

Early gastric stump cancer following distal gastrectomy

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Abstract

Background—Gastric stump cancer (GSC) is usually diagnosed at an advanced stage, and consequently the prognosis is poor.

Aims—To investigate the clinicopathological characteristics of GSC at an early stage to assist in its identification, and thereby improve its prognosis.

Methods—Forty three patients with resected early GSC were compared with 156 patients with resected primary early cancer in the upper third of the stomach.

Results—Sixty five per cent (28/43) of the early GSC patients showed the elevated type endoscopically, although the frequency of the depressed type in GSC has tended to increase in the past five years. This occurred in less than 26% (40/156) of the primary early cancers. Half of the early GSCs were located on the lesser curvature (47%), and revealed differentiated adenocarcinoma (81%) histologically. The male:female ratio of early GSC cases was about 6:1, which was much higher than that in patients with primary early cancer. The five year survival rates of patients with early GSCs and early primary cancers were 84% and 95%, respectively. GSC had a favourable prognosis, if it was detected at an early stage.

Conclusion—To detect early GSC, our results suggest that special attention should be given to elevated as well as depressed lesions on the lesser curvature of the stomach, particularly in men, during endoscopic examinations.

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Keywords: gastric stump cancer; early gastric cancer; prognosis; endoscopy

The prognosis of primary gastric cancer after gastric resection has improved notably due to early diagnosis by endoscopic examination and progress in operative techniques. However, gastric stump cancer (GSC) is usually diagnosed at an advanced stage, and its prognosis is unfavourable compared with that of primary cancer.¹ Only a few authors have reported five year survival rates of GSC, which are usually less than 10%.^{2,3}

GSCs are now being detected at a relatively early stage, mainly due to screening programmes for gastrectomised patients, and their prognosis is improving. Sasako and colleagues⁴ and Ikeguchi and colleagues⁵ have reported five year survival rates of 57% and 52.5%, respectively, when stump cancer is resected curatively. Furthermore, Pointner *et al* reported a five year survival rate of 74% for early GSC.⁶ These findings suggest that the detection of early stump cancer is important in improving its prognosis, though little is known about its characteristics. We know that it is difficult to detect early cancer by endoscopic examination since the inner space is narrow and the surface of the mucosa is often reddish and uneven due to postoperative gastritis after gastrectomy.

Therefore, we compared the endoscopic clinical and pathological characteristics of early GSC to those of primary early cancer located in the upper third of the stomach.

Patients and methods

Between 1962 and 1995, 7466 patients, including 133 with GSC, underwent surgery for gastric cancer at the National Cancer Center Hospital, Tokyo. Of these, 43 patients with early GSC who had previously received distal gastrectomy for benign (21 patients) and malignant (22 patients) diseases were evaluated. Generally, the patients with gastric or duodenal ulcer had not undergone gastrectomy, except as emergency surgery, as the worldwide use of antiulcer drugs is increasing. As we were interested in determining how to detect early stump cancer through endoscopic observation, early GSC was defined as gastric cancer that occurred five years or more (from five to 36 years) after curative gastrectomy regardless of the original disease. This definition was used as it reduced the recurrence factor to the minimum in patients with previously malignant disease; furthermore, in two patients early GSC occurred five years after gastrectomy for gastric ulcer.

Early GSC and primary early cancer were histologically defined as adenocarcinoma infiltrating the mucosal or submucosal layer. The

Table 1 Comparison of early gastric stump cancers in previously benign disease and previously malignant disease

| | Benign disease (n=21) | Malignant disease (n=22) | Total (n=43) |
|---------------------------------|--------------------------|-----------------------------|-----------------|
| Age at operation (y) | | | |
| Original operation | 42.8 | 56.6* | 49.9 |
| Operation for gastric remnant | 63.5 | 65.2 | 64.4 |
| Interval between operations (y) | 23.8 | 9.8* | 15.3 |
| Male:female ratio | 6.0 | 6.3 | 6.2 |
| Macroscopic type | | | |
| Elevated | 11 (52) | 17 (77) | 28 (65) |
| Depressed | 10 (48) | 4 (18) | 14 (33) |
| Flat | 0 (0) | 1 (5) | 1 (2) |
| Histological type | | | |
| Differentiated | 17 (81) | 18 (82) | 35 (81) |
| Undifferentiated | 4 (19) | 4 (18) | 8 (19) |
| Five year survival rate (%) | 88 | 82 | 84 |

*Significantly different from previously benign group, p<0.001. Numbers in parentheses are per cents.

