

Early Gastric Cancer

A 25-Year Surgical Experience

Jean Moreaux, M.D., and Joëlle Bougaran, M.D.

From the Centre Médico-Chirurgical de la Porte de Chiosy, Paris, France

Objective

Special emphasis has been placed on pathologic features, survival after surgical treatment, and prognostic factors.

Summary Background Data

Incidence is much lower in Western countries than in Japan. All degrees of tumor differentiation met in invasive cancer may be found. Prognosis is remarkably good, compared with advanced gastric cancer.

Methods

After reexamination of the pathologic specimens of 115 patients, 101 patients were included in this study; 58 were male. Mean age was 60.7 years. Preoperative biopsies were positive in 88%. The lesion was located in the antrum in 78 patients. Subtotal gastrectomy was performed in 85 patients and total gastrectomy in 13 patients with a RI lymph node resection.

Results

Cancer was extended to submucosa in 68.3%, poorly differentiated in 48.5%, and multifocal in 12.9% of patients. Lymph node involvement was present in 18.8%. Secondary deaths ($n = 25$) were in relation with the cancer in 6 patients only. The 5-, 10-, 15-, and 20-year actuarial crude survival rates were 88, 65, 58, and 51%, respectively. The survival rate was significantly higher for mucosal lesions than for submucosal lesions ($p < 0.01$). Survival showed no significant correlation with lymph node involvement, tumor size, and differentiation.

Conclusions

Subtotal gastrectomy is recommended, except for proximal lesions, with survey of the gastric stump. Prognosis is significantly better for cancers limited to mucosa. Early gastric cancer is not a specific entity. Transitions between early and advanced carcinomas, especially observed in the poorly differentiated carcinomas with signet ring cells, suggest that this type of cancer should be a precursor of the invasive gastric carcinomas.

In 1962, the Japanese Endoscopic Society defined early gastric cancer (EGC) as a carcinoma limited to the mucosa and submucosa layers regardless of the presence

of lymph node metastases. This type of cancer was described in France in a well-documented book in 1939.¹ Its incidence in Western countries is much lower than in Japan.

This retrospective study is a review of our 25-year experience in the surgical management of EGC with diagnostic modalities, pathologic findings, and long-term fol-

Address reprint requests to Jean Moreaux, 19 avenue de Tourville, 75007 Paris, France.

Accepted for publication July 15, 1992.

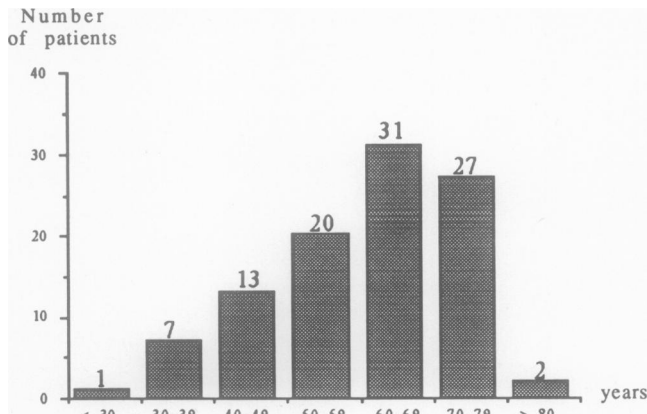


Figure 1. Age distribution.

low-up. All the pathologic specimens were reexamined and special emphasis has been placed on pathologic features and prognostic factors.

PATIENTS AND METHODS

From 1965 to 1990, 115 patients underwent operations for a gastric cancer which was classified as EGC. All these patients were referred to the same surgeon (the first author), operated on, and followed in the same hospital over the same period. There was no postoperative adjuvant therapy. The hospital is a 180-bed public surgical unit, which has no connection with a major medical center. Patients with EGC coexisting with diffuse gastric polyposis and patients with EGC found in an adenomatous polyp removed endoscopically had been previously excluded. Pathologic specimens concerning the 115 patients were reexamined by the same pathologist (the second author) who had already examined the fresh material macroscopically and histologically in 61 patients. All the original slides of the resected stomach and regional lymph nodes were reviewed. Additional sections were taken when necessary, stained with hematoxylin and eosin, with PAS and Alcian blue, and immunohistochemical identification of intracellular keratin was achieved in 58 patients, using an indirect antibody technique.

Eight patients were excluded because EGC was associated with an advanced gastric cancer in seven patients and with an advanced esophageal cancer in one patient. Six patients were excluded after the reexamination of the specimens: in two patients tumor spread had already extended into the muscularis proper of the gastric wall on additional sections; in four patients the presence of sparse signet ring cells in the muscularis proper of the gastric wall and/or the subserosa was revealed with stains for mucin and immunohistochemical demonstration of

cytokeratin. A total of 14 patients were excluded and this study concerns 101 patients.

