REVIEW ARTICLE

Postoperative Pancreatic Fistula: A Surgeon's Nightmare! An Insight with a Detailed Literature Review

Prasad Seetharam, Gabriel Sunil Rodrigues

Kasturba Medical College, Manipal University, Manipal – 576104, India

ABSTRACT

Context Postoperative fistula formation is an important complication following pancreatic resections. **Objective** A large volume of literature without uniform conclusions is available regarding various controversies about postoperative pancreatic fistulae. The term postoperative pancreatic fistula includes fistula resulting from any surgery involving pancreas, most commonly pancreaticoduodenectomy and distal pancreatectomy. In this review, we have tried to present a comprehensive account of postoperative pancreatic fistula with particular emphasis on important controversies clouding the subject. **Methods** We performed Medline literature search for relevant articles using the key words pancreas, pancreatic cancer, pancreatectomy, pancreatoduodenectomy, Whipple's operation, postoperative, complications, fistula, management and treatment in various combinations with the Boolean operators AND, OR and NOT. **Conclusions** Postoperative pancreatic fistula is a troublesome complication of pancreaticoduodenectomy. Although the risk factors for postoperative pancreatic fistula have been extensively described, none of the methods recommended for preventing postoperative pancreatic fistula have been conclusively proved to be effective. While endoscopic treatment and percutaneous treatment form important aspects of treatment of postoperative pancreatic fistula, surgery may be required for select cases.

INTRODUCTION

Pancreaticoenteric anastomosis (pancreaticojejunostomy) is still considered the "Achilles heel" of pancreaticoduodenectomy (PD). Among high volume centers, while the mortality rates following pancreatic surgery has come down to less than 5%, the morbidity still remains high, ranging from 30-50% [1]. Traditionally, postoperative pancreatic fistula (POPF) has been regarded as the most frequent major complication following pancreatic resection and reconstruction. However, a recent study has observed that the incidence of POPF is significantly lower in recent times and ranks third among different complications evaluated in terms of frequency and severity [2]. The significance of POPF lies in the fact that in addition to being a life-threatening complication, it prolongs the hospital stay and adds on to hospital costs.

CLASSIFICATION

High or Low Output Fistula

A fistula is termed a high output fistula when the output is greater than 200 mL in 24 hours and low output when the output is less than 200 mL in 24 hours. However, the incidence of spontaneous resolution is similar for both the groups [3].

Received November 29th, 2014 – **Accepted** February 09th, 2015
Keywords complications; Pancreatectomy; Pancreaticoduodenectomy; Postoperative Period; Fistula
Correspondence Gabriel Sunil Rodrigues
Department of General Surgery
Kasturba Medical College, Manipal University,
Manipal – 576104, India
Phone +91 9448501301
E-mail gabyrodricks@gmail.com

Pure or Mixed Fistula

A fistula that drains only pancreatic juice is called a pure fistula, while a fistula which drains pancreatic juice mixed with enteric contents, is a mixed fistula. The output of a pure POPF contains inactive pancreatic enzymes and is relatively inert. The output of a mixed POPF contains activated proteases, which can cause further complications like necrosis and hemorrhage.

End or Side Fistula

An end fistula results from disruption of main pancreatic duct. The two portions of pancreas are not continuous and tend to heal separately. This condition is termed *"disconnected duct syndrome"*. End fistulae are unlikely to heal on conservative management because of discontinuity from the gastrointestinal tract and the remaining pancreatic duct. Also end fistulae are not amenable to transpapillary stent placement. On the contrary, in a side fistula, the continuity of the pancreatic duct is maintained. The probability of a side fistula healing with conservative management is more [3]. Side fistulae can be inflammatory or postoperative, the latter respond better to medical treatment than inflammatory fistulae.

EPIDEMIOLOGY

POPF commonly occur following either PD or distal pancreatectomy (DP).

Fistulae after PD

The incidence ranges from 0-24% with an average fistula rate of 12.9% following PD [4]. The mortality rate from a major pancreatic fistula is up to 28% and the usual cause of death is retroperitoneal sepsis and hemorrhage [5-7].

Fistulae after DP

POPF is a common complication after DP with an incidence of 5-28% [7].

DEFINITION

The word 'fistula' is used to describe an abnormal passage from one epithelialized surface to another. A thorough literature search does not yield an unanimous definition for POPF. The issue is further complicated with usage of terms like leak, leakage, collection, anastomotic failure and anastomotic insufficiency. Pancreatologists worldwide have used the following various definitions to describe POPF.

- Drainage fluid of more than 50 mL in 24 hours with an amylase content of more than 3 times the normal serum amylase activity for more than 10 days after operation [8, 9].
- Drainage fluid of more than 10 mL in 24 hours with the amylase at least 3 times the normal serum activity, 3 or 4 days postoperatively [10, 11].
- Fluid drainage for more than 7 days postoperatively containing amylase activity of more than 3 times the serum activity [12].
- The concept of clinically significant leak has been suggested which incorporates fever (>38^0 C), leukocyte count of greater than 10000 cells/mm^3, sepsis and/or the need for drainage [13].

An International Study Group on Pancreatic Fistula (ISGPF) formed by an international consortium of 37 leading pancreatic surgeons from 15 countries reviewed the literature, discussed their clinical experiences with POPFs and has proposed a definition and classification [1]. ISGPF has defined POPF as 'an abnormal communication between pancreatic ductal epithelium and another epithelial surface, containing pancreas derived enzyme rich fluid.' Interestingly, this definition also includes clinically asymptomatic patients and for the same reason a grading system (Grade A, B and C) has been proposed to assess the severity of POPF [1] (Table 1).

Michelle *et al*. have used a classification scheme for grading complications arising after PD and is applicable to all complications arising from PD and not just POPF [2] (Table 2).

RISK FACTORS FOR POPF

Risk factors can be classified as

- Patient factors
- Disease related factors

Patient Factors

Though male sex is seen to be associated with increased risk for POPF, no specific reason has been found for this phenomenon [12]. Similarly age greater than 70 years is associated with increased risk for POPF [14]. Other risk factors for POPF that have been evaluated in various studies include duration of jaundice, creatinine clearance and intraoperative blood loss [15]. But none of these are found to have a definitive relation with POPF.

Disease Related Factors

Pancreatic texture, pancreatic pathology, high pancreatic juice output, pancreatic duct size and biochemical parameters are factors seen to contribute towards POPF.

