



## *Original article*

# Early gastric cancer: Report of 58 cases

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### **Abstract:**

**Background.** This retrospective study was carried out to review our surgical experience and to define the clinicopathologic profile of early gastric cancer in a Western country with one of the highest incidences in the world.

**Methods.** Fifty-eight patients who had gastric surgery for early gastric cancer were included in this study.

**Results.** The incidence of early gastric cancer was 13.9% of the patients with resected gastric cancer (58/416). The mean age of these 58 patients at diagnosis was  $56.8 \pm 12.3$  years (range, 30–81 years) and the male:female ratio was 2.4:1. The most common presenting symptom was epigastric pain (52.4%). All patients were treated by surgical resection. Tumors were typically located in the antrum (72.4%), with a predominance of lesser curvature lesions (89.7%). Macroscopically, the majority of the lesions (63.8%) were excavated (types IIc and III). Thirty tumors were intramucosal and 28 extended into the submucosa. Thirty were of the intestinal type and 28 of the diffuse type. The rate of regional lymph node metastasis was 10.4%. The overall 5-year survival rate was 93.9%.

**Conclusions.** The excellent response to surgical resection of early gastric cancer reported by Japanese authors is reproducible in Western countries even in the presence of regional lymph node metastasis. For this reason an aggressive surgical approach should be taken for all early gastric cancer.

**Key words:** gastric cancer, early, surgery

### **Introduction**

Early gastric cancer (EGC) is defined [1] as an adenocarcinoma confined to the mucosa or the submucosa regardless of the presence of lymph node metastasis. In contrast with the low overall survival rate

for patients operated for advanced gastric cancer (AGC), results of surgery in patients with EGC are excellent. In fact the 5-year survival rate for these patients is better than 85% in many large European [2–4], North American [5–7], and Japanese [8–10] series.

In Japan, EGC has been diagnosed in more than 60% of patients presenting with gastric cancer [11]. In Europe and the United States, considerably lower rates 8.8% and 4% of all resected cases, respectively, have been reported [12,13] which suggests that some EGC are being missed in Western countries. However, recent studies [7,14] describe an increasing frequency of diagnosed EGC in Western countries.

During the past few decades there has been a worldwide decrease in the incidence of gastric cancer [15]; however, Portugal still has one of the highest incidences in the world [16]. This retrospective study is a review of the experience of a single surgical department in Portugal. Special emphasis has been placed on clinicopathologic features, treatment, and long-term follow-up.

### **Patients and methods**

From January 1, 1974, through December 31, 1996, 416 patients underwent a gastrectomy for gastric cancer at the second Department of Surgery, University Hospital of Coimbra, Portugal. Fifty-eight of the 416 patients (13.9%) were diagnosed with EGC with no evidence of any other malignancy.

According to the criteria defined by the Japanese Gastroenterological Society [17] the gross appearance of the carcinomas was classified into five types: I, protruded; IIa, superficial elevated; IIb, flat; IIc, superficial depressed; and III, excavated.

The World Health Organization (WHO) [18] and Lauren's [19] classifications were used for microscopic characterization of the tumors. Papillary adenocarci-

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noma and tubular adenocarcinoma were grouped together and designated as “differentiated”. Papillary and tubular adenocarcinomas were classified as “intestinal type” according to Lauren’s classification, and poorly differentiated adenocarcinomas and signet-ring cell carcinomas were classified as “diffuse type”. Because mucinous carcinomas were found to have structural characteristics in common with both the intestinal and the diffuse types, they were classified as intestinal on diffuse by their structural features.

In our report, N1 refer to metastasis in lymph nodes within 3 cm of the tumor and N2 to metastasis in lymph nodes further than 3 cm from the tumor.

D1 lymphadenectomy included N1 lymph nodes; an incomplete D2 lymphadenectomy included N1 lymph nodes and the nodes along the left gastric and hepatic common arteries.

Survival curves were computed by the Kaplan-Meier method and differences between survival curves were compared with the Maentel-Haenzel test. Differences were considered significant at the 5% level.

## Results

### *Clinical presentation and diagnosis*

There were 41 men and 17 women in the study; the male-to-female ratio was 2.4:1. The mean age at diagnosis was  $56.8 \pm 12.3$  years (range, 30–81 years) and the condition was most common in the fifth (25.8%) and sixth (31.1%) decades of life.

The most common presenting symptom was epigastric pain (52.4%). A preoperative diagnosis of EGC was established, by endoscopic biopsy, in 86% of the patients. In the remainder, the diagnosis was made intraoperatively.