Table 2 Comparison of early gastric stump cancer and primary early gastric cancer in the upper third of the stomach

| | Early gastric stump cancer | Primary early gastric cancer |
|-----------------------------|----------------------------|------------------------------|
| Number of patients | 43 | 156 |
| Age at operation (y) | 64.4 | 60.3 |
| Male:female ratio | 6.2 | 2.8* |
| Macroscopic type | | |
| Elevated | 28 (65) | 40 (26)* |
| Depressed | 14 (33) | 113 (72)* |
| Flat | 1 (2) | 3 (2) |
| Histological type | | |
| Differentiated | 35 (81) | 126 (81) |
| Undifferentiated | 8 (19) | 30 (19) |
| Depth of invasion | | |
| Mucosa | 24 (56) | 82 (53) |
| Submucosa | 19 (44) | 74 (47) |
| Five year survival rate (%) | 84 | 95 |

*Significantly different from early stump cancer, $p < 0.001$. Numbers in parentheses are per cents.

data obtained regarding early GSC were compared with data from 156 patients with primary early gastric cancer in the upper third of the stomach, the location where early GSC arises.

The site of the tumour within the stomach was classified as lesser curvature, greater curvature, anterior wall, or posterior wall. In addition, the macroscopic type of the tumour, the histological type, and depth of infiltration were analysed according to the rules of the Japanese Research Society for Gastric Cancer (JRS GC).⁷ Briefly, macroscopic type was classified as either elevated type (I, IIa, IIa+IIc), depressed type (IIc, IIc+IIa, III), or flat type (IIb). The depth of infiltration was classified histologically, as follows: m, infiltration into mucosa; sm, infiltration into submucosa. Cancers were classified by the predominant histological type, as follows: differentiated type (papillary, well differentiated, and moderately differentiated adenocarcinoma) or undifferentiated type (poorly differentiated adenocarcinoma, signet ring cell, and mucinous carcinoma).

Table 3 Site of cancer in the stomach in early gastric stump cancer and primary early gastric cancer in the upper third of the stomach

| | Lesser curvature | Anterior wall | Greater curvature | Posterior wall |
|--------------------------------------|------------------|---------------|-------------------|----------------|
| Early gastric stump cancer (n=43) | 20 (47) | 4 (10) | 10 (23) | 9 (20) |
| Primary early gastric cancer (n=156) | 71 (46) | 17 (11) | 9 (5) | 59 (38) |

Numbers in parentheses are per cents.

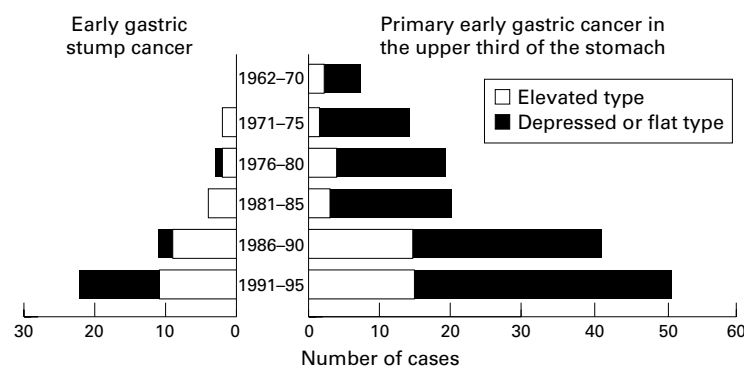


Figure 1 Changes with time in macroscopic findings between early gastric stump cancer and primary early gastric cancer in the upper third of the stomach.

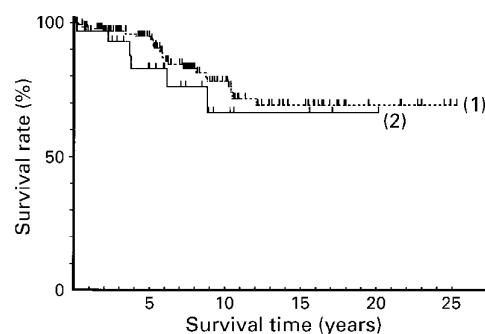


Figure 2 Five year survival rates of early gastric stump cancer ((1); n=43); and primary early gastric cancer in the upper third of the stomach ((2); n=156).

STATISTICAL ANALYSIS

The statistical analysis system (SAS) was used in this study. The patients with early GSC who had previously received distal gastrectomy for benign disease were compared with those with malignant disease, and the patients with early GSC were compared with those with primary early gastric cancer in the upper third of the stomach. The data were analysed for significance using Wilcoxon and χ^2 tests. Survival was evaluated by the Kaplan-Meier method and analysed by the Wilcoxon test.

Results

COMPARISON OF EARLY GSC WITH PREVIOUSLY BENIGN OR MALIGNANT DISEASE

Table 1 summarises the clinical data of patients who had early stump cancer. The interval between distal gastrectomy and detection of early GSC was longer for patients with previously benign disease ($p < 0.001$). This is due to the fact that patients with benign diseases underwent previous gastric surgery at a younger age. In fact, the mean age at the time of the operation for early GSC was almost identical in the two groups. There was no significant difference in the male:female ratio, macroscopic type, or histological type between two groups. Macroscopically, the frequency of the elevated type tended to be higher in previously malignant disease than in previously benign disease.