Macroscopic classification was made according to the outlines prepared by the Japanese Gastroenterological Society. Histologic differentiation was grouped into the following three types of adenocarcinoma based on the outlines proposed by the WHO classification:² well differentiated, moderately differentiated, and poorly differentiated with or without signet ring cells. The regional lymph nodes of the stomach were designated, according to the general rules proposed by the latest TNM-classification of the UICC.³

Clinical, surgical and pathological data, based on the 101 patients, were registered on a computer. Follow-up was available for all patients except one. Most of the patients were reviewed yearly during the 5 postoperative years. Postoperative gastroscopy has been routinely performed since 1975. The survival rates have been calculated by the actuarial method, and not age-adjusted, the operative mortality included. Statistical analysis was performed using the chi-square test and the *t*-test of Student-Fisher.

RESULTS






Fifty-eight patients were men and 43 were women (the male:female ratio being 1.3:1). The age ranged from 28 to 82 years with a mean age of 60.7 years (59.9 years in men and 61.8 years in women). The peak incidence was between 60 and 80 years of age (Fig. 1). This population represents 15% of all gastric carcinomas treated surgically in the unit during the same period. If this experience is divided into 5 periods of 5 years, the incidence of EGC remained stable.

Most of the patients reported epigastric pain (74%). Initial symptoms are listed in Table 1. Duration of preoperative symptoms was recorded in 88 patients, and classified into four time intervals: less than 3 months in 16 patients (18.1%) from 3 to 6 months in 13 patients (14.8%), from 6 to 12 months in 19 patients (21.6%) and more than 1 year in 40 patients (45.5%); 19 patients had

Table 1. PRESENTING SYMPTOMS (n = 101)

Symptoms	Number of Patients	Per cent
Epigastric pain	74	73.3
Dyspepsia	11	10.9
Bleeding	5	5
Weight loss	4	3.9
Anemia	1	1
No symptoms	6	5.9

Table 2. MACROSCOPIC TYPE ACCORDING TO THE JAPANESE CLASSIFICATION

Type I		12	11.9%
Type II			
Superficial			
IIa Elevated		9	8.9%
IIb Flat		16	15.8%
IIc Depressed		47	46.5%
Type III			
Excavated		17	16.7%

been previously treated for a duodenal or gastric peptic ulcer and 3 patients had been operated on for a colorectal malignancy. Associated medical diseases were present in 31 patients; ischemic heart disease (n = 6), hypertension (n = 5), and respiratory insufficiency (n = 5) were the most common illnesses. At the beginning of this experience,⁴ all patients had one or more barium meal examinations that revealed appearance of superficial gastric mucosal abnormalities or gastric ulcers; 97 patients underwent one or several endoscopic examinations. The lesion was believed to be compatible with the diagnosis of EGC in 79 patients (81%). There was some macroscopic suspicion of malignancy in 6 patients and the endoscopic examination was considered normal or subnormal in 12 patients. Carcinoma was identified by endoscopically directed gastric biopsies in 85 patients (88%); 12 patients were operated on without exact diagnosis, 10 of them during the first decade of this study.

All patients were operated on. The lesion was located in the antrum in 78 patients, in the fundus in 14, in the gastric cardia in 5 and in a gastric stump in 3. These 3 patients had undergone previous distal gastrectomy, in 2 patients for a first EGC, 4 and 5 years before, respectively, and in 1 patient for a double carcinoma (one EGC and one carcinoma invading the muscular proper) 7 years before.

Subtotal distal gastrectomy was performed in 85 patients; continuity was restored by a Billroth I procedure in 59 patients, a Billroth II procedure in 24 patients, and a Roux-en-Y jejunal loop in 2 patients. Total gastrectomy was performed in 13 patients, partial resection of the gastric stump in 2, and proximal esophagogastrectomy in 1 patient.

Lymph node resection was performed in all patients, limited to perigastric nodes (R 1 in the Japanese classification). Gastric resection was associated with cholecystectomy for gallstones in nine patients, hiatal hernia repair for esophageal reflux in two patients, and segmental transverse colectomy for synchronous colonic carcinoma peroperatively discovered in one patient.

The distribution of the lesions according to the macroscopic Japanese classification is given in Table 2; when carcinoma showed diverse morphologic patterns, the predominant pattern was only considered. Type IIc lesions were the most common in this series (46.5%). The lesions were divided into three groups according to their larger diameter; for multifocal lesions, the largest lesion was only considered. The largest diameter was less than 2 cm in 35 patients, from 2 to 5 cm in 55 patients (54.4%) and more than 5 cm in 11 patients.

EGC was limited to the mucosa in 32 patients (31.7%) and extended to the submucosa in 69 patients (68.3%). The submucosal carcinomas were divided into two subgroups: those with only a few scattered cells or glandular structures under the muscularis mucosa (n = 51) (50.5%) and those with an extensive invasion (n = 18) (17.8%).

