

Table 1. Incidence of nodal metastasis by depth of invasion (surgical T) from databases of major Japanese hospitals [data taken from 3]

Mucosal cancer	pN0	pN1	pN2	total	95% CI
Differentiated type	496 (98.0%)	9 (1.8%)	1 (0.2%)	10/506 (2.0%)	1.0–3.6%
Undifferentiated type	320 (93.6%)	20 (5.8%)	2 (0.6%)	22/342 (6.4%)	4.1–9.6%
Submucosal cancer	pN0	pN1	pN2		
Differentiated type					
Tumor size					
<1.5 cm	232/242 (95.9%)	10/242 (4.1%)	0/242 (0%)		
1.6–2.0 cm	147/164 (89.6%)	12/164 (7.3%)	5/164 (3.0%)		
>2.1 cm	431/513 (84.0%)	57/513 (11.1%)	25/513 (4.9%)		
Total	810/919 (88.1%)	79/919 (8.6%)	30/919 (3.3%)		

Depth of invasion was decided by inspection and palpation during operation.

of nodal metastasis observed for various types and stages of gastric carcinoma. As a result, it is now widely accepted by Japanese surgeons that such an extended lymphadenectomy (D2) is not inevitable for certain subsets of early gastric cancer with a very rare chance of nodal involvement [4–7] (table 1).

The detection rate of early gastric cancer has also increased in recent times due to the development of diagnostic methods and widespread use of mass screening [8, 9]. The incidence of aged patients has increased due to a prolonged lifespan [10]. Therefore, recent trends in the management of EGC show that Japanese surgeons have been increasingly adopting more conservative methods to preserve the quality of life while at the same time maintaining a high level of radicality, such as endoscopic mucosal resection (EMR) or function-preserving gastrectomies for EGC.

Lymph Node Metastasis from EGC

Distant metastasis from EGC is extremely rare, and peritoneal seeding is unlikely because the tumor is completely confined to the gastric wall. The only possible local spread is via the lymphatic route. The incidence and extent of nodal metastasis from EGC is closely related to the depth of tumor invasion [11]. Mucosal cancers rarely metastasize (3% or less), while nearly 20% of EGC invading the submucosa metastasize to the regional nodes, and the incidence approaches 50% in T2 tumors [12].

Treatment Guidelines for EGC

A patient with early gastric cancer is usually assigned as stage IA (T1N0), stage IB (T1N1) or stage II (T1N2). Less extensive surgeries are advocated for stage IA and stage IB in the guidelines (table 2). Since T2 tumor has a high incidence of nodal metastasis, the accuracy of preoperative diagnosis is the key to perform less extensive treatment, since understaged patients will have insufficient treatment.

Less extensive resection is defined as modified gastrectomy (table 3) in the guidelines according to the Japanese Classification of Gastric Carcinoma [13]. The guidelines also introduced optional treatment methods, such as pylorus-preserving, vagal nerve-preserving, and laparoscopic assistance.

Stage IA (T1N0). EMR or modified gastrectomy (MG) is indicated for this stage according to table 4. EMR should be indicated for patients with small mucosal cancer with no lymph node metastasis. Vigorous retrospective studies have been made in Japan. Databases containing several hundreds or even thousands of patients with EGC who have undergone surgery with lymphadenectomy have been analyzed to identify the specific features of EGC without lymph node metastasis [6, 7, 14].

It is now accepted that a tumor satisfying all the following conditions is suitable for EMR: (1) tumor confined to the mucosal layer; (2) tumor of elevated type (I or IIa), or depressed type (IIc) without ulcer or ulcer scar (endoscopically no fold convergence); (3) well or moderately differentiated adenocarcinoma; (4) tumor <2.0 cm [15].

Table 2. Japanese treatment guidelines [data taken from 3]

T	N			
	N0	N1	N2	N3
T1 (M)	IA EMR (wel or mod, ≤2 cm, ul (-)) MGA (else)	IB MGB (≤2 cm) D2 (>2 cm)	II D2	IV D3
T1 (SM)	IA MGA (wel or mod, ≤1.5 cm) MGB (else)	IB MGB (≤2 cm) D2 (>2 cm)	II D2	IV D3
T2	IB D2	II D2	IIIA D2	IV D3
T3	II D2	IIIA D2	IIIB D2 (D3)	IV D3
T4	IIIA D2 extended	IIIB D2 extended	IV D2 extended	IV D3 extended

Table 3. Type of gastrectomy [data taken from 3]

Gastrectomy	Area of resection	Dissection	Option
Modified A	<2/3	D1 + No.7 ¹	Vagus-preserving
Modified B	<2/3	D1+No.7, 8a, 9	Pylorus-preserving
Laparoscopic			
Standard	≥2/3	D2	
Extended	≥2/3	D2	D3
	Combined resection		

¹No. 7 nodes along the left gastric artery; No. 8a nodes along the common hepatic artery (antero-superior group), and No. 9 nodes around the celiac artery.

In case of lower third cancer, No. 8a nodes should be dissected. Standard gastrectomy includes proximal, distal or total gastrectomy associated with D2 according to the size and location of the tumor (Japanese Classification of Gastric Carcinoma issue by Japanese Gastric Cancer Association).

Conditions 2–4 are diagnosed by endoscopy and biopsy. The EMR is then performed and the resected specimen retrieved. When the histological examination confirms condition 1 for the specimen, the procedure is considered curative.

Mucosal cancer that does not meet this condition should be treated by MG A. MG A is also indicated for

Table 4. Treatment methods for stage IA [data taken from 3]

Depth of invasion	Histology	Size	Methods
Mucosa (M)	Differentiated	≤2 cm	EMR
Mucosa (M)	Else		MG A
Submucosa (SM)	Differentiated	≤1.5 cm	MG A
Submucosa (SM)	Else		MG B

the differentiated submucosal cancer <1.5 cm in diameter. Submucosal cancer that does not meet this condition should be treated by MG B.

Stage IB (T1N1). As shown in table 4, MG B or standard gastrectomy is indicated for stage IB cancer according to the T and N categories. If the T1N1 tumor is <2.0 cm in diameter, MG B is indicated, and the T1N1 tumor >2.1 cm or T2N0 tumor is treated by standard gastrectomy.

Treatment Details

Endoscopic Mucosal Resection

Endoscopic treatment mainly using laser therapy was primarily employed as a palliative treatment for patients with high operative risks or incurable disease [16]. Tada et al. [17] first described the technique of 'strip biopsy' in

1984 and developed it into a method for the cure of mucosal gastric cancer. The revolutionary point of this technique is that not only a polypoid but also a depressed mucosal lesion can be removed along with the surrounding normal mucosa, which provides sufficient material for histological confirmation of tumor cell infiltration.

