



Complications in Biliopancreatic Surgery

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Abstract

The complications of biliopancreatic surgery have a very variable range of incidence showing surgical procedures with low incidence of complications such as simple cholecystectomy and complex or very complex procedures such as pancreatic resections followed by high incidence of postoperative complications. The purpose of this editorial is to examine a number of specific complications unique to biliopancreatic surgery such as: pancreatic fistula in relation to the different types of pancreatic-digestive anastomosis and biliary injuries after biliary surgery. Pancreatic and biliary surgical complications include a large range of conditions with overlapping clinical presentations and diverse therapeutic choices. The true incidence of pancreatic and biliary complications is difficult to determine due to selection and reporting bias. The treatment of these complications continues to evolve and patients may require endoscopic, surgical, and/or percutaneous techniques.

Keywords: Pancreatic surgery; Biliary surgery; Pancreatic fistula; Biliary injuries

Introduction

This editorial reviews the more common postoperative pancreatic and biliary surgical complications, their prevention and treatment. There are medical and surgical complications common to major surgical procedures but our purpose is to examine a number of specific complications unique to biliopancreatic surgery. The evaluation and study of these surgical complications should be connected with each intervention that can be related to the pathology. The specific complications of biliopancreatic surgery have a very variable range of incidence showing surgical procedures with low incidence of complications such as simple cholecystectomy and complex or very complex procedures such as pancreatic resections followed by high incidence of postoperative complications. In this manuscript we have assessed the complications with the classification proposed by Clavien-Dindo, based on the therapy used to treat the complication [1,2].

Complications in Pancreatic Surgery

Acute and chronic pancreatitis, benign and malignant tumors, may require pancreas surgery. Surgical treatment of pancreatic disease often has very challenging steps, based on the location, the close connections of the gland with other structures (superior mesenteric artery and vein), and the management of the resected pancreas. Therefore the pancreatic surgery can result in complications and high postoperative morbidity rates can occur. Pancreatic resections are the major surgical procedures, such as duodenopancreatectomy, Frey's intervention, etc., with operative mortality rates less than 5%, showing a stable reduction (data referred to the last two decades), but also a stable high morbidity rates (30-60%) [3].

The majority of perioperative complications of pancreatic surgery are not life-threatening, with less than 10% requiring reoperation [4]. However these morbidities complicate the postoperative period with prolonged hospital stay and delay in adjuvant therapy for cancer patients. Our study will examine the most frequent specific complications.

Pancreatic Fistulas

Pancreatic Fistula (PF) is the most relevant complication of pancreatic surgery. A pancreatic-digestive anastomosis typically completes the pancreatic surgery and fistula results from an anastomotic leak. The incidence of PF range from 3 to 50%. This very variable incidence may come from variety of assessment. In fact this variety of assessment has been in the past years the cause of great difficulties of clinical evaluation of this morbidity. From the data of the literature there were 26 definitions of PF between 1991-2000. Each definition was arbitrarily assigned a score based on daily fluid output criteria and timing of fistula development [5]. We can find in the literature a very variable incidence of PF (Table 1). Then has been proposed by International Study Group on

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Table 1: Incidence of PF in the literature.

Authors	Incidence %
Bassi C 2001, Buchler MW 2003	2-20
Suzuki Y 2002, Alexakis N 2004	8-50
Van Berge JM IV 2001	80
Doglietto GB 2006	37

Table 2: Grading of PF.

Criteria	No fistula	Grade A	Grade B	Grade C
Drain amylase level	<3 times normal SA*	>3 times normal SA*	>3 times normal SA*	>3 times normal SA*
Clinical conditions	Well	Well	Often well	Ill appearing
Specific treatment	No	No	Yes/No	Yes
US/CT if obtained	Negative	Negative	Negative/Positive	Positive
Persistent drainage (> 3 weeks)	No	No	Usually yes	Yes
Signs of infection	No	No	Yes	Yes
Readmission	No	No	Yes/No	Yes/No
Sepsis	No	No	No	Yes
Reoperation	No	No	No	Yes
Death related to fistula	No	No	No	Yes

*Serum amylase (SA)

pancreatic fistula a shared definition and classification of PF [6].

