
The Advantages of Pylorus-preserving Pancreatoduodenectomy in Malignant Disease of the Pancreas and Periapillary Region

J. H. G. KLINKENBIJL, M.D.,* G. P. VAN DER SCHELLING, M.D.,* W. C. J. HOP, M.Sc.,†
R. VAN PEL, M.D.,‡ H. A. BRUINING, M.D., Ph.D.,* and J. JEEKEL, M.D., Ph.D.*

The aim of this study was to establish whether the pylorus-preserving pancreatoduodenectomy (PPPD) is a safe and radical procedure in malignant disease of the head of the pancreas and periampillary region, without increased morbidity and mortality rates compared with the standard Whipple's procedure. During the period 1984 to 1990, a Whipple's procedure (n = 44) or PPPD (n = 47) was performed in 91 patients. In-hospital mortality rates were 2% after PPPD and 5% after Whipple's procedure. Median duration of the resection procedure and median blood loss in the PPPD group were 210 minutes and 1800 mL, respectively. After Whipple's procedure, these figures were 255 minutes and 2500 mL, both significantly different ($p < 0.01$) as compared with PPPD. No difference was found during follow-up with respect to days of gastric suctioning, start of liquid diet, normal diet, complaints of ulcer disease, postoperative complications, recurrence of disease, and survival. In all patients, curative resection was performed with comparable TNM (tumor, nodes, metastases) staging. The number of tumor-containing duodenal or gastric resection margins did not differ in both groups of patients (two patients after PPPD, two patients after Whipple's procedure). Hospital stay was significantly ($p = 0.02$) shorter after PPPD; median 14 days, compared with median 18 days after Whipple's procedure. The advantage of the PPPD is that it is an easier and less time-consuming operation, with less blood loss, a shorter hospital stay, and better weight gain ($p = 0.02$) during follow-up. In conclusion, PPPD is a safe and radical procedure for cancer in the head of the pancreas or periampillary region, with the same survival and appearance of loco-regional recurrence and distant metastases as after standard Whipple's resection.

SINCE WHIPPLE ET AL. in 1935 described the first resection of the head of the pancreas for malignant disease, many modifications have been reported.¹ Watson² described the first pylorus-preserving pancreatoduodenectomy (PPPD) in 1944. This technique was not applied, however, until Traverso and Longmire³ in 1978 used the PPPD in two patients. The expected advantages

From the Department of General Surgery, University Hospital Dijkzigt; the Department of Epidemiology and Biostatistics,† Erasmus University; and the Department of Pathology,‡ Erasmus University; Rotterdam, The Netherlands*

of the PPPD above the standard Whipple's resection with partial gastrectomy were less dumping, improved gastrointestinal function, and reduced jejunal ulceration. Conversely, prolonged hospital stay because of delayed gastric emptying has been reported. Furthermore, in malignant disease, radicality of the PPPD has been argued with respect to the duodenal resection margin.⁴⁻⁹

We reviewed the hospital charts of patients with cancer of the pancreas head or periampillary region after resection by means of standard Whipple's procedure or PPPD during the period 1984 to 1990. Both treatment modalities were compared with respect to radicality of the resection, morbidity rate, and mortality rate. The aim of this study was to establish whether PPPD is a safe and radical procedure in malignant disease of the head of the pancreas and periampillary region, with acceptable morbidity and mortality rates compared with the standard Whipple's procedure.

Materials and Methods

From 1984 to 1990, 113 patients underwent a Whipple's resection or PPPD, 13 for a benign disease like pancreatitis or villous adenoma of the pancreas or duodenum, and four for malignant disease of origin other than pancreas head or periampillary region. Ninety-six patients underwent Whipple's resection or PPPD for cancer of the head of the pancreas or periampillary region. None of these patients underwent total pancreatectomy. In four patients, a resection was performed despite of tumor growth in lymph nodes outside the resection area (N1b) and in one patient with liver metastases. These patients were excluded from analysis.

Address reprint requests to J. Jeekel, M.D., Ph.D., Department of General Surgery, University Hospital Dijkzigt, Dr. Molewaterplein 40, 3015 GD, Rotterdam, The Netherlands.

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This study concerned 91 patients with cancer of the head of the pancreas ($n = 50$) or periampullary region ($n = 41$), 34 women and 57 men, with a mean age of 60 years. In 45 patients, a standard Whipple's resection with partial gastrectomy was performed; in 46 patients, a PPPD was done. In the group of patients with cancer of the head of the pancreas ($n = 50$), 25 PPPD resections and 25 standard Whipple's resections were performed. In the group of patients with periampullary cancer ($n = 41$), 21 PPPD resections and 20 Whipple's resections were performed.

