Adenocarcinoma of the Gastric Cardia

The Choice of Gastrectomy

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A retrospective study of 101 patients with adenocarcinoma of the gastric cardia treated with proximal subtotal, extended proximal subtotal, total, and extended total gastrectomy demonstrated the following: 1) There were no five year survivors among patients with TNM stage III and IV disease. 2) Surgical treatment was curative only in the presence of stage I and II disease, where extended total gastrectomy resulted in a significantly higher survival rate than proximal subtotal gastrectomy ($p < 0.03$). 3) Proximal subtotal gastrectomy resulted in a high incidence of local recurrence, particularly when it was applied in patients with stage I and II neoplasms. 4) There were no significant differences in operative mortality between the four procedures. Since the choice of operative procedure makes a difference only in patients with TNM stage I and II disease, intraoperative classification should be considered in the management of adenocarcinoma of the cardia. Classification should be based on lymph node biopsy unless the neoplasm has spread beyond the confines of gastrectomy.

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THE SURGICAL TREATMENT of adenocarcinoma of the gastric cardia has three main objectives: 1) to remove the tumor and prevent or relieve obstruction of the esophagus; 2) to obtain tumor-free margins around the primary neoplasm, and 3) to remove those regional lymph nodes which are likely to be involved by metastasis. The first two objectives are usually achieved by proximal subtotal gastrectomy (Fig. 1). Unfortunately these lesions metastasize to all the regional nodes of the stomach (Fig. 2). The only procedure which can encompass the primary neoplasm with the entire lymphatic drainage of the stomach is an extended total gastrectomy—a total gastrectomy combined with splenectomy, distal pancreatectomy and celiac node dissection (Fig. 1).

Extended total gastrectomy has not been adopted as the procedure of choice for the management of neoplasms of the cardia.[13] An argument against it is that adenocarcinomas of the cardia have such a poor prognosis that surgical treatment is essentially palliative; hence, one should perform proximal subtotal gastrectomy which is less extensive and more simple from a technical point of view.[2,3] Some authors advocate proximal subtotal gastrectomy for primary lesions confined to the cardia and reserve total or extended total gastrectomy for those neoplasms which extend toward the lesser curvature of the stomach.[4,5,16] In order to encompass the disease in the area of the lesser gastric curvature, surgeons have devised various modifications of proximal subtotal gastrectomy, none of which includes the pyloric and greater curvature lymph nodes (Fig. 1). Thus, despite the lapse of almost eight decades since total[19] and proximal subtotal gastrectomy[24] were initiated in clinical practice, their place in the management of adenocarcinoma of the cardia has not been clearly defined as yet.

It is generally conceded that the majority of adenocarcinomas of the gastric cardia are incurable by surgical means because 70–80% of them have already spread beyond the confines of gastrectomy at the time of exploration.[3,10,17] This fact should be taken into account in comparing the results of surgical treatment because the patients with advanced lesions outnumber those with potentially curable, early ones. In this setting, proper classification of the disease permits a more meaningful comparison of therapeutic procedures. The present report concerns a group of patients with adenocarcinoma of the gastric cardia treated with four different types of gastrectomy. The study was mainly based on the TNM system of tumor classification; additional parameters, however, were considered. These were the size and location of the primary neoplasm in relation to the esophagus and the stomach, the extent of esophageal involvement, the

