

Pancreatic surgery: evolution and current tailored approach

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Abstract: Surgical resection of pancreatic cancer offers the only chance for prolonged survival. Pancretic resections are technically challenging, and are accompanied by a substantial risk for postoperative complications, the most significant complication being a pancreatic fistula. Risk factors for development of pancreatic leakage are now well known, and several prophylactic pharmacological measures, as well as technical interventions have been suggested in prevention of pancreatic fistula. With better postoperative care and improved radiological interventions, most frequently complications can be managed conservatively. This review also attempts to address some of the controversies related to optimal management of the pancreatic remnant after pancreaticoduodenectomy.

Keywords: Pancreatic cancer; pancreatic resection; pancreatic fistula; total pancreatectomy; pancreatic anastomosis

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Introduction

Pancreatic cancer is an uncommon type of cancer, the incidence of which has been on the rise worldwide, likely correlated with an increased incidence of obesity. Pancreatic cancer rates are highest in North America and Europe, where the frequency of its occurrence puts it in the eighth place (1,2). Although it is not very common, its significance lies in the fact that it is most often diagnosed in the late stage of the disease, it is almost always fatal, surgical treatment is rather complex and there is no adequate adjuvant treatment. Moreover, it is the only type of cancer in Europe of which increased mortality is anticipated in 2014 (3). Five-year survival rate in Europe and North America is around 6%, which makes it the fourth cause of death according to cancer mortality statistics (1,2). However, within the 10% of patients who have been diagnosed in the early, localised stage, the 5-year survival rate rises to 25% (4,5).

There has been immense progress in surgical treatment of pancreatic cancer patients since Kausch and the first pancreaticoduodenectomy of periampullary tumor (6), Whipple and his modification of pancreaticoduodenectomy in the 1930's (7), Priestley and the first successful total

pancreatectomy reported in 1944 (8), and Traverso and Longmire with pylorus-preserving pancreaticoduodenectomy in 1978 (9) (*Table 1*). Despite the initially high mortality and morbidity following surgical treatment (12,13), with the development of surgical technique and concentration of patients in high-volume centres, as well as with improvement in perioperative care, the rate of morbidity and mortality following pancreaticoduodenectomy has dropped to acceptable levels. Morbidity and mortality following total pancreatectomy have also become more acceptable, as well as long term outcome with better blood glucose regulation and exocrine insufficiency management which has been made possible by developing novel insulin formulations and pancreatic enzyme supplements. Improved management of endocrine and exocrine insufficiency following total pancreatectomy and the discovery of novel clinical entities, such as IPMN (intraductal papillary mucinous neoplasm), have revived what was once a rare surgery, with an increased number of procedures and widened indications for surgical treatment.

Despite its complications, curative resection is the single most important factor determining the outcome in patients with pancreatic adenocarcinoma (14). Surgery remains the

Table 1 History and evolution of pancreaticoduodenectomy

1909: Kausch 2-stage procedure, first cholecystectomy, followed 6 weeks later by resection of the head of pancreas, pylorus, first and second half of duodenum, with gastroenterostomy, closure of common bile duct and anastomosis of pancreas and the third part of duodenum (6)
1935: Whipple 2-stage procedure, first posterior gastroenterostomy, ligation and division of the common bile duct with cholecystogastrostomy, followed by resection of the duodenum and pancreatic head, with closure of pancreatic stump (7)
1940: Whipple completed the procedure in a single stage, in 1942, modification of the procedure with pancreaticojejunostomy (10)
1946: Waugh and Clagett first used pancreaticogastrostomy (11)
1978: Taverso and Longmire reported pylorus preserving pancreaticoduodenectomy (9)

Table 2 Risk factors for pancreatic leak

Pancreas related
Soft pancreatic parenchyma
Small size pancreatic duct
Ampullary, duodenal, cystic and bile duct neoplasms
Patient related
Male sex
Age >70 years
Cerebrovascular disease
Duration of jaundice
Procedure related
Type of pancreatic anastomosis
Use of somatostatin
Surgeon's experience
Intraoperative blood loss

principal treatment for pancreatic cancer and offers the only chance for cure (15,16).

