Endoscopic Management of Pancreatic Fistula and Leaks

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Introduction

Pancreatic fistula with leakage of pancreatic fluid into adjacent or distant spaces, structures, or organs result from a disruption of the pancreatic ductal system. Pancreatic fistula involve either the main pancreatic duct or one of its side branches and may occur in the course of (recurrent) episodes of acute pancreatitis, chronic pancreatitis, pancreatic malignancy, pancreatic resection, or trauma [1–6].The clinical consequences depend on multiple factors including etiology, site and extent of the disruption, the rate of secretion of pancreatic juice, the location of the leak relative to anatomic tissue planes, and the presence of downstream obstruction of the pancreatic duct caused by strictures or calculi [3, 6]. A small leak from one of the side branches of an otherwise unobstructed pancreatic duct may resolve spontaneously, whereas a persistent leak from a major main pancreatic duct disruption may be complicated by pseudocyst formation, internal fistula formation causing ascites or pleural effusion, and external pancreatic fistulas. Leakage of pancreatic secretions can cause significant morbidity due to infection, malnutrition, and skin excoriation.

Pancreatic fistulas have iatrogenic or non-iatrogenic causes. The former include (1) pancreatic resection and operative trauma, which typically occur in the tail of the pancreas during splenic surgery, left renal/adrenal surgery, or mobilization of the splenic flexure of the colon; (2) percutaneous drainage of a pancreatic fluid collection (pseudocyst or walled-off pancreatic necrosis); (3) complications of endoscopic interventions during endoscopic retrograde cholangiopancreatography (ERCP); and (4) intraoperative core biopsy of pancreatic masses. Non-iatrogenic causes include acute and chronic pancreatitis, most frequently caused by gallstones or alcohol, and penetrating or blunt abdominal trauma.

Following pancreatic duct disruption, pancreatic juice leaks into the peripancreatic area creating a peripancreatic fluid collection which, depending on local factors, may lead to the formation of a fluid collection, internal pancreatic fistula or external pancreatic fistula (Table 33.1).

The development of an outer wall of granulation tissue over a period of 4–6 weeks may confine the peripancreatic fluid collection to the retroperitoneum, lesser sac, or mediastinum and marks the development of a pseudocyst.

Persistent leakage of pancreatic fluid can lead to the development of an internal fistula due to spontaneous erosion into a neighboring hollow viscus (colon, duodenum, stomach, or esophagus), peritoneal or pleural cavities, or mediastinum, lesser sac, retroperitoneum, or perihepatic space. If the leak occurs anteriorly into the peritoneal cavity, it results in pancreatic ascites. A posterior communication may track into the pleural cavity or mediastinum resulting in pancreaticopleural fistula. External fistulae are pathological communications that connect any part of the gastrointestinal tract with the skin. This may occur spontaneously but usually follows after a surgical or radiological intervention of a peripancreatic fluid collection, debridement of pancreatic necrosis, or after a pancreatic resection. The likelihood of developing an external fistula increases greatly if percutaneous drainage is performed in the setting of disconnected pancreatic duct syndrome.

Signs and Symptoms

The clinical manifestations of pancreatic fistulas vary based on the size, location, and site of communication (e.g., peritoneal or pleural cavity, another hollow viscus or the skin). Patients with internal pancreatic fistulas may be asymptomatic. Symptoms of an internal pancreatic fistula

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Table 33.1 Manifestations of pancreatic fistula and leaks

1. Pancreatic fluid collections (pseudocysts)
2. Internal pancreatic fistula
Pancreaticoperitoneal (pancreatic ascites)
Pancreaticopleural
Pancreaticobronchial
Pancreaticomediastinal
Pancreaticopericardial
3. External (cutaneous) pancreatic fistula

may include vague abdominal pain, nausea, vomiting, and abdominal distension. Patients may have fever, features of sepsis, and gastrointestinal bleeding with hematemesis, melena, or hematochezia. Pancreatic ascites usually develops slowly and is associated with a variable intensity of abdominal pain and distension. Ascites may be associated with weight loss, anorexia, weakness, and severe malnutrition. Symptoms of thoracopancreatic fistulas include cough, shortness of breath, chest pain, and dysphagia [7]. These patients may have unilateral or bilateral pleural effusions with dullness to percussion over the thorax and diminished breath sounds on physical examination. External pancreatic fistula is associated with drainage of pancreatic fluid from an abdominal wound. Patients may have weight loss due to malnutrition, symptoms of dehydration due to fluid and electrolyte loss, and/or fever due to an infection.

