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, 700–16 000 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-

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

priate 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 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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