After successful EMR, however, close follow-up of the patient by endoscopy is mandatory, because multifocal lesions, either synchronous or metachronous, are not uncommon in the stomach [18]. A second or third lesion will again be removed by EMR if it satisfies the above criteria.

EMR has already become an essential tool for treatment in Japan [19]. Large series of up to 400 EMRs in a single institution are presented at congresses [20]. Various techniques, such as endoscopic submucosal resection, are being tested for safer and wider resection and expansion of inclusion criteria [19, 21, 22]. Although no prospective study has been published in the English literature, a prospective, nationwide collection of EMR cases will be performed in the future, and the above criteria will no doubt undergo modifications.

D2 Gastrectomy for EGC

Gastrectomy with D2 lymphadenectomy has long been the standard treatment for gastric cancer in Japan as already mentioned. Recently, European surgeons have also advocated it as treatment of choice for EGC [23–25], because of excellent outcomes of retrospective series comparable to Japanese results. Although modified gastrectomies are described in the guidelines in Japan, gastrectomy with D2 dissection is considered reasonable for 'seemingly early gastric cancer', firstly because N2 nodes can be involved from submucosal EGC, though the incidence is low, and secondly because the diagnosis of EGC is not always accurate [26], leaving the possibility of the tumor being T2 or deeper.

Modified Gastrectomy for EGC

Various modified gastrectomies for EGC have been devised in Japan, aimed at preserving the function of the stomach. All these operations are employed after careful patient selection, again based on the guidelines defined by lymph node studies, so as not to decrease the survival rate. The published studies are classified as phase II or pilot, and the functional comparison with conventional counterparts is a retrospective one, with historical controls. Then, accuracy of a diagnosis of depth of invasion is most important to perform surgery with limited nodal dissection.

Total Gastrectomy without Splenectomy. For EGC in the proximal stomach, total or proximal gastrectomy is performed. According to the Japanese Classification of Gastric Carcinoma, D2 for proximal tumors includes dissection of the splenic hilar nodes. However, metastasis to this area from EGC is extremely rare [17, 27]. Even in T2 tumors, the splenic hilar metastasis is seldom seen unless the primary tumor is located on the greater curvature. Therefore, the spleen should be preserved in these tumors, especially in view of the additional morbidity associated with splenectomy.

Proximal Gastrectomy. At least for early gastric cancer, the benefit of a total gastrectomy with splenectomy has not been seen and is limited. Therefore, for EGC in the proximal third of the stomach, proximal gastrectomy is being tested in some institutions with or without preservation of the vagal nerves [27–29]. Proximal gastrectomy is currently indicated for EGC only when we can preserve at least half of the stomach to keep radicality of operation and capacity of the remnant stomach.

All regional nodes except for the splenic hilum nodes (No. 10) and distal splenic nodes (No. 11d) can be dissected as in the standard D2 operation, although the dissection of the lesser curvature nodes (No. 3) was incomplete at the distal part. An antireflux procedure such as jejunal interposition (physiological sphincter) and new gastric fundus formation is routinely added.

Proximal gastrectomy was prospectively evaluated in the one arm study in our institution and the survival data was almost identical to that after total gastrectomy, and was satisfactory [27]. The literature reported that improved post-operative absorption [30, 31] and body weight recovery is good as compared to total gastrectomy. Pylorus function is also preserved with this method by preserving vagus nerves including hepatic and pyloric branches, which is the same as pylorus-preserving gastrectomy. Reflux esophagitis may be a possible sequela.

Simple esophagogastrotomy produced a higher incidence of reflux esophagitis [32, 33], despite several modifications. Minimizing the incidence of esophagitis has been required for routine use of this gastrectomy. Recent efforts including the jejunal interposition method produced good results [27, 34].

Pylorus-Preserving Gastrectomy (PPG). PPG was originally applied for peptic ulcers [35] and has also been applied for early gastric cancer [36–40]. The distal two-thirds of the stomach are resected but a pyloric cuff of about 2 cm is preserved. A recent report showed the benefit of a longer cuff for gastric motility. Infrapyloric vessels are occasionally preserved to maintain the blood sup-

ply of a longer pyloric cuff. The result of infrapyloric node dissection preserving these vessels should be evaluated. Vagal nerves are identified and preserved to maintain pylorus function. Furthermore, preservation of the celiac branch of the posterior vagal trunk has also been done in combination with a PPG by several Japanese surgeons.

All regional nodes, except suprapyloric nodes (No. 5), can be dissected as in the standard D2 operation. PPG is currently indicated for EGC in the middle stomach from which nodal metastasis to No. 5 is extremely uncommon [39]. Since a pyloric cuff is retained, PPG is not desirable for lesions located in the distal antrum.

The literature reports that the incidence of post-gastrectomy dumping syndrome, bile regurgitation, and gall bladder stone formation is decreased, and body weight recovery is good as compared to Billroth-I reconstruction [37–39]. However, these benefits have not been proven by a prospective randomized trial. Emptying disturbance may be a possible sequela.

Segmental Gastrectomy. A gastrectomy with a more limited resection of the stomach body is the segmental gastrectomy. This is indicated for mucosal tumor in the mid-gastric body. A segment of the stomach containing the tumor is resected with [41] or without preservation of the Latarjet branch of the vagal nerve [42]. The hepatic and pyloric branches are preserved. Lymphadenectomy is limited to the perigastric regions close to the resected segment, but for lesser curve tumors the nodes along the left gastric artery can also be dissected. Functional results are generally satisfactory.

Wedge Resection. An attempt at local wedge resection with regional lymphadenectomy was reported [43]. Several reports showed the possibilities for developing sentinel node-guided surgery for gastric cancer [44, 45].

Laparoscopic Surgery. Laparoscopic surgery for gastric cancer is underway in some institutions. Laparoscopy-assisted gastrectomy with nodal dissection was performed and was being evaluated in some reports. The evaluation of survival should be very strict, since the survival rate of open surgery operation is quite good. The literature reported faster recovery, less pain, and shorter hospital stay. However, the benefit of quality of life might be only better cosmesis. A multicenter randomized controlled trial will be needed in the near future [46].

Laparoscopic local resection of the stomach: Two types of laparoscopic local resection, laparoscopic wedge resection by the lesion-lifting method [47] and intragastric mucosal resection [48], have been performed in Japan for early gastric cancer. Since the target of laparoscopic local

resection is early gastric cancer without lymph node metastasis, expansion of inclusion criteria of endoscopic treatment may cause a decrease in the number of patients treated by this method. The lesion-lifting method is carried out by retracting the metal rod, piercing the lesion through the abdominal and gastric wall, and wedge resection is carried out with endoscopic staplers [47]. Intragastric mucosal resection is performed through trocars, which are placed in the gastric lumen [48].

