

 ORIGINAL ARTICLE

Pancreatic fistula after pancreaticoduodenectomy: the conservative treatment of choice

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Abstract

Background: A pancreatic fistula (PF) is the most common complication after pancreaticoduodenectomy (PD), and its reported incidence varies from 2% to 28%. The aim of the present study was to analyse the treatment of a complicated PF comparing the surgical approach with conservative techniques.

Methods: From January 2000 through to August 2006, 121 patients were submitted for PD. The study consisted of 70 men and 47 women, with a median age of 60 years (SD \pm 12). The main indications for PD were pancreatic duct carcinoma in 52 patients (44.5%), ampullary carcinoma or adenoma in 18 (15.4%) and islet cell tumour in 11 (9.4%). Reconstruction by pancreaticogastrostomy was performed in 65 patients (55.6%), and pancreaticojejunostomy in 52 patients (44%).

Results: Thirty-five patients (30%) developed a PF. Amongst these, 20 were managed conservatively and 14 were reoperated. These two groups of patients were compared with patients without a PF for analysis. There was no significant difference in the mean age, the gender ratio, American Society of Anesthesiologists (ASA) classification, surgical time and blood replacement, number of associated procedures, vascular resection and type of reconstruction between the three groups. There were five post-operative deaths (4.2%), three patients (21.4%) in the surgical treatment group ($P < 0.01$). Mean total number of complications ($P = 0.02$) and mean length of hospital stay ($P < 0.001$) were greater in the surgical group. The medium delay between the pancreatic resection and reoperation was 10 days (range, 3–32 days). Completion splenopancreatectomy was required in five patients whereas conservative treatment including debridement and drainage was applied in nine patients.

Conclusion: The surgical approach for a PF is associated with a higher mortality and morbidity. There is no advantage in performing completion pancreatectomy (CP) instead of extensive drainage as a result of the same mortality and morbidity rates and the risk of endocrine insufficiency. In cases of complicated PF, radiological or surgical conservative treatment is recommended.

Keywords

pancreatic fistula, pancreaticoduodenectomy, postoperative complications, pancreatic resection

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Introduction

Over the past three decades, operative mortality rates after pancreaticoduodenectomy (PD) have decreased dramatically.^{1–3} An increase in experience and continuous improvements in surgical techniques have led to this decline, and in many high-volume centres the mortality rate is lower than 4%.^{4–8} However, the post-

operative morbidity rate is still high, between 30% to 50%.^{9–12} A pancreatic fistula (PF) is the most common complication after PD, and its reported incidence varies from 2% to 28%.^{7,9–17} A great deal of effort has been made to minimize its occurrence, using different methods for reconstruction, mainly drainage into either a jejunal loop (pancreaticojejunostomy) or the remaining stomach (pancreaticogastrostomy). Occlusion of the pancreatic

stump without any anastomosis in cases of small atrophic pancreas, biological adhesives to seal the anastomosis, somatostatin analogues to inhibit pancreatic secretion or a number of different anastomosis surgical techniques have also already been used to reduce the PF rate and none of these have demonstrated a clear advantage.^{15,18–29}

Developments in diagnosis methods and radiological intervention techniques have been responsible for an increase in the conservative management of PF. However, the leakage of pancreatic anastomosis can lead to bleeding from adjacent large vessels, severe pancreatitis, peritonitis and/or sepsis. In these cases, the conservative approach is not possible, and the risk of post-operative death is high.^{2,3,5,6,12,16,30,31,33}

Surgical management of a complicated PF can vary from simple drainage of the anastomotic region to completion pancreatectomy (CP) in the case of uncontrollable anastomotic leakage and peritonitis.³² Favourable outcomes after CP have been reported,^{32,33} but an important disadvantage of this option is pancreatic endocrine insufficiency. The aim of the present study is to analyse the treatment of a complicated PF comparing the surgical approach with conservative techniques.

Patients and methods

We reviewed the medical records of 121 patients who underwent PD between 1 January 2000 and 31 August 2006. Four patients without anastomosis of the pancreatic remnant were not included. Data collection was performed retrospectively using operation records, patient's files and discharge letters.