Complications of pancreaticoduodenectomy

Pancreaticoduodenectomy is indicated for patients with neoplasma of the head of the pancreas, ampullary, duodenal and distal bile duct neoplasms. It is also performed for chronic pancreatitis and rarely for trauma. Although high mortality rate approaching 25% and morbidity rates up to 60% (12,13) were initially related to pancreaticoduodenectomy, in the last few decades there has been a significant decline in mortality rates which is now 3-5% in highly specialized centres (17-19). On the other hand, there are still numerous possible postoperative complications related to pancreaticoduodenectomy and morbidity rates are as high as 30-60% (20-24). Most common local complications are delayed gastric emptying with prevalence of 8-45% (25-30), pancreatic fistula with reported rates from 2% to 22%

(20,23,24,30-34), infectious complications, most commonly intra-abdominal abscesses, with prevalence from 1-17% (30,35) and hemorrhage. Postoperative bleeding occurs in 3-13% of patients (5,17). Hemorrhage within the first 24 hours is result of the inadequate hemostasis at the time of surgery, a slipped ligature, bleeding from an anastomosis or diffuse hemorrhage from the retroperitoneal operation field, most likely caused by underlying coagulopathy, frequently seen in jaundiced patients (36,37). Late hemorrhage, occurring 1-3 weeks after surgery, is often caused by an anastomotic leak with erosion of retroperitoneal vessels (38) with mortality rates from 15% to 58% (39,40). Other causes of late hemorrhage are pseudoaneurysm and bleeding from the pancreaticojejunostomy. Management includes completion pancreatectomy or formation of pancreatic neoanastomosis (36). Other, not so common, complications are cholangitis, colonic and biliary fistulas. Within the systemic complications group, cardiopulmonary and neurological complications prevail (34,36). Over the years the most significant pancreaticoduodenectomy complication was the development of pancreatic leak and fistula (33,41,42) due to its frequency of occurrence and high mortality. However, with the refinement of surgical techniques, improved postoperative intensive care and concentration of patients in high-volume centres decreased mortality, this also resulted in decline of pancreatic fistula incidence. Depending on the definition used, the incidence of pancreatic fistula used to be 10-29% (43). Nowadays, according to the International Study Group Pancreatic Fistula Definition the incidence of pancreatic fistula is from 2% to 10% in the centres of excellence (30,34,41). The seriousness of pancreatic fistula can be seen in its possible consequences, such as septicemia and hemorrhage, which makes it the leading risk factor for postoperative death, longer hospital stay and increased hospital costs after pancreaticoduodenectomy even today. Risks for developing the fistula can be divided into a few groups (Table 2). The first group is pancreas related. One

Table 3 Trials of pancreatic management

Variables	Authors	Number of patients	Pancreatic fistula (%)
Trials comparing outcomes of the use of somatostatin and analogues	Büchler <i>et al.</i> 1992 (53)	125 somatostatin vs. 121 control	17.6 vs. 38
	Friess <i>et al.</i> 1995 (54)	122 vs. 125	12 vs. 28
	Yeo <i>et al.</i> 2000 (55)	104 vs. 107	11 vs. 9
	Sarr <i>et al.</i> 2003 (56)	135 vs. 140	24 vs. 23
	Suc <i>et al.</i> 2004 (57)	122 vs. 108	17 vs. 19
Trials comparing outcomes of PG and PJ	Yeo <i>et al.</i> 1995 (58)	73 PG vs. 72 PJ	12 vs. 11
	Duffas <i>et al.</i> 2005 (59)	81 vs. 68	16 vs. 20
	Bassi <i>et al.</i> 2005 (60)	69 vs. 82	13 vs. 16
Trials comparing outcomes after duct stenting	Winter <i>et al.</i> 2006 (61)	115 with stent vs. 119 no stent	11.3 vs. 7.6
	Poon <i>et al.</i> 2007 (62)	60 vs. 60	6.7 vs. 20
	Pessaux <i>et al.</i> 2011 (63)	77 vs. 81	26 vs. 42
Trials comparing outcomes after different anastomotic technique	Marcus <i>et al.</i> 1995 (64)	68 duct-to-mucosa vs. 18 invag	4.4 vs. 5.5
	Bassi <i>et al.</i> 2003 (65)	144 duct-to-mucosa vs. invag	13 vs. 15
	Berger <i>et al.</i> 2009 (66)	97 duct-to mucosa vs. 100 invag	24 vs. 12
	Peng <i>et al.</i> 2007 (67)	106 binding vs. 111 invag	0 vs. 7.2

