

# Pancreatic fistula after pancreatic head resection

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**Background:** Pancreatic resections can be performed with great safety. However, the morbidity rate is reported to be 40–60 per cent with a high prevalence of pancreatic complications. The aim of this study was to analyse complications after pancreatic head resection, with particular attention to morbidity and pancreatic fistula.

**Methods:** From November 1993 to May 1999, perioperative and postoperative data from 331 consecutive patients undergoing pancreatic head resection were recorded prospectively. Data were analysed and grouped according to the procedure performed: classic Whipple resection, pylorus-preserving pancreatoduodenectomy (PPPD) or duodenum-preserving pancreatic head resection (DPPHR).

**Results:** Pancreatic head resection had a mortality rate of 2.1 per cent; the difference in mortality rate between the three groups (0.9–3.0 per cent) was not significant. Total and local morbidity rates were 38.4 and 28 per cent respectively. DPPHR had a lower morbidity, both local and systemic, than pancreatoduodenectomy. The prevalence of pancreatic fistula was 2.1 per cent in 331 patients, and was not dependent on the procedure or the aetiology of the disease. Reoperations were performed in 3.9 per cent of patients, predominantly for bleeding and non-pancreatic fistula. None of the patients with pancreatic fistula required reoperation or died in the postoperative course.

**Conclusion:** A standardized technique and a continuing effort to improve perioperative management may be responsible for low mortality and surgical morbidity rates after pancreatic head resection. Pancreatic complications occur with Whipple, PPPD and DPPHR procedures with a similar prevalence. Pancreatic fistula no longer seems to be a major problem after pancreatic head resection and rarely necessitates surgical treatment.

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## Introduction

The safety of pancreatic resection has increased in recent years, and the mortality rate has decreased to between 0 and 6 per cent in specialized units<sup>1–4</sup>. Large series of pancreatoduodenectomies without operative death have been reported by single institutions<sup>5–8</sup>. The morbidity rate after pancreatic resection is still in the range of 40–60 per cent, and many reports state that pancreatic fistulas and their septic sequelae are important contributors to surgical morbidity and mortality<sup>9</sup>. However, the reasons for the observed decrease in mortality rate are not entirely clear. They certainly include a perfected perioperative management and optimized care in the intensive care unit after pancreatic head resection<sup>4</sup>, but improvements in surgical technique, attention to detail, standardized reconstruction of the gastrointestinal tract and the formation of specialized units for the treatment of pancreatic disease are crucial in

this development. Data from prospective randomized trials recently demonstrated that perioperative administration of octreotide also contributed to a reduction in surgical morbidity<sup>10–14</sup>.

This report includes three groups of patients undergoing either a classic Whipple operation, pylorus-preserving pancreatoduodenectomy (PPPD) or duodenum-preserving pancreatic head resection (DPPHR). In a prospective clinical audit, postoperative morbidity after pancreatic head resection was analysed in 331 consecutive patients with special emphasis on the prevalence of surgical complications and pancreatic fistula.

## Patients and methods

A database was established to prospectively record patients with pancreatic disease. The primary aim was to determine morbidity and mortality rates after pancreatic surgery.

From 1 November 1993 to 31 May 1999 data were collected on standardized data sheets from 615 patients undergoing pancreatic resection (436 of 615) or palliative and exploratory procedures (179 of 615). The variables were grouped into demographics, indications, preoperative evaluation and risk assessment, operation and postoperative course. The present analysis includes in-hospital data for all patients undergoing pancreatic head resection during this time interval ( $n = 331$ ).

### Standard treatment protocol

Before operation, the majority of patients (97.9 per cent; 324 of 331) underwent contrast-enhanced abdominal computed tomography, typically in combination with endoscopic retrograde cholangiopancreatography (ERCP) (81.6 per cent; 270 of 331). Recently, all-in-one magnetic resonance imaging has replaced ERCP as a standard examination<sup>15</sup>. The extent of the pancreatic pathology and the infiltration into other organs and retroperitoneal vessels in patients with neoplasm were determined. In patients with malignant tumour, the common bile duct was decompressed by an endoscopically inserted stent in 43.3 per cent (75 of 173), corresponding to 52 per cent of patients with a bilirubin level above 40  $\mu\text{mol/l}$ . In patients with chronic pancreatitis or benign tumour, 29 and 17 per cent presented with a bilirubin level above 40  $\mu\text{mol/l}$ , and 8.4 and 3 per cent had an endoscopic stent inserted, respectively. Rarely, the obstructed common bile duct was decompressed by percutaneous transhepatic cholangiography and drainage (1.8 per cent; six of 331). Standard preoperative risk assessment included a stress electrocardiography and a pulmonary function test.