A survey by the Japanese Society for Endoscopic Surgery [49] showed low perioperative morbidity and zero mortality, and possibly shorter hospital stay. There is a report of local recurrence [47].

Laparoscopy-assisted distal gastrectomy: Laparoscopy-assisted Billroth-I gastrectomy for early gastric cancer was first performed in 1991 by Kitano et al. [50], and the Billroth-II gastrectomy was reported in 1992 by Goh and Kum [51]. Laparoscopy-assisted gastrectomy is still in the developmental phase around the world, while the number of patients with early gastric cancer treated by LADG has increased significantly in Japan.

The guidelines described LADG as one of the optional treatments in MG. Even D2 gastrectomy can be attempted safely at the proper time [52]. LADG is still performed in only a limited number of hospitals in Japan.

The survey of the Japan Society for Endoscopic Surgery showed low morbidity-mortality rates of LADG, similar to open distal gastrectomy [49]. A small randomized study showed some advantages including less pain and less impaired pulmonary function after LADG to open distal gastrectomy [53]. A multicenter randomized controlled trial is needed to confirm the clinical advantages of LADG including medical expenses.

Investigational Treatment for Non-Early Cancer

Superextended Para-Aortic Lymphadenectomy

Since 1980, more extended lymphadenectomy than D2 procedures have been practiced in many Japanese specialized centers. The literature reported that 20–30% of patients with non-early gastric cancer had microscopic metastasis present in the para-aortic nodes [54–57]. The 5-year survival for these patients has reached 14–30% after superextended systematic dissection.

In addition to D2 lymphadenectomy, lymph nodes around the upper abdominal aorta were dissected, primarily for ultimate local tumor control. However, this

dissection may not only increase operative morbidity but also may affect the function of other abdominal organs. To evaluate the survival benefit and operative complications of D2 gastrectomy and extended para-aortic dissection in gastric cancer surgery, a multi-institutional randomized controlled trial was conducted on behalf of the Japan Clinical Oncology Group. Although the morbidity for the superextended surgery group was slightly higher, the hospital mortality rate was as low as 0.8% in each group [58].

Total Gastrectomy with Spleen Preservation

Japanese retrospective studies revealed that 15–20% of patients with non-early carcinoma in the proximal stomach have nodal metastasis in the splenic hilum [59] and the 5-year survival rate after dissection is 20–25% [60, 61], and therefore pancreas-preserving splenectomy [62] is part of the standard operation in specialized centers. However, even in Japan, there are several studies

that report on the lack of benefit of splenectomy [63–66]. Recent European clinical trials of gastrectomy showed that splenectomy is an important risk factor for post-operative morbidity and mortality [67, 68].

To evaluate the role of splenectomy in potentially curative total gastrectomy for proximal gastric carcinoma in terms of survival benefit and post-operative morbidity, a multi-institutional randomized controlled trial was conducted on behalf of the Japan Clinical Oncology Group [69]. Since metastasis in the splenic hilum is frequently found for the tumor invading the greater curvature, the tumor invading greater curvature will be excluded [70].

Conclusion

The latest developments in surgery for gastric cancer could be described as wide variations of surgical treatment according to the stage of disease based on new procedures. Further evaluation is required to prove the superiority to standard techniques.

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Short communication

Increasing body mass index in Japanese patients with gastric cancer

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Abstract

We studied the body mass index (BMI) of 986 patients who underwent potentially curative gastrectomy for gastric cancer at the National Cancer Center Hospital, Tokyo, in 1971, 1981, 1991, and 2001. The median BMI increased from 20.8 kg/m² in 1971 to 22.6 kg/m² in 2001 ($P < 0.01$). The increase was significant in both early and advanced gastric cancers, and in males, but not in females. The proportion of overweight patients (BMI ≥ 25.0 kg/m²) increased from 9.2% in 1971 to 24.0% in 2001. Obese patients (BMI ≥ 30.0 kg/m²) were rare. In conclusion, surgeons at the National Cancer Center Hospital, Tokyo, are increasingly having to operate on fat patients, but obese patients are still uncommon compared to the West.

Key words Body mass index · Gastric cancer · Gastrectomy · Operative morbidity

Introduction

Operative morbidity and mortality rates for gastric cancer in Asian countries have been reported to be better than those in the West [1]. Possible explanations for this are that Western gastric cancer patients are older and fatter, and more frequently have significant comorbidities compared with their Asian counterparts. While it is true that Japanese surgeons have developed and practiced surgical techniques in thin and fit patients, there is a consensus that Japanese patients are becoming fatter and sometimes require special caution or even technical modifications to the D2 lymphadenectomy and postoperative management. In order to validate this impression, we examined the changes in body mass index (BMI) of Japanese patients over the past three decades.

Offprint requests to: T. Sano

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Subjects and methods

The National Cancer Center Hospital, Tokyo, is a specialized referral center, established in 1963, where more than 10 000 gastric cancer patients have undergone gastrectomy. The vast majority of patients are residents of the metropolitan area. We reviewed the records of all of the patients who underwent potentially curative gastrectomy (R0) at our hospital in the years 1971, 1981, 1991, and 2001 — a total of 986 patients. We excluded patients with noncurative operations, as these patients may have had considerable weight changes preoperatively due to gastrointestinal obstruction, cachexia, ascites, or other conditions related to advanced malignancy. The height and weight data were collected from the preoperative summary charts or anesthetic records. The disease was categorized as either early or advanced according to the histological depth of tumor invasion (pT1 vs pT2/3/4).

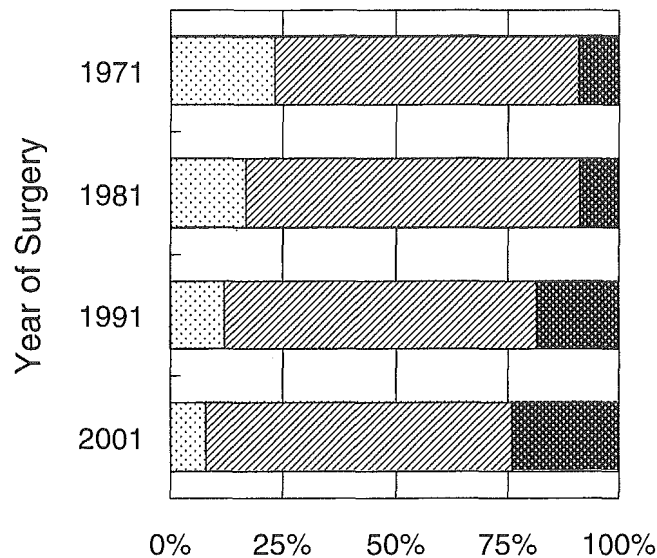
The BMI was calculated as the weight in kilograms divided by the square of the height in meters (kg/m²), and was categorized according to the WHO cutoff points [2], i.e., underweight, less than 18.5 kg/m²; normal, from 18.5 to 24.9 kg/m²; and overweight, 25.0 kg/m² or more. The trends of BMI and patients' age were statistically examined using Dunn's test for multiple comparisons setting the values of 1971 as the reference.