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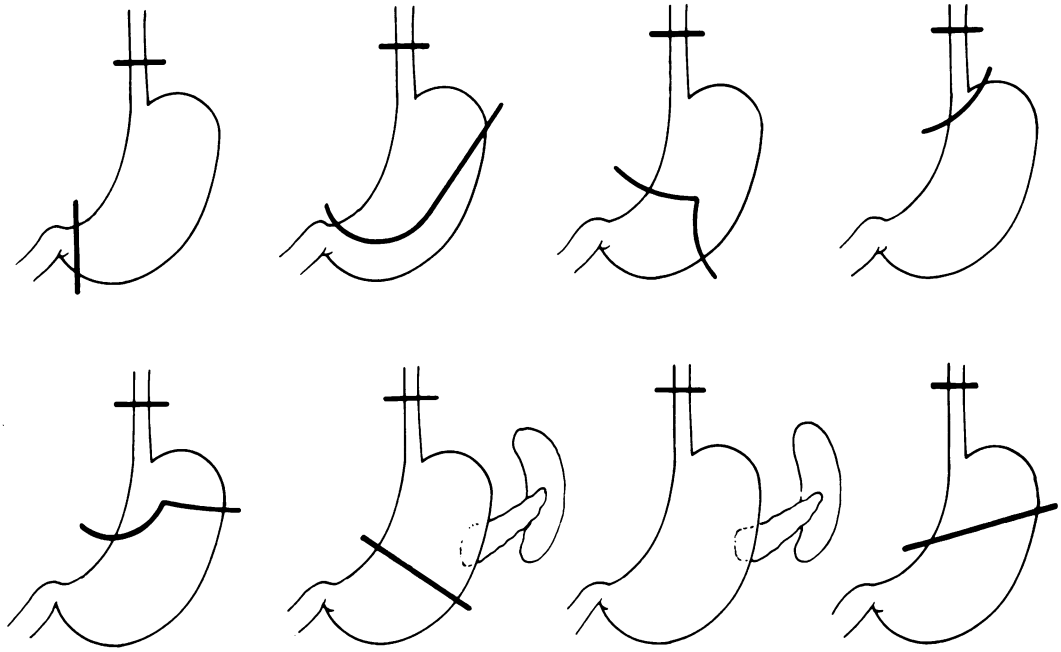

FIG. 1. Types of gastric resection used in the management of neoplasms arising in the cardia of the stomach.

adequacy of esophageal resection etc. The four procedures were compared according to operative mortality, incidence of local recurrence and survival rate.

Materials and Methods

The study includes 101 patients with primary adenocarcinoma of the gastric cardia treated by gastrectomy during a 20-year period ending in August of 1975. Patients who received adjuvant chemotherapy, immunotherapy and radiation therapy were excluded. Patients with a history of gastric surgery for ulcer and those who had neoplasms containing elements of squamous cell carcinoma were also excluded. Seventy patients were males and 31 were females. Their median age was 61 and the range was 34–79 years.

Four types of gastrectomy were used: 1) Proximal subtotal (n = 46). This procedure involved resection of the distal esophagus, the spleen and the proximal stomach cephalad to a line connecting the junction between the mid and lower third of the lesser curvature to the middle of the greater curvature. 2) Extended proximal subtotal (n = 10). In addition to the structures resected by proximal subtotal gastrectomy, this procedure involved dissection of the celiac nodes and resection of the distal pancreas en bloc.[14] 3) Total (n = 6). This type of resection included the distal esophagus, the entire stomach, the first part of the duodenum, the spleen and both omenta. 4) Extended total (n = 35). In addition to the structures resected by total gastrectomy, this procedure included the distal pancreas and the celiac nodes.[11,14] Gastrointestinal continuity was restored as follows: In patients undergoing proximal and extended proximal subtotal gastrectomy the esophagus was anastomosed to the gastric remnant either end-to-side (n = 48) or end-to-end (n = 8). In patients treated with total and extended total gastrectomy the esophagus was anastomosed to a loop of jejunum either end-to-end Roux-en-Y (n = 24), or end-to-side (n = 17). A Hunt-Lawrence pouch was constructed in four patients.[11]

Resected neoplasms were classified according to the TNM system[1] on the basis of information obtained from the operative and the pathology reports (Table 1). Tumor size was that recorded in the pathology reports and it was defined as the maximum diameter of the primary lesion. Esophageal invasion was defined as the

