

**Original Article****Risk Factors And Outcome of Pancreatic Fistula after Consecutive Pancreaticoduodenectomy with Pancreaticojejunostomy for Patients with Malignant Tumor**

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**ABSTRACT**

**Objective:** Pancreatic fistula (PF) is a common complication after pancreaticoduodenectomy (PD) and there is no consensus regarding the criteria to define PF. The study was undertaken to determine the risk factors for PF according to the definition of the International Study Group on Pancreatic Fistula (ISGPF) and to delineate its impact on patient outcome.

**Methods:** Between March 1994 and May 2009, data from 153 consecutive patients with malignant tumors underwent a PD with pancreaticojejunostomy in the Peking University People's Hospital were recorded prospectively. A total of 24 factors were examined with univariate analysis and multivariate logistic regression analysis was used to estimate relative risks, and their 95% confidence intervals (95% CI) and odds ratio (OR).

**Results:** Our institution belonged to medium-volume center and PF occurred in 30 patients (19.6%). Pancreatic texture, early postoperative hemorrhage and pancreatic pathologies correlated with PF rates significantly in univariate analyses. But in multivariate regression, soft gland (OR, 4.934; 95% CI, 1.132–7.312) and early postoperative hemorrhage with conservative therapy (OR, 4.130; 95% CI, 1.057–21.112) were predictive. The mean postoperative length of stay in patients with PF was longer (32.7±23.9 versus 60.5±56.2 days) than patients without PF ( $P=0.001$ ). Overall 30-day mortality was not affected by the development of PF ( $P=0.657$ ). There was no difference in reoperation rates between patients with and without PF (10.0% versus 6.5%,  $P=0.787$ ). Concerning the sum of postoperative complications, there were 36 complications for 30 patients with PF, while 64 for 123 patients without PF. When patients with distal cholangiocarcinoma, ampullary and duodenal cancer were considered as a whole for survival analysis, the median survival for patients with PF was 20 months, whereas the median survival for patients without PF was 26 months. Kaplan-Meier survival curves for patients with and without PF were not statistically different ( $P=0.903$ ).

**Conclusion:** Soft texture and early postoperative hemorrhage with conservative therapy are independent correlates of increased rate of PF. Anastomotic technique for pancreaticojejunostomy does not have impact on the development of PF in our experience. PF contributes to early postoperative morbidity and the length of hospital stay, but it does not affect postoperative 30-day mortality, reoperation rate and overall survival.

**Key words:** Pancreaticoduodenectomy; Pancreatic fistula; Morbidity; Mortality; Surgical outcome

**INTRODUCTION**

Although improved operative technique and

postoperative care decrease mortality after pancreaticoduodenectomy (PD)<sup>[1]</sup>, the rate of pancreatic fistula (PF) is not improved in recent large series which have reported failure of the pancreaticoenteric anastomosis in 10.2%–26.7% of patients worldwide<sup>[2–6]</sup>. The rate of PF is considered intolerable when compared with leak

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rates of most other gastrointestinal anastomoses. Prior retrospective analyses of surgical series have indicated several important risk factors for PF after PD: surgical volume<sup>[7]</sup>, general health, pancreatic fibrosis, and pancreatic pathology<sup>[8]</sup>. A number of methods for reducing the incidence of PF have been proposed and analyzed. Many of these involve technical features of the anastomosis, including site of reconstruction<sup>[9]</sup>, anastomotic technique<sup>[10]</sup>, and use of somatostatin analogue<sup>[2]</sup>. Some investigators even advocated omitting the anastomosis entirely, with occlusion of the remnant duct<sup>[3]</sup>. To further determine the risk factors for PF in patients who underwent PD with pancreaticoduodenostomy for malignant tumors and to define its effects on outcomes, a univariate and multivariate analysis was conducted using a prospective single-institutional database.

## MATERIALS AND METHODS

### Patient Selection

Between March 1994 and May 2009, 153 consecutive patients with malignant tumors underwent a PD with pancreaticojejunostomy. The patient was not included when acute pancreatitis was found simultaneously in operation. Details of these patients were entered into a prospective database. There were 106 men (69.3%) and 47 women (30.7%), with a mean age of  $58.5 \pm 10.5$  years (range from 26 to 80 years). All patients had elective operations after full workup and control of preoperative conditions. Indications for PD were malignant diseases (Table 1).

### Operation and Postoperative Care

PD was performed without pylorus preservation, and reconstruction was performed by intussusception with an end-to-side or end-to-end pancreaticojejunostomy for all patients. Hepaticojejunostomy was located about 12 cm distal to pancreaticojejunostomy. Gastrojejunostomy or jejunojejunostomy was located about 40 cm distal to hepaticojejunostomy. The jejunal limb was brought up to the supramesocolic region through an avascular zone of the transverse mesocolon. If possible, a fine silastic tube was placed in the pancreatic duct with several perforations and fixed at the edge of transected pancreas with 10 cm left in the jejunal loop. In the year of 2003 and 2004, the tube was brought out of the jejunal wall to the outside with the aim of diverting pancreatic

secretions from the body for the majority of patients. Lymphadenectomy was routinely performed with skeletonization of the hepatic artery from the hepatic pedicle to the celiac axis. Closed drains were placed in the vicinity of the pancreatic and biliary anastomosis, and they were removed when the volume of drainage was less than 5 ml for continuous 3 d. Somatostatin analogues were given for 7 days in 135 patients as prophylaxis for PF. After induction of anesthesia, intravenous antibiotic prophylaxis was administered for all patients and repeated every 4 hours during the operative procedure. All patients had nasogastric aspiration for at least 7 d. Oral diet was initiated 7 days after operation if there was no PF or other intraabdominal complications.

### Definitions of PF

According to selected North American standards<sup>[11]</sup>, high-volume centers were defined as those operating on 20 patients or more per year, medium-volume centers operated on between 5 and 19 patients per year, low-volume centers operated on between 1 and 4 patients per year, and very low-volume centers operated on less than 1 patients per year. Mortality and morbidity were defined, respectively, as death or complication occurring within 30 d after operation. PF was defined, according to the International Study Group on Pancreatic Fistula (ISGPF)<sup>[12]</sup>, as a drain output of any measurable volume of fluid on or after postoperative day 3 with an amylase concentration greater than three times the serum amylase activity. Three different grades of PF (Grade A, B, and C) were defined according to the clinical impact on the patient's hospital course<sup>[12]</sup>. Patients with PF would be asymptomatic (Grade A) or poorly symptomatic requiring conservative treatment (Grade B), whereas others would develop abscesses, peritonitis, sepsis, and hemorrhage with a high mortality rate which necessitate interventional procedures (Grade C). Delayed gastric emptying (DGE) was defined as the need for nasogastric decompression after postoperative day 10<sup>[13]</sup>. Wound infection was defined as presence of pus requiring wound opening. Intraabdominal collection was defined as postoperative fluid collection treated by puncture or drainage. Pulmonary infection was defined as a suggestive radiographic study with fever and requirement for antibiotics. Sepsis was diagnosed when systemic inflammatory response syndrome with positive peripheral blood culture appeared<sup>[14]</sup>. Infectious complications were proved bacteriologically by