Results and discussion

The patient demographics and BMIs are shown in Table 1. The male/female ratio was almost constant, while the median patient age in 2001 was significantly higher than that in the other three periods in both males and females. The proportion of early gastric cancer in potentially curative cases steadily increased, from 41.8% in 1971 to 61.8% in 2001.

Table 1. Patient demographics and body mass indices

Year of surgery	1971	1981	1991	2001
Number of patients	153	184	232	417
Age in years; median (range)	58 (19–80)	57.5 (27–83)	59 (31–87)	62 (26–87)
Sex ratio (M/F)	1.5	2.0	2.1	1.8
Early cancer (%)	41.8	53.8	56.6	61.8
BMI; median (range)	20.8 (14.6–31.2)	20.9 (12.0–34.2)	21.8 (14.8–35.3)	22.6 (15.0–31.8)
Male	20.5	21.0	22.8	23.0
Female	21.1	20.6	20.7	21.9

**Fig. 1.** Trend of body mass index (BMI) distribution. Dotted bars, BMI < 18.5; gray hatched bars, normal; dark gray bars, BMI > 25

The median BMI increased from 20.8 kg/m² in 1971 to 22.6 kg/m² in 2001 ($P < 0.01$). The increase was statistically significant in males but not in females. The median BMI in patients with early cancer (22.1 kg/m²) was significantly higher than that in patients with advanced cancers (21.5 kg/m²; Mann-Whitney U -test; $P = 0.013$), possibly reflecting disease-related weight loss in the advanced group. In both early and advanced cancers, the patients' median BMI increased significantly from the first two periods to the last two periods.

In 1971, only 9.2% of patients were overweight, while 22.9% were underweight. In 2001, in contrast, 24.3% of patients were overweight, while only 7.9% were underweight (Fig. 1). Obese patients (BMI ≥ 30.0 kg/m²) were rare at all times (0.7% in 1971 and 1.4% in 2001). These results confirm that surgeons in our institution are operating, with increasing frequency, on older and fatter patients with gastric cancer, especially in the past 20 years.

The trend seems to reflect the changes in age and BMI of the Japanese population. The median age of the

total Japanese population has increased rapidly, from 29.1 years in 1970 to 41.4 years in 2000 [3]. The National Nutrition Survey showed that, in the 20-year period from 1976 to 1995, the BMIs of Japanese men in all age groups, and that of elderly women, increased, while that in younger women, especially in metropolitan areas, decreased [4]. In addition, the expansion of indications for gastrectomy in old and obese patients in recent years may have facilitated the trend in this study, i.e., we are now frequently operating on old or overweight patients, for whom gastrectomy might not have been performed 30 years ago.

BMI does not necessarily measure the body fat volume. Interestingly, the relationship between BMI and body fat varies considerably among ethnic groups, and Asian people tend to have more fat for a given BMI than Caucasians [5]; some researchers have proposed 23.0 kg/m² instead of 25.0 kg/m² as a BMI cutoff point of overweight for Asians [6]. If we apply this criterion, 43.9% of our patients in 2001 were overweight compared with 24.2% in 1971.

Nevertheless, the majority of our patients are still normal or underweight according to the WHO criteria and, as compared to Western series, we have only limited occasions to operate on obese patients (BMI ≥ 30.0 kg/m²). Barry et al. [7], in the United Kingdom, reported that nearly half of their patients who had undergone potentially curative gastrectomy were overweight, and 7% had a BMI of more than 30 kg/m². Gretschel et al. [8], in Germany, reported that 58.8% of their 199 patients with total gastrectomy had a BMI of more than 25 kg/m² and 18.1% had a BMI of more than 30 kg/m². It is interesting that these two European groups maintain that BMI does not affect operative morbidity or survival after D2 gastrectomy, whereas Japanese surgeons report high BMI as an important risk factor for morbidity and recurrence [9,10]. This may suggest that D2 gastrectomy in obese patients requires some different surgical techniques that are not quite familiar to Japanese surgeons.

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Original article

Pancreaticoduodenectomy for advanced gastric cancer

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Abstract

Background. Although pancreaticoduodenectomy has been rarely performed for gastric cancer because of frequent morbidity and mortality, some favorable results after this procedure have been reported recently. Our objective was to present our data that might aid in the selection of patients to undergo this procedure.

Methods. Between 1970 and 2001, 23 patients who had pancreaticoduodenectomy for gastric cancer with tumor invading the pancreatic head were identified, and they were the subjects of this study. Clinical, operative, and pathological data, and morbidity and mortality rates were collected and analyzed. Survival outcome was also calculated and analyzed. **Results.** Five patients underwent this procedure for disease in the gastric remnant, 18 undergoing the procedure for primary tumors. Median operating time was 8 h (range, 6–13 h), and median blood loss was 1600 ml (range, 700–16000 ml). Regarding extent of gastrectomy, all patients with primary cancer ($n = 18$) underwent a distal gastrectomy and patients with disease in the gastric remnant ($n = 5$) underwent a completion gastrectomy. Incurable factors, including paraaortic lymph node metastasis, positive lavage cytology, or peritoneal dissemination were found in 8 patients. The postoperative morbidity rate was 73.9%; however, operation-related death was zero. The overall 5-year survival rate was 34.3%. The 5-year survival rate of the 8 patients with incurable factors was 0%, while that of the 15 patients without incurable factors was 47.4%.

Conclusion. If an R0 resection can be achieved by pancreaticoduodenectomy, this procedure should be performed for patients with tumor invading the pancreatic head. Patients with incurable factors should not be considered for pancreaticoduodenectomy.