### *Surgical treatment*

All patients were treated by surgical resection. None received adjuvant therapy. Distal sub-total gastrectomy was performed in 39 patients (67.2%), total gastrectomy in 18 patients (31.1%), and proximal sub-total gastrectomy in 1 patient. Concomitant procedures included 16 splenectomies and 2 cholecystectomies. All the splenectomies were performed as “en-bloc” resections. The extent of the lymphadenectomy performed reflected the opinions and judgments of the surgeon and varied considerably during the study period. A D1 lymphadenectomy was performed in 37 patients and an incomplete D2 lymphadenectomy in 21 patients.

### *Pathology*

All tumors were adenocarcinoma. Eighteen (31.1%) arose in stomachs with a background of precancerous

conditions (not precancerous lesions): in 14 patients (24.1%), the carcinoma was at the edge of a peptic ulcer; three carcinomas were in polyps (two in adenomatous polyps, and one in a villous polyp); and one patient had had a gastroenterostomy and truncal vagotomy for peptic ulcer (20 years previously). By contrast, severe dysplasia was observed in 12 patients.

Forty-two (72.4%) cancers were located in the distal third of the stomach, 14 (24.1%) in the middle third, and 2 (3.5%) in the proximal third. Most of the lesions (89.7%) were on the lesser curvature and on the anterior wall of the stomach (55.2%). Multicentric lesions were found in 7 patients (12.1%).

The mean size of the tumors was 2.6 cm (range, 0.5–6 cm). Thirty-one tumors (59.4%) measured between 2 and 4 cm in maximum diameter. Eighteen tumors (31.1%) were smaller than 2 cm and 9 (15.5%) were greater than 4 cm.

By macroscopic classification there were 7 (12.1%) type I, 12 (20.6%) type IIa, 2 (3.5%) type IIb, 16 (27.6%) type IIc, and 21 (36.1%) type III. When the lesions were classified into three categories: protruded (I and IIa), flat (IIb), and depressed (IIc and III); the majority (37/58) were depressed (63.8%).

Thirty of the tumors (51.7%) were intramucosal and 28 (48.3%) extended into the submucosa.

According to the WHO classification [18], there were 26 (44.8%) differentiated tumors and 23 (39.7%) signet-ring cell carcinomas. The frequency of mucinous carcinoma was 12.1% (7/58) and of poorly differentiated carcinoma, 3.4% (2/58).

Thirty (51.7%) of the tumors were intestinal type and 28 (48.3%), diffuse type, based on the histopathologic classification of Lauren [19].

All surgical margins were microscopically negative. Metastatic deposits in lymph nodes were histopathologically confirmed in 6 of the 58 patients (10.4%) (Table 1). In patients with mucosal cancer, only 3.3% (1/30) had lymph node metastasis. On the other hand, in patients with submucosal cancer, there were metastases to regional lymph nodes in 17.9% (5/28). Four of the six patients with lymph node metastases had metastatic involvement of the first-echelon lymph nodes only. Two of the patients had metastases in the second echelon lymph nodes. Clinicopathological features of the patients with EGC with lymph node metastases are shown in Table 1.

### *Survival*

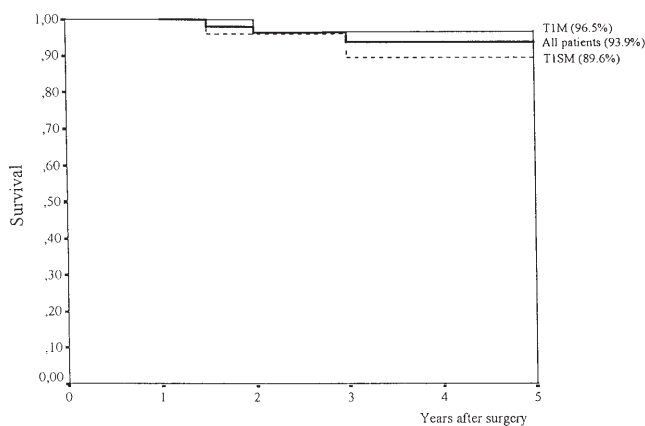
None of the patients died within 30 days of the operation and none died during their post-surgical hospital stay.

