Original article

Cancer of the gastric stump following distal gastrectomy for cancer

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Background: Cancer of the gastric stump (CGS) after distal gastrectomy for cancer has not been characterized in a large study. The aim of this study was to investigate the clinicopathological features and outcome of CGS following distal gastrectomy for cancer.

Methods: Patients with CGS following distal gastrectomy for gastric cancer diagnosed between 1970 and 2002 were reviewed retrospectively.

Results: A total of 108 patients was identified. The median interval between the initial gastrectomy and resection for CGS was 7·5 (range 1–41) years. The depth of tumour invasion was T1 in 67 patients, T2 in 16, T3 in eight and T4 in 17 patients. Endoscopic mucosal resection was performed in 25 patients with T1 tumours. R0 resection was achieved in 103 patients. The overall 5-year survival rate was 53·1 per cent. The 5-year survival rates for patients with T1, T2, T3 and T4 disease were 76, 40, 13 and 9 per cent respectively.

Conclusion: The outcome for patients with non-early CGS was poor. Early detection of CGS is important following distal gastrectomy for gastric cancer and strict surveillance is recommended for at least 10 years after the initial gastrectomy.

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Introduction

In recent decades, cancer of the gastric stump (CGS) following distal gastrectomy has accounted for 1–2 per cent of all gastric cancers in Japan[1,2]. The number of patients with CGS who had gastrectomy for benign disease continues to fall as surgical treatment of benign disease continues to diminish. Conversely, the number of patients with CGS following gastrectomy for gastric cancer is increasing, as a result of improved outcomes for patients with gastric cancer.

There have been many reports on CGS following distal gastrectomy for benign disease. The tumours are often detected at an advanced stage, 15–20 years after gastrectomy[3–7], and usually at the anastomotic site of Billroth II reconstructions[8,9]. The long-term prognosis after resection is generally comparable to that after resection of primary cancer in the proximal third of the stomach[8,10–14]. Some features of CGS following distal gastrectomy for cancer have been documented in small case series[9,15]. The aim of this study was to investigate the clinicopathological features and results of treatment of CGS following distal gastrectomy for cancer.

Patients and methods

A total of 9814 patients underwent open surgery for gastric cancer at this institution between 1970 and 2002. CGS following distal gastrectomy for cancer was identified in 108 patients over the same period. Fifty-four of these 108 patients had undergone their initial surgery at this institution and 54 patients had their primary surgery elsewhere. Initial distal gastrectomy was defined as the removal of more than two-thirds of the distal stomach. The clinicopathological data and outcome of these 108 patients were reviewed from a prospective database supported by information from medical records.

The previous distal gastrectomy was reported to be curative in all patients and so no cases of definite recurrence were included. When multiple cancers were found in the gastric stump, only the largest or most deeply invading lesion was considered for analysis.

The main locations of CGS were classified as anastomotic site, non-anastomotic site or total stump. Non-anastomotic tumours were further subdivided according to whether the bulk of the tumour was situated between the lesser curvature and the posterior wall or between the

greater curvature and the anterior wall. The cancers were classified according to histological type into differentiated adenocarcinoma (papillary, well differentiated and moderately differentiated adenocarcinoma) and undifferentiated adenocarcinoma (poorly differentiated adenocarcinoma, signet-ring cell carcinoma and mucinous adenocarcinoma). The depth of tumour invasion, lymph node status and tumour stage were recorded according to the International Union Against Cancer classification[16]. The macroscopic tumour type and extent of lymph node dissection were recorded in accordance with the Japanese Classification of Gastric Carcinoma[17].

Medical records were reviewed for preoperative medical conditions, histological results and follow-up data. Patients who had gastrectomy at this institution were usually followed up for 10 years after operation. The cumulative survival rate was calculated by the Kaplan–Meier method with 95 per cent confidence intervals (c.i.). Survival curves were compared using the log rank test.

Results

Of 108 patients who developed CGS following distal gastrectomy for gastric cancer, seven were diagnosed between 1970 and 1980, 28 between 1981 and 1991, and 73 between 1992 and 2002. The median interval between the initial gastrectomy and resection of the CGS was 7·5 (range 1–41) years, and was 10 years or less in 72 patients (66·7 per cent).

Clinicopathological data are summarized in *Table 1*. A Billroth I procedure was the most common method of reconstruction during the initial operation. The area from the lesser curvature to the posterior wall of the non-anastomotic site was most frequently involved by CGS.

