

PAPERS AND ORIGINALS

Natural history of "early" gastric cancer: results of a 10-year regional survey

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Summary and conclusions

In "early" gastric cancer the depth of invasion by the primary tumour is confined to the submucosa of the stomach. Out of 13 228 cases of gastric cancer notified to the Birmingham Cancer Registry during 1960-9, 90 (0.7%) were identified as early gastric cancer. The crude five-year survival rate of these 90 patients was 57.8% (age-adjusted rate 70.4%) compared with 3.7% (age-adjusted rate 4.7%) for all cases and 14.6% (age-adjusted rate 17.4%) for the cases treated radically. Prognostic factors established for gastric cancer pertained equally to early gastric cancer. Most of the 90 patients had had symptoms related to the gastrointestinal tract, but in contrast to patients with advanced gastric cancer only 19% had lost weight on admission.

These findings suggest that early investigation of dyspeptic symptoms would increase the detection of early gastric cancer, the most important prognostic group identified in gastric cancer.

Introduction

Gastric cancer is defined as "early" when the depth of invasion by the tumour is histologically limited to the submucosal layer of the stomach.¹ The depth of penetration by the primary lesion is closely related to survival,² and in Japan the five-year survival rate of patients with early gastric cancer was reportedly 90.4%.³ Outside Japan, however, the low incidence of the condition

makes analysis of survival difficult. Evans *et al*⁴ showed that the microscopical features of 14 early gastric cancers in Britain were similar to those seen in Japan but were unable to assess survival because of small numbers and inadequate follow-up. We have therefore identified the early gastric cancers among all gastric cancers notified to the Birmingham Cancer Registry during 1960-9 and report here the natural history of the lesion.

Subjects and methods

We reviewed all patients notified to the Birmingham Cancer Registry during 1960-9 with histologically proved adenocarcinoma of the stomach. Histological reports were analysed and the depth of invasion by the primary lesions assessed. Though lymph-node metastasis may occur in early gastric cancer,⁵ we consider here only patients with histologically normal nodes in whom the depth of penetration was clearly documented. In several patients with normal lymph nodes the depth of invasion was not documented, and we reviewed the histological sections in these cases to permit accurate identification of early gastric cancers in the period under review.

Microscopically all the early gastric cancers were confined to the mucosa and submucosa and did not penetrate the muscularis propria. Macroscopically they were classified by the method of Murakami⁶ as (I) protruded, (II) superficial, or (III) excavated. It was not possible in a retrospective review to subdivide these groups further.

Detailed analysis of all these patients was made from cancer registry information. Survival rates described as "crude" are merely the proportion of patients who were still alive at the time of assessment. These crude rates were "age adjusted"⁷ for overall survival rates. The object was to relate mortality from cancer to the general mortality at the same age, so avoiding the use of inappropriate comparisons that might be grossly disturbed by differences in the ages of patients treated.

Results

During the 10 years the registry had been notified of 13 228 cases of gastric adenocarcinoma, of which 3523 (26.6%) were treated by resection. Of these cases, we identified 90 (0.7% of the whole series) as early gastric cancer. The mean age at presentation of the 90 patients was 62.3 years, and the condition was most common in the fifth and sixth decades (table I). Fifty-nine of the patients were men and 31 women.

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Of the 90 lesions, 60 were in the pyloric antrum, 10 in the body of the stomach, two at the junction of the body and antrum, and three at the cardia; in 15 cases we could not locate the tumour accurately from reports. Macroscopically 18 of the lesions were type I, 16 type II, and 42 type III. Fourteen could not be classified. Microscopically all were adenocarcinomas: in 34 cases the depth of invasion was confined to the mucosa, and in the others the muscularis mucosa had been penetrated.

TABLE I—Age distribution of 90 patients with early gastric cancer

Age in years	25-30	30-35	35-40	40-45	45-50	50-55	55-60	60-65	65-70	70-75	75-80	80-85	85-90
No of patients	1	1	1	2	10	5	16	18	11	11	11	2	1

SYMPTOMS, DIAGNOSIS, AND MANAGEMENT

Forty-six patients had presented with a solitary symptom and 44 with a combination of symptoms (table II). The most common symptom was epigastric pain (26 cases), and weight loss occurred in only 17 cases. Twenty-one patients had presenting symptoms listed as "other," which included malaise, stomach troubles, and general weakness. Type II and type III lesions had been manifested predominantly by epigastric pain, and type I lesions by haematemesis (table II). No patient had had physical signs of a gastric primary neoplasm. The length of history varied, and in 14 cases it was a year or more.

