: early TNM stage tumors only.

tomy—29% (10/34 patients), total gastrectomy—35% (13/37 patients), and extended total gastrectomy—16% (16/98 patients). The lowest local recurrence rate was therefore achieved with the extended total gastrectomy, which showed a statistically significant difference when compared with total gastrectomy ($p < 0.05$).

Operative Mortality Rates

Forty four patients died of the surgical procedure, giving an overall operative mortality rate of 21%. High distal subtotal gastrectomy showed a lower mortality rate (13%) compared with total (23%) or extended

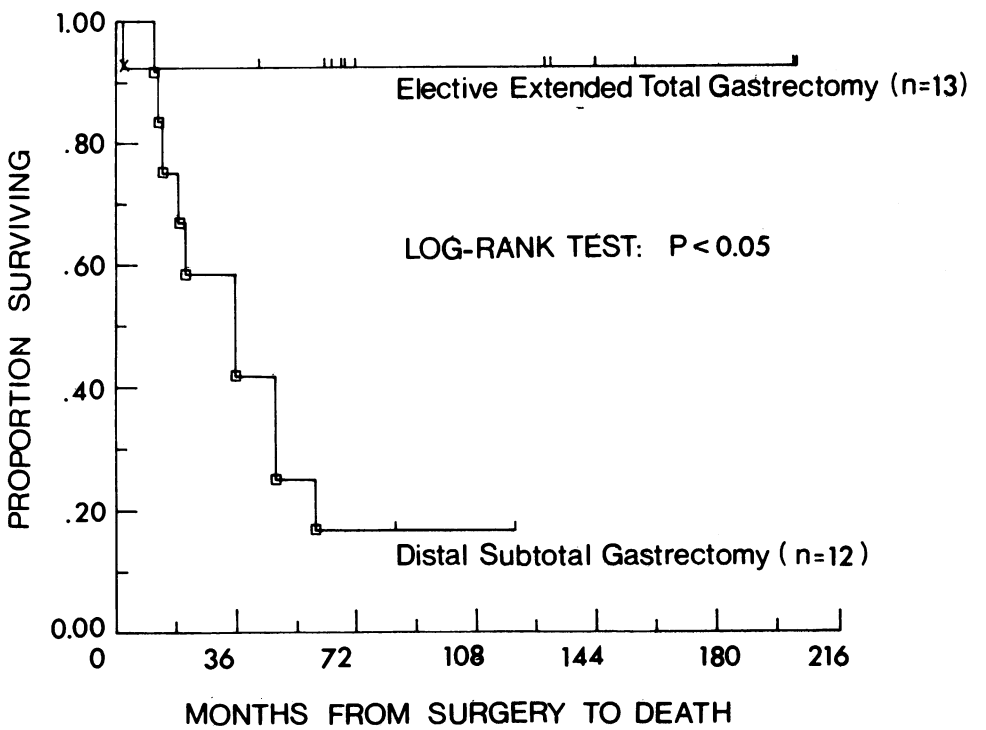

FIG. 5. Survival curves of patients treated by *elective* extended total gastrectomy and high distal subtotal gastrectomy: early TNM stage tumors only.

total (22%) gastrectomy. However, these differences were not statistically significant. Most of the deaths that occurred because of the operation were in the first 15 years of the study period. During the last five years of the study (1970–1975), the operative mortality rate dropped to 8% (3/36 patients).

Discussion

Although carcinoma of the stomach is decreasing in incidence in many western countries, it still ranks high in the list of major causes of death from carcinoma in the United States, and continues to be a major health problem in countries such as Japan, Chile, and Iceland where the disease is much more prevalent. Except in countries where mass screening programs are conducted for the early diagnosis of gastric carcinoma, these tumors continue to present clinically at a late stage of the disease. This is particularly so with carcinomas of the midstomach, which are less prone to develop early symptoms due to obstruction and hemorrhage. As indicated in the present study, many of these tumors are large and show signs of advanced local invasion or lymphatic spread. Yet, in the absence of detectable distant metastases, many of these neoplasms are totally resectable, and this is the only hope for long-term cure.

The surgeon's dilemma in these cases is often how aggressive a stance to adopt in offering surgical resection. Anatomically extensive resections are often necessary because of the position and bulkiness of the tumor, and the suspected or actual direct invasion of adjacent organ structures. Knowledge of the lymphatic drainage pathways of the midstomach, and the recorded frequencies of metastases to the various perigastric lymph node groups[13,19] (including the juxtapyloric lymph nodes, the paracardial lymph nodes, and the pancreaticolienal lymph nodes) also prompt the surgeon toward execution of an extensive regional lymphatic dissection. The decision to carry out such extensive surgical procedures must, of course, be tempered by consideration of the prospects of cure relative to the risk of operative complications and death. Such a decision has always been difficult because even though the more aggressive gastric resections (such as total radical gastrectomy or extended total gastrectomy with en bloc distal pancreatectomy) may have theoretical merit, the reported results in several series of patients have not shown any improvement in survival and cure rates as compared with standard radical subtotal gastrectomy.[2–6,8] If anything, these extensive procedures were shown to have higher operative morbidity and mortality rates.