Table 4 Solutions for pancreatic leak

Use of Somatostatin & analogues
Pancreaticogastrostomy
Binding or invaginating pancreaticojejunostomy
Pancreatic duct stenting
Pancreatic duct occlusion
Total pancreatectomy

of the most widely recognized risk factors is texture of the remnant pancreas; the relation between high rates of pancreatic fistula up to 25% (42,44-47) in the presence of soft pancreatic parenchyma has been repeatedly reported. The pancreatic duct size has been implicated as another relevant factor. Pancreatic duct diameter under 3 mm is related to a significantly higher risk of pancreatic fistula development (42,44,46,47). Pancreatic fistula development is also predisposed by pancreatic pathology: ampullary, bile duct, duodenal carcinoma and cystic neoplasms are correlated with an increased risk of pancreatic fistula (48,49). The second group of risk factors are patient related, including male sex, advanced age (older than 70) (48,50), cardiovascular disease probably due to poor blood supply of anastomosis (30), duration of jaundice (51). The last group is procedure related and includes a type of pancreaticodigestive anastomosis, use of somatostatin, surgeon's experience and increased operative blood loss (20,21,23,24,30,43-47,52).

Prevention of complications

A great deal of research has been conducted over the years aimed at decreasing the risk of pancreatic fistula occurrence (*Table 3*). It has focused on the influence that somatostatin, pancreatic duct stenting and pancreatic occlusion have on the reduction of PF rate. In addition, a number of studies have become available which compare pancreaticogastric anastomosis versus pancreaticojejunal anastomosis and different pancreaticojejunal anastomotic technique and their influence on frequency of PF occurrence (*Table 4*).

Somatostatin and analogues

Ocreotide is a synthetic long acting analogue of somatostatin, a potent inhibitor of pancreatic endocrine and exocrine secretion, and gastric and enteric secretion as well. Somatostatin and its analogue are administered postoperatively as prophylaxis. The idea behind this is that the decrease of pancreatic secretion would result in the pancreatic fistula prevention. A number of RTC have examined the benefit of somatostatin in pancreatic leakage prevention, but the results were inconsistent (68). In 2005, Connor conducted meta-analyses of ten RTCs which showed benefits of the use of somatostatin and its analog ocreotide in reducing the rate of biochemical fistula formation, pancreas-specific complications and total morbidity. The incidence of clinical anastomotic disruption and mortality

rate was not reduced (69). Cochrane Database Systematic Review from 2013 involved 2,348 patients in 21 trials. Conclusion drawn from it was that there was no significant difference in postoperative mortality, reoperation rate or hospital stay between the group of patients who were administered prophylactic somatostatin or its analogue and the group which received either placebo or nothing at all. In the somatostatin analogue group, the incidence of pancreatic fistula was lower, as was the overall number of patients with postoperative complications. On the other hand, when only patients with clinically significant fistulas were considered, there was no relevant difference between the groups. Based on the current available evidence, somatostatin and its analogues are recommended for routine use in people undergoing pancreatic resection (70).