For reconstruction after the standard Whipple's resection, a Roux-en-Y jejunal loop was used with an end-to-side or end-to-end pancreaticojejunostomy with a one-layer inverted running suture of pancreatic tissue to the jejunum. An end-to-side choledochojejunostomy was constructed on the same jejunal loop, also with a one-layer running suture. An end-to-side gastrojejunostomy was constructed with the other part of the Roux-en-Y jejunal loop. Only one jejunal loop was used after PPPD with an end-to-side one-layer running inverting pancreaticojejunostomy and an end-to-side choledochojejunostomy. Finally, an end-to-side duodeno-enterostomy with a one-layer running suture was performed on the same jejunal loop. Stents were never used for the pancreatic or bile duct. After operation, prophylactic antacid medication by ranitidine was given to all patients after PPPD and in selected cases after standard Whipple's procedure.

Operative death was defined as death during the first admission period. Tumor, nodes, metastases (TNM) staging (UICC 87) was used, with a modification for the N-stage, stage N1a indicating positive lymph nodes within the resection specimen and stage N1b indicating positive lymph nodes outside the resection specimen. During follow-up, locoregional or distant metastases were demonstrated by means of ultrasound or computed tomography with or without fine needle aspiration biopsy or histology. Median follow-up was 25 months, ranging from 1 month to 67 months.

Data on location of tumor, blood loss, and duration of operation were obtained. Postoperative information on days of gastric suction, days of liquid nutrition, and days of normal nutrition, occurrence of ulcer disease, and gastric stasis were obtained. Pathologic examination of the resection specimen was performed, with special attention to the resection margins. All resection margins were reviewed by one pathologist. During follow-up in the outpatient department, information on nutritional status, weight, ulcer disease with or without medication, locoregional recurrence, and distant metastases was obtained.

In Table 1, data on gender, age, tumor localization, and TNM staging of both treatment groups are presented. There were no significant differences between the two groups with respect to any of these parameters.

Quantitative data were compared using Mann-Whitney's test. The chi square test was used in cases of qual-

TABLE 1. Various Patient Characteristics According to Treatment

Characteristic	Treatment	
	PPPD	Whipple
Gender		
Men	30 (64%)	27 (61%)
Women	17 (36%)	17 (39%)
Age (yr)	62 (41-79)	60 (27-78)
Localization		
Head	26 (55%)	24 (55%)
Periampullary	21 (45%)	20 (45%)
T stage		
T1	9 (19%)	13 (29%)
T2	34 (72%)	24 (55%)
T3	4 (9%)	7 (16%)
N stage		
NO	34 (74%)	28 (65%)
N1a	12 (26%)	15 (35%)

Data given are numbers of patients or mean (range) in case of age.

itative data. Survival was calculated and compared using life-table methods (Kaplan Meier, log-rank test). The limit of statistical significance was considered to be $p \leq 0.05$ (two-sided).

Results

Median duration of the operation performed in the PPPD group was 210 minutes (range, 160 to 270 minutes), with a median blood loss of 1800 mL (range, 850 to 3050 mL). In the group of patients with a standard Whipple resection, median operation time was 255 minutes (range, 180 to 335 minutes), and median blood loss was 2500 mL (range, 1400 to 3600 mL). This difference was significant for duration of operation and blood loss. The in-hospital mortality rate was 2% (1/47) after PPPD and 5% (2/44) after standard Whipple's resection. The morbidity rate after resection did not differ significantly with respect to days of gastric suction, start of liquid meals, normal meals, and complaints of duodenal or gastric ulceration. Postoperative complications and re-explorations were similar in both groups of patients, and leakage of the pancreaticojejunostomy occurred two times in the group of patients after PPPD, and five times after standard Whipple resection. Hospital stay was significantly shorter after PPPD than after Whipple's resection (median, 14 days; range, 8 to 85 days; and median, 19 days; range, 9 to 184 days) (Table 2). The TNM classification was similar in both groups of patients. Review of the duodenal resection margins in the group of patients after PPPD showed tumor-containing resection margins in two patients; after standard Whipple's resection in two patients, a tumor-containing duodenal resection margin was found. Considering all the resection margins, including pancreas and common bile duct, no difference was observed. In patients after standard Whipple's procedure or PPPD with cancer of the head of the pancreas, significantly more tumor-