Pancreatic Texture

The texture of pancreas is usually related to the underlying disease process. It is widely accepted that a fibrotic pancreatic remnant in chronic pancreatitis holds the pancreatic anastomosis well, while a soft friable pancreas found in pancreatic or periampullary cancer usually betrays. This concept has been substantiated by several studies. A review of 2644 patients who had undergone PD before 1991 reported a fistula rate of 5% in chronic pancreatitis, 12% in pancreatic cancer, 15% in ampullary cancer and 33% in bile duct cancer [16]. Yeo *et al*. [17] found that there was a strong association between pancreatic texture and the pancreatic fistula rate. In their study, none of the 53 patients with hard pancreatic remnants developed pancreatic fistula, whereas 19 of 75 patients (25%) with soft pancreatic texture developed

Table 1. Grading system to assess the severity of POPF

Grade	A	B	C
Clinical conditions	Well	Often well	Ill appearing/ Bad
Specific treatment	No	Yes/No	Yes
Ultrasonography/ Computed tomography	Negative	Negative/ Positive	Positive
Persistent drainage	No	Usually yes	Yes
Reoperation	No	No	Yes
Death related to POPF	No	No	Possibly yes
Signs of infections	No	Yes	Yes
Sepsis	No	No	Yes
Readmission	No	Yes/ No	Yes/ No

Table 2. Classification scheme for grading complications arising after PD applicable to all complications arising from PD and not just postoperative pancreatic fistula (POPF)

Grade	Definition
I	Any definition from the normal post-operative course without pharmacologic treatment or surgical, endoscopic and radiological interventions. Allowed therapeutic regimens are drugs such as antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy. This grade also includes wound infections opened at the bed side.
II	Requiring pharmacologic treatment with drugs other than ones allowed for grade I complications. Blood transfusion and total parenteral nutrition are also included
III -IIIa -IIIb	Requiring surgical, endoscopic or radiologic intervention. Intervention not under general anesthesia. Intervention under general anesthesia.
IV -IVa -IVb	Life threatening complication requiring Intermediate care/ Intensive care unit management. Single-organ dysfunction Multiorgan dysfunction
V	Death of a patient
Suffix "d"	If the patient suffers from a complication at the time of the discharge, the suffix "d" (for disability) is added to the respective grade of complication (including resection of pancreatic remnant). This label indicates the need for a full follow-up to fully evaluate the complication.

POPF. Other studies too show similar results regarding POPF and pancreatic texture [18, 19].

High Pancreatic Juice Output

In the setting of a nondilated duct in a soft textured pancreas, a high pancreatic juice output has been considered as an important factor contributing to POPF [20, 21]. Ishikawa *et al*. [22] reported significantly reduced POPF rates after PD among patients who received preoperative radiation therapy compared with patients who did not and they have even suggested that preoperative radiation therapy might reduce the risk of POPF by decreasing pancreatic secretion.

Size of the Pancreatic Duct

A small sized pancreatic duct has been suggested as a risk factor for POPF [7, 21]. In a study, which included 62 patients who underwent PD, the incidence of POPF was 4.88% among patients with a pancreatic duct size greater than or equal to 3 mm and was 38.1% in those with ducts smaller than 3 mm [23].

Biochemical Parameters

Various biochemical parameters like serum bilirubin, serum albumin, blood urea nitrogen (BUN), serum amylase and N-benzoyl-L-tyrosyl-p-aminobenzoic acid (BT-PABA) excretion test values have been evaluated as risk factors for POPF. A normal preoperative BT-PABA test value has been suggested as a risk factor for POPF [19].

TECHNICAL ASPECTS

Appropriate management of the pancreatic remnant has been one of the core issues regarding prevention of POPF. Some of the recommended methods for the management of pancreatic remnant include

1. Pancreatic duct ligation
2. Pancreatic duct obliteration
3. Pancreaticojejunostomy (PJ)
4. Pancreaticogastrostomy (PG)

Pancreatic Duct Ligation

Ligation of the pancreatic duct of the pancreatic remnant was one of the earliest practices in the management of the pancreatic remnant. However, this procedure is associated with a high incidence of pancreatic fistula, infection and inevitable pancreatic insufficiency [24]. Even though ligation technique was uniformly associated with a high incidence of fistula, the resultant complications were not fatal because of the non-activated enzymes in the fistula output. Bartoli and colleagues [16] in a meta-analysis concluded that although ligation was associated with a significantly higher fistula rate compared with anastomosis, the mortality rates were not significant.

Pancreatic Duct Obliteration

Obliteration of the pancreatic duct with fibrin glue [25] or synthetic polymers [26] have shown to result in a low pancreatic fistula rate of 4% to 7%. This technique carries the advantage of being technically easier and less time consuming to perform as compared with pancreaticoenteric anastomosis. However it has the disadvantage of being incomplete and is associated with physiological disturbances.

Pancreaticojejunostomy (PJ)

Jejunum is a good choice for reconstructing the drainage of pancreatic remnant because of its good vascularity and mobility. The anastomosis between pancreatic remnant and jejunum could be

- End-to-side duct-to-mucosa anastomosis, wherein the pancreatic duct is anastomosed to the mucosa on the antimesenteric border of the jejunum. The cut margin of the pancreas is then circumferentially opposed to the jejunal wall with seromuscular sutures
- End-to-end invagination technique (dunking method), wherein end-to-end anastomosis between pancreatic remnant and jejunum is achieved in two layers. The inner layer approximates the cut margin of the pancreas to the full thickness of the jejunal wall. The sutures of this layer should incorporate pancreatic duct so as to splay the duct. The outer layer circumferentially opposes the capsule of the pancreas to the seromuscular coat of the jejunum
- End-to-side invagination technique, which is similar to dunking method, except that the anastomosis is between the cut surface of the pancreatic remnant to the antimesenteric aspect of the jejunum

Comparison of Different Techniques of PJ's

The debate on the technique of PJ having a favorable outcome remains unsettled. Although several studies have compared various techniques of PJ, a consensus is yet to be arrived at. Studies from 1980s did not find any significant difference in the pancreatic fistula rate among different techniques of PJ [27]. A meta-analysis of 2361 patients who underwent PD before 1991 found significantly higher incidence of POPF with end-to-side invagination anastomosis compared with duct-to-mucosa anastomosis (16). Few non-randomized studies have suggested that duct-to-mucosa anastomosis may be associated with lower POPF rate compared with invagination technique [28-30]. Studies have also compared continuous and interrupted duct-to-mucosa anastomosis, wherein continuous duct-to-mucosa anastomosis was found to have a significantly lower leakage rate [31, 32].

Retrospective studies comparing duct-to-mucosa and dunking technique for PJ have not found any statistical difference between the two in preventing anastomotic failure [33]. Marcus *et al*. [21] found that duct-to-mucosa anastomosis was associated with a low pancreatic fistula rate in low risk patients with dilated pancreatic duct or firm fibrotic pancreas, whereas end-to-end invagination

technique was safer in high risk patients with small ducts or soft friable pancreas and this opinion is shared by other workers as well [33].

To summarize, there is still no consensus regarding the choice of anastomotic technique for PJ. Different techniques find their application among different group of surgeons. It is preferable for pancreatic surgeons to have more than one technique in their armamentarium for managing the pancreatic remnant. Ultimately a well-designed prospective randomized study will be required to prove the superiority of one technique over the other.