Key words Gastric cancer · Pancreaticoduodenectomy · Combined resection of adjacent organs

Introduction

Complete removal of all evaluable disease, i.e., R0 resection, is vital to a successful outcome in gastric cancer treatment. Extended surgery is occasionally required for advanced gastric cancer with infiltration of adjacent organs to achieve complete tumor clearance. For locally advanced gastric cancer with infiltration of the pancreatic head or duodenum, pancreaticoduodenectomy (PD) is required. However, this procedure has been rarely performed because of substantial morbidity and mortality [1]. Prior to the 1990s, few reports regarding PD for gastric cancer had been published [2]. Only Kishimoto et al. [3] and Scott et al. [4] referred to a long survivor after this procedure in their reports about gastrectomy with combined resection. Recently, with current advances in operative techniques and in nutritional support, some favorable results of the patients undergoing this procedure have been reported [5–7]. However, only a few reports with a large number of cases have been published so far. In the current study, we present our data that might aid in the selection of patients to consider who should undergo this procedure.

Subjects and methods

A retrospective review of our prospective database, spanning from 1970 to 2001 and containing 9349 patients, identified 195 (2.1%) who had locally advanced cancer with macroscopically suspected infiltration of the pancreatic head. We included patients with pancreatic head invasion from metastatic lymph nodes, and excluded type 4, linitis plastica cancer. Of the 195 patients identified, 23 underwent PD with presumed curative intent, and they were the subjects of this study.

In these 23 patients, clinical data, including age, sex, symptoms, and primary tumor or tumor in the gastric remnant, were collected and analyzed, using the appro-

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Table 1. Patients undergoing pancreaticoduodenectomy

	Disease	Stage	pT	pN	P	CY	Adjuvant Chemo.	Combined resection	Recurrence	FUT (months)	Status	
1	63/F	Primary	IV	4	1	0	0	—	Liver	N	13	DOD
2	42/M	Primary	IIIB	3	1	0	ND	—	—	—	157	DOC
3	64/M	Primary	IIIB	2	2	0	0	—	—	—	182	NED
4	67/M	Primary	IV	3	2	0	ND	—	—	—	87	DOC
5	76/M	Primary	IV	4	3	0	0	—	Colon	Unclear	4	DOD
6	67/M	Primary	IIIB	4	0	0	0	+	—	—	26	DOC
7	65/M	Primary	IV	4	3	0	1	+	—	N	6	DOD
8	74/F	Primary	IV	2	3	0	0	—	Colon	H	34	AWD
9	70/M	Primary	IV	4	2	0	0	—	Colon	N, H	14	DOD
10	62/M	Primary	II	2	0	0	0	—	Colon	—	52	NED
11	65/M	Primary	IV	4	2	0	0	—	—	N	36	AWD
12	65/F	Primary	IV	4	2	0	0	—	—	N, H, spleen	12	DOD
13	58/M	Primary	IV	4	3	0	0	—	Colon	N	6	DOD
14	60/M	Primary	IIIB	2	2	0	0	—	Colon	—	12	NED
15	64/M	Primary	IV	4	2	1	1	—	Colon	Unclear	19	DOD
16	51/F	Primary	IIIB	2	2	0	0	—	—	H	11	DOD
17	61/M	Primary	IV	4	1	0	ND	—	—	H	4	DOD
18	70/M	Primary	IV	4	3	0	1	—	—	N, lung	4	DOD
19	60/M	Remnant	IV	4	2	1	1	—	—	N	13	DOD
20	57/M	Remnant	IV	4	1	0	0	—	Liver, colon	N, H	26	DOD
21	64/F	Remnant	IIIB	4	0	0	0	—	—	N	64	DOD
22	47/M	Remnant	IV	4	3	0	0	—	—	N	17	DOD
23	60/M	Remnant	IIIB	4	0	0	0	—	Colon	P	4	AWD

Primary, Primary tumor; remnant, tumor of the gastric remnant; P, peritoneal dissemination; CY, lavage cytology; ND, not done; N, lymph node; H, liver; FUT, follow-up time; NED, no evidence of disease; AWD, alive with disease; DOC, dead of other cause; DOD, dead of disease; unclear, site of recurrence unclear

appropriate nonparametric tests. Operative data, including operating time, blood loss, hospital stay, extent of gastrectomy, extent of lymphadenectomy, and combined resection with PD, were also evaluated. Pathological data, including pT, pN stage, site of tumor, and incurable factors, such as paraaortic lymph node metastasis (pN3), peritoneal dissemination, and positive lavage cytology, were analyzed according to the Japanese classification. Perioperative morbidity and mortality were also investigated.

The survival data of the 195 patients with tumors invading the pancreatic head, including the 23 PD patients, were calculated by the Kaplan-Meier method and analyzed by the log-rank method.

Results

Demographics

Of the 195 patients with tumors invading the pancreatic head, 151 (77%) underwent resection, and the remaining 44 underwent only an exploration or a bypass surgery. In 68 patients, an R0 resection was carried out. In 45 patients with R0 resections, a lesser pancreatic resection (not PD) was performed because of a slight degree of tumor infiltration. The remaining 23 patients (12%) underwent PD (Fig. 1).

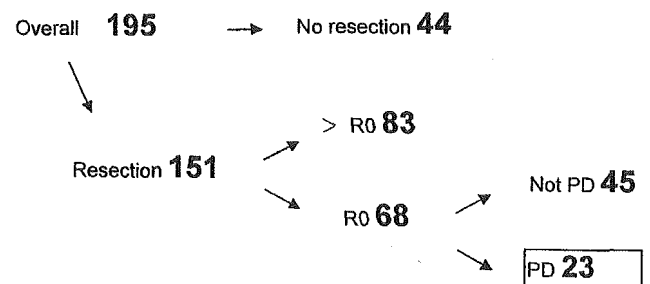


Fig. 1. Patients with tumors invading the pancreatic head. *No resection*, patients undergoing only exploration or bypass operation. *Not PD*, patients undergoing R0 resection, but with a lesser pancreatic resection than pancreaticoduodenectomy (PD)

In the 23 patients undergoing PD, the median age at the time of resection was 64 years (range, 42–76 years), with a male-to-female ratio of 18:5 (Table 1). Twenty-one patients (91.3%) were symptomatic, most commonly with abdominal pain ($n = 13$) and symptoms due to obstruction, including fullness and vomiting ($n = 11$).

Eighteen patients underwent the PD procedure for primary cancer and 5 for gastric remnant cancer following previous Billroth I gastrectomy. Of the 5 patients with gastric remnant cancer, 4 had undergone distal partial gastrectomy for gastric cancer. Two of these

patients had early cancers; and the other 2 had advanced disease. The disease-free intervals were 1.5 and 6 years for those with advanced cancers and 8 and 10 years in those with early cancers. The fifth patient had had a partial gastrectomy for a benign gastric ulcer 30 years previously.