There were 70 men and 47 women, with a median age of 60 years (SD \pm 12). Indication for PD was pancreatic duct carcinoma in 52 patients (44.5%), ampullary carcinoma or adenoma in 18 (15.4%), islet cell tumour in 11 (9.4%), intraductal papillary mucinous neoplasm in 4 (3.4%) duodenal carcinoma in 4 (3.4%), cystoadenoma in 2 (1.7%) and chronic pancreatitis in 8 (6.8%). In nine (7.7%) cases, PD was performed as part of a more extended resection of advanced cholangiocarcinoma or gallbladder cancer. Other indications existed in nine patients (7.7%), such as peripancreatic metastasis or invasion of colonic, gastric or renal cell cancer.

Surgical technique

None of the 117 resections had pylorus preservation and extend of gastric resection was not standardized. There was, however, a tendency towards a limited antrectomy. Reconstruction by pancreatogastrostomy was performed in 65 patients (55.6%) and pancreatojejunostomy in 52 patients (44%). After PD, choice of the type of reconstruction (pancreatogastrostomy or pancreatojejunostomy) was decided according to the surgeon's preference and was not influenced by the consistence of the pancreas. In cases of cancer, a standard peripancreatic lymphadenectomy was performed, without extended retroperitoneal lymph node dissection. A silicone drain was routinely placed near the pancreatic anasto-

mosis in all patients. If the post-operative course was uneventful, a CT-scan was systematically performed on post-operative day (POD) 7 and in the absence of pathological findings the drain was removed. The presence of gas bubbles and/or liquid collection near the anastomosis were considered as radiological signs of PF even in the absence of amylase-rich fluid in the drain. In this situation drain withdrawal was delayed.

Tube gastrostomy and a feeding jejunostomy were not used. Thirteen patients (11.1%) had vascular resection and 8 (6.8%) had additional major organ resections (e.g. liver or colonic resection).

Complications

A PF was defined as a drain output of any measurable volume of fluid after POD 3 with amylase content greater than three times the serum amylase activity (CB). Post-operative mortality was defined as death occurring in the first 30 post-operative days or before discharge from the hospital. Delayed gastric emptying was defined as intolerance to oral intake and need for nasogastric decompression after the 7th post-operative day.

Other complications were categorized and defined as any of the following: intra-abdominal abscess (fluid requiring drainage and with positive bacterial culture); wound infection; post-operative bleeding (requiring transfusion, endoscopic or operative intervention); bile leakage (bilious drainage from intra-operatively placed drains or bile collection requiring drainage); cardiac (myocardial infarction or new-onset arrhythmia requiring intervention); pulmonary (pneumonia, effusion requiring drainage, or reintubation); sepsis (fever, leukocytosis, or bacteremia requiring medical and/or surgical intervention); and reoperation in the first 30 postoperative days or before discharge from the hospital.

Pancreatic leakage was generally treated by maintenance of the drain placed near the pancreaticodigestive anastomosis. Percutaneous drainage was performed if the patient developed a concomitant intra-abdominal abscess or fluid collection diagnosed by tomography. Relaparotomy was performed for post-operative haemorrhage and intra-abdominal collection when the interventional methods were not possible or the patient showed clinical deterioration.

In the absence of reliable guidelines, the management of the PF at the time of relaparotomy was left to the discretion of the operating surgeon. However, conservative treatment, including a thorough peritoneal lavage, drainage and the control of sepsis using large spectre antibiotherapy, was the preferred approach whenever considered possible. In the presence of massive peritoneal contamination as a result of complete disunion of the pancreatic anastomosis CP was undertaken.

Statistical analysis

Data analyses were performed using SPSS® software (SPSS, Chicago, IL, USA). For statistical comparisons of the patients

groups, a two-tailed χ^2 and *t*-test were used. Quantitative variables were tested using a Mann–Whitney *U*-test. Values of $P < 0.05$ were considered significant.

Results

Management of pancreatic leakage

Thirty-five patients (30%) developed PF. Amongst these, 20 were managed conservatively and 14 were reoperated. These two groups of patients were compared with patients without PF for analysis (Table 1). The conservative treatment included the maintenance of the drain placed at the time of operation in 14 patients (70%) and percutaneous drainage in the other 6 (30%). Mean age, gender ratio and American Society of Anesthesiologists (ASA) classification were similar in the three groups. The percentage of malignant pathology was also similar (Table 2).