COMPARISON OF EARLY GSC AND PRIMARY EARLY CANCER IN THE UPPER THIRD OF THE STOMACH

Table 2 summarises the clinicopathological features of GSCs and primary early cancers in the upper third of the stomach. The mean age at the time of operation in early GSC did not differ significantly from that in primary early cancer. The male:female ratio in early GSC was significantly higher than that in primary early gastric cancer. Macroscopically, the elevated type was predominant in early GSC (65%), while the depressed type was predominant in primary early cancer (72%).

As table 3 shows, half of the early GSC cases (47%) were located in the lesser curvature of the gastric remnant, similar to the results seen with primary early cancer in the upper third of the stomach (46%). However, not only the number of cases but also the frequency of the depressed type in early GSC increased from

1991 to 1995 (fig 1). Eleven of 15 depressed type cases (73%) were detected from 1991 to 1995, and six of these were located on the lesser curvature in the remnant stomach.

According to the histological classification recommended by JRSGC, over 80% of the early cancers were of the differentiated type in both the stump and primary groups.

The five year survival rates of patients with early stump and primary cancers were 84% and 95%, respectively. The five year survival rate of early stump cancer did not differ significantly from that of primary early cancer in the upper third of the stomach ($p=0.2683$) (fig 2).

Discussion

Since Balfour first reported gastric stump cancer in 1922,⁸ there have been many studies of stump cancer by various investigators. The survival rate of patients with gastric stump cancer is unfavourable compared with that of cancer in the non-resected stomach,^{9,10} probably because the malignant lesion in the stomach remnant is detected at a relatively advanced stage. The symptoms of GSC are similar to those of postgastrectomy syndrome, and it is difficult to detect in its early stages by radiography. Recent progress in endoscopic examination has made it possible to detect early GSC, although few studies have evaluated its clinicopathological findings. If stump cancer is diagnosed at an early stage, the five year survival rate can be as satisfactory as that reported for early gastric cancer.^{11,12}

In our hospital, over 200 patients with gastric cancer undergo gastrectomy every year. In the future, the number of patients with GSC who have previously undergone gastrectomy for gastric cancer will be expected to increase because patients with gastric or duodenal ulcer are not now subjected to gastrectomy, except in an emergency, due to the increased use of anti-ulcer drugs. In this study, we evaluated 43 patients with early GSC who had previously received distal gastrectomy for benign or malignant diseases, because we were interested in detection of early cancer in the remnant stomach in order to improve its prognosis.

In comparing early GSCs which had been previously benign or malignant, there was a significant difference in the interval between operations. However, there was no significant difference in the mean age at operation for early stump cancer, the male:female ratio, location of the tumour in the stomach, endoscopic or histological type of tumour, or prognosis between the two groups. It is suggested that the cause of the first gastric cancer does not affect the subsequent stump cancer.

The clinicopathological characteristics of early GSC can be summarised as follows: it was predominantly found in males; it appeared more than 10 years after distal gastrectomy; half the cases (47%) were located in the lesser curvature in the remnant stomach; macroscopically and histologically, the elevated type and the differentiated type, respectively, were predominant; and the prognosis was favourable.

It is noteworthy that the elevated type was predominant in GSC and that this type was much less frequent in primary early cancers, although both cancers showed the same histological findings. There are two possibilities to explain the discrepancy in macroscopic findings between early GSC and primary early cancer. Firstly, the hypoacidic conditions in the gastric remnant might play a role in the development of elevated or differentiated carcinoma.¹³ Sano *et al* showed, using an animal model, why the elevated type of cancer will develop experimentally in hypoacidic conditions.¹³ Secondly, elevated lesions are sometimes easier to identify even in the remnant stomach with postgastrectomy gastritis. It is difficult to detect depressed or flat type cancers in the remnant stomach because of the narrow space and the reddish mucosa. Small depressed cancerous lesions might be missed. The number of cases and the frequency of the depressed type increased in early GSC, compared with primary early cancer, from 1991 to 1995, in that 11 of 22 cases showed depressed type in early GSC, and six of these were located on the lesser curvature. It is suggested that the progress of diagnostic ability by endoscopic observation, in addition to advances in endoscopic instrumentation, might contribute to early detection of the depressed type in GSC. Endoscopy is important as the frequency of the depressed type is higher in early GSC and the number of overlooked cases should be reduced to the minimum.

In conclusion, our results emphasise the fact that early detection is the only way to improve the prognosis of stump cancer, and special attention should be given to elevated as well as depressed lesions on the lesser curvature, particularly in male patients, during endoscopic examinations.

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