Duct stenting

Internal, transanastomotic stent diverts the pancreatic juice from the anastomosis, and enables easier placement of sutures reducing the risk of iatrogenic duct occlusion. Its drawbacks are possibility of migration of the stent and occlusion which may lead to pancreatic fistula formation. There are not enough studies on internal stenting and their results have been contradictory (71,72). RTC from Winter *et al.* (61), involving 234 patients, demonstrated that internal duct stenting did not reduce the rate or the severity of pancreatic fistulas. The pancreatic fistula rates were 11.3% in patients with internal stent and 7.6% in patients without internal pancreatic stent. External stent has the possibility of a complete diversion of the pancreatic juice away from the pancreaticojejunal anastomosis which prevents the activation of pancreatic enzymes by bile. The RTC by Poon *et al.*, involving 120 patients, showed that the external stent group pancreatic fistula rate was significantly lower (6.7%) compared to the group which did not undergo the same procedure (20%) (62). In prospective multicenter randomized trial from Pessaux *et al.*, it was shown that external drainage reduces pancreatic fistula rate (26% *vs.* 42%), morbidity and delayed gastric emptying after pancreaticoduodenectomy in high risk patients (soft pancreatic texture and a nondilated pancreatic duct) (63). Cochrane database systematic Review from 2013 involved 656 patients in order to determine the efficacy of pancreatic stents, both external and internal, in preventing pancreatic fistula after pancreaticoduodenectomy. The use of external or internal stents was not associated with a statistically significant change in incidence of pancreatic fistula, re-

operation rate, length of hospital stay, overall complications and in-hospital mortality. In the subgroup analysis, it was found that the use of external stents is associated with lower incidence of pancreatic fistula, the incidence of complications and length of hospital stay. The review concludes that the external stenting can be useful, but further RCTs on the use of stents are recommended (73).

Pancreatojejunal anastomosis technique

Ever since Whipple modified pancreaticoduodenectomy in 1942 by performing pancreaticojejunostomy instead of occlusion of pancreatic remnant, this type of anastomosis has been most commonly used for a reconstruction of pancreaticodigestive continuity. There have been further modifications over the years. For example, jejunal loop can be positioned in antecolic, retrocolic or retro-mesenteric fashion, or the isolated Roux loop pancreaticojejunostomy can be performed. The anastomosis can be performed as an end-to-end anastomosis with invagination of the pancreatic stump in the jejunum or as an end-to-side anastomosis with or without duct-to-mucosa suturing (*Figure 1*) (47,65,74,75). In 2002, Poon *et al.* compared duct-to-mucosa with invagination anastomosis, and found that the duct-to-mucosa anastomosis was safer (49). In 2013, Bai *et al.* conducted a meta-analysis of randomized controlled trials comparing duct-to-mucosa (467 patients) and invagination pancreaticojejunostomy (235 patients). Pancreatic fistula rate, mortality, morbidity, reoperation and hospital stay were similar between techniques (76). Peng described a binding pancreaticojejunostomy technique with a pancreatic fistula rate of 0%. This was further validated in an RTC demonstrating that the binding pancreaticojejunostomy in comparison with end-to-end pancreaticojejunostomy demonstrated significantly decreased postoperative pancreatic fistula rates, morbidity, mortality and shortened the hospital stay (67,77). However, multiple authors reported better results with binding or invaginating pancreaticojejunostomy technique in patients with soft pancreatic parenchyma and small size duct (42,64).

Type of pancreatic anastomosis

In 1946, Waugh and Clagett first introduced pancreaticogastrostomy in clinical practice (11) (*Figure 2*). There are several advantages of this anastomosis—the proximity of the stomach and the pancreas enables tension-free anastomosis, the excellent blood supply to the stomach