Carcinoma was well differentiated in 42 patients (41.5%), moderately differentiated in 10 patients and poorly differentiated or undifferentiated in 49 patients (48.5%), with signet ring cells (n = 46) or without (n = 3). Stromal reaction was sparse in intramucosal carcinomas. Fibrosis was often seen in submucosal carcinomas, particularly in poorly differentiated one. In 14 patients of this group, stromal fibrosis tended to be prominent and the gross pattern had an "infiltrative or diffuse type," like a superficial linitis plastica.

Proximal carcinomas were extended to the esophagus in 6 of 14 specimens. Distal carcinomas were extended to the duodenum in 12 of 98 specimens. Lymph node metastases were identified in 19 patients (18.8%). Lymph node involvement was limited to proximal lymph node in 15 patients (14.8%) and extended to prox-

Table 3. PATHOLOGIC FEATURES

	Number of Patients	Per cent
Size		
Diameter		
<2 cm	35	34.7
2-5 cm	55	54.4
>5 cm	11	10.9
Degree of penetration		
Mucosal	32	31.7
Submucosal	51	50.5
slight	18	17.8
extensive		
Histologic differentiation		
High	42	41.5
Moderate	10	10
Poor	46	45.5
with signet ring cells	3	3
without		
Spread		
Lymph-node involvement	19	18.8
Vascular invasion	9	8.9

Table 4. CORRELATIONS BETWEEN MACROSCOPIC TYPE AND DEGREE OF DIFFERENTIATION

	Well Differentiated	Moderately Differentiated	Poorly differentiated	
			With Signet Ring Cells	Without Signet Ring Cells
I Protruded (n = 12)	8 (66.7%)	3 (25%)	1	
II Superficial				
a—elevated (n = 9)	3 (33.3%)	2	2	2
b—flat (n = 16)	7 (43.7%)		9 (56.2%)	
c—depressed (n = 47)	17 (36.1%)	3	26 (55.3%)	1
III Excavated (n = 17)	7 (41.2%)	2	8 (47%)	
	42	10	46	3

imal and distal lymph nodes in 4 patients (3.9%). Vascular invasion was present in nine patients (8.9%). Lymph node metastases and vascular invasion were both present in four patients (3.9%).

Correlations were established between the different pathologic features listed in Table 3. Type I carcinomas were predominantly well differentiated and type IIc predominantly poorly differentiated (Table 4). Smaller lesions were predominantly well differentiated and larger lesions predominantly poorly differentiated (Table 5). Lymph node involvement rate correlated significantly with size of the lesion: 5.7% for tumor diameter less than 2 cm and 25.4% for tumor diameter from 2 to 5 cm ($p < 0.02$) (Table 6). Lymph node involvement rate correlated significantly with depth of invasion; it was present in 3% of the patients with intramucosal carcinoma, and in 26% of the patients with submucosal carcinoma ($p < 0.02$), in 17.6% of the patients with slight submucosal carcinoma and in 50% of the patients with extensive submucosal carcinoma ($p < 0.02$) (Table 7). Lymph node involvement rate correlated significantly with differentiation of cancer; it was present in 4.8% of the patients with well-differentiated carcinomas and in 30.4% of the patients with poorly differentiated carcinomas and signet ring cells ($p < 0.01$) (Table 8). Distal lymph node involvement (n = 4) was always concomitant with inva-

sive submucosal carcinoma and, in 3 of 4 patients, with poorly differentiated carcinoma and signet ring cells; in this group, the number of positive lymph nodes was 2, 3, 12, and 22, respectively. Vascular involvement was present in 3% of the patients with mucosal carcinoma and in 11.6% of the patients with submucosal carcinoma (NS) (Table 7), in 7.1% of the patients with well-differentiated carcinomas and 8.7% of the patients with poorly differentiated carcinomas and signet ring cells (NS) (Fig. 8).

Multifocal lesions were encountered in 13 resection specimens (12.9%). There were a total of 31 carcinomas for 13 patients: a double carcinoma in 8 patients, a triple carcinoma in 4 patients and a quadruple carcinoma in 1 patient. Multifocal cancers were located in the same portion of the stomach in 12 patients: 9 in the distal third and 3 in the middle third. In the patient with four foci, the upper lesion was located in the proximal third of the stomach and the lower lesion in the distal third of the stomach. The different lesions were similar in the same patient concerning macroscopic features: 6 well differentiated, 1 moderately and 6 poorly differentiated. All the lesions were limited to the mucosa in five patients, one or more lesions were extended to the submucosa in eight patients. Lymph node involvement was present in one patient; there was no vascular invasion in this group.

