



Original article

A clinicopathological study of gastric stump carcinoma following proximal gastrectomy

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Abstract

Background. We aimed to clarify the frequency and clinicopathological characteristics of gastric stump carcinoma following proximal gastrectomy.

Methods. Three-hundred and sixteen patients who had undergone curative proximal gastrectomy over a 21-year period from January 1984 through December 2004 were reviewed.

Results. Gastric stump carcinoma was observed in 17 patients (5.4%). The time interval between the initial gastrectomy and the treatment of gastric stump cancer was within 5 years in 3 patients, within 5–10 years in 8, and after 10 years in 6. Treatment included endoscopic resection ($n = 4$), completion total gastrectomy of the remnant stomach ($n = 11$), pancreatoduodenectomy ($n = 1$), and nonsurgical resection ($n = 1$). Pathologically, 9 carcinomas were differentiated and 8 were undifferentiated. In a review of reconstruction methods associated with disease stage, stage I was found in 6 of the 7 patients with esophagogastrostomy or short-segment jejunal interposition. On the other hand, stage I was found in only 3, but stage II–IV was found in 7 of the 10 patients with reconstruction by double-tract or long-segment jejunal interposition; thus, the tumor was more likely to be detected at an advanced stage after long-segment interposition ($P = 0.049$).

Conclusion. Gastric stump carcinoma following proximal gastrectomy occurred at a high frequency of 5.4% of initial resections. It is necessary to select a reconstruction method that facilitates postoperative endoscopic examination, as well as to follow up the patients after proximal gastrectomy in the long term for the early detection and early treatment of gastric stump carcinoma.

Key words Gastric stump carcinoma · Proximal gastrectomy · Jejunal interposition

Introduction

Proximal gastrectomy has been widely accepted as function-preserving surgery for early gastric cancer located in the cardiac part of the stomach [1–3]. However, the procedure has two important problems; one is the postoperative quality of life (QOL) involving reflux esophagitis [4, 5]; the other is carcinoma arising in the gastric stump. To date, only a few studies have been published on gastric stump carcinoma in patients who have undergone proximal gastrectomy [6–8], although many studies have revealed the clinicopathological findings of gastric stump cancer after distal gastrectomy [9–14]. We have experienced 17 cases of gastric stump carcinoma arising after proximal gastrectomy. This study aimed to reveal the clinicopathological features of gastric stump cancer following proximal gastrectomy.

Patients and methods

Proximal gastrectomy

We reviewed 316 curative proximal gastrectomies among 6151 patients who had undergone stomach resection between January 1984 and December 2004 at the Cancer Institute Hospital, Tokyo, Japan. Proximal gastrectomy was indicated for early gastric cancer located in the cardiac portion of the stomach, and exceptionally for bleeding gastric ulcer. The reconstruction method after proximal gastrectomy was changed during the study period. From 1984 through 1994, a double-tract method or long-segment jejunal interposition (long interposition) was adopted after resection of the upper half of the stomach. In these reconstructions, the distance between the esophagojejunal anastomosis and the jejunogastrostomy was 30 to 40 cm, and pyloroplasty was required. After 1995, as the resection range had been changed to the proximal-third or proximal

quarter of the stomach, short-segment jejunal interposition (short interposition), in which the length of the esophagogastric anastomosis or interposed jejunum was within 15 cm, was then possible. With this method, the hepatic branch, pyloric branch, and celiac branch of the vagus nerve were preserved, and pyloroplasty was not needed. During the entire study period, the double tract method was adopted in 78 patients, long interposition in 142, esophagogastronomy in 73, and short interposition in 23. Figure 1 illustrates the reconstruction methods following proximal gastrectomy.

Definition of gastric stump carcinoma

Gastric stump carcinoma was defined as: (1) carcinoma detected more than 10 years after the initial surgery for either malignant or benign disease; or (2) carcinoma detected within 10 years that was likely to have occurred independently of the initial lesion [15]. Cancers that developed at the anastomotic site or on the suture line within 10 years after the initial surgery for a malignant lesion, and those that developed at the anastomotic site or on the suture line with a positive resection margin after the initial surgery for a malignant lesion were excluded from the study.