However, previous analyses of these experiences have not given detailed consideration to the stages of the disease, as classified in the TNM scheme. As a result, any salutary effect in a small number of patients with earlier stages of neoplasm may have been completely obscured by the unfavorable outcome in a much larger number of patients who had advanced-stage tumors. This was found to be the case in the present study, in which the five-year survival rates, for all TNM stages combined, were almost identical after radical subtotal, total, and extended radical gastrectomies (Fig. 2). However, for early-stage tumors in which disease was limited to the gastric wall and the immediately adjacent perigastric lymph nodes (T1-4 N0 and T1-4 N1), a distinctly better five-year survival rate of 48% was achieved by radical total gastrectomy (6/8) and extended total gastrectomy (15/36), as compared with 17% (2/12) for radical subtotal gastrectomy. The theoretical merit of extensive resection coupled with wide regional lymphadenectomy for early-stage disease is also borne out by the remarkable five-year survival rate of 93% achieved by elective extended total gastrectomy in 13 patients, in three of whom the tumor had invaded an adjacent organ, and in eight of whom the tumor had metastasized to the immediate juxtagastric (N1) lymph nodes. These results suggest that submicroscopic deposits had been present within the wide expanse of vicera and lymphatic tissues resected by extended total gastrectomy, even though only limited disease was detected by histopathologic examination.

Similar reasoning can be applied to explain the relative inefficacy of extensive resection procedures performed for more advanced cases of carcinoma of the midstomach. Only six of the 157 patients in the N2, N3 and M1 tumor groups were saved by resections performed with curative intent in this series. It seems reasonable to assume that a majority of the patients with advanced-stage tumors already had clinically occult liver, distant lymphatic, or peritoneal foci of disease beyond the scope of even the most extensive procedure at the time of surgery. Extensive radical resection in this group of patients is difficult to justify unless some palliative objective can be accomplished, the risk of operative mortality can be lowered, and some form of adjuvant therapy can be offered to control residual microscopic disease. The decision in a given case could be made much easier if, in the absence of obvious distant disease, a simple method for the intraoperative determination of the extent of nodal involvement (N0 and N1 versus N2 and N3) could be applied. Unfortunately, extensive node sampling is tedious and often unhelpful; it may also jeopardize the potentially curable patient because of the likelihood of tumor cell spillage.

The operative mortality rate of 22% for patients who had extended total gastrectomies in this series is excessive. However, many of these patients were treated during the earlier years of the period studied (1955–

1970), and had died from hemorrhagic shock, cardiopulmonary complications, and intra-abdominal sepsis. Today, with improved anesthetic techniques, innovations in the physiologic management of critically ill patients, modern antibiotics, and the feasibility of long-term parenteral nutritional support, death from operative and postoperative complications due to these extensive resections can be minimized. In fact, during the last five years of the period studied (1970–1975), the operative mortality rate had dropped to 8%.

The present study was not carried out with the objective of establishing extended total gastrectomy as the best operative procedure for carcinoma of the midstomach. Rather, it was done to obtain data and evidence in support of the need for a widely encompassing organ and lymphatic field resection suggested by previous pathoanatomic studies.[13,19] In this retrospective study, such evidence was found by comparing extended total gastrectomy, radical total gastrectomy, and radical subtotal gastrectomy, which were the types of procedures chosen and performed during the study period at one institution. It must not be concluded, however, that similar or even superior results may not be achievable with other conceptually similar procedures. For example, high distal subtotal gastrectomy, with resection of the distal pancreas and spleen, and regional lymphadenectomy had been suggested by Paulino[16]; this would avoid the complications of total gastrectomy and the attendant risks of an esophageal anastomosis. Also, if extensive regional lymphadenectomy is the main objective, an obvious question is whether or not the distal pancreas must be resected even if it is not directly invaded, for the celiac and superior pancreatic lymph nodes can be dissected off the superior border of the pancreas and the splenic vessels. Omitting pancreatic resection can reduce the morbidity rate, since leakage of pancreatic fluid is associated with a high incidence of septic complications.

If there is a need for a widely encompassing organ and lymphatic resection for carcinoma of the midstomach, as suggested by this study, the following clinical studies would be desirable to further define the optimal therapy for these tumors. From the surgical standpoint, a prospective randomized trial can be conducted of total gastrectomy versus high subtotal gastrectomy, combined in each case with regional lymphadenectomy and splenectomy. The lymphadenectomy can be further studied by the randomized performance of celiac and superior pancreatic nodal dissections with or without en bloc resection of the distal pancreas. From the standpoint of adjuvant therapy, all of these patients are justifiable candidates for clinical trial with the currently available modalities and regimens, so long as appropriate stratification of the study design takes into account the extent of nodal disease (N0,N1,N2 and N3) so that any salutary effects in a subset of patients would not be masked by the overwhelming lack of efficacy with the others. Until these clinical trials are undertaken and the results reported, extended total gastrectomy with splenectomy, distal pancreatectomy and en bloc regional lymphatic dissection would seem to be the surgical procedure of choice for the curative treatment of most patients with adenocarcinoma of the midstomach. Good surgical judgment must dictate which individual patient would not be a good candidate for such a procedure. The histopathologic proof of advanced nodal involvement (N3) or the presence of concomitant medical disease with poor physiologic status would be reasonable contraindications for operation.

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