The classification of PF is based on some criteria: output of fistula, pure pancreatic fistula or mixed, side or total interruption of main pancreatic duct.

- High output fistulas have the output in 24 hours greater than 200 ml. On the contrary in the low output fistulas the leak is less than 200 ml in 24 hours.
- The separation between pure and mixed fistula has very important clinical significance. The pure fistula drains only pancreatic juice that contains inactive pancreatic enzymes and is relatively inert without other clinical manifestations. The mixed fistula drains pancreatic juice with biliary and enteric juice. In the mixed fistula there are activated proteases, which can cause some complications such a peripancreatic necrosis, hemorrhage, etc.
- The type of interruption of the main pancreatic duct allows a further distinction between end and side fistula. The end fistula is characterized by complete section of the duct. This pathological condition is present in pancreatic-enteric anastomosis dehiscence with the distal pancreatic stump or also in case of traumatic disruption of main pancreatic duct. In the latter condition, that can be termed “disconnected duct syndrome”, there are two portions of the pancreas, both secreting, that can heal separately with great difficulty, and for which is not applicable the conservative management. On the contrary the end fistula from pancreatic-enteric anastomosis leakage especially with pure output of pancreatic juice can heal with conservative management. In the same way a side fistula, with continuity of the pancreatic duct, has the probability of healing with conservative treatment.

The postoperative PF usually occurs following the pancreatic surgery: pancreaticoduodenectomy, resection of distal pancreas, resection/wirsung-jejunostomy in the treatment of chronic

pancreatitis, enucleoresection. The international assessment and definition of PF allows an important progress in its treatment. The definition of the International Study Group on Pancreatic Fistula (ISGPF) is the following: “an abnormal communication between pancreatic ductal epithelium and another epithelial surface, containing fistulas derived enzyme rich fluid”. Beside the definition, the classification proposes a grading system to assess the severity of the fistula. The grading system plans three levels of severity: Grade A, B and C. (Table 2). The grading is based on some criteria: drain amylase level, clinical conditions, sepsis, persistent drainage longer than 3 weeks, US/CT findings, use of specific treatment, reoperation, readmission, signs of infection, death. For postoperative fistula due to pancreatic anastomotic leakage after PD can be identified the risk factors. There are three types of risk factors: patient’s related risk factors, disease related risk factors, and surgical procedure related risk factors.

Patients factors [5,7-17]. There are a lot of patient’s related risk factors that have been tested in various studies. Male sex, advanced age (> 70 years), duration of jaundice, creatinine clearance abnormality, intraoperative blood loss, coronary disease have been evaluated as risk factors for pancreatic fistula. The results of these studies show [18] only a general correlation between patient’s factors and risk of pancreatic fistula: the altered general conditions of the patients (prolonged jaundice, abnormal creatinine clearance, coronary disease, etc.), advanced age, intraoperative complications may interfere with the healing of the pancreatic anastomosis. In short these factors do not play a role quantitatively definable.

Disease factors

The risk factors for pancreatic fistula connected with pathological features of the pancreas are in great evidence. The pancreatic parenchyma texture can be soft, intermediate or hard, linked to disease. The reports in the literature confirm the greater incidence of the fistula following anastomotic leakage in the patients with soft pancreatic parenchyma (20-30%) rather than the patients with intermediate or hard texture [6,19-23]. A fibrotic pancreatic stump, especially if chronic pancreatitis is present or if durable ductal obstruction (neoplastic or not) causes the glandular sclerosis, facilitates pancreatico-enteric anastomosis, with low risk of anastomotic leakage. On the contrary can be difficult to perform the anastomosis with a soft pancreatic parenchyma, characterized by high incidence of anastomotic leakage. In fact the pancreatic or periampullary diseases without main pancreatic duct obstruction and then without pancreatic tissue sclerosis present high risk of anastomotic leakage: duodenal adenocarcinoma, distal cholangiocarcinoma, benign islet tumors, duodenal adenoma, etc: Besides the structure of the parenchyma, should be considered for risk factor of fistula also the size of main pancreatic duct. The size of the duct is connected with the ductal obstruction (neoplastic or not) or the chronic flogosis. Pancreas with dilated ducts and generally with hard parenchyma shows less risk of anastomotic leakage and fistula; whereas if the size of the duct is small (3 mm or less) the risk of pancreatic fistula is higher. Other risk factors for pancreatic fistula together a small size of pancreatic duct is a high pancreatic juice output [24].