Survival data were available for 57 patients. Forty patients had a minimum follow-up time of 5 years

**Table 1.** Early gastric cancer with lymph node metastasis: Pathologic features and outcome

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Sex/Age (years)	W/45	M/69	W/80	M/64	M/53	M/56
Location	A	A	A	M	M	A
Size (cm)	2	1,2	2	1,5	3	3
Macroscopic type [17]	III	III	Iic	Iia	Iic	Iic
Depth of invasion	Submucosa	Mucosa	Submucosa	Submucosa	Submucosa	Submucosa
Histologic type (WHO [18])	Signet	Differ.	Signet	Signet	Signet	Signet
Lauren [19]	Diffuse	Intestinal	Diffuse	Diffuse	Diffuse	Diffuse
Lymph node metastasis	N1	N1	N1	N2	N1	N2
Outcome	NED	NED	NED	DOD	NED	NED
Time from operation	76 Months	68 Months	56 Months	6 Months	4 Months	40 Months

M, Men; W, women; A, lower portion of the stomach; M, middle portion of the stomach; signet, signet ring cell carcinoma; diff, differentiated carcinoma; NED, no evidence of disease; DOD, dead of gastric cancer disease  
See text for definition of N1 and N2



**Fig. 1.** Five-year survival of 58 patients with early gastric cancer. T1M, T1 cancer invasion to mucosa; T1SM, T1 cancer, invasion to submucosa

(range, 64–244 months) from the date of the resection. In the remaining 17 patients, the follow-up time ranged from 9 to 55 months. The 5-year survival rate overall was 93.9% (Fig. 1). The 5-year survival rate for patients with mucosal cancer was 96.5% and that for patients with submucosal cancer was 89.6% (non-significant difference).

Three patients died of recurrent or metastatic gastric cancer. The clinicopathological features of these patients are shown in Table 2.

## Discussion

The frequency of EGC in Japan, which represents approximately half of all cancers diagnosed by mass survey [20,21], has not yet been reproduced in Western countries. Mass screening for gastric cancer, which may

explain the high incidence in Japan, is economically impractical in the Western hemisphere, given its low rate of incidence.

However, some recent studies [7,14] have described an increase in the relative frequency of EGC in Western countries because of the routine performance of endoscopies and biopsies.

The relative frequency of EGC in the present study (13.9% of resectable gastric carcinomas) is similar to that reported in some European series [3,14]. However, it is higher than the results reported in European multicenter retrospective study [12] and it is also higher than North American results [13].

The evidence that patients presenting with EGC are younger than those with AGC [22,23] was also confirmed by our experience. At presentation, patients with EGC were, on average, 4 years younger than those with AGC resected during the same period, a significant difference ( $P = 0.03$ ). The average age of our patients with EGC was similar to the reported age in the Japanese experience [24,25]. The male-to-female ratio in the present series is higher than that in most published series. It is also higher than the ratio we found for AGC.

In our study, as in others [26,27], there was no difference in the clinical presentation of patients with EGC compared with that in patients with AGC. The present study is in agreement with others [14,27] indicating that epigastric pain is the most common presenting symptom in patients with EGC.

Although the difference is not significant, the duration of symptoms in EGC tends to be longer than in AGC [22]. A previous history of peptic ulcer is not uncommon [6,14,22,28] and may explain the duration of symptoms before diagnosis. In the present series, a high percentage of the carcinomas (24.1%) were at the edge of a peptic ulcer.

**Table 2.** Pathological data for three patients who died from recurrent or metastatic early gastric cancer

Location of tumor	Size (cm)	Macroscopic type [17]	Depth of invasion	Microscopic classification		Lymph node stage	Site of recurrence	Interval between operation and death
				Histologic type [18]	Lauren [19]			
M	1.8	IIa	sm	Signet	Diffuse	N2	Liver	9 Months
C	2	III	sm	Poor	Diffuse	No	Liver	18 Months
M	4	I	m	Differ.	Intestinal	No	Local	24 Months

M, Middle third of the stomach; C, upper third of the stomach; m, mucosa; sm, submucosa; signet, signet ring cell carcinoma; poor, poorly differentiated adenocarcinoma; differ, differentiated adenocarcinoma

The major method for the diagnosis of EGC is endoscopic biopsy (86% in the present series). However multiple biopsies (no fewer than eight to ten) must be taken from each lesion seen on endoscopy [6,29], even if there is no macroscopic suspicion of malignancy [30]. For the diagnosis of gastric cancer the sensitivity of direct brush cytology (55–80%) is less than that of biopsy but is additive to the overall accuracy [31]. In our opinion the two methods should be regarded as complementary in the pathologic diagnosis of EGC.

In our experience, more than 70% of EGCs were antral in location. Similar results have been reported in North America [22,23] and Europe [32]. In contrast, more than half of the lesions described in large Japanese series [10,25,33] were found in the middle third of the stomach.