All patients received prophylactic antibiotics perioperatively (piperacillin 4 g, ornidazole 1 g) together with a daily dose of subcutaneous low molecular weight heparin. Octreotide was started during induction of anaesthesia and given for 7 days after operation (three doses of 0.1–0.2 mg per day subcutaneously). Perioperative and postoperative pain management included epidural anaesthesia or patient-controlled analgesia in all patients. After operation, patients were transferred to the intensive care unit overnight or to an intermediate care unit.

The surgical techniques of classic pancreatoduodenectomy (Whipple), PPPD and DPPHR have been described previously<sup>16–20</sup>. However, the technique of the pancreatic anastomosis is described here. Briefly, the preferred end-to-side Roux-en-Y pancreatojejunostomy to the left pancreatic remnant was created as follows. An outer layer of interrupted 5/0 polydioxanone sutures included the majority of the cut surface of the pancreas. The inner row of 5/0 polydioxanone interrupted stitches included at least three

mucosa-to-duct sutures posteriorly and anteriorly. Careful attention was paid to ensure that the pancreatic duct was not obstructed to avoid postoperative acute pancreatitis. Using the same technique, an end-to-end pancreatojejunostomy including duct-to-mucosa sutures was used in a minority of cases. Pancreaticogastrostomy was not performed nor were the pancreatic or biliary anastomosis stented.

In cases of cancer, lymph node dissection along the hepatoduodenal ligament, common hepatic artery, vena cava, superior mesenteric vein and the right side of the superior mesenteric artery was a standard part of the procedure. A 12-mm 'LightFlow' capillary silicone drain (Willy Rüschi, Kernen, Germany) was placed close to the pancreatojejunostomy and brought out through the left abdominal wall to monitor pancreatic leakage. A second separate drain was left to drain the area of the hepaticojejunostomy.

Pancreatic tumours were classified according to the standards of the World Health Organization, and staged using the TNM classification system<sup>21,22</sup>.

All complications were recorded prospectively in the database. Morbidity was determined with respect to the number of patients. However, local and systemic complications also appear in a complete list which includes all complications for all patients. The mortality rate was defined as the total in-hospital death rate. Delayed gastric emptying (DGE) was defined as the need for a nasogastric tube for more than 10 days after operation. A pancreatic fistula was defined as secretion of 30 ml or more of amylase-rich drainage fluid (more than 5000 units) per day for more than 10 days. A biliary fistula was diagnosed if there was persistent secretion of bilirubin-rich drainage fluid for more than 5 days. Bleeding was defined as the need for more than 2 units of packed red blood cells (RBCs) more than 24 h after operation, or relaparotomy for bleeding.

### Statistical analysis

For comparison between the three different procedures, the results of the classic Whipple procedure were compared with those of both PPPD and the DPPHR. Statistical evaluation was carried out using two-tailed  $\chi^2$  analysis and the Mann-Whitney  $U$  test to determine the level of significance in unpaired groups with non-parametric distribution where appropriate. Significance was defined at the 5 per cent level.

### Results

From 1 November 1993 to 31 May 1999, 436 pancreatic resections were performed. For this analysis, patients undergoing total pancreatectomy (5.0 per cent; 22 of 436),

left pancreatectomy (14.7 per cent; 64 of 436) and atypical resections/tumour enucleations (4.4 per cent; 19 of 436) were excluded. All patients undergoing pancreatic head resection (75.9 per cent; 331 of 436) during this time interval were analysed in the present study. The mean age was 58 (median 58; range 18–87) years and the male : female ratio was 1:1.4 (137:194). In patients with chronic pancreatitis, malignant tumours and benign tumours of the pancreatic head the mean (median) ages were 48 (49), 64 (68) and 65 (67) years, and the male : female ratios were 1:0.5 (91:42), 1:0.9 (92:81) and 1:0.9 (12:11) respectively. The perioperative risk was assessed according to the American Society of Anesthesiologists (ASA) classification; 22 per cent of patients had a significantly raised perioperative risk, corresponding to the ASA class III group.