Operative/technical factors. The pancreatic stump in the past two decades has been submitted to various surgical procedures that have been assessed and compared based on postoperative fistula rates. These surgical techniques are pancreatojejunostomy, pancreatogastrostomy, invagination of pancreatojejunal anastomosis,

position of the stent in pancreatico-enteric anastomosis, etc. [5-7,19-23,25,26]. The results of the comparison of various techniques did not permit an unbeatable conclusion in favor of a technique or another. Moreover there are other risk factors for pancreatic anastomotic fistula related to surgical treatment: more complex intervention for advanced stages of disease including vascular resections for mesenteric-portal invasion, jaundice associated coagulopathy, etc. In summary the increased intraoperative blood loss is an important risk factor for developing PF. Intraoperative blood loss exceeding 1500 ml increases significantly the risk of postoperative PF.

Risk of PF following enucleoresection of little nodular lesions of the pancreas (e.g. insulinoma) and distal pancreatectomy [27,28]. The enucleoresection can cause fistula if the walls of main or other ducts have been damaged during surgical procedure. Usually there are partial lesions of the duct. In this case the fistula, well drained, can be treated with conservative option. The distal resection of pancreas with or without splenectomy can be followed by postoperative fistula. The favorable conditions in this setting are the normal transpapillary flow of pancreatic secretion that, if necessary can be improved with endoscopic sphincterotomy and effective drainage of pure PF. The conservative treatment should be the usual therapeutic choice.

Technical features of pancreatic – digestive anastomosis

The PF is a most common morbidity of pancreatic surgery with a very variable incidence from the literature. Its incidence ranges from 6 to 30-40% [5-10,19-23,25,26]. In these same reports the mortality ranges from 1, 4 to 5%. The clinical impact of PF consists of clinical conditions, specific treatment required, persistence of drainage, signs of infection, sepsis, reoperation, etc. The starting point of definition of postoperative PF is the drain amylase level plus than 3 time's normal serum amylase, from the third postoperative day. The majority of postoperative PF comes from leakage of digestive anastomosis of remnant pancreas. Therefore the formality of pancreato-digestive anastomosis is the first step in the prevention of anastomotic leakage. There are two choices for pancreatic-digestive anastomosis: pancreaticojejunostomy and pancreaticogastrostomy. In the perspective of the safety of the anastomosis there are not the advantage data for either type of anastomosis. The safety of anastomosis is based on the skills of the surgeon about each specific procedure.

Pancreaticojejunostomy (PJ) can be performed such as:

- End-to-end anastomosis with some variations: one layer (suture passage within the main duct and full thickness of the jejunal wall); two layers (the inner layer approximates the cut pancreatic surface passing within the main pancreatic duct to the full thickness of the jejunal wall; the other layer approximates the capsule of the pancreas to the seromuscular of the jejunum).
- End to side such as duct to mucosa anastomosis performing two layers suture.
- End to end invagination technique. The remnant pancreas is invaginating into the jejunum [29-34].

The comparison between these surgical techniques showed the overlapable results based on the rate of anastomotic leakage. This final conclusion emphasizes that the success (outcomes) of some surgical procedures lies on the specific skill of the surgeon performing a specific technique of pancreaticojejunal anastomosis and overall on the pathologic characteristic of the pancreatic tissue (fibrosis or not) and of the size of main pancreatic duct.

Pancreaticogastrostomy (PG): end to side anastomosis between the pancreatic stump and posterior wall of the stomach. The anastomosis can be performed following the technique of invagination of remnant pancreas into the stomach or suturing full thickness gastric wall with main pancreatic duct.