Pancreaticogastrostomy (PG)

PG involves an anastomosis between residual pancreatic stump and posterior wall of stomach. The anastomosis is accompanied by implantation of the pancreatic stump into stomach or by creating a mucosa-to-mucosa anastomosis. PG as a technique for reconstruction after PD was first introduced in 1946 [34]. However not much attention was paid to this technique until in 1990s when there was an emergence of renewed interest in PG. Proponents of PG claim the following potential advantages over PJ [24]

- The natural close apposition between stomach and pancreas facilitates a tension free anastomosis
- A long jejunal loop with its retained secretion that may exert a traction effect on anastomosis is avoided
- The thick and vascularized gastric wall provides excellent blood supply to the anastomosis
- There is incomplete activation of pancreatic enzymes in the stomach because of acidic environment absence of enterokinase
- Provision for easy monitoring of duct patency by nasogastric amylase estimation in the early postoperative period and long term access for radiological and endoscopic evaluation

The major complication with PG is gastrointestinal bleeding presumably from the pancreatic stump [35].

PJ *versus* PG

Several studies have compared PJ and PG with respect to the incidence of POPF. Published single institutional studies have favored PG over PJ [36, 37]. A large meta-analysis has shown a significantly lower incidence of pancreatic fistula after PG as compared to end-to-end or end-to-side PJ [16]. In this meta-analysis, there were no significant differences in mortality between the two groups. However the definition of pancreatic fistula was not uniform among studies included in this meta-analysis.

A prospective, randomized single institution study comparing PG with PJ concluded that the incidence of POPF as well as other postoperative complications and length of postoperative stay were similar among PG and PJ groups [9]. A meta-analysis concludes that PG is the safer method of reconstruction following PD, as PJ is associated with a higher incidence of POPF [38]. However another recent systematic review and meta-analysis of randomized control trials show no differences in outcomes irrespective of the method of pancreatic anastomosis after PD [39].

PREVENTION OF POPF

The measures recommended to prevent POPF following PD can be considered under following categories

- Pharmacological measures
- Preoperative irradiation
- Modifications in operative techniques

Pharmacological Measures

A high pancreatic juice output in a soft pancreas is an important risk factor for POPF. Hence it appears rational to hypothesize that inhibition of exocrine pancreatic secretion in the postoperative period may reduce the incidence of POPF. Somatostatin and its octapeptide analogue have been used by various groups to reduce the pancreatic juice secretion and thereby prevent POPF (Figure 1). A German group was the first to report reduced complication rate after PD with perioperative infusion of somatostatin [40]. Subsequently many other studies have evaluated the effect of somatostatin/octreotide in preventing and lowering the incidence of POPF.

Most European studies which included various pancreatic surgeries for different pancreatic pathologies opined that somatostatin/octreotide reduces the incidence of POPF [10, 11, 41, 42]. On the contrary, American studies did not show any benefit from prophylactic use of octreotide [17, 43]. The exact reasons for the different outcomes between European and American trials are not clear but the suggested reasons were [44]

- Difference in the study designs - The European trials were all multi-institutional and thus the surgical techniques were not standardized, while the American studies were conducted in a single institution with a high volume of pancreatic surgery
- Inclusion of various pancreatic procedures in the European trials, whereas the American trials concentrated exclusively on PD
- Heterogeneity in the pathological diagnosis
- Different criteria used for defining pancreatic fistula

It has been suggested that for PD's performed by highly specialized units, octreotide may not have a benefit with already low POPF rates, whereas it may have a potential benefit in operations performed by less experienced surgeons [17]. A meta-analysis regarding the prophylactic use of octreotide in pancreatic resections on the fore mentioned randomized control studies concluded that [44]

- There were no significant differences between octreotide and control groups in the frequency of local complications
- There were no significant differences between octreotide and control groups in the frequency of local or systemic complications which often develop as a consequence of pancreatic anastomotic leakage

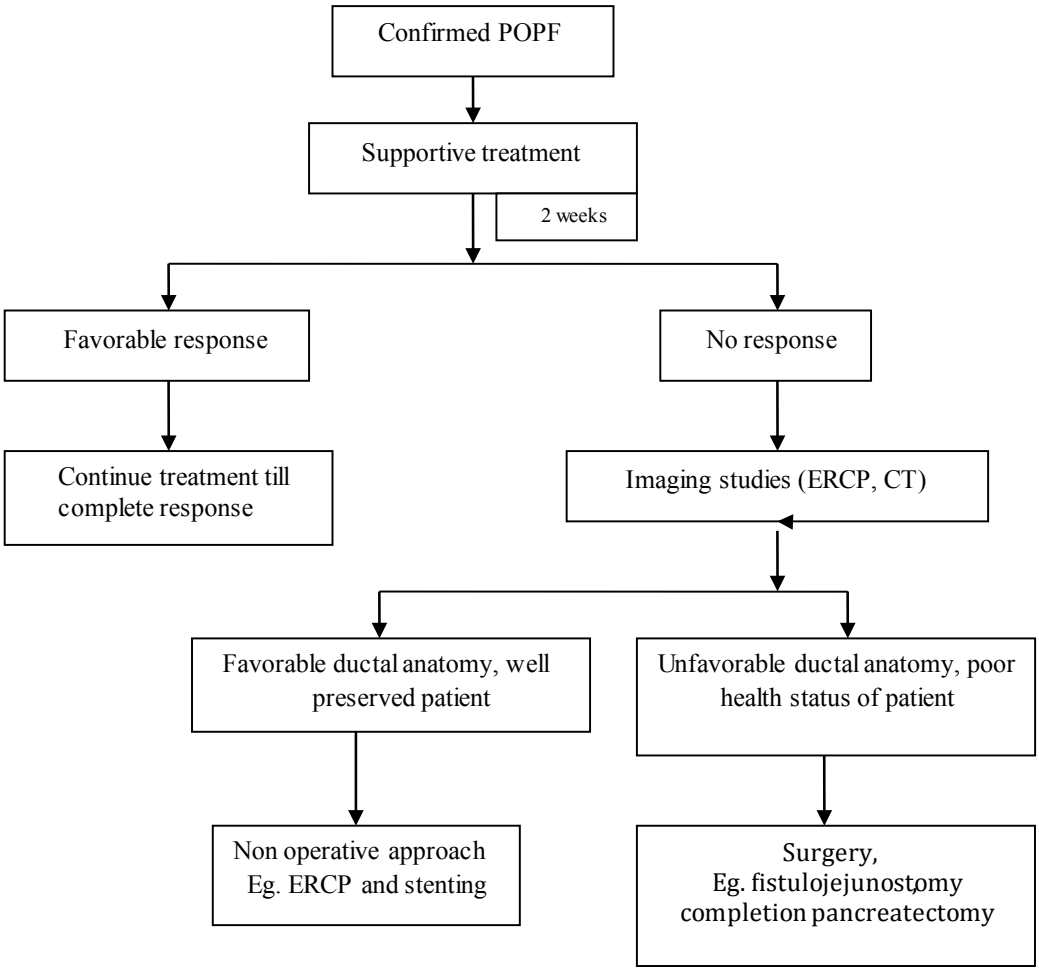

Figure 1. Management of POPF

Table 3 summarizes data of prospective randomized trials on 'prophylactic use of somatostatin/octreotide following pancreatic resection' [44]. Thus it may be conclude that the use of somatostatin/octreotide cannot be recommended for the prevention of POPF following pancreatic surgery. Pasireotide, a long acting somatostatin analogue has shown promising results in reducing POPF [48].