The lesion most commonly seen other than the carci-

Table 5. CORRELATIONS BETWEEN SIZE (largest diameter) AND DEGREE OF DIFFERENTIATION

	Well Differentiated	Moderately Differentiated	Poorly differentiated	
			With Signet Ring Cells	Without Signet Ring Cells
<2 cm (n = 35)	20 (57.1%)	2	13 (37.1%)	
2–5 cm (n = 55)	21 (38.1%)	5	27 (49.1%)	2
>5 cm (n = 11)	1	3	6 (54.5%)	1

Table 6. CORRELATIONS BETWEEN LYMPH-NODE INVOLVEMENT, VASCULAR DIFFUSION AND SIZE OF THE TUMOR (largest diameter)

	Lymph Node Involvement	Vascular Diffusion
<2 cm (n = 35)	2 (5.7%)	3
2-5 cm (n = 55)	14 (25.4%)	5
>5 cm (n = 11)	3 (27.2%)	1

noma was chronic atrophic gastritis with intestinal metaplasia (n = 68). Associated moderate dysplasia was observed in nine specimens.

There was one postoperative death (1%). This patient, 81 years old, with mental disorientation died after subtotal gastrectomy and cholecystectomy on the second postoperative day with psychic disorders. Autopsy limited to the abdomen and thorax did not find any explanation for this death. The postoperative complications are listed in Table 9.

Of the 100 patients surviving the operation, 25 died, 74 were alive at the time of the study, and 1 was lost of follow-up 1 year after the operation. The causes of death were recurrence of the gastric cancer in 6 patients, unrelated causes in 14 patients and unknown causes in 6 patients whose mean age was 77 years. The global 5-, 10-, 15-, and 20-year cumulative survival rate was 88, 65, 58, and 51%, respectively (Fig. 2). The 5-, 10-, and 15-year survival rates were significantly higher for the mucosal invasion group (92, 86, and 86%, respectively) than those for the submucosal invasion group (86, 56, and 45%, respectively) (Fig. 3) (p < 0.01). There were no significant differences in the 5- and 10-year survival rates between the slight submucosal invasion group (87 and 73%, respectively) and the extensive submucosal invasion group (94 and 61%, respectively). The 5-, 10-, and

Table 7. CORRELATIONS BETWEEN LYMPH-NODE INVOLVEMENT, VASCULAR INVASION, AND DEGREE OF PENETRATION

	Lymph Node Involvement	Vascular Diffusion	Lymph Node + Vascular Invasion
Mucosal (n = 32)	1 (3%)	1 (3%)	0
Submucosal			
Slight (n = 51)	9 (17.6%)	6 (11.8%)	2 (8.3%)
Extensive (n = 18)	9 (50%)	2 (11.1%)	2 (8.3%)
	19	9	4

Table 8. CORRELATIONS BETWEEN LYMPH-NODE INVOLVEMENT, VASCULAR DIFFUSION, AND DEGREE OF DIFFERENTIATION

	Lymph Node Involvement	Vascular Diffusion
Well differentiated (n = 42)	2 (4.8%)	3 (7.1%)
Moderately differentiated (n = 10)	2 (20%)	2 (20%)
Poorly differentiated (n = 49)		
With signet ring cells (n = 46)	14 (30.4%)	4 (8.7%)
Without signet ring cells (n = 3)	1	0

15-year survival rates were higher for patients with negative lymph nodes (90, 66, and 60%, respectively) than those for patients with positive lymph nodes (79, 61, and 41%, respectively) but the difference is not significant (Fig. 4). Among the four patients with positive distal lymph nodes, two were alive without recurrences at the time of the study, one was alive with recurrence and one had died from recurrence. The 5- and 10-year survival rates were similar for patients with carcinomas less than 2 cm in diameter (91 and 65%, respectively) and for patients with carcinomas from 2 to 5 cm in diameter (91 and 75%, respectively). The 5- and 10-year survival rates were similar for poorly differentiated carcinomas with signet ring cells (87 and 69%, respectively) and for the other carcinomas (89 and 65%, respectively).

Among the patients alive at the time of the study, one patient who had been reoperated for cancer in the gastric stump, had no obvious signs of recurrence, and another patient was in bad condition with recurrence in the gastric stump and peritoneal dissemination. The recurrence patterns evaluated through eight patients (six who died

Table 9. POSTOPERATIVE COMPLICATIONS (n = 101)

	Number of Patients	Number of Reoperations
Wound complications		
Sepsis	3	3
Abdominal complications		
Duodenal stump fistula	1	1
Small bowel obstruction	2	2
Pelvic abscess	1	1
General complications		
Respiratory	3	
Cardiovascular	2	
Pulmonary embolism	2	
Urinary	2	