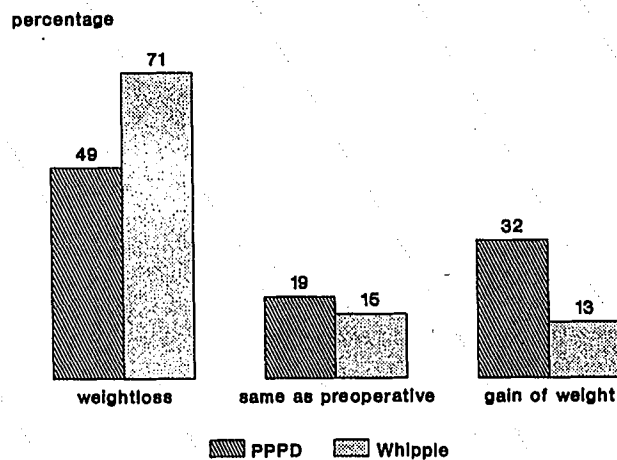
TABLE 2. Direct Postoperative Course According to Treatment

	PPPD (n = 47)	Whipple (n = 44)
Gastric suction	4 (1-39)	4 (1-45)
Liquid diet	7 (1-39)	7 (3-45)
Normal diet	9 (2-39)	9 (6-71)
Ulcer disease	3 (6%)	1 (2%)
Antacid medication	30 (64%)	18 (41%)*
Abscess wound	2 (4%)	1 (2%)
Abscess intra-abdominal	5 (11%)	3 (7%)
Bleeding	2 (4%)	2 (5%)
Leakage pancreatojejunostomy	2 (4%)	5 (11%)
Relaparotomy	11 (23%)	17 (39%)
Hospital stay	14 (8-85)	19 (9-184)*

Data given are medians (range) in days of numbers (percentages) of patients

* $p < 0.05$.

containing resection margins were found compared with the patients with periampullary cancer ($p = 0.02$). During follow-up, with a mean duration of follow-up of 25 months (range, 1 to 67), no difference was found with respect to complaints of ulcer disease. Significantly more patients after PPPD received antacid medication, because this was prescribed routinely. Weight changes after operation during follow-up in the outpatients department were significantly more favorable after PPPD (Fig. 1). Local recurrence was found eight times after PPPD and 11 times after Whipple's resection. No influence was seen of tumor-containing resection margins in case of local recurrence: in 5 of 13 patients, local recurrence was found in cases of tumor-containing resection margins, in 14 of 75 patients when the resection margins were negative. Calculated by life-table methods, differences were not significant. Local recurrence was found after a mean follow-



Mann-Whitney's test overall $p = 0.02$

pppd/wp

FIG. 1. Weight changes during follow-up in the outpatient department. Data given are numbers (percentages) of patients. Postoperative deaths are excluded.

up of 11 months (range, 3 to 38 months). Liver metastases were found after a mean of 10 months (range, 3 to 19 months) in 13 patients after PPPD and in 10 patients after Whipple's resection. Metastases elsewhere and peritonitis carcinomatosa were found in 18 patients after PPPD and in 15 patients after Whipple's resection, with means of 12 months and 11 months (range, 2 to 29 months and 2 to 38 months, respectively) (Table 3). In patients with cancer of the head of the pancreas, local recurrence, liver metastases, metastases elsewhere, and peritonitis carcinomatosa were found significantly more, and survival was also significantly shorter in this group of patients irrespective of type of resection performed (Fig. 2).

No difference in survival was found after PPPD or standard Whipple's procedure, with a 1-year survival of 56% for both groups of patients and 2-year survival of 38% after PPPD and 26% after Whipple's procedure ($p = 0.18$). Cause of death was recurrence of disease in 35 patients, three patients died of causes other than malignancy. Eleven patients are alive with local recurrence of disease or distant metastases.

Discussion

Presently the standard procedure for malignancy of the head of the pancreas or periampullary region is the Whipple's resection.¹ To reduce postoperative morbidity and mortality rates, Traverso and Longmire³ in 1978 reintroduced the PPPD after Watson proposed this technique first in 1944.^{2,3} Expected advantages of this procedure were less dumping, improved gastrointestinal function, and reduced jejunal ulcers. Postoperative gain of weight and a better quality of life were reported.^{4,5,8,10-13} Some authors doubted the radicality of PPPD, others mentioned a prolonged hospital stay mainly as a result of delayed gastric emptying.^{7,14-16} Grace et al.⁹ reported in 1990 that PPPD is a safe and radical procedure with lower morbidity and mortality rates in patients with benign and malignant disease in the periampullary region.⁹ During the study period, we were in the unique situation to compare the two techniques in a comparable group of patients. Duration of operation and blood loss during operation were signifi-

TABLE 3. Number of Patients With a Local Recurrence, Liver Metastases, Other Metastases, or Peritonitis Carcinomatosa According to Localization

	Head of Pancreas (n = 50)	Periampullary (n = 41)	Significance (log-rank)
Local recurrence	13 (36%)	6 (11%)	$p = 0.04$
Liver metastases	18 (43%)	5 (15%)	$p < 0.01$
Other metastases	13 (55%)	7 (21%)	$p = 0.06$
Peritonitis carcinomatosa	12 (31%)	1 (5%)	$p < 0.01$

The cumulative (life-table) percentage at 3 years is given in parentheses.