Preoperative Irradiation

Preoperative irradiation of the pancreas reduces the exocrine function, as the pancreatic acinar cells are very sensitive. This forms the basis for the concept of preoperative irradiation to reduce the incidence of POPF. Preoperative irradiation is particularly relevant in pancreatic malignancy where there is twin benefit of increasing resectability as well as reducing the incidence of POPF. A retrospective study by Ishikawa *et al*. substantiates this concept [22].

Technical Modifications to Prevent POPF

The technical considerations regarding management of pancreatic remnant following PD, has already been described. Few other technical innovations suggested to combat POPF are as follows

Pancreatic Duct Stent or Drainage

The use of a transanastomotic stent to drain pancreatic secretions may help to divert away pancreatic secretion from the anastomosis. It also allows more precise placement of sutures, thereby preventing pancreatic duct injury by sutures. A controlled study in a canine model has demonstrated that the use of internal stent could prevent anastomotic leakage and occlusion in PJ anastomosis [49]. Clinical studies have also reported internal stenting of the anastomosis reduces the incidence of POPF following PJ thereby promoting early discharge from the hospital [50, 51]. External drainage/diversion of pancreatic juice has the additional advantage of preventing the activation of pancreatic enzymes by the bile soon after the surgery. Studies have reported a low incidence of POPF with the use of external pancreatic duct drainage [52-54].

Fistulation Method

Okamoto A *et al*. have recommended this method wherein the pancreatic drainage tube was used without a duct to mucosa anastomosis in PJ after PD [55]. The pancreatic remnant was anchored to the seromuscular layer of the jejunum with a single layer of suture. The drainage tube was brought out externally through the jejunal loop for complete external diversion. With this technique the authors have reported a POPF rate of 3% in 162 patients. Some surgeons have reported the use of internal venting drains that traverse the bowel with their tips located intraluminally near the pancreatic anastomosis [56, 57]. Such venting drains serve to prevent the distension of jejunal loop and reduce the incidence of POPF.

Table 3: Prospective randomized trials on 'prophylactic use of somatostatin/octreotide following pancreatic resection'.

Study	Groups	No of patients	No of fistulae
Buchler *et al.* [10]	Octreotide	125	22 (18%)
	Placebo	121	46 (38%)
Pederzoli *et al.* [11]	Octreotide	122	11 (9%)
	Placebo	130	24 (18%)
Montorsi *et al.* [41]	Octreotide	111	10 (9%)
	Placebo	107	21 (20%)
Friess *et al.* [42]	Octreotide	122	12 (10%)
	Placebo	125	28 (22%)
Lowy *et al.* [43]	Octreotide	57	7 (12%)
	No treatment	53	3 (6%)
Yeo *et al.* [17]	Octreotide	104	11 (11%)
	Placebo	107	10 (9%)
Gouillate *et al.* [45]	Somatostatin-14	38	2 (5%)
	Placebo	37	8 (22%)
Sarr *et al.* [46]	Valpreotide	135	(30.4%)
	Placebo	140	(26.4%)
Suc *et al.* [47]	Octreotide	122	21 (17%)
	Placebo	108	20 (19%)

1. Use of Separate Roux-en-Y Limbs for Pancreatic Anastomosis: This technique serves to prevent pancreatic enzyme activation by biliary secretion. Studies have reported "zero" POPF rates with the use of defunctioning jejunal loop for pancreatic remnant anastomosis [58, 59].
2. Level of Pancreatic Transaction: The pancreatic neck is a watershed between celiac and superior mesenteric arterial supply. Thus pancreatic transaction at the neck may compromise the PJ anastomosis. Transaction of the pancreas about 1.5 to 2 cms to the left of the neck after evaluating the pancreas by Doppler resulted in reduced POPF (4.5%) in a series of 40 patients [60].
3. Reinforcement of Pancreatic Anastomosis with Fibrin Sealant: Fibrin sealant has been used to reinforce the pancreaticoenteric anastomosis [61], but no significant benefit in reducing pancreatic anastomotic leak was noted [62].
4. Temporary Fibrin Glue Occlusion of the Main Pancreatic Duct: It was hypothesized that if resorbable glue is used to temporarily occlude the main pancreatic duct, the exposure of the healing pancreatico enteric anastomosis with pancreatic proteases can be prevented. With the intention of increasing the efficacy of the glue, aprotinin, which delays the dissolution of the glue was added [63]. A randomized control study testing this concept has shown that, temporary ductal occlusion by intra-canal injection of fibrin decreases neither the rate nor the severity of intra-abdominal complications after pancreatic resection [64].
5. Measures to prevent POPF following DP

- Ligation of the main pancreatic duct, combined with fish mouth pancreatic closure and reinforcement of the sutures with fibrin glue after DP [12]
- Fibrin glue sealing of the pancreatic stump intraoperatively has been considered feasible, safe and reliable and will complement other prophylactic methods [12]
- Closure of pancreatic stump with a gastric or jejunal seromuscular flap [65]
- Ultrasonic dissector without suture closure of the pancreatic stump is shown to reduce the incidence of POPF in a non-fibrotic pancreas [66]
- A recent systematic review and meta-analysis has suggested that stapler closure or anastomotic closure reduces the rates of POPF following DP as compared with suture closure [67].

TREATMENT

The treatment of POPF can be conveniently considered under the following headings

Control of Sepsis

Though antibiotic therapy is not indicated routinely, in the presence of clinical sepsis, targeted antibiotic therapy should be given based on the culture results. Abdominal imaging is required to detect intra-abdominal collections needing drainage.

Maintenance of Fluid and Electrolyte Balance and Nutrition

Maintenance of nutrition and metabolic function is critical. The rationale behind nutritional therapies is two fold. First, nutritional therapy aims to compensate for the impaired nutrition resulting from reduced delivery of pancreatic secretions to the gut. Second, by limiting the volume of fistula output, it might increase the likelihood of spontaneous closure. There is evidence that total parenteral nutrition (TPN) reduces pancreatic secretion by 50% to 70% compared with enteral nutrition [68, 69]. Enteral feeding beyond the ligament of Treitz is probably equally effective at reducing pancreatic exocrine secretion and has many advantages [70, 71]. Commercially available feeds may be given through a correctly placed nasojejunal feeding tube for 2 to 3 weeks, but if longer nutritional support is anticipated, a percutaneous feeding jejunostomy is usually required. Madiba *et al*. successfully used oral enteral nutrition in 15 consecutive patients with low-output external fistulas [72]. This approach may represent a suitable alternative in a well, stable patient with low-output fistula if it does not cause increased output.