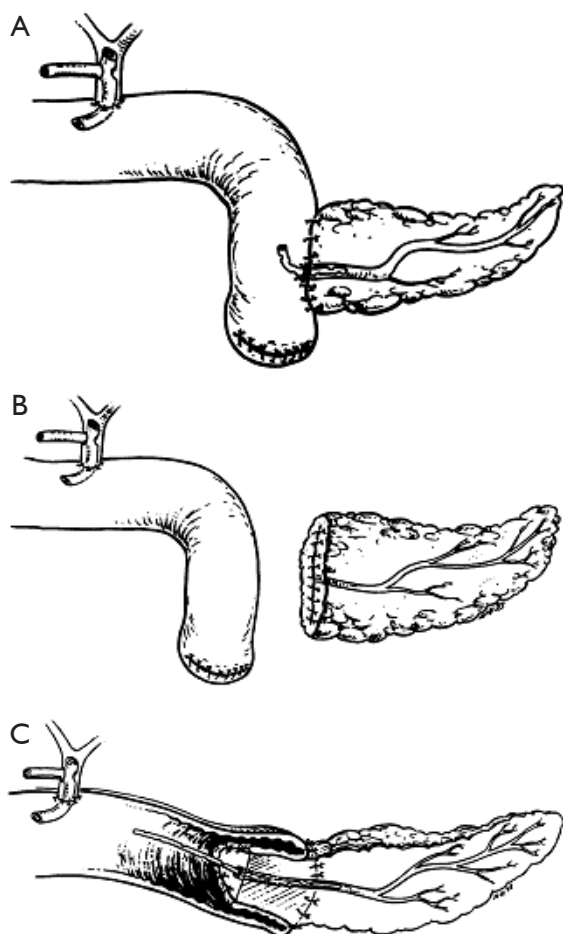


Figure 1 Different ways of doing the anastomosis for a pancreaticoduodenectomy. (A) End-to-side pancreaticojejunostomy; (B) oversewing of the pancreatic remnant; (C) end-to-end pancreaticojejunal invagination

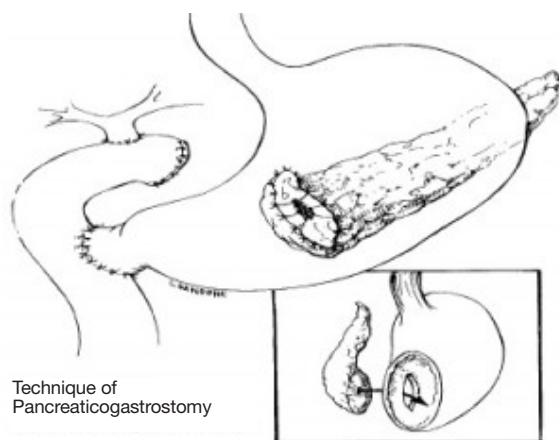


Figure 2 Pancreaticogastrostomy.

enhances the anastomotic healing, the acidity of the stomach content inactivates pancreatic enzymes, and the lack of enterokinase in the stomach prevents the conversion of trypsinogen to trypsin and subsequent activation of the pancreatic enzymes, which reduces the risk of pancreatic leakage due to anastomosis autodigestion (78). Yeo *et al.* were first to conduct prospective randomized trial comparing pancreaticojejunostomy and pancreaticogastrostomy, but this trial failed in finding a significant difference in pancreatic fistula incidence (58). Statistically relevant difference regarding pancreatic fistula rates, postoperative complications or mortality has not been found in two RTCs from Duffas *et al.* (59) and Bassi *et al.* (60) as well. In 2014 Menahem *et al.* published their meta-analysis of seven randomized controlled trials, involving 562 patients with pancreaticogastrostomy and 559 patients with pancreaticojejunostomy after pancreaticoduodenectomy. The pancreatic fistula rate was significantly lower in the PG group (11.2%) than in the PJ group (18.7%). The biliary fistula rate was also significantly lower in the PG group (2% *vs.* 4.8%) (79). Liu *et al.* dealt with the same RTCs, but focused also on morbidity, mortality, hospital stay, reoperation and haemorrhage and intra-abdominal fluid collection. As well as having lower incidence of pancreatic and biliary fistula, the PG group showed a significantly lower incidence of intra-abdominal fluid collection and shorter hospital stay (80).

Duct occlusion

In 1935 Whipple reported on the first series of results after pancreaticoduodenectomy, at which time he did not anatomize pancreas with digestive tract. Since there was a high PF incidence rate, he abandoned the aforementioned concept and implemented pancreaticojejunostomy as a standard part of surgical procedure. Where there was suture ligation of the pancreatic duct, without anastomosis, the rates of pancreatic fistulas was as high as 80% (64,81,82). In a randomized controlled trial, conducted by Tran *et al.*, involving 86 patients with duct occlusion and 83 patients with pancreaticojejunostomy, it was revealed that the ductal occlusion group had a significantly higher pancreatic fistula rate (17% *vs.* 5%), but it failed to show any relevant difference regarding other postoperative complications, mortality and exocrine insufficiency. After 3 and 12 months, there were significantly more patients with diabetes mellitus in the ductal occlusion group (83). Occlusion of the main pancreatic with fibrin glue was also abandoned (83,84) based on results from several RCTs because of high fistula

rates and higher incidence of postoperative diabetes mellitus (83,85).