Operative data

The median operating time for PD was 8 h (range, 6–13 h), with a blood loss of 1600 ml (700–16000 ml). The median length of postoperative hospital stay was 37 days (range, 25–92 days). Regarding extent of gastrectomy, patients with primary cancer ($n = 18$) underwent a distal gastrectomy and those with gastric remnant cancer ($n = 5$) underwent a completion gastrectomy. As to extent of lymph node dissection, 14 patients underwent D2 lymphadenectomy and 9 underwent D3. In 9 patients, a combined resection of the colon was performed because of direct infiltration of the mesocolon (Table 1). Two patients underwent a partial hepatectomy because of a direct invasion of the liver. Modified Child's method was selected for a reconstruction for all patients. Two patients received postoperative adjuvant chemotherapy of 5-fluoruracil (5-FU) after surgery.

Pathology

Resection specimens from all patients revealed adenocarcinoma of gastric origin. In 7 patients, infiltration of the pancreatic head could not be confirmed histopathologically. Regarding site of tumor, 18 primary tumors involved the antrum, and 11 of these tumors extended into the duodenum.

Incurable factors, including pN3, peritoneal dissemination, and positive lavage cytology were found in eight patients (Table 1). No patient in this series had a visceral metastasis. In 6 patients, pN3 was found. These patients had been considered as negative for pN3 intraoperatively, but the finding was changed to positive by pathological examination postoperatively. Of these 6 patients, 2 also had positive lavage cytology. Two patients had positive lavage cytology and peritoneal dissemination synchronously; the peritoneal dissemination was a single nodule that was removed easily at operation.

Seventeen patients developed recurrences. The most common recurrence sites were nodal, in 11 patients, followed by liver, in 6; peritoneum in 1; lung in 1, spleen in 1, and unclear, in 2.

Morbidity and mortality

Postoperative complications were seen in 17 patients (73.9%; Table 2). Pancreatic fistula was the most

Table 2. Postoperative morbidity

	<i>n</i>
Postoperative morbidity	17 (73.9%)
Pancreatic fistula	10 (43.5%)
Abdominal abscess	3 (13.0%)
Anastomotic or jejunal stenosis	3 (13.0%)
Cholangitic infection	3 (13.0%)
Anastomotic leakage	2 (8.7%)

Table 3. Survival of patients with tumor invading the pancreatic head

	<i>n</i>	Median survival (months)	5-Year survival rate (%)
Overall	195	10	13.6
No resection	44	7	0
Resection	151	12	17.7
>R0	83	8	7.9
R0	68	21	29.3
Not PD	45	22	28.1
PD	23	17	34.3

No resection, Patients who underwent only exploration or bypass operation; not PD, patients who underwent R0 resection but received a lesser pancreatic resection than PD

common. All patients who developed this complication recovered, after receiving drainage and continuous irrigation, using double-lumen drainage tubes. No operation-related death occurred in this series.

Regarding the long-term postoperative morbidity, body weight at 12 months was maintained within 10% of the preoperative weight in all patients who lived for more than 1 year. Serum albumin levels were not decreased. However, two patients who underwent PD with completion gastrectomy required total parenteral nutrition (TPN) at home, for 1 and 3 years, respectively, after discharge from hospital, because of malnutrition. Postoperative pancreatic endocrine function was adequate in all patients, but three patients required pancreatic exocrine enzyme support postoperatively.

Survival

In the 195 patients with tumors invading the pancreatic head, the 5-year survival rate was 13.6%. Of these 195 patients, the 68 patients who underwent an R0 resection showed a better survival outcome, with a 5-year survival of 29.3%. In patients who had R0 resections, there was no significant difference in survival between patients who underwent PD and those not receiving PD (Table 3).

In the 23 PD patients, the median follow-up time was 13 months (range, 4–182 months). The status of the

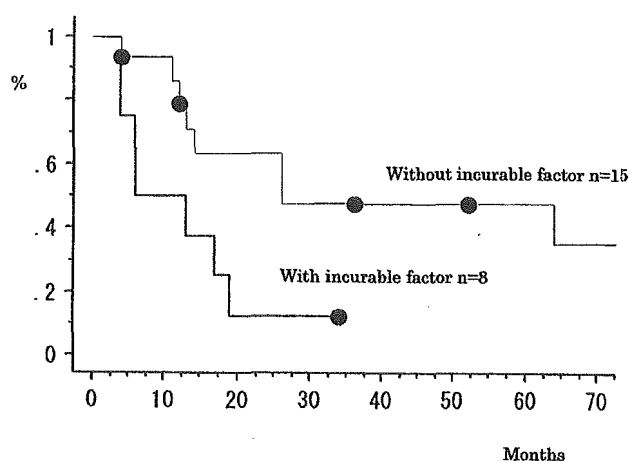


Fig. 2. Survival curves of patients undergoing pancreaticoduodenectomy (PD). The overall 5-year survival rate and the median survival of the 8 patients with incurable factors were 0% and 6 months, respectively, and these values in the 15 patients without incurable factors were 47.4% and 26 months ($P = 0.035$)

patients was as follows: no evidence of disease, 3; alive with disease, 3; dead of other causes, 3; and dead of disease, 14. The overall 5-year survival rate was 34.3%. The 5-year survival rate and the median survival of the 8 patients with incurable factors (pN3, positive lavage cytology, and peritoneal dissemination) were 0% and 6 months respectively, while these values in the 15 patients without incurable factors were 47.4% and 26 months (Fig. 2). Four patients have survived for more than 5 years.

Discussion

In our data, of 195 patients with tumors invading the pancreatic head, 23 (12%) underwent PD. This procedure has been rarely performed because of high morbidity and mortality rates. Prior to the 1990s, there had been only a few reports about this procedure [2–4]. Recently, with current advances in operative techniques, nutritional support, and antibiotics, some favorable results have been reported [5–11]. Ohashi [9] reported a large number of patients (145) undergoing this procedure. The 5-year survival rate of patients undergoing PD in that study was 6%, and it was approximately equal to the result for patients undergoing more than R0 resection in our data. Thus, it is inferred that Ohashi's subjects included patients with far-advanced tumors that could not be removed by this procedure. With proper indications, PD could account for 10% of surgeries for tumors invading the pancreatic head, and the number of patients who would have this procedure would be around 30, even at a large institution.

In our study, tumor infiltration of the pancreatic head could not be confirmed in 7 patients (30%) histopathologically. Such patients, theoretically, could have avoided this procedure; however, inconsistency between macroscopic and microscopic findings of infiltration has been reported to be 30%–50%, often because of inflammatory reactions surrounding the tumor [8,12]. Even if the latest diagnostic modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasound (EUS) are used, it is very difficult to distinguish between inflammatory reactions and tumor infiltration before operation. Intraoperative ultrasound could be more helpful than these modalities, but it was not used in any patients in the present series. It seems that inconsistency at a level of around 30% is unavoidable at present.