Skin Protection

Pancreatic secretions are activated on contact with enteric secretions and also undergo auto activation on exposure to air [73]. Thus, even pure fistulas have the potential to cause severe skin necrosis if the effluent is left in contact with skin. External fistulas are optimally managed with a pouching system using skin protection such as karaya. If a drain is not in place, the fistula opening should be catheterized. The involvement of a stoma therapist is frequently of great value.

Role of Somatostatin Analogues

Somatostatin is an endogenous peptide that inhibits pancreatic secretion. At present, the longer acting analog,

octreotide is used in the management of pancreatic fistulas. Theoretically a decrease in the fistula output improves the nursing care and nutritional management in POPF. There is strong evidence that somatostatin analogs reduce fistula output, but only one trial has shown a significant reduction in closure time for pancreatic fistula [74]. Somatostatin analogs have not been shown to increase the incidence of closure of POPF.

Percutaneous Treatment

A persistent POPF following PD has been successfully treated by percutaneous dilation of jejunal stenosis with gelatin sponge occlusion of the fistula tract [75]. Reports of successful treatment of persistent POPF with fibrin glue [76] and prolamine [77] are available. However animal model studies indicate that prolamine obliteration of the pancreatic duct causes severe local inflammatory changes in the pancreas. Reports regarding the use of articulated, steerable T-tubes to bridge the disconnected pancreatic segments or to establish drainage into adjacent gut are available [78].

Role of Endoscopic Retrograde Cholangiopancreatography (ERCP)

One of the most important predictors for the spontaneous closure of a pancreatic fistula is the ductal anatomy. ERCP serves to demonstrate the ductal anatomy, site of fistula and downstream obstruction. ERCP can be therapeutic when stents are used to bridge ductal disruptions and bypass calculi and inflammatory stenosis. The timing of ERCP is controversial [79], but there is evidence that extending the period of no operative therapy beyond 3 weeks increases the mortality rate [80]. Most authorities recommend ERCP in a fistula that has persisted for at least 2 weeks. With an ERCP, ductal anatomy will be defined, in particular the presence of end leaks, downstream stenosis and calculi. Fistulas unlikely to close spontaneously may be defined and an early management plan formulated. There is little to be gained by continued conservative management in the presence of unfavorable anatomic factors once the patient is in positive nitrogen balance. The first report of use of pancreatic stents in the treatment of internal and external pancreatic fistulae was published in 1993 [81]. The success rate of endoscopic pancreatic stenting in more recent series has been 75-100% with an average success rate of 40 (85%) in a total of 47 patients [4]. The technique comprises of placing a 5-7 French diameter stent of variable length and preferably across the site of ductal disruption [79, 82-84]. Stents are retrieved 10-14 days of the closure of the external fistula. Complications include stent migration, stent occlusion and localized duct inflammation [82]. Table 4 summarizes studies, which have used stents to treat POPF with success rates.

Table 4. Studies that have used stents to treat POPF with success rates

Study	Patients	Method	Success Rate
Costamagna *et al.* [82]	16	Nasopancreatic drain	12/16 (75%)
Boerma *et al.* [81]	15	Pancreatic duct stent	13/15 (87%)
Howard *et al.* [77]	7	Pancreatic duct stent	7/7 (100%)
Kozarek *et al.* [80]	9	Pancreatic duct stent	8/9 (89%)

Surgery

Most external pancreatic fistulae can be effectively managed by non-surgical means. Surgery will be required for those in whom nonclosure has been predicted and who are not suitable for stenting. This group largely consists of patients with an end fistula. The choice of appropriate procedure depends on the ductal anatomy, site of the leak and the duration of the fistula. Available surgical options include

Fistulojejunostomy

Anastomosis of the fibrous fistula tract to adjacent gut was the earliest described successful operation for pancreatic fistula [85] and remains a relatively safe, straight forward, and effective operation [86]. This is frequently the operation of choice. The fistula tract is isolated, dissected out as close to the pancreas as is safe, and anastomosed to a Roux-en-Y loop of jejunum. Occasionally, the fistula tract is more easily drained into the stomach. This procedure requires a mature fistulous tract. It should preferably be attempted in low output fistulae older than thirty days.

Patients with a high output anastomotic leak from pancreatoenteric anastomosis with signs of severe sepsis or hemorrhage that cannot be managed by other means should undergo laparotomy [8, 7, 19, 87]. Surgical options in such situations include

- Completion pancreatectomy
- Drainage of the anastomosis
- Reconstruction of anastomosis

In complicated POPF, tissues in the pancreatic and peripancreatic region will be inflamed, hemorrhagic, edematous and fragile. Pancreatic remnant tends to be necrotic. Dissection in such a setting is likely to be extremely difficult and potentially hazardous. This forms the rationale for completion pancreatectomy as a salvage procedure in POPF particularly when associated with serious complications like peritonitis and hemorrhage. However, studies have shown high mortality rates with completion pancreatectomy and the optimal management remains controversial [5, 6, 88, 89].

CONCLUSIONS

- POPF continues to haunt pancreatic surgeons even despite of all advances in surgical field
- Use of a common suitable nomenclature facilitates comparability among various studies
- Normal BT-PABA test, soft-friable pancreas and a small sized pancreatic duct are well acknowledged risk factors for POPF
- There is no difference in surgical outcomes with respect to POPF between PG and PJ

- None of the methods recommended for preventing POPF have been conclusively proved to be effective
- Treatment of POPF is predominantly non-surgical. Endoscopic therapy and percutaneous treatments are important therapeutic modalities. Surgical intervention may be required in select cases

Conflict of Interest

Authors declare to have no conflict of interest.

References

1. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, Neoptolemos J. et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005; 138:8-13. [PMID: 16003309]

2. DeOliveira ML, Winter JM, Schafer M, Cunningham SC, Cameron JL, Yeo CJ, Clavien PA. Assessment of complications after pancreatic surgery. A novel grading system applied to 633 patients undergoing pancreaticoduodenectomy. Ann Surg 2006; 244:931-7. [[PMID: 17122618]

3. Zinner MJ, Baker RR, Cameron JL. Pancreatic cutaneous fistulas. Surg Gynecol Obstet 1974; 138:710-2. [PMID: 4823372]

4. Alexakis N, Sutton R, Neoptolemos JP. Surgical treatment of pancreatic fistula. Dig Surg 2004; 21:262-4. [PMID: 15308865]

5. Böttger TC, Junginger T. Factors influencing morbidity and mortality after pancreaticoduodenectomy: critical analysis of 221 resections. World J Surg 1999; 23:164-72. [PMID: 9880426]

6. Cullen J, Surr M, Ilstrup D. Pancreatic anastomotic leak after pancreaticoduodenectomy: incidence, significance and management. Am J Surg 1994; 168:295-8. [PMID: 7524375]