Patients who underwent pancreatic head resection were grouped according to the operative procedure. A Whipple procedure was performed in 25.1 per cent (83 of 331), PPPD in 40.1 per cent (133 of 331) and DPPHR in 34.7 per cent (115 of 331). The majority of patients underwent an elective procedure (98.8 per cent; 327 of 331). However, four patients underwent emergency resection for either a salvage operation after unsuccessful local resection of a pancreatic sarcoma (one), a large bleeding ulcer penetrating into the head of the pancreas (one), perforation of the common bile duct and pancreatic head during ERCP (one) or an actively bleeding tumour of the Papilla of Vater (one). *Table 1* lists the pathology results in the resected specimens.

DPPHR was carried out in 86.5 per cent of patients with chronic pancreatitis. In all patients who had DPPHR an intraoperative histological sample of the resected specimen was obtained to exclude pancreatic cancer. A Whipple procedure and PPPD were performed in 5.3 per cent (seven of 133) and 8.3 per cent (11 of 133) of patients with chronic pancreatitis. In patients with benign tumours and in malignant periampullary disease, PPPD was the preferred choice of duodenopancreatectomy in 61.7 per cent of cases. PPPD was done in 54.5 per cent of patients with pancreatic cancer (61 of 112); the remaining patients underwent a classic Whipple procedure. Of the 61 patients with malignant periampullary tumours other than pancreatic cancer, 72 per cent (44 of 61) underwent PPPD and 28 per cent had a Whipple resection. The majority of benign tumours (16 of 23) were resected by PPPD.

The intraoperative blood loss, transfusion of RBCs and operative times are given in *Table 2*. In 38.7 per cent (128 of 331) no blood or blood products were transfused during or after operation. In 9.1 per cent of patients (30 of 331) vascular structures had to be repaired or resected and reconstructed for oncological or technical reasons (*Table 2*).

Patients were in hospital for a median of 14 (mean(s.d.) 19(15); range 6–118) days and stayed in the intensive care

**Table 1** Pathology in 331 specimens after pancreatic head resection

|                        | Malignant  | Benign     |
|------------------------|------------|------------|
| Periampullary tumours  |            |            |
| Pancreatic             | 112 (33.8) | 0 (0)      |
| Ampullary              | 22 (6.6)   | 5 (1.5)    |
| Distal bile duct       | 20 (6.0)   | 2 (0.6)    |
| Duodenum               | 1 (0.3)    | 2 (0.6)    |
| Cystic tumours         | 1 (0.3)    | 11 (3.3)   |
| Neuroendocrine tumours | 11 (3.3)   | 0 (0)      |
| Other tumours          | 6 (1.8)    | 3 (0.9)    |
| Chronic pancreatitis   | —          | 133 (40.2) |
| Other indications      | —          | 2 (0.6)    |
| Total                  | 173 (52.3) | 158 (47.7) |

Values in parentheses are percentages

**Table 2** Details of operative procedures in 331 patients who underwent pancreatic head resection

|   |                      |
|---|----------------------|
| Intraoperative data*                        |                      |
| Blood loss (ml)                             | 1500(921) (100–6000) |
| RBC transfusion (units)                     | 1.9(2.2) (0–15)      |
| Operating time (min)                        | 421(111) (220–780)   |
| Vascular resection for tumour infiltration† | 19 (5.7)             |
| Vascular repair for technical problems†     | 11 (3.3)             |
| Pancreatojejunostomy‡                       |                      |
| End to end                                  | 34 (10.3)            |
| End to side                                 | 294 (88.9)           |
| Side to side                                | 118 (35.6)‡          |