Morbidity after PD was in Ohashi's study [9] 51.6% and 37.8% in that of Shchepotin et al. [11]. Regarding mortality, these authors reported rates of 6.3%, and 10.8%, respectively. Buchholtz et al. [1] recommended that PD should not be performed for gastric cancer because of an unacceptable risk, with no greater degree of palliation. The morbidity rate in our series (73.9%) was higher than the rates in these previous reports [9,11], to be sure. However, the operative mortality rate was 0% and all surviving patients could resume a regular life. Pancreatic fistula was the most common complication in this series. This is critical, as it may lead to intraabdominal abscess and rupture of arterial aneurysm. This complication was diagnosed by the detection of infectious drain discharge with a high concentration of amylase ($>10000\text{IU/l}$). For the early detection of pancreatic fistula, the concentration of amylase in the drain discharge is checked routinely after PD. When pancreatic fistula has developed, continuous drainage is performed, initially. If there is infection, continuous irrigation, using double-lumen drainage tubes, is done. To achieve better control of this complication, the medical staff including not only the surgeon but also nursing staff, have to be skilled at careful drain management. Therefore, this procedure should be performed only at institutions where PD for pancreatic cancer is frequently performed.

No patient in our series developed diabetes mellitus after PD, and only three required pancreatic exocrine enzyme support postoperatively. However, after PD with completion gastrectomy, two patients required TPN at home for a long period because of malnutrition. Total gastrectomy combined with PD should be considered very carefully, as nutritional problems may be severe.

The overall prognosis of patients with tumors invading the pancreatic head was poor; however the 5-year survival rate of patients undergoing R0 resection was about 30% in this series. In the patients with R0 resec-

tions, there was no significant difference in survival between those requiring PD and those not requiring PD. Thus, to achieve R0 resection is an important objective, irrespective of whether or not PD is performed.

Ajisaka et al. [5] and Shchepotin et al. [11] reported that the 5-year survival rates of patients undergoing PD were 35% and 17%, respectively. In a study of 26 patients undergoing PD combined with right hemicolectomy, Yonemura et al. [10] reported that the 5-year survival rate of 13 patients with tumors infiltrating the pancreatic head was 55%. In our series, the 5-year survival rate for such patients was 34.3%. In PD patients without incurable factors, the 5-year survival rate was higher, at 47%, and 4 patients have survived for more than 5 years. Careful application of the PD procedure can achieve improved survival outcome. Kodama et al. [13] and Habu et al. [14] mentioned that a small amount of peritoneal dissemination and limited liver metastasis, respectively, were not contraindications for PD. However, most patients in the present series who had incurable factors died of the disease soon after operation. Incurable factors, such as pN3, positive lavage cytology, peritoneal dissemination, and visceral metastasis, should be regarded as a contraindication for PD.

In summary, the results after PD for patients with advanced gastric cancer with tumors invading the pancreatic head were acceptable from the aspects of morbidity, mortality, and survival benefit. If an R0 resection can be achieved by PD in such patients, this procedure should be performed. Patients with incurable factors should not be considered for PD. The combination of PD and total gastrectomy should be considered with caution.

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Delayed Gastric Emptying after Distal Gastrectomy for Gastric Cancer

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ABSTRACT

Background/Aims: Gastric surgery may potentiate delayed gastric emptying. The aims of the study were to determine the frequency and causes of delayed gastric emptying in patients who had undergone distal gastrectomy for gastric carcinoma and to assess which factors predispose to its development.

Methodology: 209 patients, who had undergone gastrectomy, were evaluated.

Results: Delayed gastric emptying occurred in 4.3% of patients receiving a Billroth-I, and 15.5% of patients receiving a Roux-Y reconstruction ($p=0.01$). The patients who had these consecutive symp-

toms following Roux-Y operation were all clinically diagnosed as having Roux stasis syndrome. The delayed gastric emptying after Roux-Y operation was more frequent in patients receiving extensive lymph node dissection than those receiving conventional dissection ($p<0.05$). The symptoms spontaneously subsided, and postoperative body weight loss was not significant.

Conclusions: In spite of the strong association between delayed gastric emptying and the Roux-Y procedure, it enables a relatively early return to oral intake.

KEY WORDS:

Gastric cancer; Reconstruction; Stomach; Roux-en-Y; Stasis; Gastrointestinal surgery

INTRODUCTION

Roux-Y reconstruction of gastrojejunal continuity is an established means of draining the gastric remnant after distal gastrectomy. The main advantage of the Roux-Y operation is that it prevents bile and pancreatic juice from reaching the gastric mucosa, but the gastrojejunostomy may cause the delayed gastric emptying of both solids and liquids, and delayed gastric emptying is part of the so-called Roux-en-Y stasis (Roux stasis) syndrome. This syndrome was described by Mathias *et al.* (1) in 1985, and it was diagnosed based on clinical criteria, which included epigastric fullness, epigastric pain, nausea, and vomiting of food. In the more severe form of the syndrome, weight loss and gastric bezoars may develop. The prevalence of the syndrome has ranged from 10% to 30% (2,3), but the factors leading to its development are not well known. Roux-Y reconstructions have recently been frequently used after gastrectomy for gastric malignant disease, and thus the incidence of delayed gastric emptying has been tending to increase. Once it occurs, patient's QOL is reduced and the hospital stay is prolonged.

The aims of the present study were to determine the frequency of the delayed gastric emptying retrospectively, including the Roux stasis syndrome, in patients who had undergone distal gastrectomy for gastric malignant disease and to identify predisposing factors.

METHODOLOGY

A total of 209 adult patients (134 men and 75 women) with gastric adenocarcinoma underwent dis-

tal gastrectomy during a 3-year period from 1999 through 2001. Mean patient age was 63 ± 12 years (range: 29 to 85 years). According to the 13th edition of the Japanese classification of gastric carcinoma (4), 129 patients (61%) had stage I disease, 21 (10%) had stage II disease, 29 (14%) had stage III disease, and 28 (13%) had stage IV disease. Billroth-I reconstruction was performed in 116 patients (56%), Billroth-II reconstruction in 9 patients (4%), and Roux-en-Y reconstruction after gastrectomy in 84 patients (40%). Fourteen patients were excluded because of major surgical postoperative complications (anastomotic leakage; 4, abdominal abscess; 6, pancreatic fistula; 2, severe pancreatitis, and ileus; 2). Among 209 patients, 18 were diagnosed with delayed gastric emptying based on the criterion that postoperative oral feeding was prohibited because of postprandial pain, nausea, or vomiting and the postoperative hospital stay was more than 25 days. Abdominal X-ray, upper GI series, and endoscopic examinations were performed to rule out other causes that might produce similar clinical symptoms, such as remnant gastritis, anastomotic stricture, and intestinal obstruction.