Intra-operative parameters are given in Table 2. There was no significant difference in the surgical time and blood replace-

ment between the three groups. Pancreas texture, Wirsung diameter, number of associated procedures and vascular resection rate were similar. The different types of pancreatic reconstruction were not related to PF occurrence and reoperation.

There were five postoperative deaths for the entire series, with an overall mortality rate of 4.2%. Two deaths occurred in the group without PF (2.4%), as a result of mesenteric artery thrombosis and severe pneumonia, respectively. Three patients (21.4%) died in the surgical treatment group ($P < 0.001$). There was no mortality in group 2. Post-operative complications, including PF, occurred in 54 out of the 117 patients, with an overall post-operative morbidity rate of 46.1%. The mean total number of complications for the group without PF was 0.36 ± 0.5 , compared with 0.8 ± 0.77 ($P = 0.002$) for conservative treatment group and 2.21 ± 0.73 ($P < 0.001$) for the surgical group, excluding PF itself. The mean length of hospital stay for the group without PF was 21 ± 9 days, 42 ± 17.5 days for the

Table 1 Groups characteristics

	No of PF (<i>n</i> = 82) (70%)	PF conservative treatment (<i>n</i> = 21) (18%)	PF surgical treatment (<i>n</i> = 14) (12%)	<i>P</i>
Gender (male : female)	44 : 38	15 : 6	10 : 4	0.450
Age, mean (range), years	59 (22–80)	62 (45–83)	59 (43–82)	0.600
ASA				
I	37 (45)	8 (38)	6 (43)	0.663
II	41 (50)	13 (62)	8 (57)	
III	4 (5)	0 (0)	0 (0)	
Malignancy	71 (87)	16 (76)	12 (85.7)	0.496

PF, pancreatic fistula; ASA, American Society of Anesthesiologists
Values in parentheses are percentages unless indicated otherwise

Table 2 Intra-operative parameters

	No of PF (<i>n</i> = 82) (70%)	PF conservative treatment (<i>n</i> = 21) (18%)	PF surgical treatment (<i>n</i> = 14) (12%)	<i>P</i>
Surgical time, min	372 (240–720)	325.5 (240–600)	450 (300–670)	0.233
Red blood cells units transfusions	0.7 (0–12)	0,6 (0–5)	0,7 (0–4)	0.952
Pancreas texture				
Hard	52 (63.5)	8 (38)	7 (50)	0.094
Soft	30 (36.5)	13 (62)	7 (50)	
Wirsung diameter				
<5 mm	36 (44)	12 (57)	9 (64)	0.257
>5 mm	46 (56)	9 (43)	5 (36)	
Associated procedure	3 (3.6)	3 (14)	2 (14.2)	0.114
Vascular resection for tumour infiltration	11 (13.4)	1 (4.7)	1 (7.1)	0.467
Reconstruction				0.245
Pancreatogastrostomy	49 (60)	12 (57)	5 (36)	
Pancreatojejunostomy	33 (40)	9 (43)	9 (64)	

PF, pancreatic fistula
Values in parentheses are percentages, unless indicated otherwise

Table 3 Mortality and morbidity

	No of PF (<i>n</i> = 82) (70%)	PF conservative treatment (<i>n</i> = 21) (18%)	PF surgical treatment (<i>n</i> = 14) (12%)	<i>P</i>
Post-operative hospital stay (days)	21 ± 9	42 ± 17.5	63 ± 27	<0.001 ^a 0.008 ^b
No. of complications, ^c mean ± SEM	0.36 ± 0.5	0.80 ± 0.77	2.21 ± 0.73	<0.001 ^a 0.002 ^b
Delayed gastric emptying	6 (7.3)	7 (33.3)	10 (71.4)	<0.001
Wound infection	4 (4.8)	2 (9.5)	2 (14)	0.377
Biliary fistula	4 (5.7)	2 (9.5)	1 (7.1)	0.712
Abdominal bleeding	4 (4.8)	1 (4.7)	4 (28.5)	0.008
Cardiac	3 (3.6)	1 (4.1)	1 (7.1)	0.249
Pulmonary	3 (3.6)	0	3 (21.4)	0.510
Sepsis	3 (3.6)	0	4 (28.5)	<0.001
Mortality	2 (2.4)	0	3 (21.4)	0.01

PF, pancreatic fistula

^aNo of PF compared with surgical treatment

^bConservative treatment compared with surgical treatment

^cOther than PF

Values in parentheses are percentages, unless otherwise indicated

conservative treatment group and 63 ± 27 days for the surgical group (*P* < 0.001) (Table 3).