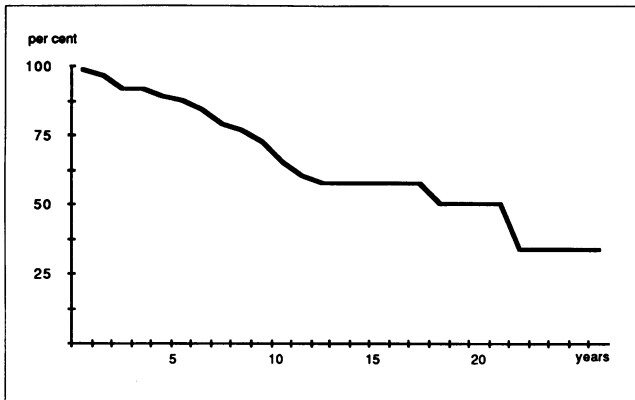


Figure 2. Global actuarial survival curve after gastrectomy for early gastric cancer.

and two still alive) were hematogenic metastasis (n = 4) to the liver, lung or bone (n = 3), peritoneal and/or ovarian metastasis (n = 3), and recurrence in the residual stomach (n = 3) concomitant with metastasis (n = 2) or isolated (n = 1). A higher risk of recurrence was associated with submucosal invasion, present in the eight patients and with positive lymph nodes present in five of the eight patients. Death in relation with hematogenic or peritoneal recurrences (n = 6) occurred 1 year, 2, 9 (n = 2), 11, and 12 years after gastric resection.

DISCUSSION

The prevalence of EGC, in our experience, has not changed over the 20 last years and was stable around 15% with regard to patients who underwent operations for gastric carcinomas. Progress in endoscopic diagnosis did not modify the rate of detected cases in French studies.⁵ Stability of EGC frequency is similar in European

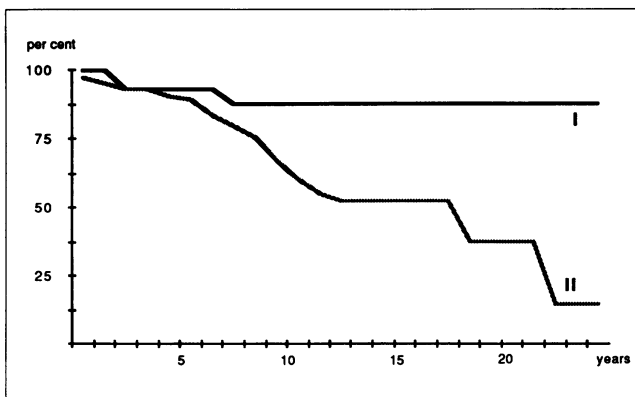


Figure 3. Actuarial survival curves related to cancer depth. I: Patients with cancer limited to mucosa. II: Patients with cancer extended to submucosa.

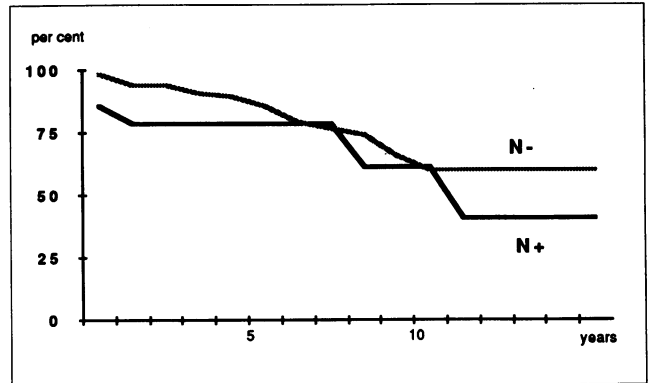


Figure 4. Actuarial survival curves related to lymph node invasion. N-: Patients with negative nodes. N+: Patients with positive nodes.

series⁶⁻⁹ and in North American series¹⁰⁻¹² but with a lower percentage. On the contrary, proportions are much different in Japanese series¹³⁻¹⁵ in which the percentage of EGC had risen to 30 or 40%. The higher frequency of gastric adenocarcinoma in Japan and the policy of endoscopic mass screening may explain this difference.

European and North American patients with EGC are on average more than 60 years old, 5 to 10 years older than Japanese patients with EGC. Sex ratio was stable in our series over this period and, like in other series, there was a slight male predominance. In Japan, Mori et al. reported a female predominance in younger patients,¹⁶ and a high male predominance in patients with early carcinoma in the gastric cardia.¹⁷

Type IIc was the most common macroscopic form in our series, like in Japanese series.^{13,15} Incidence of submucosal cancer was higher (68.3%) in our series than in most of the series^{7,10,12-14,18,19} where incidence of mucosal cancer was almost equal or even higher than that of submucosal cancer. The depth of invasion of the submucosal cancer was divided into two subgroups according to the slight or extensive degree of penetration. Johansen¹⁹ and Inoue et al.¹⁴ emphasized also the necessity of dividing the submucosal cancer into subgroups. Lymph node involvement rate was about similar in all the series, and correlated, like in our series, with the degree of penetration of the tumor,^{13,20-22} the size of the tumor,^{13,21,22} and the differentiation of the tumor.¹³ Poorly differentiated cancers were found in approximately half of the patients in our series and in only one third of the patients in the other Western and Japanese series.^{13,14,19,23} The incidence of EGC with signet ring cells has increased in Japan;¹³ in our experience, it remained stable over this period of 25 years. Multifocal lesion rate was almost similar in other series and varied in the literature from 7.8²⁴ to 21%.²⁵