Sixty-seven patients (62·0 per cent) had early CGS (T1); 41 of these cancers were mucosal and 26 submucosal. Early gastric cancer was the diagnosis in 38 (70 per cent) of the 54 patients who had undergone their initial surgery at this institution. Depressed-type early gastric cancer (IIc or IIc + III) predominated, followed by protruded-type early cancer (I, IIa) and then type 3 non-early cancer. Differentiated adenocarcinoma was the most prevalent histological type (*Table 1*).

The distribution of tumour location according to the interval between the initial gastrectomy and resection of the CGS and type of reconstruction is shown in *Table 2*. The area from the lesser curvature to the posterior wall of the non-anastomotic site was most frequently involved by CGS, regardless of the interval or reconstruction method.

The surgical procedures and curability are shown in *Table 3*. Twenty-five patients with T1 disease underwent endoscopic mucosal resection (EMR) and the remaining 83 had open surgery. Completion gastrectomy with at least D2 lymphadenectomy, completion gastrectomy with D1, and distal gastrectomy or local resection of the gastric

Table 1 Clinicopathological features in 108 patients

Median (range) age (years)	67 (44–91)
Sex ratio (M : F)	85 : 23
Median (range) interval (years)*	7·5 (1–41)
Previous reconstruction	
Billroth I	71 (65·7)
Billroth II	28 (25·9)
Roux-en-Y	9 (8·3)
Tumour location	
Anastomotic	14 (13·0)
Non-anastomotic	
Lesser curvature to posterior wall	71 (65·7)
Greater curvature to anterior wall	18 (16·7)
Total stump	5 (4·6)
Depth of invasion	
T1	67 (62·0)
T2	16 (14·8)
T3	8 (7·4)
T4	17 (15·7)
Macroscopic type	
0–I or 0–IIa	30 (27·8)
0–IIb	3 (2·7)
0–IIc or 0–III	37 (34·3)
1 or 2	14 (13·0)
3	18 (16·7)
4	4 (3·7)
5	2 (1·9)
Histological type	
Differentiated	70 (64·8)
Undifferentiated	38 (35·2)

Values in parentheses are percentages. *Time interval between the initial operation and resection of cancer of the gastric stump.

Table 2 Tumour location in relation to interval and previous reconstruction

		Non-anastomotic		
	Anasto-motic	Lesser–posterior	Greater–anterior	Total stump
Interval (years)*				
1–5 ($n = 40$)	4 (10)	29 (73)	7 (18)	0 (0)
6–10 ($n = 32$)	5 (16)	22 (69)	3 (9)	2 (6)
11–15 ($n = 18$)	1 (6)	13 (72)	2 (11)	2 (11)
≥ 16 ($n = 18$)	4 (22)	7 (39)	6 (33)	1 (6)
Previous reconstruction				
Billroth I ($n = 71$)	7 (10)	47 (66)	14 (20)	3 (4)
Billroth II ($n = 28$)	5 (18)	17 (61)	4 (14)	2 (7)
Roux-en-Y ($n = 9$)	2 (22)	7 (78)	0 (0)	0 (0)

Values in parentheses are percentages. *Time interval between the initial operation and resection of cancer of the gastric stump. Lesser–posterior, lesser curvature to posterior wall; greater–anterior, greater curvature to anterior wall.

stump with D0 were performed in 49, 30 and four patients respectively. Of the 79 patients who underwent either D1 or D2 lymphadenectomy, 74 resections were considered curative (R0) and five non-curative (R1/2) (*Table 3*). R0 resection was achieved in all patients with T1 or T2, seven of eight with T3, and 13 of 17 patients with T4 disease. Factors precluding curative resection were peritoneal dissemination in four patients and multiple liver metastases in one. There were two hospital deaths following curative surgery for T3 disease, from acute heart failure and anastomotic leakage. Lymph node metastasis was confirmed pathologically in one patient with T1 disease, five with T2 disease, three with T3 disease and 15 patients with T4 disease.

The overall 5-year survival rate was 53·1 (95 per cent c.i. 43·4 to 61·9) per cent. Five-year survival rates in patients grouped according to depth of tumour invasion, lymph node status and tumour stage are shown in *Table 4*. T3 or more, lymph node involvement and stage III or higher were associated with very low 5-year survival rates. Death from recurrence was confirmed in six of 16 patients with T2 disease, five of eight with T3 disease and 11 of 17 with T4 disease, and all but one of these deaths occurred within 4 years after surgery for CGS. The most common type of recurrence was peritoneal dissemination (eight patients), followed by nodal disease (five) and liver metastasis (two). No patient with T1 disease died from recurrence during a median follow-up of 44 (range 2–233) months.