Postoperative follow-up

Postoperative follow-up after the double-tract method or long interposition was conducted annually by postoperative fluoroscopy and computed tomography (CT) scan. Endoscopy was also carried out every year, but observation by this method was insufficient in many patients with these reconstruction methods.

After esophagogastronomy or short interposition, upper endoscopy as well as CT scan was conducted annually. Follow-up after 5 years was performed at the patient's request at our institute or at a nearby hospital.

In the present study, we reviewed gastric stump cancers after proximal gastrectomy in terms of clinicopathological features at the initial surgery, reconstruction methods, time to the treatment of gastric stump cancer, and pathological findings of the gastric stump carcinomas. The terms used here are based on the *Japanese classification of gastric carcinoma* (second English edition) [16]. Statistical analysis was performed by using Fisher's exact test.

Results

Gastric stump carcinoma was found in 17 (5.4%) of the 316 patients who had undergone curative proximal gastrectomies. Table 1 and Table 2 show the clinicopatho-

Table 1. Clinicopathologic characteristics of patients at initial surgery

Number of patients	17
Sex	
Male	15
Female	2
Age (years)	
Average	59.3
Range	39–71
Reconstruction	
Double-tract	3
Interposition ^a	7
EG	3
Short interposition ^b	4
Macroscopic type	
0-IIa	3
0-IIc	12
Histology	
Differentiated	13
Undifferentiated	2
Tumor depth	
m	7
sm	7
mp	1
Degree of lymph node metastasis	
n0	12
n1	3
n2	0
Stage	
I	14
II	1

EG, esophagogastronomy; Interposition, jejunal interposition

^aLong-segment jejunal interposition of 30- to 40-cm length

^bShort-segment jejunal interposition of 5- to 15-cm length

logical characteristics of the 17 patients. At the initial surgery, the lesions in 2 patients were benign; one was a bleeding gastric ulcer and the other was an adenoma, confirmed on the postoperative pathological examination, but which had been preoperatively diagnosed as carcinoma. Of the 15 malignant lesions, all but 1 was at an early stage; pathologically 13 of them were differentiated and the remaining 2 were undifferentiated tumors. After the proximal gastrectomy, 3 patients had reconstruction by esophagogastronomy, 3 by the double-tract method, and 11 by jejunal interposition, including 4 with short interposition. The time to treatment of the gastric stump carcinoma was within 5 years in 3 patients, within 5–10 years in 8, and after 10 years in 6. Treatment of the gastric stump carcinoma included endoscopic resection in 4 patients, total completion gastrectomy of the gastric remnant in 11, and pancreaticoduodenectomy in 1. One patient did not receive surgical treatment. Pathologically, 9 carcinomas were differentiated and 8 were undifferentiated. When examined in relation to the initial disease, differentiated tumor in the gastric stump carcinoma was found in 9 of the 13 patients with differentiated histology in the initial disease. The 2 undifferentiated initial lesions had, again,