7. van Berge Henegouwen MI, De Wit LT, Van Gulik TM, Obertop H, Gouma DJ. Incidence, risk factors and treatment of pancreatic leakage after a pancreatoduodenectomy: drainage versus resection of pancreatic remnant. J Am Coll Surg 1997; 185:18-24. [PMID: 9208956]

8. Büchler MW, Friess H, Wagner M, Kulli C, Wagener V, Z'Graggen K. Pancreatic fistula after pancreatic head resection. Br J Surg 2000; 87:883-9. [PMID: 10931023]

9. Yeo CJ, Cameron JL, Maher MM, Sauter PK, Zahurak ML, Talamini MA, Lillemoe KD, Pitt HA. A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. Ann Surg 1995; 222:580-8. [PMID: 7574936]

10. Büchler M, Friess H, Klempa I, Hermanek P, Sulkowski U, Becker H, Schafmayer A, Baca I, Lorenz D, Meister R, et al. Role of octreotide in prevention of post operative complications following pancreatic resection. Am J Surg 1992; 163:125-30. [PMID: 1733360]

11. Pederzoli P, Bassi C, Falconi M, Camboni MG. Efficacy of octreotide in the prevention of complications of elective pancreatic surgery. Br J Surg 1994; 81:265-9. [PMID: 8156354]

12. Suzuki Y, Kuroda Y, Morita A, Pujino Y, Ykawamura T, Saitoh Y. Fibrin glue sealing for the prevention of pancreatic fistula following distal pancreatectomy. Arch Surg 1995; 130:952-5. [PMID: 7661678]

13. Lowy AM, Lee JE, Pisters PW, Davidson BS, Fenoglio CJ, Stanford P, Jinnah R, Evans DB.Prospective, randomized trial of octreotide to prevent pancreatic fistula after pancreaticoduodenectomy for malignant disease. Ann Surg 1997; 226:632-41. [PMID: 9389397]

14. Matsusue S, Takeda H, Nakamura Y, Nishimura S, Koizumi S. A prospective analysis of the factors influencing pancreaticojejunostomy performed using a single method, in 100 consecutive pancreaticoduodenectomies. Surg Today 1998; 28:719-26. [PMID: 9697265]

15. Yeh TS, Jan YY, Jeng LB, Hwang TL, Wang CS, Chen SC, Chao TC, Chen MF. Pancreaticojejunal anastomotic leak after pancreaticoduodenectomy-multivariate analysis of perioperative risk factors. J Surg Res 1997; 67:119-25. [PMID: 9073557]

16. Bartoli FG, Arnone GB, Ravera G, Bachi V. Pancreatic fistula and relative mortality in malignant disease after pancreaticoduodenectomy. Review and statistical meta-analysis regarding 15 years of literature. Anticancer Res 1991; 11:1831-48. [PMID: 1685076]

17. Yeo CJ, Cameron JL, Lillemoe KD, Sauter PK, Coleman J, Sohn TA, Campbell KA, Choti MA. Does prophylactic octreotide decrease the rate of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo controlled trial. Ann Surg 2000; 232:419-29. [PMID: 10973392]

18. Al-Sharaf K, Ihse I, Dawiskiba S, Andrèn-Sandberg A. Characteristics of the gland remnant predict complications after subtotal pancreatectomy. Dig Surg 1997;14:101-4. [PMID: 172522]

19. Sato N, Yamaguchi K, Chijiiwa K, Tanaka M. Risk analysis of pancreatic fistula after pancreatic head resection. Arch Surg 1998;133:1094-8. [PMID: 9790207]

20. Hamanaka Y, Nishihara K, Hamasaki T, Kawabata A, Yamamoto S, Tsurumi M, Ueno T, Suzuki T. Pancreatic juice output after pancreatoduodenectomy in relation to pancreatic consistency, duct size and leakage. Surgery 1996; 119:281-7. [PMID: 8619183]

21. Marcus SG, Cohen H, Ranson JH. Optimal management of the pancreatic remnant after pancreaticoduodenectomy. Ann Surg 1995; 221:635-45. [PMID:]

22. Ishikawa O, Ohigashi H, Imaoka S, Teshima T, Inoue T, Sasaki Y, Iwanaga T, Nakaizumi A.Concomitant benefit of preoperative irradiation in preventing pancreatic fistula formation after pancreatoduodenectomy. Arch Surg 1991; 126: 885-9. [PMID: 1854249]

23. Yang YM, Tian XD, Zhuang Y, Wang WM, Wan YL, Huang YT. Risk factors of pancreatic leakage after pancreaticoduodenectomy. World J Gastroenterol 2005; 11:2456-61. [PMID: 15832417]

24. Sikora SS, Posner MC. Management of pancreatic stump following pancreatico duodenectomy. Br J Surg 1995; 82:1590-7. [PMID: 8548218]

25. Marczell AP, Stierer M. Partial pancreaticoduodenectomy (Whipple procedure) for pancreatic malignancy: occlusion of a non-anastomosed pancreatic stump with fibrin sealant. HPB Surg 1992; 5:251-9. [PMID: 1356420]

26. Di Carlo V, Chiesa R, Pontiroli AE, Carlucci M, Staudacher C, Zerbi A, Cristallo M, Braga M, Pozza G. Pancreatoduodenectomy with occlusion of the residual stump with Neoprene injection. World J Surg 1989; 13:105-10. [PMID: 2543144]

27. Grace PA, Pitt HA, Tompkins RK, DenBesten L, Longmire WP Jr. Decreased morbidity and mortality after pancreatoduodenectomy. Am J Surg 1986; 151:141-9. [PMID: 3946745]

28. Matsumoto Y, Fujii H, Miura K, Inoue S, Sekikawa T, Aoyama H, et al. Successful pancreatojejunal anastomosis for pancreaticoduodenectomy. Surg Gynecol Obstet 1992; 175:555-62. [PMID: 1360173]

29. Howard JM. Pancreatojejunostomy: leakage is a preventable complication of the Whipple resection. J Am Coll Surg 1997; 184: 454-7. [PMID: 9145064]

30. Hosotani R, Doi R, Imamura M. Duct-to-mucosa pancreaticojejunostomy reduces the risk of pancreatic leakage after pancreatoduodenectomy. World J Surg 2002; 26:99-104. [PMID: 11898041]

31. Tsuji M, Kimura H, Konishi K, Yabushita K, Maeda K, Kuroda Y. Management of continuous anastomosis of pancreatic duct and jejunal mucosa after pancreaticoduodenectomy: historical study of 300 patients. Surgery 1998; 123:617-21. [PMID: 9626311]

32. Hwang TL, Jan YY, Chen MF. Secural pancreaticojejunal anastomosis for the pancreaticoduodenectomy. Hepatogastroenterology 1996; 43:275-7. [PMID: 8682478]

33. Batignani G, Fratini G, Zuckermann M, Bianchini E, Tonelli F. Comparison of Wirsung-jejunal duct-to-mucosa and dunking technique for pancreatojejunostomy after pancreatoduodenectomy. Hepatobiliary Pancreat Dis Int 2005; 4:450-5. [PMID: 16109535]