Similar to findings in other European [14] and in North-American [28] and Japanese [10,25,34] series, we found that most lesions (63.8%) were of the depressed or excavated types. Also, as reported previously [8,14], protruded tumors (type I and IIa) were mostly differentiated intestinal type carcinomas (72%), whereas depressed or excavated types displayed both diffuse and intestinal patterns.

The excellent outcome of EGC is attributable to its lower incidence of lymph node metastasis [24,34]. Approximately 90% of EGCs are reported to be node-negative [24,25,28]. The incidence of lymph node metastasis in patients with EGC has been reported as varying from 1.9% to 7% in patients with intramucosal cancer and from 7.4% to 20.9% in patients with submucosal cancer. In the present series, the frequency of metastasis to lymph nodes was 3.3% in patients with intramucosal cancer and 17.9% in those with submucosal cancer. The overall rate of regional lymph node metastasis was 10.4%.

There have been many reports [10,24,25,33,34] of the relation between lymph node metastasis and various characteristics of EGC. These studies indicate that the frequency of lymph node metastasis increases with

depth of invasion and size of tumor and varies with macroscopic features. Some authors [8,33] have reported that the frequency of lymph node metastasis was higher in protruding type cancers, while others [25,34] observed a higher frequency in cancers with depression. In our experience, lymph node metastases were more frequent in submucosal cancers with depression (IIc and III types) and in signet ring cell carcinomas.

Although tumor recurrence after gastric resection is rare, it is not uncommon. Recurrence rates of 16% [14,28] and 34% [32] have been reported in Western countries, significantly higher than that reported by Japanese authors [35,36].

The higher recurrence rate in the Western hemisphere has been attributed to inadequate gastric resection and lymphadenectomy [13]. Another potential cause of the higher recurrence rate in the Western hemisphere is misdiagnosis of advanced tumors as EGC [37]. The strict criteria and exhaustive histologic review used by Japanese pathologists probably eliminate these “contaminating” cases [37].

The extent of lymphadenectomy remains a controversial issue in the management of EGC [9,33,34]. In Japan the prognosis for patients with EGC has improved markedly since 1973 [38]. These positive results are attributable to established surgical treatment including gastrectomy and D2 lymph node dissection [24]. However, the viewpoint that D2 lymphadenectomy is the optimal procedure remains controversial, since the rate of secondary lymph node metastasis is only 0–24% and 2.3–8.9% for mucosal and submucosal cancers, respectively [8,24,25].

Because of this lower incidence of lymph node metastasis, some surgeons advocate that removal of the N1 nodes is sufficient treatment for most patients, with a more extensive lymphadenectomy recommended when N2 involvement is detected intraoperatively [39]. However, up to 10% of patients in most EGC series have shown lymph node metastasis, and about 2.5–3.5% had metastatic deposits in second-echelon lymph nodes [9,10,24,25,33,36].

On the other hand, accurate intraoperative determination of whether lymph node metastasis is present is difficult. For these reasons we feel that a more aggressive surgical approach should be used for all EGC if there is potential for cure. In recent years, our policy has been to perform an incomplete D2 lymphadenectomy which includes the perigastric or N1 lymph nodes and the nodes along the left gastric and hepatic common arteries.

In our opinion, sub-total gastrectomy is an adequate surgical resection for EGC of the antrum. We reserve total gastrectomy for lesions of the middle and upper third of the stomach. Multicentricity has been used as a rationale for routine total gastrectomy [2], but reports from the US [23,28], Europe [14,32], and Japan [10,36] of series involving higher percentages of subtotal gastrectomies show a low recurrence rate and excellent 5-year survival.

In recent years in Japan, endoscopic treatment, including laser ablation, multiple or strip biopsies, or chemical injection, has been increasingly used for the treatment of EGC. With strict selection criteria, a cumulative curative rate of 98.4% has been reported [40]. According to Maekawa et al. [25], the best results would be expected in patients who have tumors of the differentiated type measuring 20mm or smaller without depression, since lymph node metastases were rare in these variants. In our opinion, endoscopic therapy should be limited to patients who are not candidates for gastric resection (elderly or other high-risk patients) and those refusing operative resection.

In conclusion, the excellent response to surgical resection of EGC reported by Japanese authors is reproducible in Western countries even in the presence of regional lymph node metastasis. At least for this reason an aggressive surgical approach, including extended lymphadenectomy, should be taken for all early gastric cancers.

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