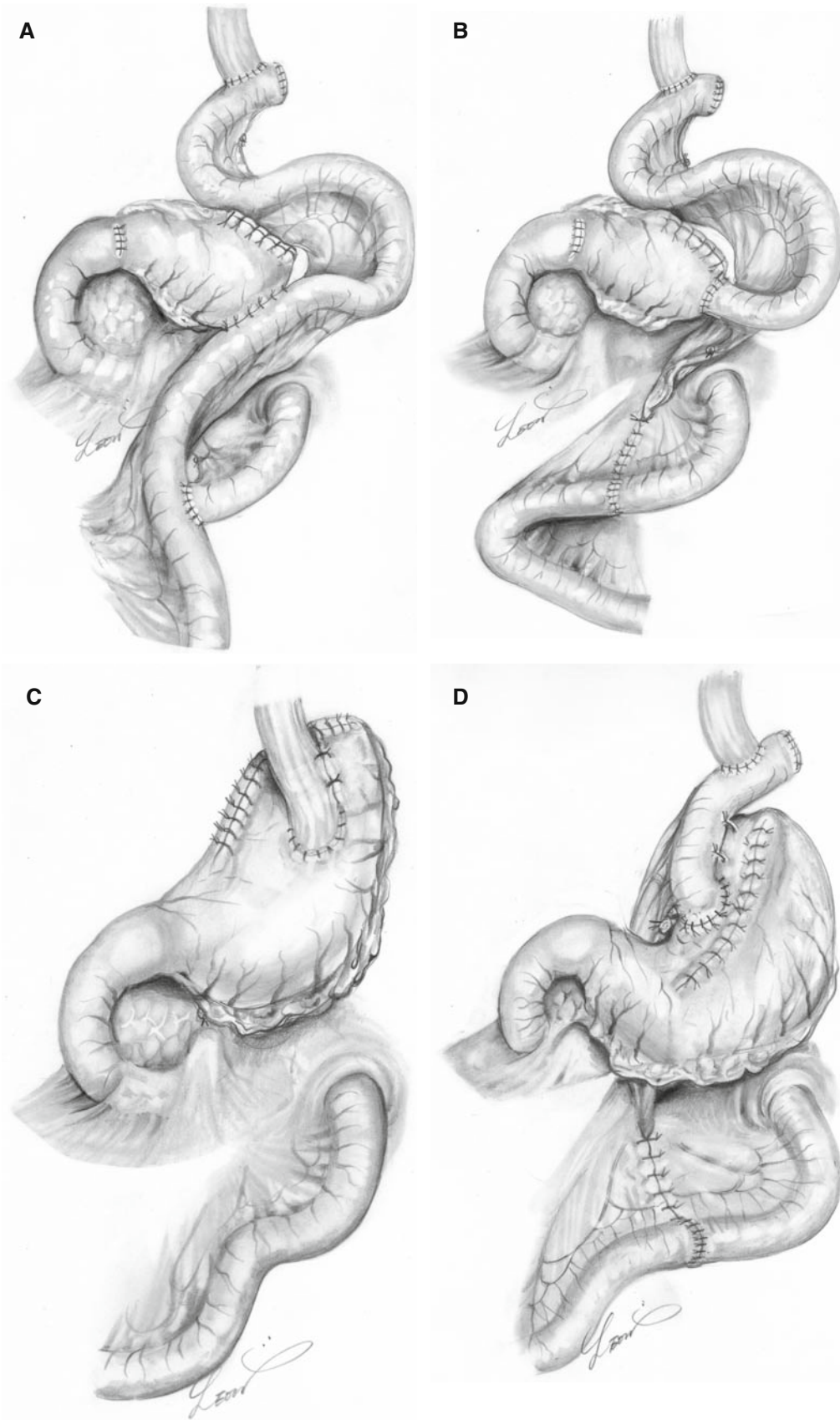


Fig. 1A–D. Reconstruction methods following proximal gastrectomy. **A** Double-tract reconstruction; **B** long-segment jejunal interposition; **C** esophagogastrostomy; **D** short-segment jejunal interposition

Table 2. Clinicopathologic characteristics of 17 patients at surgery for gastric stump carcinoma