TABLE II—Incidence of symptoms in all 90 patients with early gastric cancer and in type I, type II, and type III lesions. Figures are numbers of patients (percentages in parentheses)

	All patients (n=90)	Macroscopic classification*		
		Type I (n=18)	Type II (n=16)	Type III (n=42)
Epigastric pain	26 (28.9)	1 (5.6)	6 (37.5)	17 (40.5)
Vomiting	21 (23.3)	2 (11.1)	3 (18.8)	14 (33.3)
Other (malaise, weakness, etc) .. .	21 (23.3)	4 (22.2)	1 (6.3)	5 (11.9)
Abdominal pain	17 (18.9)	3 (16.7)	5 (31.3)	4 (9.5)
Weight loss	17 (18.9)	3 (16.7)	3 (18.8)	5 (11.9)
Anorexia	13 (14.4)	2 (11.1)	2 (12.5)	5 (11.9)
Indigestion	11 (12.2)	1 (5.6)	3 (18.8)	6 (14.3)
Haematemesis, melaena	6 (6.6)	4 (22.2)	0	0
Dysphagia	1 (1.1)	0	0	0
Not known from data	4 (4.4)	1 (5.6)	0	3 (7.1)

*Fourteen lesions could not be classified.

The method of diagnosis was evaluated in 54 patients. In 40 cases barium studies had been performed, 37 of which had shown abnormalities and three nothing abnormal. Fourteen patients were diagnosed at laparotomy. Fibreoptic endoscopy had been used in only one of these patients.

Fifty patients had shown evidence of gastric disease preoperatively, though in only 23 was carcinoma suspected (table III). In 29 cases we could not establish the preoperative diagnosis. At operation a further

TABLE III—Preoperative diagnoses in 90 patients with gastric cancer

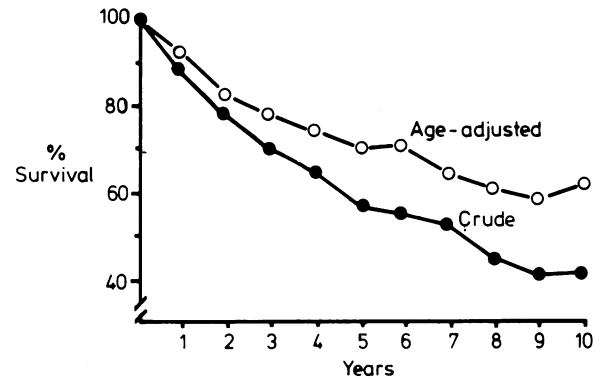
Gastric carcinoma	23	Pernicious anaemia with dyspepsia and weight loss	1
Gastric ulcer	18	Abdominal pain	1
Gastric neoplasm	5	Gall stones	3
Gastric polyp	1	Gastric mass at sympathectomy .. .	1
Pyloric stenosis	3	Not known from data	29
Haematemesis	4		
Duodenal ulcer	1		

nine patients had been thought to have malignant lesions, so that in 32 patients the lesion had been thought to be malignant either before or at operation.

All patients had been treated by surgical resection: 74 had had a partial gastrectomy, seven total gastrectomy, and six local excision. In three cases the operation was not recorded. Five patients had died postoperatively—that is, within 30 days—two after total gastrectomy.

SURVIVAL AND FACTORS INFLUENCING SURVIVAL

The crude five-year survival rate of the 90 patients (figure) was 57.8% (age-adjusted rate 70.4%) and the crude 10-year survival 41.1% (age-adjusted rate 64.2%). Of the patients with type I, type II, and type III lesions, 11 (61.1%), 11 (68.8%), and 24 (57.1%) respectively survived five years. The crude five-year survival rate of all 76 patients with macroscopically classified lesions was 60.5%. The 34 patients with lesions confined to the mucosa had a crude five-year survival of 70.6%.



Crude and age-adjusted survival rates of 90 patients with early gastric cancer.

Of the three patients aged under 40 at presentation, two survived five years; of the others, seven of the 12 aged 40-49, 17 of the 21 aged 50-59, 17 of the 29 aged 60-69, eight of the 22 aged 70-79, and one of the three aged over 80 survived five years. The 31 women had a crude five-year survival rate of 67% and the 59 men a crude five-year survival of 52%.

Fourteen patients had had a history of 12 months or more, and 13 of these survived longer than five years, the single death occurring after four years. Of the patients with a history of under 12 months, 56 had a crude five-year survival rate of 48%.

Of the 74 patients treated by partial gastrectomy, three had died postoperatively and 45 (61%) survived five years or more. The seven total gastrectomies had resulted in two postoperative deaths, and of the remaining five patients, four survived five years or more. There were no postoperative deaths after local excision, and three of the six patients had survived for five years.

CAUSES OF DEATH

In 61 cases the cause of death was established from death certificates; in 21 cases accurate diagnoses had been established at operation or necropsy. Five patients had died postoperatively, and the longest interval to death was 16 years. Thirty-one had died with recurrent or metastatic gastric cancer and 25 from unrelated causes. Eight patients had had proved recurrence in the gastric stump. The incidence of cancer-related death was highest within five years after operation (table IV), 67.7% of such deaths occurring during this period.