Endotracheal anesthesia and a standard midline laparotomy incision were used for all patients in our institution. The gastroduodenostomy and gastrojejunostomy were performed end-to-end by the Albert-Lembert suture method. The jejunal anastomosis was placed 20cm distal to the gastrojejunal anastomosis in the Roux-en-Y reconstruction and was performed end-to-side by the Albert-Lembert suture method. Main trunk vagal nerve entering the celiac axis was preserved in 28 patients (13%), and vagotomy was per-

gastric carcinoma (4), and 7 (54%) had stage II, III, and IV disease. D0 or D1 lymphadenectomy was performed in 2 patients (15%), D2 lymphadenectomy in 6 patients (38%), and D3 lymph node dissection in 6 patients (46%). The operation time was 285±74 minutes, and the operative blood loss was 517±386mL (Table 3). Delayed gastric emptying prolonged the postoperative hospital stay to 42.5±11.8 days. Oral feeding was stopped because of obstructive symptoms on 9.9±2.8 POD (Table 2), and restarted on 26.0±9.5 POD. Upper gastrointestinal series (performed in 9 cases), endoscopy (performed in 8 cases), or both showed that 6 patients had jejunal-mucosal edema at the anastomosis, and 3 of the 13 patients who had the delayed gastric emptying after a Roux-Y operation had ulceration on the proximal side of the anastomosis (Table 2). Moreover, no patients had bile reflux in the stomach remnant. Among the 5 patients who had delayed gastric emptying following the Billroth-I operation, postoperative endoscopy (performed in 3 patients) showed that 3 patients had anastomotic edema and none had anastomotic ulceration (Table 2). All 13 patients after Roux-Y gastrectomy were able to restart oral feeding by 46 POD, and they were discharged from hospital without their symptoms. They did not have significant postoperative body weight loss a month after discharge, compared with the group without delayed gastric emptying following a Roux-en-Y operation (Table 3).

The analysis to identify factors predisposing to delayed gastric emptying after Roux-en-Y reconstruction revealed that delayed gastric emptying was more common in the D3 lymph node dissection group than in the D0-2 dissection group ($p=0.004$) by univariate and multivariate analysis (Tables 3 and 4). Patient gender, age, stage, truncal vagotomy by sectioning the main nerves entering the celiac axis, operation time, intraoperative blood loss, and preoperative status were not significantly associated with the development of delayed gastric emptying. The postoperative hospital stay of the patients with delayed gastric emptying was much longer than that of the patients who did not have delayed emptying (Table 3). Moreover, when the 3 cases with anastomotic ulceration were excluded from the 13 cases with delayed gastric emptying after Roux-en-Y reconstruction, the remaining 10 patients were considered to have developed "Roux stasis syndrome". Comparison of these 10 patients with the other 71 cases revealed that postoperative delayed emptying was also more common in the D3 lymph node dissection group than in the D0-2 dissection group ($p=0.027$).

DISCUSSION

Gastric surgery may potentiate or induce delayed gastric emptying and result in chronic gastroparesis (6). Since the changes in gastric emptying following the various forms of vagotomy, drainage procedures, gastric resection, and the several methods of gastrointestinal reconstruction have been discussed previously, further discussion is unnecessary other than to emphasize the increased postoperative risk of delayed

TABLE 3 Characteristics of Patients with Delayed Gastric Emptying after Distal Gastrectomy with Roux-en-Y Reconstruction

	Delayed gastric emptying (n=13)	No delayed gastric emptying (n=71)
Sex (male/female)	8/5	50/21
Age (years)	61±12	63±11
Stage (I/II-IV)	6/7	26/45
Operation time (min)	285±74	268±67
Operative blood loss (mL)	517±386	510±356
Truncal vagotomy (-/+ #)	2/11	11/60
Lymph node dissection (D0-2/D3)	7/6*	62/9
Diabetes	2	5
Preoperative pyloric stenosis	0	3
Postoperatively hospital stay (days)	42.5±11.8**	19.9±5.3
Body weight loss*** (kg)	7.3±4.2	5.6±2.3

* $p=0.004$; ** $p<0.05$, compared to "No delayed gastric emptying"; *** Body weight loss between before the operation and one month after discharge; #Vagotomy -: gastrectomy without truncal vagotomy; vagotomy +: gastrectomy with truncal vagotomy.

TABLE 4 Delayed Gastric Emptying Factors after Roux-en-Y Gastrectomy on Multivariate Analysis

Parameters	P value	Hazard ratio	95% Confidence interval
Stage (I vs. II-IV)	0.051	9.60	0.989-93.183
Vagotomy (- vs. +)	0.688	0.68	0.105-4.412
Lymph node dissection (D0-2 vs. 3)	0.004	0.03	0.002-0.313
Diabetes (- vs. +)**	0.403	2.5	0.292-21.403

P values were calculated using a Cox hazard model; *Vagotomy -: gastrectomy without truncal vagotomy; vagotomy +: gastrectomy with truncal vagotomy; **Diabetes -: had not diabetes; diabetes +: had diabetes.

gastric emptying in predisposed persons. Patients with obstructive ulcer disease have been reported to be at increased risk of postoperative gastric atony (7). The prevalence of delayed gastric emptying after gastrectomy has been reported to range from 5% to 30% (2,3,5,8). Delayed gastric emptying has also been reported to continue to affect a considerable number of patients (24%) after gastric surgery and be particularly common in patients with diabetes, malnutrition, and gastric or pancreatic cancer (8). In this study, Roux-en-Y reconstruction after gastric cancer resection caused significantly more delayed gastric emptying than Billroth-I reconstruction. The clinical features of patients showing delayed emptying, such as postoperative hospital stay, the days when oral feeding was stopped and restarted, and upper GI series findings did not differ according to whether a Billroth-I or Roux-en-Y operation had been performed. Other factors may cause delayed gastric emptying after Roux-en-Y operations.

The Roux-en-Y operation is reported to be superior to either Billroth I or II reconstruction for preventing bile reflux into gastric remnant and gastritis (9,10) and to prevent carcinoma of the remnant stomach (11). Moreover, Roux-en-Y reconstruction is supposed to cause anastomotic leakage rarely, compared to Billroth-I reconstruction. From these points of view, we

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