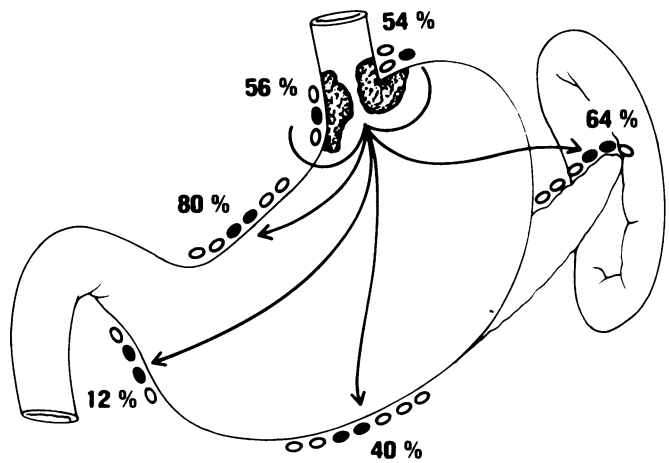

FIG. 2. Incidence of regional node metastasis in patients undergoing gastrectomy for adenocarcinoma of the cardia. Modified after McNeer and Pack.[14]

TABLE 1. *The TNM System for the Classification of Cancer of the Cardia*

Classification	Explanation
T1	Primary neoplasm confined to the mucosa
T2	Primary neoplasm extending to serosa
T3	Primary neoplasm extending through serosa
T4	Primary neoplasm infiltrating the stomach diffusely
TX	Degree of gastric involvement unknown
N0	Regional nodes free of metastasis
N1	Metastasis to nodes adjacent to the primary
N2	Metastasis to nodes in both gastric curvatures or to remote regional nodes
NX	Extent of nodal involvement unknown
M0	Absence of distant metastasis
M1	Distant metastasis present
Stage I	T1, T2, T3 with N0 M0
Stage II	T4, N0, M0 or T1–T4 with N1M0
Stage III	T1–T4 with N2M0
Stage IV	Any T and N with M1

length of esophagus grossly occupied by tumor. Esophageal margin was defined as the distance from the line of esophageal transection to the palpable edge of the primary. These dimensions had been measured in fresh specimens and do not correspond to *in vivo* dimensions because resected esophagi shrink to about half their original size.[15]

Results

Tumor Staging

Classification of the 101 neoplasms according to the TNM system revealed that most of them had already caused involvement of multiple regional lymph nodes and/or distant metastasis at the time of resection (Table 2). Thus, stage III and IV lesions constituted a 69% majority, while early-stage neoplasms were relatively rare. The same classification demonstrated that stage I and II tumors were generally managed with proximal subtotal gastrectomy while extended total gastrectomy was mainly reserved for advanced stage neoplasms (Table 2). Actually, half of all proximal subtotal resections were done for stage I and II lesions while only seven out of the 39 extended total resections were done for such tumors ($p < 0.05$, chi-square test).

TABLE 2. *Classification of Resected Neoplasms According to the Stage of Their Disease*

Gastrectomy	Number of Patients	TMN Stage I	II	III	IV
Proximal subtotal	46	9	11	15	11
Ext. prox. subtotal	10	1	2	6	1
Total gastrectomy	6	1	—	3	2
Ext. total gastrectomy	39	3	4	21	11
Total number of patients	101	14	17	45	25

TABLE 3. *Classification of Resected Neoplasms According to Size (Maximum Diameter—in Centimeters)*

Gastrectomy	Total	TNM Stage I	II	III	IV
Proximal subtotal	6	5.5	6	6.5	7
Ext. prox. subtotal	7.5	5.5	6	8	9
Total gastrectomy	8	6.5	10	8	9
Ext. total gastrectomy	8.5	7.8	11	8.5	8.5
Total	7	6	7	7.5	8

Tumor Size

There was no correlation between tumor size and stage of the disease (Table 3). Despite a gradual increase in tumor size from stage I to stage IV, the difference between the two groups was not statistically significant (Rank Sum Test). Actually, the median maximum diameter of stage IV lesions was only two centimeters larger in comparison to that of stage I neoplasms (Table 3). Proximal subtotal gastrectomy was frequently used for the management of smaller neoplasms while the larger tumors were managed with extended total gastrectomy. The difference between the two procedures was particularly evident in stages I and II although it was not statistically significant (Rank Sum Test).