Discussion

The term "early" gastric cancer may be inappropriate, implying a condition related to carcinoma-in-situ. This is not the

TABLE IV—Causes of 56 deaths (percentages in parentheses)

	Within five years of operation	After five years	Total
Recurrent or metastatic disease	21 (67.7)	10 (40.0)	31 (55.4)
Unrelated causes	10 (32.3)	15 (60.0)	25 (44.6)
Total	31 (55.4)	25 (44.6)	56 (100)

case, however, as it characteristically shows invasion, and lymph-node metastases have been observed in 8.8% of mucosal lesions and 17.4% of submucosal lesions.⁵ Spread to lymph nodes reportedly greatly affects survival,⁸ but we could not confirm this since we reviewed only patients without evidence of lymph-node metastases. The incidence of early gastric cancer in our series (0.7%) was comparable with the incidence of 1% in Japan between 1946 and 1950 but not with the incidence there of 24.1% between 1966 and 1970.² During the study period fiberoptic endoscopy was not generally available and this procedure may increase the detection of early gastric lesions in Britain. Evans *et al*⁴ reported an incidence of 1% before the adoption of routine endoscopy and 10% afterwards.

Many features in gastric carcinoma apply to early gastric cancers. They were more common in men than women, and the highest incidence occurred between the ages of 55 and 65. Survival, however, was significantly better. The crude five-year survival⁷ rate of all patients from the first six years was 3.7% (age-adjusted rate 4.7%), and the crude five-year survival after radical treatment was 14.6% (age-adjusted rate 17.4%). The crude five-year survival of the 90 patients with early gastric cancer was 57.8% (age-adjusted rate 70.4%). The prognosis in patients under 70 was better than in the older age group, and established prognostic factors such as sex⁷ and length of pre-operative history⁹ pertained equally to early gastric cancer. Although early gastric cancer is associated with increased survival at five and 10 years, the true effect of increasing the detection of early gastric cancer cannot be fully evaluated until the effect on yearly gastric cancer mortality rates is known.

Early gastric cancers present with symptoms referable to the gastrointestinal tract (table II) and may be diagnosed pre-operatively. In advanced gastric carcinoma 78% of patients have lost weight on admission to hospital¹⁰; however, this was not a constant feature of the early lesions. Most patients with early lesions had had gastric disease diagnosed preoperatively (table III); undoubtedly, with the advent of fiberoptic endoscopy and double-contrast radiology many more would have had histologically proved gastric cancers preoperatively.

All 90 patients were treated surgically. As only 32 had cancer diagnosed either preoperatively or at the time of operation, probably resection did not always include removal of appropriate lymph nodes.¹¹ Desmond *et al*¹² showed that revisional surgery for histological gastric carcinomas of macroscopic benign disease was associated with a five-year survival rate of 56%; in patients not subjected to further surgery, however, the five-year survival was 23%. In our series most patients had partial gastrectomies, and the results were good when compared with other results for gastric cancer in Britain. The high postoperative mortality among the few patients having total gastrectomies corresponded with the 21% postoperative mortality reported by Longmire.¹³ Hence radical subtotal gastrectomy with excision of appropriate primary, secondary, and tertiary lymph nodes should probably be recommended.¹¹ Follow-up to assess the residual stomach for evidence of malignancy should include regular endoscopy during the first five years, since most cancer-related deaths occur during this time (figure, table IV). The Japanese results with the management of gastric cancer differ appreciably from those seen elsewhere,¹⁴ but this may be a different lesion. Evans *et al*⁴ failed to identify any macroscopic or microscopical differences in early gastric cancer. Our retrospective study permitted identification and assessment of this group, establishing that an early lesion is the most important prognostic factor in gastric cancer. Direct comparisons with the Japanese results can be made only when similar methods of diagnosis, resection, and histological staging are used.

The increase in the number of patients seen with early gastric cancer in Japan was associated with the introduction of mass screening of asymptomatic populations. The pick-up rate of screening was 0.37%¹⁵ in a country with a gastric cancer mortality rate of 68 per 100 000 population. In the West Midlands the mortality rate was 23 per 100 000,¹⁶ and mass screening would be difficult to justify on economic grounds. The

detection of early lesions may be increased with more clinical awareness and investigation of dyspeptic patients, preferably before weight loss begins. Screening programmes should be considered for dyspeptic patients over the age of 40 living in high-risk environments, such as Stoke-on-Trent⁹ and the coal-mining areas of Wales.¹⁷

The incidence of gastric cancer is decreasing in America,¹⁸ Japan,¹⁹ and the West Midlands (J Waterhouse, personal communication, 1980). Even so, it continues to rank second as a contributory cause of death from cancer in the West Midlands (J Waterhouse). As in Japan, advanced gastric cancer will remain the most frequently encountered lesion, and efforts should be made to improve treatment. Chemotherapy and radiotherapy are being evaluated under the guidance of the British stomach cancer group, and radical excision of the primary growth with removal of appropriate primary, secondary, and tertiary draining lymph nodes must be undertaken to provide exact staging and clearance of the lesion. In combination with efforts to diagnose gastric cancer at an early stage this may produce benefits in the treatment of the condition, which has shown no noticeable improvement over the past 30 years.

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Requests for reprints should be sent to JWLF.

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