\*Values are mean(s.d.) (range); †values in parentheses are percentages; ‡A DPPHR needs an additional side-to-side anastomosis. The technique used for the end-to-side pancreatic reconstruction is described in the text. RBC, red blood cell

unit or an intermediate care unit for a median of 1 (mean 2; range 1–71) day. Data related to the postoperative course are summarized in *Tables 3* and *4*. Some 61.6 per cent of patients had an uncomplicated postoperative course but, although the mortality rate was 2.1 per cent, a total local and systemic morbidity rate of 38.4 per cent after pancreatic head resection was recorded. The morbidity rate includes the 12 per cent of patients who had a postoperative course complicated by more than one local and/or systemic complication. The reoperation rate was 3.9 per cent (13 of 331) and included predominantly patients with haemorrhagic complications (four of 13) and non-pancreatic fistula (five of 13). The colonic fistulas resulted in three patients with anastomotic breakdown after segmental colon resection. In two of three patients with biliary fistula the leak was surgically repaired. None of the reoperations was done for a pancreatic fistula and no completion pancreatectomy was necessary. *Table 3* also shows that systemic complications

were encountered in 19.3 per cent of patients and that cardiopulmonary complications were common (12.1 per cent).

**Table 3** Deaths, reoperations and morbidity after 331 pancreatic head resections

|                                   | No. of patients | Reoperation | Death |
|-----------------------------------|-----------------|-------------|-------|
| Deaths                            | 7 (2.1)         |             |       |
| Reoperations                      | 13 (3.9)        |             |       |
| Total patients with complications | 127 (38.4)      |             |       |
| Complications                     |                 |             |       |
| Local                             |                 |             |       |
| Delayed gastric emptying          | 54 (16.3)       | 1           |       |
| Septic complications              | 17 (5.1)        |             |       |
| Wound sepsis                      | 13 (3.9)        |             |       |
| Intra-abdominal abscess           | 4 (1.2)         |             |       |
| Fistula                           | 13 (3.9)        |             |       |
| Pancreatic                        | 7 (2.1)         |             |       |
| Colonic                           | 3 (0.9)         | 3           |       |
| Biliary                           | 3 (0.9)         | 2           | 1     |
| Bleeding                          | 12 (3.6)        | 4           |       |
| Cholangitis                       | 7 (2.1)         |             |       |
| Liver necrosis                    | 3 (0.9)         | 1*          | 1     |
| Common bile duct occlusion        | 1 (0.3)         | 1           |       |
| Small bowel obstruction           | 2 (0.6)         | 1           | 1     |
| Chylous ascites                   | 1 (0.3)         |             |       |
| Neurological                      | 3 (0.9)         |             |       |
| Systemic                          |                 |             |       |
| Cardiopulmonary                   | 40 (12.1)       |             | 3     |
| Neurological                      | 10 (3.0)        |             |       |
| Renal                             | 5 (1.5)         |             |       |
| Catheter sepsis                   | 3 (0.9)         |             |       |
| Other                             | 6 (1.8)         |             | 1     |

Values in parentheses are percentages. \*One patient was reoperated for suspected intra-abdominal sepsis, which was not confirmed intra-operatively

Fistulas remain potentially dangerous complications following pancreatic head resection. However, the rate of 3.9 per cent included all fistulas; a pancreatic fistula was encountered in 2.1 per cent of patients (seven of 331). The pancreatic fistula rate in patients with chronic pancreatitis was 2.3 per cent (three of 133) and was no different from that in patients without pancreatitis (2.0 per cent; four of 198). One patient with a pancreatic fistula presented after operation with an abdominal abscess that was drained interventionally. The remaining six pancreatic fistulas healed with initial bowel rest and prolonged administration of octreotide. In six additional patients the postoperative course was complicated by a biliary (three) or colonic (three) fistula. Five of 13 patients with a fistula required reoperation, three patients with breakdown of the colonic anastomosis and two of three patients with biliary leaks. Although the presence of a pancreatic fistula was not associated with death, one patient with a biliary fistula died late in the postoperative course, resulting in a mortality rate of 8 per cent (one of 13) in the fistula group. However, the fistula-associated mortality rate in the study overall was only 0.3 per cent (one of 331).

The mortality rate was 2.1 per cent (seven of 331). Three of the seven patients died from local complications and four as a consequence of systemic complications (*Table 3*).