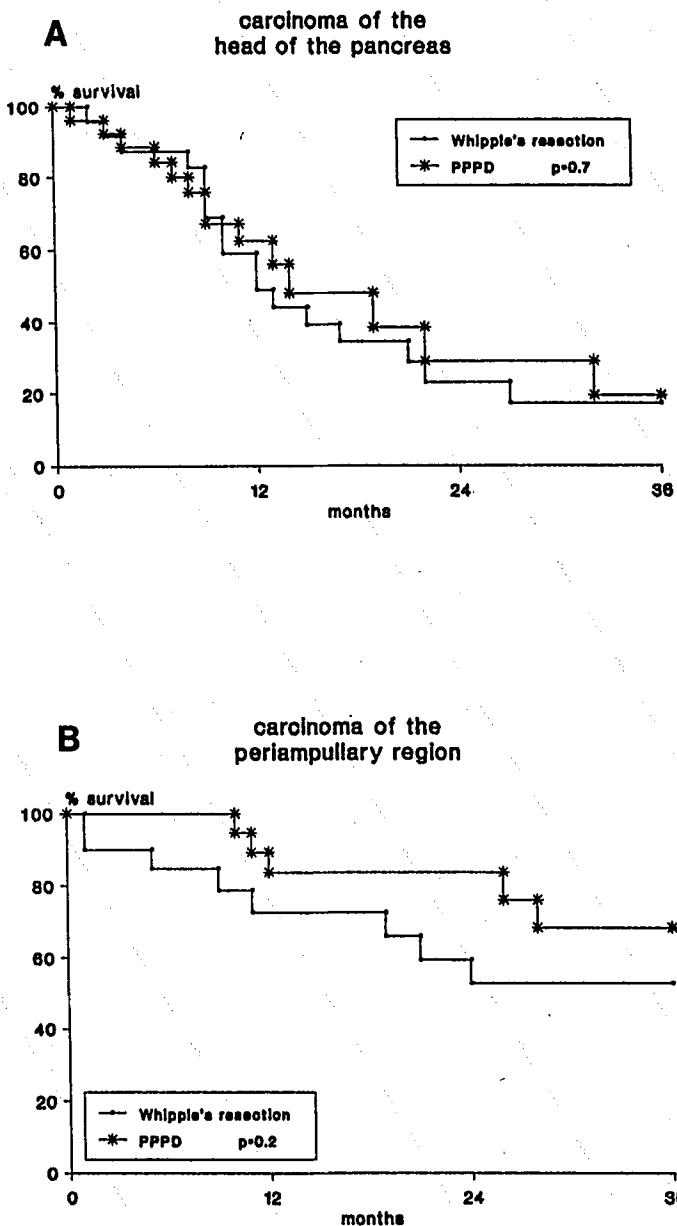


FIG. 2. Survival according to treatment for patients with cancer of the head of the pancreas (A) and periampullary region (B).

cantly less after PPPD. Operative mortality rate of both procedures was not significantly different. In particular, no great differences were observed with respect to gastric emptying and complaints of ulcer disease, claimed to be disadvantages of PPPD. Moreover, hospital stay was significantly shorter after PPPD. Surgical complications and the need for re-explorations were similar in both groups of patients.

As discussed before, irradicality and locoregional recurrence might be expected more frequently after PPPD. In our series, however, no difference was observed in tumor-containing resection margins, all reviewed by one pathologist. Locoregional recurrence was observed in 11

patients (20%) after Whipple procedure, in eight patients (17%) after PPPD, and in similarly staged patients according to the TNM staging. During follow-up in the outpatient department, ulcer disease occurred equally in both groups. More patients in the PPPD group received antacid medication because it was given routinely as prophylaxis. Gain of weight appeared to be significantly better in patients after PPPD. No difference in survival was observed between the two groups of patients after intentionally curative resection. There also was no difference in postoperative in-hospital mortality rate, 2% after PPPD and 5% after standard Whipple's procedure. In conclusion, PPPD can be a radical and safe procedure for cancer of the head of the pancreas and periampullary region. No differences in morbidity and mortality rates were found between the two procedures. The advantage of PPPD is that it is an easier and less time-consuming operation, with less blood loss and a shorter hospital stay. During follow-up, gain of weight appears to be better after PPPD. Therefore, quality of life seems to be better, which is especially of importance when life expectancy is so low.

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