Several suggestions for prevention of postoperative pancreatic fistula (POPF)

There are some options for prevention or control of postoperative fistula. The management of pancreatic remnant after pancreaticoduodenectomy plays a relevant role in the prevention of POPF. Preventive function can be hypothesized for pharmacological inhibition of exocrine pancreatic secretion in the postoperative period. Peri-postoperative infusion of somatostatin-octreotide may reduce the pancreatic juice secretion and consequently the incidence of the POPF. The data of the literature about the results of these therapeutic procedures are not overlapable [14,35-38]. Pancreaticojejunal or pancreaticogastric anastomoses are the main surgical procedures that can condition the incidence of POPF (see above). Some other technical detail may be important to prevent the fistula. Main pancreatic duct stent has been proposed and employed. The stent allows, with transjejunal or transgastric passage, the external drainage of pancreatic juice avoiding the activation of pancreatic enzymes by the bile. The use of T – tube transanastomotic biliary drainage can be proposed because can establish the almost complete separation of biliary and pancreatic secretions and an eventual POPF should be pure fistula [39]. Other technical solutions are the use of separate Roux-en-Y limbs for pancreatic anastomosis or with the reduction of pancreatic remnant after duodenopancreatectomy. The closure of pancreatic stump without digestive anastomosis has been also proposed. In this way the purpose is to obtain a guided and isolated PF. After ligation of the main pancreatic duct, the closure of pancreatic stump can be performed with stitch suture or stapler closure. Can be used also after the closure of pancreatic remnant or as reinforcement of pancreatic anastomosis the fibrin sealant.

The treatment of POPF encompasses some therapeutic procedures (medical or surgical) based on the type of intervention (duodenopancreatectomy, distal pancreatectomy, enucleoresection, etc.) and the definition and grade of this complication following on one hand the classification proposed by Clavien, based on the therapy used to treat the complication, and the other hand the definition and classification proposed by International Study Group on Pancreatic Fistula (ISGPF).

Complications in Biliary Surgery

Biliary surgery (gallbladder and biliary tract procedures) presents very variable range of complexity from simple cholecystectomy to treatment of cholangiocarcinoma or biliary tract injuries repair. The incidence of biliary injuries relative to cholecystectomy, with open or laparoscopic approach, range from 0.2 to 0.8% [40]. The biliary leak after biliary surgery can be caused by a lot of factors, almost always due to iatrogenic injuries or complications of percutaneous, surgical, endoscopic interventions. The etiology of these complications can be summarized as follow:

- Abdominal operations: cholecystectomy, pancreaticobiliary resection, hepatic resection, gastroduodenal surgery, hepatic transplantation, biliary anastomosis.
- Percutaneous procedures: transhepatic drainage/dilation, liver biopsy, radiofrequency tumor ablation, liver biopsy.

- Endoscopic retrograde cholangiography: biliary perforation.

The most common causes of postcholecystectomy biliary leakage are cystic duct stump leak (frequency range from 60 to 70% of this complication), duct of Luschka injuries (10-20%). The bile leakage can complicate all bilioenteric anastomosis. The incidence of this complication is not exactly established, but we can consider that its range is from 2 to 5%. The frequency of this complication is, on the whole, very low but in selected cases should be evaluated the employ of biliary transanastomotic drainage such as T-tube. The most significant complication of biliary-hepatic surgery is the bile duct injuries. Numerous types of bile duct lesions can be considered. There is a useful classification of common bile duct injury [41] the Way-Stewart classification. This classification encompasses four classes of bile duct injuries:

- Class I: common bile duct (CBD) mistaken for cystic duct but recognized; cholangiogram incision in cystic duct extended into CBD.
- Class II: lateral damage of common hepatic duct (CHD) from cautery or clips placed on duct; associated bleeding, poor visibility.
- Class III: CBD mistaken for cystic duct not recognized; CBD, CHD, R, L hepatic ducts transected and/or resected.
- Class IV: RHD mistaken for cystic duct, RHA mistaken for caustic artery, RHD, RHA transected. Lateral damage of the RHA from cautery or clips placed on duct [42].

Various measures have been suggested to reduce the risk of biliary injuries during biliary intervention, mostly cholecystectomy, that can be very complex procedure if acute or chronic inflammation is present in the triangle of Calot. Others risk factors are abnormal biliary anatomy, short cystic duct and also improper surgical maneuvers (excessive cephalad or lateral retraction of gallbladder, excessive use of cautery, etc.). The first maneuver useful in the risk reduction should be the antegrade dissection of gallbladder [43]. Strasberg et al. [44] have proposed the "critical view of safety". This method encompasses three actions:

- The triangle of Calot must be rid of fat and fibrous tissue.
- The gallbladder infundibulum should be disconnected from the gallbladder bed.
- Only two structures can be connected with gallbladder.