Extent of Esophageal Invasion and Location of the Main Tumor

The median length of gross esophageal invasion for the entire series was 2.8 cm (Table 4). Tumors managed with proximal subtotal gastrectomy had invaded a longer segment of esophagus as compared with tumors managed with other procedures although the difference between the four types of gastrectomy was

TABLE 4. *Extent of Esophageal Invasion, Dimensions of the Esophageal Margins and Incidence of Histologically Positive Margins*

Gastrectomy	Esophageal Invasion, Median	Esophageal Margins, Median	Positive Margins (Incidence)
Proximal subtotal	3.2 cm (0.4–5.0)	2 cm (0–4.5)	43% (20/46)
Ext. prox. subtotal	2.9 cm (0.8–3.8)	2.5 cm (0–4.2)	40% (4/10)
Total gastrectomy	2.3 cm (0.2–4.0)	2.2 cm (0–6)	33% (2/6)
Ext. total gastrectomy	2.2 cm (0.3–3.8)	2.6 cm (0–5.5)	26% (10/39)
Average	2.8 cm (0.3–5.0)	2.3 cm (0–6)	36% (36/101)

not significant (Rank Sum Test). Subtraction of the length of esophageal invasion from the diameter of the main neoplasm defines the length of gastric invasion. Thus, the median diameter of lesions managed with proximal subtotal gastrectomy was 6 cm (Table 3) and the median length of esophageal invasion was 3.2 cm which means that these neoplasms were located almost exactly at the gastroesophageal junction. Neoplasms managed with extended total gastrectomy showed evidence of rather extensive gastric invasion. The median tumor diameter was 8.5 cm while the median length of esophageal invasion was only 2.2 cm (Table 3 and 4). Lesions managed with other procedures were intermediate.

Esophageal Margins

Table 4 presents the median length of macroscopically tumor-free esophageal margins obtained in each of the four procedures under comparison. Although margins were smaller in patients treated with proximal subtotal gastrectomy, the difference between the four groups was not statistically significant (Rank Sum Test). In 36 patients the esophagus was transected through an area invaded by the neoplasm, as permanent section examination of the specimen revealed (Table 4). Twenty of these so-called histologically positive margins were encountered in patients treated with proximal subtotal gastrectomy. The incidence of positive margins was lower in the other three groups; the difference however between them was not statistically significant.

Mortality

The overall operative mortality for the entire series was 15% (15/101). Extended proximal subtotal gastrectomy resulted in the highest mortality rate (40%) followed by total (14%), extended total (13%) and proximal subtotal gastrectomy (11%). The difference between the four procedures was not statistically significant. Dehiscence of the esophageal anastomosis resulted in 10 deaths, three of which occurred after extended proximal, three after proximal subtotal, three after extended total and one after total gastrectomy.

Local Recurrence

One-third of the patients who survived their treatment developed recurrence of the disease in the area of gastric resection (Table 5). Patients treated with proximal subtotal gastrectomy had the highest incidence of local recurrence and those treated with extended total gastrectomy the lowest ($p < 0.01$, chi-square test). The difference between the two procedures was particularly evident in TNM stages I and II ($p < 0.01$, Table 5). On the other hand, their difference was minimal in stages III and IV. Local recurrences in general were more common in patients with early rather than advanced-stage disease as Table 5 indicates ($p < 0.05$).

TABLE 5. *Incidence of Local Recurrence following Gastrectomy for Adenocarcinoma of the Cardia**

Gastrectomy	All Stages	Stage I, II	Stage III, IV
Proximal subtotal	49%† 20/41	70%§ 12/17	33% 8/24
Ext. prox. subtotal	17% 1/6	0% 0/3	33% 1/3
Total gastrectomy	33% 2/6	0% 0/1	40% 2/5
Ext. total gastrectomy	15%† 5/33	0%§ 0/7	20% 5/25
All patients	32% 28/86	46%‡ 12/26	27%‡ 16/60

* Patients dying in the immediate postoperative period were excluded.
† $p < 0.01$.
‡ $p < 0.05$.
§ $p < 0.01$.