The present study is in agreement with other reports about the high predominance of epigastric pain among the presenting symptoms. The long duration of preoperative symptoms in a high percentage of cases is emphasized like in other series. Endoscopy combined with biopsies was a very important process in the diagnosis of EGC and has led to the decline of barium meal examination. Endoscopic appearance of the lesions may strongly suggest EGC. All of the gastric cavity must be minutiously explored because multifocal lesions were observed in all series. Multiple biopsies have to be taken from each lesion even if there is no macroscopic suspicion of malignancy. Endoscopic biopsies allow diagnosis of gastric carcinoma but cannot distinguish early from advanced gastric cancer. Endosonography is an important progress for the confirmation of the superficial lesion and the research of lymph node metastases. The preoperative differentiation between mucosal and submucosal cancers is often not achieved even with endoscopic endoluminal ultrasound. The accuracy of endosonography is high in elevated lesions (I, IIa) and poorer in depressed lesions (IIc and III), especially those associated with ulceration.²⁰

Subtotal gastrectomy was the most common operation performed in all series which included a majority of lesions located in the middle and distal part of the stomach. Total gastrectomy was mainly indicated in lesions located in the upper part of the stomach or in the gastric cardia or in a gastric stump. Noguchi et al.²⁶ reported on 178 cases of synchronous multiple EGC. Fewer than one-third of the smaller lesions were diagnosed preoperatively and, in 13% of their patients, the smaller lesions were located in the upper third of the stomach with the main lesion in the lower third of the stomach. The possibility of missing one of the multiple foci may be an argument for routinely performing total gastrectomy in EGC.²⁷ On the basis of our experience, multifocal lesions recognized in 13 patients were located on the same portion of the stomach in 12 patients. The risk of missing a proximal lesion is not high enough, in our opinion, to justify a routine total gastrectomy but it is important to evaluate the whole stomach before and during the operation, to examine the resection specimen in the operating theater and to send it for frozen section if adequate excision is doubtful. Annual endoscopic surveillance is also necessary to investigate the gastric remnant.²⁸ In the collective series of Santoro et al.,²⁹ subtotal distal resection compared with total gastrectomy was associated with a higher 5-year survival rate in EGC located in the lower and middle third of the stomach. Pyloric preserving gastrectomy was proposed for EGC located in the middle third of the stomach.³⁰ Partial resection of the gastric remnant as the treatment of choice in patients with early gastric stump carcinoma cannot be recommended.³¹

There has been some controversy about the extent of lymphadenectomy in addition to gastrectomy. In this series, a R1 lymphadenectomy was routinely performed. For Japanese authors,^{14,32-35} a R2 operation should be the standard surgical procedure. In fact, for mucosal cancers, the rate of metastases to group 2 lymph nodes was 0 in our series and between 0 and 2.4% in other series;²⁰ for submucosal cancers, it was 5.8 in our series and between 2.3 and 8.9% in other series.²⁰ A selective policy should be adopted, depending on size and depth of the primary lesion. In cancers confined to the mucosa, in type I and IIa lesions, in small and well differentiated adenocarcinomas, lymph node dissection can probably be limited to the R1 operation (Hioki et al.). The current problem lies in the difficulty of accurately diagnosing preoperatively the depth of cancer invasion and in discriminating mucosal from submucosal cancer by endoscopy or other methods.¹⁴

The prognosis of EGC is remarkably good, compared with advanced gastric cancer. In most of the series, the 5-year survival rate is about 90%. It often exceeds 90% and is close to 100% in Japanese series. The 10- and 20-year survival rates are less favorable in our series than in Japanese series. Age of patients appears to be the major discrimination between Japan and Western countries²³ and in our series, postoperative mortality was included in the calculation of the survival rate, crude survival rate was only considered and proportion of submucosal lesions was higher than that in other series.

Invasion of the submucosa layer was, in our series, the only significant prognostic factor; the depth of cancer invasion within the wall of the stomach is considered in most of the series of gastric cancer as the best predictor of the survival rate. The claim by several investigators^{12,14,20,21} that prognosis of EGC is also associated with the presence of lymph node metastases is not supported by the present study and by others,^{13,18} but the prognosis in the patients with metastases to secondary lymph nodes appears poor (recurrence in 2 of 4 patients in our series), the 5-year survival rate being less than 50%.³⁴ In these patients with a high risk of recurrence, a postoperative adjuvant therapy should be performed.²¹ There was no survival advantage for patients with carcinomas less than 2 cm in diameter in our series. There was no significant differences in the survival rate based on histopathologic type in our series and in other series.^{7,12} The presence of signet ring cells was not associated with a worse prognosis. Even completely undifferentiated forms demonstrated a long survival if treated in the early stage.