These maneuvers cannot give the total certainty of avoiding the biliary injuries but can give a considerable reduction of the risk mostly in the complex surgical conditions.

These injuries can be recognized during operative procedures (15-30%) or in the postoperative period, early or late.

Discussion

Clinical presentation

The surgical drain, if present, can show the evident biliary component. If there isn't the drain, the bile leakage forms a collection, usually in the surgical site, or widespread in the peritoneal cavity. The clinical presentation ranges from general discomfort to abdominal pain, fever, septic conditions, expected evolution of bile peritonitis.

Diagnosis

The first diagnostic step is the suspicion based on the alteration of normal postoperative course. The diagnostic phase can employ the common exams. Laboratory data can show serum bilirubin increase and leukocytosis. At imaging exams (US, CT) can be detected intrabdominal fluid collection. An important diagnostic exam for postoperative bile leakage is the cholangiography performed by different ways: operative drain, if present; biliary drainage (T-tube), endoscopic retrograde cholangiography, percutaneous transhepatic cholangiography. The access to biliary tree in some cases allows several therapeutic actions (simple drainage, prosthesis, stent, etc.). A noninvasive imaging exam is the magnetic resonance cholangiopancreatography that cannot have therapeutic role.

Management

The minor bile leaks, usually after cholecystectomy can be treated with decompression of biliary tree by ERCP and endoscopic sphincterotomy with or without biliary stent. In some cases should be necessary percutaneous drainage of intrabdominal fluid biliary collections. If the transpapillary access is not possible can be employed the percutaneous way (PTC) to biliary tree. The major bile duct injury usually requires surgical intervention. The timing of treatment can be conditioned by several factors: time of recognition of lesion, the type of lesions, the skills of the surgeons. The lesion detected at time of intervention (e.g. laparoscopic cholecystectomy) should be treated with primary repair or hepaticojejunostomy (usually end to side Roux-en-Y loop). On the other hand if the injury has been detected in the early postoperative period with CT scan the first step of treatment is the (percutaneous) drain collections. The following step is the anatomical definition of biliary lesion by PTC with biliary drainage. In this way we can control the biliary leak that allows waiting 4-6 weeks to organize the definitive repair as hepaticojejunostomy. In any case the biliary injury can be followed by long-term morbidity, multiple radiological and surgical procedures and also mortality. Clinical manifestations due to biliary injuries in the later postoperative period are biliary strictures and cholangitis. Biliary strictures can be due also to bilio-digestive anastomosis following biliary resections for malignant or benign diseases. Biliary lithiasis can be complicated by retained stones following surgical treatments such as cholecystectomy or choledocolithotomy. Moreover biliary pancreatitis, sometime recurrent, may be the complication of incomplete treatment of papillary stenosis due to stones passage through duodenal papilla. Finally postoperative pancreatitis can occur following biliary surgery. The other specific complications of pancreatic surgery are the following: delayed gastric emptying after PD (incidence 20-40%), postoperative hemorrhage (incidence 2-15%) following pancreatic resection in the immediate postoperative period or delayed 10-15 days after surgery. Gastrojejunal anastomosis fistulas after PD with incidence 0.4-7.4%, enteric fistulas after laparotomies/relaparotomies as treatment of infected pancreatic necrosis (high incidence 41-75%), intrabdominal abscess following necrosectomy for infected pancreatic necrosis after acute pancreatitis (incidence 13-26%), after PD (incidence 11%) and pancreatic-enteric anastomosis (incidence 7%).

Conclusions

Pancreatic and biliary surgical complications include a large range of conditions with overlapping clinical presentations and diverse therapeutic choices. The true incidence of pancreatic and biliary complications is difficult to determine due to selection and reporting

bias. The treatment of these complications continues to evolve and patients may require endoscopic, surgical, and/or percutaneous techniques.

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