The indication for pancreatic head resection in the DPPHR group was always chronic pancreatitis, and the patient population was therefore demographically and aetiologically different from that of the other two groups. With respect to reoperation and mortality rates, there were no significant differences between the three procedures (*Table 4*). The total morbidity rate was lowest after DPPHR. The differences in morbidity were significant between the Whipple group and both the PPPD and the DPPHR

**Table 4** Comparison of procedures in 331 patients who underwent pancreatic head resection

|                          | Whipple | PPPD       | P    | DPPHR     | P     |
|--------------------------|---------|------------|------|-----------|-------|
|                          | (n=83)  | (n=133)    |      | (n=115)   |       |
|                          | n       | n          |      | n         |       |
| Pathology                |         |            |      |           |       |
| Neoplasia                | 75 (90) | 121 (91.0) |      | 0 (0)     |       |
| Chronic pancreatitis     | 7 (8)   | 11 (8.3)   |      | 115 (100) |       |
| Other                    | 1 (1)   | 1 (0.8)    |      | 0 (0)     |       |
| Hospital death           | 2 (2)   | 4 (3.0)    | 0.55 | 1 (0.9)   | 0.41  |
| Complications            | 46 (55) | 54 (40.6)  | 0.05 | 27 (23.5) | <0.01 |
| Local                    | 34 (41) | 40 (30.1)  | 0.1  | 18 (15.7) | <0.01 |
| Systemic                 | 24 (29) | 27 (20.3)  | 0.2  | 13 (11.3) | 0.01  |
| Delayed gastric emptying | 27 (33) | 27 (20.3)  | 0.04 | 0 (0)     | 0.01  |
| Pancreatic fistula       | 0 (0)   | 4 (3.0)    | 0.11 | 3 (2.6)   | 0.30  |
| Reoperation              | 4 (5)   | 5 (3.8)    | 0.71 | 4 (3.5)   | 0.88  |

Values in parentheses are percentages. PPPD, pylorus-preserving pancreatoduodenectomy; DPPHR, duodenum-preserving pancreatic head resection

groups. Pancreatic fistula rates were not significantly different between the three groups. However, since DGE was the most frequent complication after pancreatoduodenectomy, and was not observed after DPPHR, the difference in morbidity is in large part explained by this complication. The Whipple group exhibited a higher DGE rate than the PPPD group ( $P=0.04$ ). If complications other than DGE were analysed, the complication rates did not differ significantly, 23 per cent in the Whipple group, 20 per cent after PPPD and 24 per cent after DPPHR. Likewise, when DGE was excluded, the local morbidity was similar in the three groups ( $P>0.12$ ): 8 per cent for Whipple resection, 9.8 per cent for PPPD and 16 per cent for DPPHR.

## Discussion

Surgery of the pancreatic head originally had a high risk of complications, but resection is the treatment that offers the best long-term survival in patients with malignant tumours of the pancreatic head, as demonstrated in a recent study by Sener *et al.*<sup>23</sup> of more than 100 000 patients with pancreatic cancer. The reduced mortality rate after pancreatic resection has been a major achievement in surgery over recent decades<sup>2-8</sup>. The results of many centres indicate that a mortality rate below 5 per cent is a prerequisite for the performance of pancreatic resection today. Recent studies have also demonstrated that a comparable low mortality rate can be achieved in elderly patients, even in octogenarians, if the perioperative risks are assessed carefully and patients selected accordingly<sup>8,24,25</sup>. Pancreatic surgery should probably be concentrated in specialized units to improve quality of care and to reduce costs<sup>26-28</sup>. The present mortality rate of 2.1 per cent reflects the experience of other centres that perform a large number of pancreatic resections<sup>1,2,4,7,29,30</sup>. Pancreatic fistula and intra-abdominal abscess are still regarded as severe and relatively frequent complications that contribute substantially to the mortality rate after pancreatectomy<sup>30</sup>. Indeed, the pancreatic fistula rate has been reported to be above 10 per cent in several centres of excellence<sup>7,25,31,32</sup>.

A low prevalence of local and systemic causes of death after pancreatic head resection was observed, and these causes did not include pancreatic fistula. This finding is different from that of the Johns Hopkins group which reported a 15 per cent prevalence of pancreatic fistula. The Johns Hopkins reoperation rate of 4 per cent was almost identical to that reported here, but six of nine patients reoperated for leaks of the pancreatojejunostomy died in the postoperative course<sup>7</sup>. Likewise, Trede *et al.*<sup>4</sup> reported a fatal outcome in 24 per cent of 25 patients with pancreatic leaks in a series of 557 pancreatojejunostomies. In a recent

study by van Berge Henegouwen *et al.*<sup>33</sup> on the outcome when pancreatic fistula followed pancreatoduodenectomy, a high mortality rate of 28 per cent was noted and early completion pancreatectomy was recommended. The present study indicates that pancreatic fistulas and their associated mortality rate could be reduced in the future if patients were to receive improved perioperative management routinely, including interventional drainage of intra-abdominal collections.