Referring to our material, only 6 of 26 patients who died (23%), died of carcinoma. Recurrences were also the cause of death in 17.5% in the series of Ichiyoschi et al.³⁶ Hematogenic metastases were observed in 4 of the 8 patients with recurrence in our series, in 47 to 68% of all

cases of recurrence according to Ichiyoshi et al.³⁶ Among the hematogenic metastases, bone metastases were unusually frequent ($n = 3$) and in two cases, they were the first manifestation of recurrence, confirmed by histologic examination. Peritoneal and/or ovarian metastases were almost as frequent as hematogenic metastases in this series (3 of 8), occurring in patients with undifferentiated cancers. Recurrence in the residual stomach can be attributed to invasion from the lymph node metastases or can be considered as another cancer. Differentiating between synchronous and metachronous lesions is difficult.²⁸ A regular follow-up should be performed in all the patients operated on for EGC because synchronous upper lesions could have been missed in the preoperative examination at the time of the initial gastrectomy. A recurrent lesion in the residual stomach can be detected at an early stage and resection can be performed curatively.^{36,37}

There was another interesting finding in our study: the late occurrence of death from recurrence in 4 of 6 patients; 2 died 9 years after the operation, 1 died after 11 years, and 1 after 12 years. For late deaths in other elderly patients, it is difficult, without autopsy, to be sure that there is no recurrence of the gastric cancer; on the contrary, obvious metastases may be in relation with the frequent occurrence of other malignancies.^{5,18,23}

The question remains whether EGC is an entity different from invasive gastric carcinoma or an early stage of the same disease. There are many arguments in favor of the second proposition. All histologic types and all degrees of differentiation met in advanced gastric cancer, are also found in the early types. Early and invasive gastric cancer may be associated on the same specimen (7 patients in our experience). Transitions between early and invasive carcinomas are often met. It might be difficult to determine whether invasion into the muscularis proper of the gastric wall has taken place. Six patients with lesions who have been classified as EGC, were excluded from this series after reexamination of the specimens; four of these patients were transferred in the group of linitis plastica after demonstration of sparse signet ring cells beyond the submucosal layer, with stains for mucin and immunohistochemical examination. In a group of 14 patients included in this series, the pathologic appearance of the EGC was also very close to a localized linitis plastica: extensive invasion in the submucosa, sparse signet ring cells in an important stromal fibrosis, and lymph node metastases ($n = 10$) involving multiple lymph nodes ($n = 6$). Histochemical examinations could not demonstrate any signet ring cells beyond the submucosa; metastases occurred in three of these patients after 1 and 2 years, respectively. This type of EGC seems to be the precursor of the linitis plastica of the stomach. The different forms of EGC may represent

early stages of all types of advanced cancer. Although mass screening measures have increased the prevalence of EGC and curability of adenocarcinoma of the stomach in Japan, the low incidence of EGC in Western countries and the high cost of mass screening programs make a similar strategy impractical in Europe.

Acknowledgment

The authors thank Miss Josette Cloix for excellent technical assistance.