The high incidence of local recurrence following proximal subtotal gastrectomy could not be attributed to histologically positive esophageal margins which were rather common in this group of patients. This is because positive margins were encountered in only eight of 24 patients who developed recurrence at the site of the esophageal anastomosis; of these eight patients, only four had been treated with proximal subtotal gastrectomy. Furthermore, positive esophageal margins were present in only two of 12 stage I and II patients who developed anastomotic recurrence after proximal subtotal gastrectomy.

Survival

Analysis of survival data using a TNM classification failed to demonstrate any significant differences between the four types of surgical treatment (Fig. 3). The survival curves in Figure 3 were computed by means of the Kaplan Meier method[8] and the logrank test[18] was used for the difference. The five-year actuarial survival rate following extended total and extended proximal subtotal gastrectomy was 12%, and that following proximal subtotal was 6%. There were no five-year survivors among patients treated with total gastrectomy. The difference in survival between the four procedures was not statistically significant.

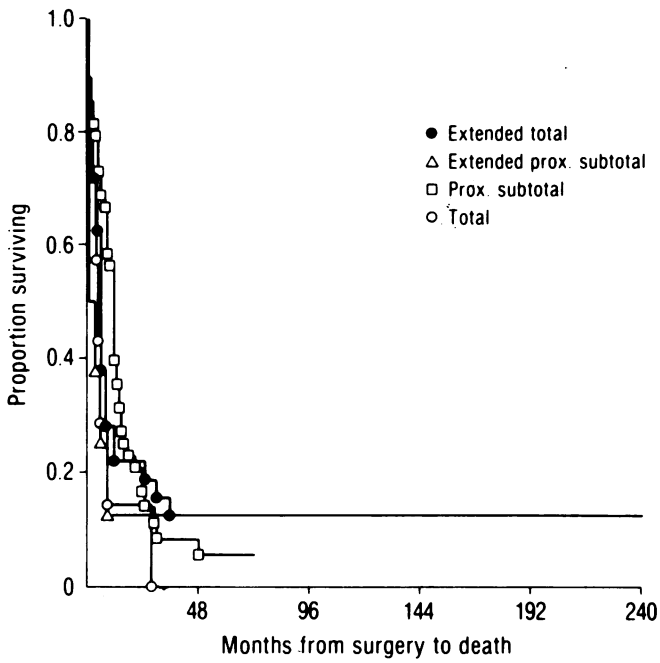

FIG. 3. Actuarial survival curves of patients treated with four different types of gastrectomy.

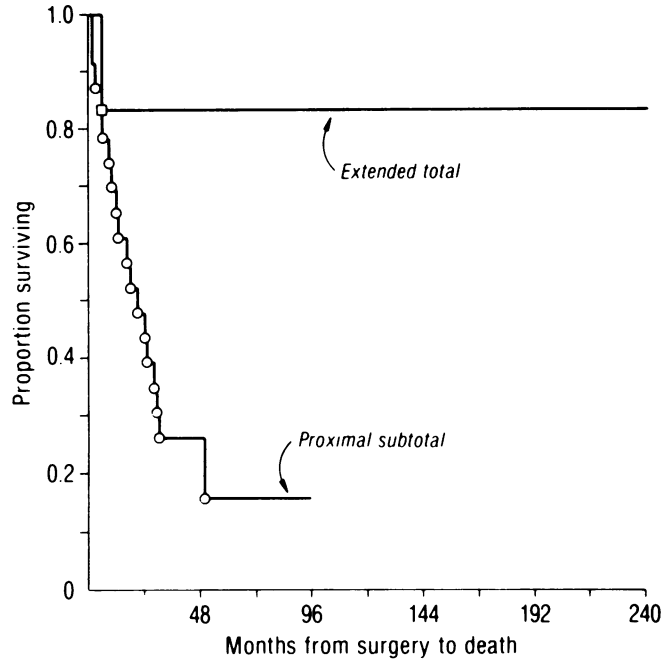

FIG. 5. Actuarial survival of stage I and II patients treated with extended total and with proximal subtotal gastrectomy.