Treatment

Surgical interventions for complications after pancreatoduodenectomy are nowadays rare, as low as 4% in centers of excellence (33,34) and 85-90% of patients with pancreatic fistula can be treated conservatively by means of fluid management, parenteral nutrition, suspension of oral intake and antibiotics administration. Lower percentage of surgical interventions can also be attributable to more advanced radiologic interventions for intrabdominal fluid collections, fistulas and bleeding. Indications for surgical intervention are clinical deterioration of the patient, disruption of pancreatic anastomosis, signs of spreading peritonitis, abdominal abscess, haemorrhage, and wound dehiscence. Delayed hemorrhage can be managed, if a patient is stable, by angiographic embolization of the bleeding vessel. In the remaining number of cases, emergency surgery is indicated (86,87). The type of surgical procedure depends on the underlying cause, and includes procedures such as peripancreatic drainage, control of hemorrhage, disruption of the pancreatic anastomosis without a new anastomosis or a conversion in another type of pancreatic anastomosis and a completion pancreatectomy (68,78).

Completion pancreatectomy has nowadays become a rare procedure, owing to improvements in conservative treatment and radiologic interventions. Completion pancreatectomy is indicated in patients with pancreatic anastomotic leak accompanied by sepsis or bleeding (88). Owing to the seriousness of the patient's condition, this procedures postoperative mortality is between 38% and 52% (89,90).

Total pancreatectomy

Total pancreatectomy was first performed in 1943 by Rockey (91), but the patient died soon after it. In 1944 Priestley performed the first successful total pancreatectomy (8). During the 1950's this procedure was popularised by Ross (92) and Porter (93) who considered it to be safer than pancreatoduodenectomy with pancreatojejunostomy, because pancreatic anastomosis related morbidity and mortality was avoided. Because of high local recurrence rates and poor long-term survival after Whipple operation, combined with the erroneous belief that pancreatic adenocarcinoma is a

multicentric disease, total pancreatectomy was thought to be an oncologically more radical procedure (94,95). Later reports revealed disadvantages of this procedure: long-term survival after total pancreatectomy was similar or lower than after pancreatoduodenectomy (96), morbidity and mortality were as high as 37% (95-97), with obligatory development of brittle diabetes mellitus and exocrine insufficiency. Development of steatohepatitis with progressive liver failure (98) is another potential long-term complication. Without advantages of oncologic radicality and with diabetes mellitus and malabsorption difficult to control, total pancreatectomy was abandoned for treating pancreatic tumors.

Number of total pancreatectomy procedures has been on the rise over the last two decades, for which several reasons can be named. Concentrating patients in high-volume centres and enhancements in surgical techniques have resulted in morbidity and mortality decline, the rates of which are now as low as 35% and 5% respectively (99-101) and are comparable to those following pancreatoduodenectomy. The second reason lies in the development of novel insulin formulations and better pancreatic enzyme preparations. While exocrine insufficiency can be relatively easily managed using pancreatic enzyme supplements, the control of endocrine insufficiency demands intensive insulin programmers, extensive patient education and continuing care (102). Total pancreatectomy is followed by not only insulin insufficiency, but also of glucagon and pancreatic polypeptide insufficiency, which leads to development of diabetes mellitus with tendencies to severe hypoglycemia. However, with intensive insulin programmers utilizing multiple daily insulin injections or pumps, and with glucagon rescue therapy, glycemic control can be achieved with satisfactory levels of HbA1c, similar to those in patients with insulin-dependent diabetes from other causes (99,102-104) and quality of life comparable to those of the patients after PPPD (99,100).

The third reason is the existence of broader spectre of indications which now include in situ neoplasia with malignant potential such as intraductal papillary mucinous neoplasm and multifocal islet cell neoplasm; hereditary pancreatitis and familiar pancreatic cancer syndromes. Other indications include locally advanced or multicentric pancreatic adenocarcinoma, neuroendocrine tumors, metastases in the pancreas, end-stage chronic pancreatitis with disabling pain, trauma, unsafe pancreatic anastomosis and completion pancreatectomy after dehiscence pancreato-enteric anastomosis (98,99,102).