In the surgical group, there were significant increases in the following complications: delayed gastric emptying, intra-abdominal bleeding and sepsis. There were no differences in rates of wound infection, biliary fistula, cardiac and pulmonary complications (Table 3).

Reoperation for PF

The mean age of the patients was 59 years (22–80 years). There were 10 men (71%) and 4 women (29%). Patients were preoperatively scored as ASA I (six patients) or ASA II (eight patients). Surgical findings of the 14 patients that were submitted for relaparotomy are detailed in Table 4. The medium delay between pancreatic resection and reoperation was 10 days (3–32 days).

Overall, completion splenopancreatectomy was required in five patients, whereas conservative treatment, including debridement and drainage, was applied in nine patients. Three patients (14.2%) died in the early post-operative period (8, 16 and 20 days after surgery) as a result of multiorgan failure and sepsis. All of them showed diffuse peritonitis at the time of reoperation, two patients were submitted for completion pancreatectomy and the other one for debridement and drainage.

Seven patients had post-operative medical complications: pneumopathy (*n* = 3), renal failure (*n* = 2), cardiac arrhythmia (*n* = 1) and mental confusion (*n* = 1). Six patients (43%) had delayed gastric emptying. Mean hospital stay was 63 ± 27 days for survivors.

Discussion

The International Study Group on Pancreatic Fistula Definition (ISGPF) has recently proposed a standardized definition of PF

which seems to be widely accepted.³⁴ In this classification, three grades of severity have been described. Overall, any fistula that requires reoperation is classified as Grade C. However, in this latter group of patients, two situations should be distinguished depending on a finding of localized sepsis or diffuse peritonitis. Although surgical conservative treatment is mainly used in the case of localized collection, the management of diffuse peritonitis still remains ill defined. In the last decade, conservative treatment has been suggested instead of CP. In our study, we analysed the two types of treatment and our results support the use conservative management.

Using a non-restrictive definition of PF, according to the ISGPF proposition, 30% of our patients experienced pancreatic leakage. Most of them were grade A or B (21/35). However, a remaining large proportion of PF (grade C) was reoperated. However, comparative analyses of preoperative and intra-operative data failed to predict severity of PF. Overall, mortality and morbidity, especially delayed gastric emptying, were significantly greater in the cases of reoperation for PF. Consequently, the hospital stay was longer in such cases. We showed that reoperation for PF has a significant deleterious impact on post-operative course as compared with non-surgical management.

In the situation where surgery seems mandatory, two strategies are available: CP or conservative treatment. Initially, CP was the main surgical approach reported for the treatment of complicated PF. In the last decade, this treatment has been restricted to patients with peritonitis. At the present time, the use of CP is under debate whereas conservative management has emerged as a salvage solution equally efficient to CP. The two main arguments to perform CP are sterilization of the source of infection and the decreased need for reoperation.^{32,33} However, CP is technically demanding, leading in most cases to splenectomy, and more rarely to total