Vascular resection usually aims to increase local radicality and to obtain tumour-free resection margins. Vascular resection was performed in 5.7 per cent of patients with malignant tumours to achieve a radical ( $R_0$ ) resection of pancreatic cancers predominantly infiltrating into the retropancreatic vessels. The renewed interest in vascular resection during surgery for periampullary cancer is a consequence of recent evidence that the complication rate of radical pancreatoduodenectomy is not increased in experienced hands<sup>34,35</sup>. Furthermore, survival after radical pancreatoduodenectomy, including segmental vein or artery resection, is similar to or better than that of standard resection<sup>36,37</sup>.

The most frequent surgical complications after pancreatic head resection were DGE, septic complications, fistulas and bleeding. Since DGE is only observed after pancreatoduodenectomy and usually has a prevalence of 15 to over 40 per cent<sup>8,38-40</sup>, the local and total morbidity rates after DPPHR were significantly lower than those in the other two groups. The other complications had a similar prevalence in all three groups. In patients with chronic pancreatitis, the difference in the DGE rate may have been responsible for the slower postoperative recovery after PPPD compared with DPPHR<sup>41,42</sup>.

The septic complication rate reported here includes wound sepsis as well as intra-abdominal abscess. The prevalence of septic complications in this series was lower than that in other large series, which report a prevalence of 8-15 per cent<sup>8,37,43</sup>. Four intra-abdominal abscesses occurred (1.2 per cent) and were drained by an interventional radiologist in three, with full recovery.

Compared with other reports, the pancreatic fistula rate of 2.1 per cent was low, and a similar prevalence of pancreatic fistula was observed in the three procedure groups. Pancreatic fistulas were always of low output (less than 200 ml/day), were treated conservatively in six patients and interventionally in one, did not result in death and, in contrast to biliary and colonic fistulas, did not necessitate reoperation. Completion pancreatectomy for a pancreatic fistula should therefore be an exception after pancreatic head resection. Although these results contradict recommendations from other groups<sup>31,33,44,45</sup>, many centres report a higher prevalence of fistula and intra-abdominal

sepsis. Reoperation for pancreatic fistula and completion pancreatectomy may be necessary only in those with an early high-output pancreatic fistula in combination with early postoperative multiple organ failure. In contrast, the majority of biliary and colonic fistulas were managed by reoperation. One of the patients with a biliary fistula died in the postoperative period after the reoperation, giving a mortality rate of 8 per cent in all patients with a fistula.

Patients without chronic pancreatitis did not have a higher prevalence of pancreatic fistula than those with chronic pancreatitis, who had a firm, fibrotic or calcified pancreas. In both groups the rate was 2 per cent; technical factors described earlier as well as adequate perioperative management may determine the prevalence of this potentially dangerous complication. Octreotide reduces the rate of postoperative fistula after pancreatic resection and perioperative administration of octreotide is cost effective in patients undergoing pancreatic head resection<sup>10-14</sup>. The controversy over the routine use of octreotide in pancreatic resection may be difficult to resolve<sup>46</sup>. Interinstitutional comparisons may be inconclusive since differences in surgical technique may contribute significantly to postoperative results.

In conclusion, this audit confirms the findings of recent large international series that pancreatic head resection can safely be performed by either a Whipple procedure, PPPD or DPPHR, with a comparably low mortality rate in all three groups. In this study patients undergoing DPPHR had a lower local and systemic morbidity rate than those undergoing pancreatoduodenectomy, supporting the use of DPPHR in treating chronic pancreatitis. Pancreatic fistula after pancreatic head resection has become a rare complication and in general does not require reoperation. With attention to technical detail and a continuing effort to improve perioperative management, pancreatic fistula may be a vanishing problem after pancreatic head resection, and this may lead to a further reduction in surgical morbidity.

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