A less pessimistic outlook was obtained when the survival data were analyzed according to the stage of the disease at the time of resection (Fig. 4). Thus, the five-year actuarial survival rates of TNM stage I and II patients were 47 and 27% respectively. There were no survivors after the fourth postoperative year among individuals with stage III and IV disease regardless of operative procedure. Because surgical treatment did not "cure" any patient with advanced stage disease, further analysis dealt only with patients with stage I and II lesions. Evaluation of total and extended proximal subtotal gastrectomy was not possible because only a few patients with stage I and II tumors were treated with these procedures. The results of extended total and proximal subtotal gastrectomy in Stage I and II are shown in Figure 5. The two survival curves were computed by means of the Kaplan Meier procedure.[8] The logrank test for the difference yielded a p value of less than 0.03 (two-sided test) in favor of extended total gastrectomy. Thus, the choice between the four types of gastrectomy made a difference only in patients with TNM stage I and II disease where extended total gastrectomy resulted in a significantly higher five year actuarial survival rate (83%) as compared with proximal subtotal gastrectomy (16%).

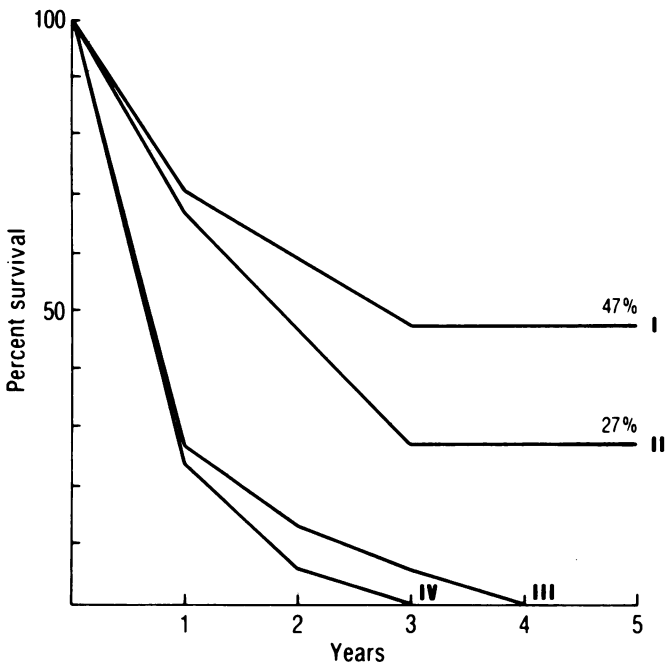

FIG. 4. Actuarial survival curves of patients undergoing gastrectomy. Analysis following TNM staging.

Discussion

Adenocarcinomas of the gastric cardia are relatively rare neoplasms although it is reported that their relative incidence among gastric adenocarcinomas has increased in recent years.[2,3] Their prognosis is worse in comparison with squamous carcinomas of the distal esophagus and adenocarcinomas of the corpus and distal stomach.[4,5,15,23] Untreated they eliminate 25% of the patients in six months and 75% of them in one

year.[17] The present report indicates that surgical treatment can be curative provided it is properly selected and properly applied.

Surgeons dealing with neoplasms of the cardia have traditionally based their therapeutic strategy upon pathoanatomic data showing a high incidence of pyloric, greater curvature and pancreatolienal lymph node metastasis in those patients.[5,12,22] Application of this knowledge in clinical practice would suggest that the only procedure which can encompass all these nodes is an extended total gastrectomy. Involvement however, of such remote lymph node basins by metastasis, classifies the disease in TNM stage III. According to this study, stage III patients were incurable by surgical means regardless of the type of gastrectomy used, as none of them survived longer than four years. The five year survival rate of similar patients was only 6% in another study.[3]

In addition to pathoanatomic observations, therapeutic strategy is often based upon survival data obtained without using a TNM classification. This approach is misleading because advanced lesions, which constitute the vast majority of neoplasms of the cardia, outnumber the potentially curable ones and determine the overall prognosis.[2–5,7,10,16,20,21,23] Thus, plotting of survival data without a previous TNM classification in Figure 3 showed no difference between the four types of gastric resection under study. Based on this result, one might conclude that proximal subtotal gastrectomy should be the procedure of choice because it is the least extensive and the easiest to perform. This conclusion proved erroneous when the survival data were plotted following classification of the resected neoplasms.