Table 4 Patients and operative findings

Patient no./gender/years	Surgical indications	Anast.	Reintervention (operative day)	Operative findings	POHS (days)	Death
1/M/55	Ampullary carcinoma	PJ	Completion pancreatectomy, splenectomy (6)	PJ leakage, peritonitis	8	Yes
2/F/49	Pancreatic duct Carcinoma	PJ	Debridement and drainage (17)	PJ leakage, intra-abdominal abscess (peripancreatic retrogastric)	32	No
3/M/59	Pancreatic duct Carcinoma	PG	Completion pancreatectomy, splenectomy (5)	PG leakage, pancreatitis	85	No
4/M/82	Bile duct Carcinoma	PJ	Debridement and drainage (12)	Diffuse peritonitis	16	Yes
5/M/72	Pancreatic duct carcinoma	PJ	Biliary intubation, drainage (9)	PJ leakage, HP leakage, peritonitis	52	No
6/M/52	Pancreatic duct carcinoma	PJ	Hemostasis, debridement and drainage (5)	PJ leakage, haemoperitoneum	42	No
7/M/58	Chronic pancreatitis	PJ	Completion pancreatectomy, splenectomy (9)	PJ leakage, peritonitis	42	No
8/M/43	Pancreatic duct carcinoma	PJ	Completion pancreatectomy, splenectomy (32), GDA ligation	PJ leakage, GDA haemorrhage	105	No
9/M/62	Pancreatic duct carcinoma	PJ	Debridement and drainage (6)	PJ leakage, peritonitis	61	No
10/F/75	Pancreatic duct carcinoma	PG	Debridement and drainage (13)	PG leakage, intra-abdominal abscess (retrogastric)	45	No
11/M/66	Ampullary carcinoma	PG	Debridement and drainage (12)	PG leakage, intra-abdominal abscess (retrogastric)	35	No
12/F/69	Duodenal carcinoma	PG	Completion pancreatectomy, splenectomy (5)	PG leakage, peritonitis	20	Yes
13/F/47	Pancreatic duct carcinoma	PG	Debridement and drainage (3)	PG leakage, haemoperitoneum	14	No
14/M/48	Islet cell tumor	PJ	Debridement and drainage (5)	PJ leakage, haemoperitoneum	95	No

Anast, anastomosis; PJ, pancreaticojejunostomy; PG, pancreaticogastrostomy; POHS, post-operative hospital stay; HP, hepaticojejunostomy; GDA, gastroduodenal artery

gastrectomy. Moreover, definitive endocrine insufficiency with potential lethal severe hypoglycemia is a major pitfall of this approach. In our experience, even in cases of reoperation, most patients (9/14) did not undergo CP. Among the five patients who underwent CP, splenic conservation was not possible. Two of these (40%) patients died during the post-operative course. Overall, we are in accordance with the mortality rate after CP ranging from 0% to 80%.^{32,33,35–37} However, only four studies reported their experience of CP with a reduced number of patients. As a result of the small sample size, no conclusion can be drawn.

On the other hand, conservative treatment is now more frequently applied even in cases of diffuse peritonitis. Most of the patients reported herein were conservatively treated even in the case of diffuse peritonitis (3/9) with (3/9) or without associated haemorrhagic complications. The remaining patients (3/9) had localized abscesses which were not radiologically accessible. Gueroult *et al.* speculated that CP avoids reoperation.³² However, in their study, they did not compare CP with conservative treatment. In our experience, none of the patients were reoperated after 'salvage' drainage. Moreover morbidity did not differ between CP and drainage. Although the mortality rate was not statistically significant, there is a tendency for an increased mortality rate after CP (40%) as compared with drainage (11%). In the case of leakage requiring surgical drainage, several authors reported a mortality rate ranging from 0% to 33%,^{16,37–40} which is lower than the mortality rate reported after CP (0 to 80%). Again, the number of reoperations was similar, irrespective of the use of CP or drainage to treat PF. Our experience, which corroborated with several authors, shows that the conservative approach was not related to increased reoperations when compared with CP.

After PD, haemorrhage occurs in more than 10% and is strongly related to local sepsis and anastomotic leakage.^{12,41} In our study, four patients reoperated for PF had an associated haemorrhage, a higher rate when compared with patients without PF, or with PF treated conservatively. The association between PF and haemorrhage has been reported and some authors suggested that pancreatic remnant resection is necessary to prevent rebleeding.⁴² In this series, three patients were treated by laparotomy without CP and relaparotomy was not necessary. Drainage of intra-abdominal collection and fistula may avoid pancreatic fluid contact with dissected vessels, preventing hemorrhage.

Conclusion

This study demonstrated that the surgical approach for PF is associated with higher mortality and morbidity rates, as compared with the conservative approach. In case of PF requiring surgical treatment, it seems that there is no advantage in performing a completion as compared with extensive drainage, owing to the same mortality and morbidity rates, and given the risk of severe endocrine insufficiency in case of CP. Radiological or surgical conservative treatment of a PF should be the preferred option.

Conflicts of interest

None declared.

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