	Reconstruction	Interval ^c	Treatment	Initial pathology ^d	Pathology ^e	T	N	Stage	Prognosis (months)	Status
1	EG	2.2	Total gastrectomy	Differentiated	Differentiated	sm	0	I	72	Alive
2	EG	2.7	Total gastrectomy	Differentiated	Differentiated	m	0	I	35	Alive
3	EG	6.7	EMR	Differentiated	Differentiated	m	—	I	12	Alive
4	Short interposition ^b	6.4	EMR	Differentiated	Differentiated	m	—	I	25	Alive
5	Short interposition	9.4	EMR	Undifferentiated	Undifferentiated	m	—	I	6	Alive
6	Short interposition	12.2	EMR	Differentiated	Differentiated	m	—	I	4	Alive
7	Short interposition	7.6	Total gastrectomy	Differentiated	Differentiated	ss	3	IV	4	Alive
8	Double tract	2.5	Total gastrectomy	Differentiated	Differentiated	m	0	I	62	Alive
9	Double tract	10.2	Total gastrectomy	Differentiated	Differentiated	sm	0	I	11	Alive
10	Double tract	10.8	Total gastrectomy	Differentiated	Undifferentiated	si	2	IV	26	Dead
11	Interposition ^a	5.3	Total gastrectomy	Adenoma	Undifferentiated	si	3	IV	1	Dead
12	Interposition ^a	7.8	Total gastrectomy	Differentiated	Undifferentiated	ss	2	III	49	Dead
13	Interposition	8.1	No operation	Differentiated	Undifferentiated	si	2	IV	8	Dead
14	Interposition	8.7	Whipple operation	Differentiated	Undifferentiated	sm	2	IV	52	Dead
15	Interposition	17.1	Total gastrectomy	Differentiated	Differentiated	sm	0	I	11	Alive
16	Interposition	21.8	Total gastrectomy	Gastric ulcer	Undifferentiated	sm	2	II	2	Alive
17	Interposition	22.5	Total gastrectomy	Undifferentiated	Undifferentiated	ss	2	III	6	Alive

EG, esophagogastrostomy; Interposition, jejunal interposition; EMR, endoscopic mucosal resection

^aLong-segment jejunal interposition of 30–40 cm length^bShort-segment jejunal interposition of 5–15 cm length^cTime interval (years) from initial gastrectomy to treatment of gastric stump carcinoma^dPathology at initial surgery (proximal gastrectomy)^ePathology at the surgery for gastric stump carcinoma

undifferentiated pathology in the gastric stump carcinomas (Table 3). With regard to the stage of the gastric stump cancers, stage I disease was found in 9 patients, stage II in 1, stage III in 2, and stage IV in 5. When we reviewed the reconstruction methods associated with cancer stage, gastric stump carcinoma was detected at stage I in all 3 patients with reconstruction by esophagogastrostomy and 3 of the 4 with reconstruction by short interposition. On the other hand, stage I was found in only 3 of the 10 patients with a long-interposition or double-tract reconstruction; in contrast, these reconstruction methods were associated with stage II, III, or IV disease in 7 of the 10 patients with such reconstruction. Thus, gastric stump carcinomas were more likely to be detected at an advanced stage after a double-tract or long jejunal interposition reconstruction method (Table 4; $P = 0.049$).

Discussion

Many studies have shown that gastric stump cancer develops after distal gastrectomy, particularly after Billroth II reconstruction, at frequencies of 0.4%–2.5%, with an increased incidence 15 years after surgery [17–20]. Reflux of duodenal fluid such as bile or pancreatic juice was reported to be associated with the development of gastric carcinoma after distal gastrectomy [21–26].

On the other hand, very few studies have been conducted on gastric stump carcinoma after proximal gastrectomy. Igami et al. [8] reported that gastric stump cancer was found in 6 (5%) of 120 patients who received

Table 3. Comparison of pathological types of initial lesion and gastric stump carcinoma

Initial lesion			Gastric stump carcinoma
Differentiated	13		Differentiated 9
Undifferentiated	2		Undifferentiated 8
Benign			
Adenoma	1		
Bleeding gastric ulcer	1		

proximal gastrectomy over a 27-year period from 1971 to 1997. Kaminishi et al. [7] showed 26 cases of gastric stump cancer following proximal gastrectomy, but the incidence was not studied because the total case number was unclear. In our review, gastric stump carcinoma was observed at a frequency of 5.4% in patients with curative proximal gastrectomies. It is presumed that gastric stump cancer develops at a higher frequency after proximal gastrectomy than after distal gastrectomy.

As for the cause of gastric stump carcinoma after proximal gastrectomy, the following reasons have been advanced: (1) the distal part of the stomach is originally a high-incidence area for gastric carcinoma; (2) postoperative hypergastrinemia promotes carcinogenesis (after resection of the fundic gland region in proximal gastrectomy, an acidity occurs and parietal cells are decreased in quantity and function [27–29]; and (3) expression of the trefoil factor family 1 [30] (TFF1; pS2), which inhibits carcinogenesis, is decreased after resection of the fundic gland region. It was reported that TFF1 knockout mice developed adenomas and carcinomas in the stomach. It is thought that such factors are contributors to the high risk of gastric carcinoma after proximal gastrectomy [31–33].