TNM classification revealed that there were no survivors among stage III and IV patients beyond the fourth year, regardless of surgical procedure. Surgical treatment was "curative" only in the presence of stage I and II disease and it was only among stage I and II patients that the choice of gastrectomy made a difference in survival. Although extended proximal subtotal and total gastrectomy could not be evaluated, extended total gastrectomy resulted in a significantly higher five-year actuarial survival as compared with proximal subtotal gastrectomy in the management of stage I and II patients. Extended total gastrectomy, a classic description of which was recently given by Lawrence,[11] was designed to include the celiac, pancreatolienal, pyloric and greater curvature lymph nodes in the resection. The fact that this procedure fails to salvage the patient when these remote nodes contain metastatic deposits, as in stage III, and it succeeds when the same nodes are not involved seems contradictory. The explanation here might be that these nodes contain submicroscopic deposits in individuals with stage I and II disease and by the time they become microscopically involved, as in stage III, the tumor has spread beyond the confines of even the most extensive gastrectomy.

Proximal subtotal gastrectomy is reportedly associated with high operative morbidity and mortality rates as compared with extended total gastrectomy.[9,16] The present study does not confirm these observations; it does show however that the procedure increased significantly the incidence of local recurrence particularly among patients with stage I and II disease. It was unclear why proximal subtotal gastrectomy, which was mostly used for early-stage, small-sized neoplasms, led to more recurrences than extended total gastrectomy, which was mainly applied for advanced-stage, large-sized and locally extensive neoplasms. Histologically positive esophageal margins could not be implicated in this difference because only a few patients with positive margins developed local recurrence. According to Payne et al.,[17] local recurrences in those patients are more often due to periesophageal neoplastic remnants than due to failure to obtain tumor free margins in the esophagus. It might be that proximal subtotal gastrectomy is more prone to local recurrence because it is a "sleeve" type of resection whereas extended total gastrectomy requires a meticulous dissection of perigastric and periesophageal tissues.

If the selection of a surgical procedure makes a difference only in patients with TNM stage I and II disease and the choice is between two procedures which differ so much in extent, one should consider classifying the disease prior to resection. Classification cannot be based on the size of the neoplasm because, as the present and other studies have shown, tumor size does not correlate with the stage of the disease.[6,12] The only way to classify the disease intraoperatively is to biopsy those regional lymph nodes which, if found invaded, would place the disease in TNM stage III. These are the pyloric, greater curvature, and pancreatolienal nodes. Spilling of neoplastic cells during biopsy is unlikely to alter the prognosis because if these nodes are involved by metastasis, the prognosis is poor. Biopsy of these will not be required in the presence of extragastric metastasis which classifies the disease as stage IV.

The present study has two limitations. First, it is retrospective. Although there were no major differences between the four types of gastrectomy with regard to the size and the location of the tumor, or the extent of esophageal invasion, the choice of operative procedure was not made at random. Thus, proximal subtotal gastrectomy was mainly used for small size neoplasms which were confined in the cardia, while ex-

tended total gastrectomy was usually applied for large tumors invading major portions of the stomach. The second limitation is that the role of extended proximal subtotal gastrectomy and total gastrectomy in the treatment of TNM stage I and II disease is not evaluated. The study showed only that extended total gastrectomy gives superior results as compared with proximal subtotal gastrectomy in the management of patients who have stage I and II disease. It also demonstrated that the choice of one type of gastrectomy over another is unimportant in patients with stage III and IV disease, where proximal subtotal gastrectomy can be chosen because it is the simplest of the four procedures. Because of these two limitations, confirmation of these findings by a prospective study will be required prior to their application in clinical practice.

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