34. Waugh JM, Clagett OT. Resection of the duodenum and head of the pancreas for carcinoma: an analysis of thirty cases. Surgery 1946; 20:224-32. [PMID: 20994806]

35. Kapur BM. Pancreaticogastrostomy in pancreaticoduodenal resection for ampullary carcinoma: experience in thirty-one cases. Surgery 1986; 100:489-93. [PMID: 3738768]

36. Morris DM, Ford RS. Pancreaticogastrostomy: preferred reconstruction for Whipple resection. J Surg Res 1993; 54:122-5. [PMID: 8479169]

37. Ramesh H, Thomas PG. Pancreaticojejunostomy versus pancreaticogastrostomy in reconstruction following pancreaticoduodenectomy. Aust N Z J Surg 1990; 60:973-6. [PMID: 2268215]

38. McKay A, Mackenzie S, Sutherland FR, Bathe OF, Doig C, Dort J, Vollmer CM Jr, Dixon E. Meta-analysis of pancreaticojejunostomy versus pancreatico gastrostomy after pancreaticoduodenectomy. Br J Surg 2006; 93:929-36. [PMID: 16845693]

39. Wente MN, Shrikhande SV, Müller MW, Diener MK, Seiler CM, Friess H, Büchler MW. Pancreaticojejunostomy versus pancreatico gastrostomy: systematic review and meta-analysis. Am J Surg 2007; 193:171-83. [PMID: 17236843]

40. Klempa J, Schwedes U, Usadel KH. Verhutung von postoperativen pancreatitischen komplikationen nach duodenopankreatetomie durch somatostatin. Chitrurg 1979; 50:429-32. [PMID: 477469]

41. Montorsi M, Zago M, Mosca F, Capussotti L, Zotti E, Ribotta G, Fegiz G, Fissi S, Roviaro G, Peracchia A, et al. Efficacy of octreotide in the prevention of pancreatic fistula after elective pancreatic resections: a prospective, controlled, randomized clinical trial. Surgery 1995; 117:26-31. [PMID: 7809832]

42. Friess H, Beger HG, Sulkowski U, Becker H, Hofbauer B, Dennler HJ, Büchler MW. Randomized controlled multicentre study of the prevention of complications by octreotide in patients undergoing surgery for chronic pancreatitis. Br J Surg 1995; 82:1270-3. [PMID: 7552016]

43. Lowy AM, Lee JE, Pisters PW, Davidson BS, Fenoglio CJ, Stanford P, Jinnah R, Evans DB. Prospective, randomized trial of octreotide to prevent pancreatic fistula after pancreaticoduodenectomy for malignant disease. Ann Surg 1997; 226: 632-41. [PMID: 9389397]

44. Poon RT, Lo SH, Fong D, Fan ST, Wong J. Prevention of pancreatic leakage after pancreaticoduodenectomy. Am J Surg 2002; 183:42-52. [PMID: 11869701]

45. Gouillat C, Chipponi J, Baulieux J, Partensky C, Saric J, Gayet B. Randomized controlled multicentre trial of somatostatin infusion after pancreaticoduodenectomy. Br J Surg 2001; 88:1456-62. [PMID: 11683740]

46. Sarr MG; Pancreatic Surgery Group. The potent somatostatin analogue vapreotide does not decrease pancreas specific complications after elective pancreatectomy: a prospective, multicenter, double-blinded, randomized, placebo controlled trial. J Am Coll Surg 2003; 196:556-65. [PMID: 12691930]

47. Suc B, Msika S, Piccinini M, Fourtanier G, Hay JM, Flamant Y, Fingerhut A, et al. French Associations for Surgical Research. Octreotide in the prevention of intra abdominal complications following elective pancreatic resection. A prospective, multicenter randomized controlled trial. Arch Surg 2004; 139:288-94. [PMID: 15006886]

48. Allen PJ, Gönen M, Brennan MF, Bucknor AA, Robinson LM, et al. Pasireotide for PostoperativePancreatic Fistula. N Engl J Med 2014; 370:2014-22. [PMID: 25162895]

49. Biehl T, Traverso LW. Is stenting necessary for a successful pancreatic anastomosis? Am J Surg 1992; 163:530-2. [PMID: 1575313]

50. Yoshimi F, Ono H, Asato Y, Ohta T, Koizumi S, Amemiya R, Hasegawa H. Internal stenting of the hepatojejunostomy and pancreaticojejunostomy in patients undergoing pancreaticoduodenectomy to promote earlier discharge from the hospital. Surg Today 1996; 26:665-7. [PMID: 8855507]

51. Shibuya T, Uchiyama K, Imai S, Shibuya J, Shoji T. Improvement of pancreaticojejunostomy in pancreaticoduodenectomy. Int Surg 1995; 80:57-60. [PMID: 7657494]

52. Hamanaka Y, Suzuki T. Total pancreatic duct drainage for leakproof pancreatojejunostomy. Surgery 1994; 115:22-6. [PMID: 8284756]

53. Mok KT, Wang BW, Liu SI. Management of pancreatic remnant with strategies according to the size of the pancreatic duct after pancreaticoduodenectomy. Br J Surg 1999; 86:1018-9. [PMID: 10460636]

54. Roder JD, Stein HJ, Böttcher KA, Busch R, Heidecke CD, Siewert JR. Stented versus nonstented pancreaticojejunostomy after pancreaticoduodenectomy: a prospective study. Ann Surg 1999; 229:41-8. [PMID: 9923798]

55. Okamoto A, Tsuruta K. Fistulation method: simple and safe pancreaticojejunostomy after pancreatoduodenectomy. Surgery 2000; 127:433-8. [PMID: 10776435]

56. Braasch JW. Pancreaticoduodenal resection. Curr Probl Surg 1988; 25:321-63. [PMID: 3391042]

57. Keck H, Steffen R, Neuhaus P. Protection of pancreatic and biliary anastomosis after partial duodenopancreatectomy by external drainage. Surg Gynecol Obstet 1992; 174;329-31. [PMID: 1348151]

58. Kingsnorth AN. Safety and function of isolated Roux loop pancreaticojejunostomy after Whipple's pancreaticoduodenectomy. Ann R Coll Surg Engl 1994; 76:175-9. [PMID: 7912489]

59. Papadimitriou JD, Fotopoulos AC, Smyrniotis B, Prahalias AA, Kostopanagiotou G, Papadimitriou LJ. Subtotal pancreatoduodenectomy: use of a defunctionalized loop for pancreatic stump drainage. Arch Surg 1999; 134:135-9. [PMID: 10025450]

60. Strasberg SM, McNevin MS. Results of a technique of pancreaticojejunostomy that optimizes the blood supply to the pancreas. J Am Coll Surg 1998; 187:591-6. [PMID: 9849731]