References

1. Gutmann RA, Bertrand L, Peristany TJ. Le cancer de l'estomac au début. Paris: Doin, 1939.
2. Watanabe H, Jass JR, Sobin LH. Histological typing of oesophageal and gastric tumours. Berlin: Springer Verlag, 1990.
3. Hermanek P, Sobin LH. TNM classification of malignant tumours. Berlin: Springer Verlag, 1987.
4. Moreaux J, Martin E, Mombet J, et al. Le cancer superficiel de l'estomac (à propos de 41 cas). Arch fr mal app digestif 1972; 61:711-724.
5. Adloff M, Schloegel M, Arnaud JP, et al. Le cancer gastrique superficiel de l'estomac: a propos d'une série de cinquante-sept cas. Ann Chir 1990; 44:713-717.
6. Allum WH, Powell DJ, McConkey CC, et al. Gastric cancer: a 25-year review. Br J Surg 1989; 76:535-540.
7. Oleagoitia JM, Echevarria A, Santidrian JI, et al. Early gastric cancer. Br J Surg 1986; 73:804-806.
8. Ovaska J, Kruuna O, Saario I, et al. Surgical treatment of gastric carcinoma. Am J Surg 1989; 158:467-471.
9. Valen B, Viste A, Haugstvedt T, and Members of the Norwegian Stomach Cancer Trial. Treatment of stomach cancer, a national experience. Br J Surg 1988; 75:708-712.
10. Bringaze WL, Chappuis CW, Cohn I, et al. Early gastric cancer. 21-year experience. Ann Surg 1986; 204:103-107.
11. Carter KJ, Schaffer HA, Ritchie WP. Early gastric cancer. Ann Surg 1984; 199:604-609.
12. Lawrence M, Shiu MH. Early gastric cancer: 28-year experience. Ann Surg 1991; 213:327-334.
13. Endo M, Habu H. Clinical studies of early gastric cancer. Hepatogastroenterol 1990; 37:408-410.
14. Inoue K, Tobe T, Kan N, et al. Problems in the definition and treatment of early gastric cancer. Br J Surg 1991; 78:818-821.
15. Sowa M, Kato Y, Nishimura M, et al. Surgical approach to early gastric cancer with lymph node metastasis. World J Surg 1989; 13:630-636.
16. Mori M, Sugimachi K, Ohiwa T, et al. Early gastric carcinoma in Japanese patients under 30 years of age. Br J Surg 1985; 72:289-291.
17. Mori M, Kitagawa S, Iida M, et al. Early carcinoma of the gastric cardia: a clinicopathologic study of 21 cases. Cancer 1987; 59:1758-1766.
18. Itoh H, Oohata Y, Nakamura K, et al. Complete ten-year postgastrectomy follow-up of early gastric cancer. Am J Surg 1989; 158:14-16.
19. Johansen AA. Early gastric cancer: current topics in pathology. In BC Morson, ed. Pathology of the Gastro-intestinal Tract. New York, 1976, pp 1-47.
20. Hioki K, Nakane Y, Yamamoto M. Surgical strategy for early gastric cancer. Br J Surg 1990; 77:1330-1334.

21. Maehara Y, Orita H, Okuyama T, et al. Predictors of lymph node metastasis in early gastric cancer. *Br J Surg* 1992; 79:245–247.
22. Sano T, Kobori O, Muto T. Lymph node metastasis from early gastric cancer: endoscopic resection of tumour. *Br J Surg* 1992; 79:241–244.
23. Lehnert T, Sternberg SS, Sprossmann M, et al. Early gastric cancer. *Am J Surg* 1989; 157:202–207.
24. Dromer M, Chome J, Fasano JJ, et al. Les cancers superficiels de l'estomac: à propos d'une série de 57 cas. *Chirurgie* 1986; 112:604–609.
25. Huguier M, Msika S, Lacaine F, et al. Early gastric carcinoma: don't miss it. *Hepato-gastroenterol* 1989; 36:33–35.
26. Noguchi Y, Ohta H, Takagi K, et al. Synchronous multiple early gastric carcinoma: a study of 178 cases. *World J Surg* 1985; 9:786–793.
27. Marrano D, Viti G, Grigioni W, et al. Synchronous and metachronous cancer of the stomach. *Eur J Surg Oncol* 1987; 13:493–498.
28. Moreaux J, Mathey P, Msika S. Gastric adenocarcinoma in the gastric stump after partial gastrectomy. *Hepato-gastroenterol* 1992; 39:517–522.
29. Santoro E, Garofalo A, Scutari F, et al. Early gastric cancer: total gastrectomy vs. distal resection. results of a study of 271 cases. *Hepato-gastroenterol* 1991; 38:427–429.
30. Kodama M, Koyama K. Indications for pylorus preserving gastrectomy for early gastric cancer located in the middle third of the stomach. *World J Surg* 1991; 15:628–634.
31. Stael von Holstein C, Eriksson S, Hammar E. Role of re-resection in early gastric stump carcinoma. *Br J Surg* 1991; 78:1238–1241.
32. Boku T, Nakane Y, Okusa T, et al. Strategy for lymphadenectomy of gastric cancer. *Surgery* 1989; 105:585–592.
33. Eriguchi M, Miyamoto Y, Fujii Y, et al. Regional lymph node metastasis of early gastric cancer. *Eur J Surg* 1991; 157:197–200.
34. Korenaga D, Haraguchi M, Tsujitani S, et al. Clinicopathological features of mucosal carcinoma of the stomach with lymph node metastasis in eleven patients. *Br J Surg* 1986; 73:431–433.
35. Okamura T, Tsujitani S, Korenaga D, et al. Lymphadenectomy for cure in patients with early gastric cancer and lymph node metastasis. *Am J Surg* 1988; 155:476–480.
36. Ichiyoshi Y, Toda T, Minamisono Y, et al. Recurrence in early gastric cancer. *Br J Surg* 1990; 77:684–690.
37. Tytgat GNJ, Offerhaus JGA, Stadt JVD, et al. Early gastric stump cancer: macroscopic and microscopic appearance. *Hepato-gastroenterol* 1989; 36:103–108.