Given that the postoperative total pancreatectomy

morbidity and mortality outcomes do not differ significantly from those after pancreatoduodenectomy (17,33,34,98,99), and the quality of life is fairly acceptable, there are no restrictions for performing total pancreatectomy on patients with indication for total pancreatectomy (99,101).

Discussion

After decreasing a 30-day mortality rate after pancreaticoduodenectomy to about 5%, surgeons have now focused their efforts on reducing morbidity, which is still as high as 30-60% (17,105-107). This mainly concerns reduction in incidence of pancreatic fistula, which is regarded the main cause of other frequent complications such as delayed gastric emptying, septic complications and intraabdominal haemorrhage.

Ever since Whipple's first pancreaticojejunostomy after pancreatoduodenectomy, surgeons have paid special attention to anastomosis between pancreatic remnant and digestive tract. In highly specialized centres pancreatic fistula incidence is from 0 to 18% (108), with death rate of 5%. Among the reports classifying pancreatic fistulas as A, B or C, following ISGPF grading system, incidence of grade C pancreatic fistulas was 2-5% (109-111). Grade C pancreatic fistulas were associated with sepsis from intraabdominal collections and bleeding, with high reoperation rate, prolonged length of hospital stay and with mortality rates from 35-40%. Soft pancreatic parenchyma is the most widely recognized risk factor for pancreatic fistula (112,113), along with three other relevant factors: duct size smaller than 3 mm, excessive intraoperative blood loss and specific pathology: ampullary, duodenal, cystic or islet cell neoplasms (111). The question is what to do when one or more risk factors for development of pancreatic fistula are present. There are multiple factors that will influence a decision which procedure to perform. First, to preserve a sufficient endocrine pancreatic function, approximately 50% of alpha and beta cells must be preserved (114). Alpha and beta cells are located predominately in the tail of the pancreas (115), so, theoretically, classical pancreaticoduodenectomy procedure should not cause endocrine insufficiency. When a pancreatic duct is occluded, without pancreatic anastomosis, pancreatic exocrine insufficiency will surely develop. Besides exocrine insufficiency, there is a significantly higher incidence of diabetes mellitus in patients with chemical occlusion of pancreatic duct in comparison with patients with a pancreaticojejunostomy (83).

On the other hand, exocrine insufficiency will also develop in 9-20% of patients after Whipple procedure (116,117). The underlying cause are probably stenosis of pancreatic anastomosis and postoperative inflammation of the pancreas and fibrosis of pancreatic parenchyma (118,119). Other factors include patient's preexisting diabetes mellitus or exocrine insufficiency, patient's overall health and performance status and patient's compliancy. A surgeon has several possibilities. First option is to perform a pancreatoduodenectomy with pancreatogastrojejunostomy, because of the lower incidence of pancreatic fistula with this type of anastomosis (79,80) or pancreatoduodenectomy with invagination pancreaticojejunostomy, recommended by a number of authors in case of soft pancreatic parenchyma and small pancreatic duct (67,113). Second option is also pancreatoduodenectomy, but with occlusion of the pancreatic remnant, either by ligation of the main pancreatic duct or by occlusion of the main pancreatic duct by Neoprene, Ethibloc or fibrin glue injection. This procedure is related to a higher incidence of pancreatic fistula, but with more benign clinical course, because pancreatic enzymes are not activated. The last option is total pancreatectomy for initial treatment of patients with multiple risk factors. With this procedure potential risks of a pancreatic fistula are eliminated, but with establishment of a total pancreatic state. Because of glycemic instability, predisposition for severe, life-threatening hypoglycemia, and need for close glucose monitoring and intense insulin programme, patient's compliance after total pancreatectomy is essential.

When a surgeon encounters such a significant problem, the decision about proper surgical management can be difficult to make. Besides purely technical challenges, patients overall health status, existing comorbidities, pancreas pathology and expected survival are crucial in the decision-making process.

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