Concerning the pathological type at the initial resection, differentiated carcinoma was more frequently observed in our study. In this regard, the possibility of selection bias cannot be denied; that is, proximal gastrectomy was more likely to be performed for differentiated carcinoma than for undifferentiated carcinoma, because the spread of undifferentiated carcinoma is unclear. Kaminishi et al. [7] reported that differentiated carcinoma was more frequent, being observed in 11 of 15 pathologically confirmed gastric stump cancers following proximal gastrectomy. In our review, the numbers of differentiated and undifferentiated tumors in the gastric stump carcinomas were almost the same. Because there have been only a few studies published on the pathological type of gastric stump carcinoma to date, its characteristics still remain unclear.

Concerning the time interval to the occurrence of gastric stump cancer, Kaminishi et al. [7] reported that occurrence within 10 years after the initial surgery was the most common period, with 11 patients (42%)

Table 4. Reconstruction methods in relation to cancer stage

	Early gastric cancer		Advanced gastric cancer	
	Stage I	Stage II	Stage III	Stage IV
Double tract	2			1
Jejunal interposition ^a	1	1	2	3
Esophagogastrostomy	3			
Short jejunal interposition ^b	3			1

^a Long-segment jejunal interposition of 30- to 40-cm length

^b Short-segment jejunal interposition of 5- to 15-cm length

showing occurrence within 5 years, 9 (35%) showing occurrence between 5 and 10 years, and 6 (23%) showing occurrence after 10 years. As we also found that most patients ($n = 11$) developed carcinomas within 10 years after surgery, it is necessary to conduct careful follow-up within 10 years. Also, as some gastric stump carcinomas were detected more than 10 years after the initial surgery, long-term follow-up even after 10 years is essential.

Reconstruction following proximal gastrectomy was conventionally focused on preventing postoperative reflux esophagitis. Thus, a double-tract method or long interposition, in which the esophagojejunal anastomosis was located 30 cm or more distant from the jejunogastrostomy, was frequently adopted. However, in patients who had had these reconstruction methods there were some difficulties in conducting endoscopic examinations of the remnant stomach. In recent years, with the increasing incidence of early gastric cancer located in the upper third of the stomach, the procedure of proximal gastrectomy has been changed, with conservation of a large part of the stomach, preservation of the vagus nerves, or the creation of a jejunal pouch. Igami et al. [8] employed esophagogastrostomy in all their patients, while Katai et al. [2] recommended the use of short interposition. Kikuchi et al. [34] also reported the efficacy of jejunal pouch interposition in an attempt to increase food intake. Still, it has remained controversial as to which reconstruction method should be used following gastric resection, and different surgical procedures have been employed.

To detect gastric stump cancer at an early stage, it is essential to conduct endoscopic follow-up of the remnant stomach. When we examined the reconstruction methods associated with disease stage, six of the seven patients who had received esophagogastrostomy or short interposition were found to have stage I disease; four of these patients were treated with endoscopic resection. Among the patients reconstructed by conventional procedures such as long interposition or the double-tract method, the incidence of stage I disease was only 30%, whereas stage IV disease was found in four of these patients (40%). After a double-tract or long-interposition reconstruction, gastric stump carcinoma was more likely to be detected at an advanced stage, even including an unresectable tumor. This indicated that a reconstruction method that facilitates postoperative endoscopic observation of the remnant stomach is useful for the early detection and early treatment of gastric stump carcinoma after proximal gastrectomy.

Proximal gastrectomy will require further efforts to improve patients' postoperative QOL. The present study clarified that there was a high frequency of gastric stump carcinoma following proximal gastrectomy. It

is necessary to select an appropriate reconstruction method that facilitates postoperative endoscopic examination. This will contribute to the early detection and early treatment of gastric stump carcinomas following proximal gastrectomy in the future.

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