61. Kram HB, Clark SR, Ocampo HP, Yamaguchi MA, Shoemaker WC. Fibrin glue sealing of pancreatic injuries, resections and anastomoses. Am J Surg 1991; 161: 479-81. [PMID: 2035768]

62. D'Andrea AA, Costantino V, Sperti C, Pedrazzoli S. Human fibrin sealant in pancreatic surgery: it is useful in preventing fistulas? A prospective randomized study. Ital J Gastroenterol 1994; 26:283-6. [PMID: 7949264]

63. Lillemoe KD, Cameron JL, Kim MP, Campbell KA, Sauter PK, Coleman JA, Yeo CJ. Does fibrin glue sealant decrease the rate of pancreatic fistula after pancreaticoduodenectomy? Results of a prospective randomized trial. J Gastrointest Surg 2004; 8:766-72. [PMID: 15531229]

64. Suc B, Msika S, Fingerhut A, Fourtanier G, Hay JM, Holmières F, Sastre B, Fagniez PL; And the French Associations for Surgical Research. Temporary fibrin glue occlusion of the main pancreatic duct in the prevention of intra abdominal complications after pancreatic resection. Ann Surg 2003; 237:57-65. [PMID: 12496531]

65. Moriura S, Kimura A, Ikeda S, Iwatsuka Y, Ikezawa T, Naiki K. Closure of distal pancreatic stump with a seromuscular flap. Surg Today 1995; 25:992-4. [PMID: 8640031]

66. Suzuki Y, Fujino Y, Tanioka Y, Hori Y, Ueda T, Takeyama Y, Tominaga M, Ku Y, Yamamoto YM, Kuroda Y. Randomized clinical trial of ultrasonic dissector or conventional division in distal pancreatectomy for non fibrotic pancreas. Br J Surg 1999; 86:608-11. [PMID: 10361178]

67. Zhang H, Zhu F, Shen M, Shi CJ et al. Systematic review and meta-analysis comparing three techniques for pancreatic remnant closure following distal pancreatectomy. Br J Surg 2015; 102:4-15. [PMID: 25388952]

68. Grant JP, Davey-McCrae J, Snyder PJ. Effect of enteral nutrition on human pancreatic secretions. JPEN J Parenter Enteral Nutr 1987; 11:302-4. [PMID: 3110448]

69. Bivins BA, Bell RM, Rapp RP, Toedebusch WH. Pancreatic exocrine response to parenteral nutrition. JPEN J Parenter Enteral Nutr 1984; 8:34-6. [PMID: 6321813]

70. Bodoky G, Harsanyi L, Pap A, Tihanyi T, Flautner L. Effect of enteral nutrition on exocrine pancreatic function. Am J Surg 1991; 161:144-8. [PMID: 1702939]

71. Duerksen DR, Bector S, Yaffe C, Parry DM. Does jejunal feeding with a polymeric immune-enhancing formula increase pancreatic exocrine output as compared with TPN? A case report. Nutrition 2000; 16:47-9. [PMID: 10674235]

72. Madiba TE, Haffejee AA, Singh B, Reddy R. Nutritional support in the management of external pancreatic fistulas. S Afr J Surg 1995; 33:81-4. [PMID: 8545731]

73. Kassell B, Kay J. Zymogens of proteolytic enzymes. Science 1973; 180:1022-7. [PMID: 4574732]

74. Pederzoli P, Bassi C, Falconi M, Albrigo R, Vantini I, Micciolo R. Conservative treatment of external pancreatic fistulas with parenteral nutrition alone or in combination with intravenous infusion of somatostatin, glucagon or calcitonin. Surg Gynecol Obstet 1986; 163:428-32. [PMID: 2877505]

75. Sheiman RG, Chan R, Matthews JB. Percutaneous treatment of a pancreatic fistula after pancreaticoduodenectomy. J Vasc Interv Radiol 2001; 12:524-6. [PMID: 11287543]

76. Wadström J, Gannedahl G, Wahlberg J, Frödin L. Persistent pancreatic fistula after pancreas transplantation treated with fibrin glue and octreotide. Transplant Proc 1995; 27:3491-2. [PMID: 8540064]

77. Buecker A, Keulers P, Guenther RW. Successful closure and embolization of a fistula between the pancreatic duct and a pseudocyst using ethibloc. Cardiovasc Intervent Radiol 1997; 20:394-6. [PMID: 9271654]

78. Cope C, Tuite C, Burke DR, Long WB. Percutaneous management of chronic pancreatic duct strictures and external fistulas with long term results. J Vasc Interv Radiol 2001; 12:104-10. [PMID: 11200342]

79. Howard TJ, Stonerock CE, Sarkar J, Lehman GA, Sherman S, Wiebke EA, Madura JA, Broadie TA. Contemporary treatment strategies for external pancreatic fistulas. Surgery 1998; 124:627-33. [PMID: 9780981]

80. Lipsett PA, Cameron JL. Internal pancreatic fistula. Am J Surg 1992; 163:216-20. [PMID: 1739176]

81. Saeed Z, Ramirez F, Hepps KS. Endoscopic stent placement for internal and external pancreatic fistulas. Gastroenterology 1993; 105:1213-7. [PMID: 8405869]

82. Kozarek RA, Ball TJ, Patterson DJ, Raltz SL, Traverso LW, Ryan JA, Thirlby RC. Transpapillary stenting for pancreaticocutaneous fistulas. J Gastrointest Surg 1997; 1:357-1. [PMID: 9834370]

83. Boerma D, Rauws EA, van Gulik TM, Huibregtse K, Obertop H, Gouma DJ. Endoscopic stent placement for pancreaticocutaneous fistula after surgical drainage of the pancreas. Br J Surg 2000; 87:1506-9. [PMID: 11091237]

84. Costamagna G, Mutignani M, Ingrosso M, Vamvakousis V, Alevras P, Manta R, Perri V. Endoscopic treatment of postsurgical external pancreatic fistulas. Endoscopy 2001; 33:317-22. [PMID: 11315892]

85. Corachan M. Sur le traitment des fistules pancreatiques. La Presse Medicale 1928; 88:1394-7. [PMID: 10827321]

86. Bassi C, Butturini G, Salvia R, Contro C, Valerio A, Falconi M, Pederzoli P. A single institution experience with fistulojejunostomy for external pancreatic fistulas. Am J Surg 2000; 179:203-6. [PMID: 8689156]

87. Farley DR, Schwall G, Trede M. Completion pancreatectomy for complications after pancreaticoduodenectomy. Br J Surg 1996; 83:176-9. [PMID: 1350387]

88. Smith CD, Sarr MG, vanHeerden JA. Completion pancreatectomy following pancreaticoduodenectomy: clinical experience. World J Surg 1992; 16:521-4. [PMID: 1350387]

89. Tamijmarane A, Ahmed I, Bhati CS, Mirza DF, Mayer AD, Buckels JA, et al. Role of completion pancreatectomy as a damage control option for post-pancreatic surgical complications. Dig Surg 2006; 23:229-234. [PMID: 16943670]