Table 3 Surgical procedures and curability

Depth of invasion	Surgical procedure	Curative (R0)	Non-curative (R > 1)
T1 ($n = 67$)	Endoscopic mucosal resection	25	0
	Distal gastrectomy or local resection* (D0)	3	0
	Completion gastrectomy (D1)	21	0
	Completion gastrectomy (≥ D2)	18	0
T2 ($n = 16$)	Distal gastrectomy or local resection* (D0)	1	0
	Completion gastrectomy (D1)	3	0
	Completion gastrectomy (≥ D2)	12	0
T3 ($n = 8$)	Completion gastrectomy (D1)	2	0
	Completion gastrectomy (≥ D2)	5	1
T4 ($n = 17$)	Completion gastrectomy (D1)	0	4
	Completion gastrectomy (≥ D2)	13	0

*Local resection of the gastric stump. Local resection was indicated for small clinical T1 tumours before the introduction of endoscopic mucosal resection. The distal part of the remnant stomach was further removed (further distal gastrectomy) when a small tumour was located at or near the anastomosis.

Table 4 Five-year survival rates

	5-year survival rate (%)	*P**
Depth of invasion		< 0·001
T1 ($n = 67$)	76 (65, 85)	
T2 ($n = 16$)	40 (20, 64)	
T3 ($n = 8$)	13 (2, 47)	
T4 ($n = 17$)	9 (1, 27)	
Lymph node status		< 0·001
N0 ($n = 84$)	74 (64, 82)	
N1 ($n = 13$)	13 (4, 42)	
≥ N2 ($n = 11$)	0 (0, 24)	
Stage		< 0·001
I ($n = 77$)	73 (62, 81)	
II ($n = 6$)	33 (10, 70)	
III ($n = 2$)	0 (0, 78)	
IV ($n = 23$)	6 (1, 21)	

Values in parentheses are 95 per cent confidence intervals. *Log rank test.

Discussion

CGS following distal gastrectomy for gastric cancer is becoming more common. Long-term exposure of the gastric mucosa to duodenal contents is thought to be one of the major causes of CGS after distal gastrectomy[18–20]. This seems true of CGS following gastrectomy for benign disease, because the anastomotic site of Billroth II reconstruction, which is constantly affected by duodenogastric reflux, is frequently involved by CGS 15–20 years or more after the initial gastrectomy[8,9]. In the present study, most gastric stump tumours following gastric cancer surgery were detected at a non-anastomotic site and within 15 years, regardless of the type of reconstruction. These results are similar to those reported by Sowa *et al.*[9].

The most common site of the non-anastomotic tumours was the area from the lesser curvature to the posterior wall, where primary early cancer in the proximal third of the stomach often develops[2]. This suggests that pre-existing mucosal changes, such as atrophic gastritis and intestinal metaplasia, rather than duodenogastric reflux, may be more relevant to the development of CGS following gastric cancer. It has been proposed that denervation during initial gastric cancer surgery might weaken the defence mechanisms of the gastric mucosa and promote the development of CGS[15].

As a result of recent advances in diagnostic techniques, especially endoscopy, both the macroscopically elevated and depressed types of early CGS are being detected with increasing frequency[2]. In the present study, early CGS was diagnosed in 38 (70 per cent) of 54 of patients who underwent initial distal gastrectomy at this institution and participated in a follow-up programme.

Current institutional policy is to perform annual surveillance endoscopy commencing 1 year after the gastrectomy for at least 10 years. Follow-up endoscopy after gastrectomy seems important for the early diagnosis of CGS.

Early gastric cancer is associated with a low incidence of lymph node metastasis and is often treated by EMR and partial gastrectomy, which provide excellent disease-free survival. However, when CGS following gastric cancer is detected at a later stage (T2 or later) the prognosis is considerably poorer and the recurrence rate high, even after curative resection. The outcome for patients with T3 or higher-stage tumours or lymph node involvement is extremely poor and worse than that of patients with primary cancers in the proximal third of the stomach of the same stage[12]. The exact reasons for this poorer survival are not clear, but the disruption of lymphatic channels at the first operation may lead to substantial changes in lymphatic flow from the gastric remnant, making surgical control of CGS with nodal disease difficult. On this basis, the authors emphasize the importance of early detection of CGS following gastric cancer.

Lifelong annual follow-up endoscopy is recommended and strict surveillance for at least 10 years after the initial gastrectomy is especially important as two-thirds of the patients destined to develop CGS will do so within this time. Careful endoscopic examination of the entire stump, particularly around the lesser curvature and posterior wall, is essential. Elevated and depressed mucosal changes should be examined histologically.

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