Physical examination findings include abdominal distension and flank dullness. A large pseudocyst may be palpable in the epigastric region and can cause symptoms by compressing adjacent organs.

Pancreatic fluid effluent may be visible from an external pancreatic fistula with skin excoriation around the fistula site. Pancreatic fluid is high in bicarbonate and protein, and in the case of high-output fistulas, fluid loss may lead to metabolic acidosis, malnutrition, and dehydration. A fistula is termed a high-output fistula when the output is greater than 200 mL per 24 h and low output when the output is less than 200 mL per 24 h [8]. A fistula that drains only pancreatic juice is called a pure fistula, while a fistula that drains pancreatic juice mixed with enteric contents is referred to as a mixed fistula. The output of a pure fistula contains inactive pancreatic enzymes and is relatively inert [9] . The output of a mixed fistula contains activated proteases, which can cause further complications like necrosis and hemorrhage. A pancreatic fistula can be either a side or end 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 pancreatic duct syndrome." End fistulae are unlikely to heal with conservative management because of discontinuity from the gastrointestinal tract and the remaining pancreatic duct. Also, end fistulae are not amenable to transpapillary stent placement.

Conditions that May Represent an Indications for Treatment

- Pancreatic ascites and pancreaticopleural fistula
- Disconnected pancreatic duct syndrome
- Postoperative pancreatic fistula

Indications

Pancreatic Ascites and Pancreaticopleural Fistula

Pancreatic ascites and pancreaticopleural fistula are an uncommon but well-recognized complication of chronic pancreatitis that are associated with significant morbidity and mortality. Internal pancreatic fistula with pancreatic ascites and pleural effusion share a common pathophysiology. The disruption of the pancreatic duct results in the formation of internal fistula communicating with peritoneal or pleural cavities, which result in ascites or pleural effusion, respectively. Alcohol-related chronic pancreatitis is considered the main cause. Pancreatic ascites and pleural effusion may initially be misdiagnosed being a consequence of alcoholic liver disease or pleural tuberculosis. Although a pancreaticopleural fistula is relatively rare, it is an important diagnostic consideration in patients with chronic pancreatitis who present with recurrent or persistent respiratory symptoms and pleural effusions. Pleural effusion generally occurs on the left, but it is not unusual to see right-sided or bilateral effusions. Although a high amylase level in pleural fluid is a characteristic of pleural effusions associated with chronic pancreatitis, this can also be due to acute pancreatitis, esophageal perforation, para-pneumonic effusions, and pulmonary or pancreatic malignancy [7, 10–12]. However, only pancreatic pleural fistula leads to pleural fluid amylase levels greater than 50,000 IU/L [10, 12]. Traditionally these patients are treated with prolonged conservative medical therapy (see further).

Disconnected Pancreatic Duct Syndrome

Disconnected pancreatic duct syndrome refers to a condition in which rupture of the main pancreatic duct results in a portion of the pancreatic gland becoming isolated from the duct proximal to the obstruction and not in communication with the papilla. This isolated segment of the pancreas will continue to secrete pancreatic secretions that cannot reach the duodenum through the distal main pancreatic duct and will be secreted freely into the abdominal cavity resulting in the formation of external or internal fistulas and peripancreatic fluid collections. The site of disconnection in more than

80% of cases is the head or neck/body portion of the pancreas [13, 14].

The most important clinical clue is a nonhealing pancreatic fistula or peripancreatic fluid collection that does not resolve with conservative medical management [15]. On imaging investigation, evidence of an intrapancreatic fluid collection or segmental necrosis along the expected course of the main pancreatic duct with viable upstream pancreatic parenchyma suggests the diagnosis of disconnected pancreatic duct syndrome. Abrupt discontinuity of the main pancreatic duct at the level of the fluid collection is usually diagnostic of a disconnected pancreatic duct syndrome. However, a focal stenosis or mechanical compression from an acute fluid collection can mimic a disrupted main pancreatic duct [15].

Postoperative Pancreatic Fistula

An important and potentially life-threatening complication of pancreatic surgery is the occurrence of a postoperative pancreatic fistula which can originate from the pancreatic remnant after distal pancreatectomy or enucleation, as well as from an anastomosis which is usually created as a pancreaticojejunostomy or pancreaticogastrostomy following pancreatic head resections or drainage procedures [16–18]. The incidence ranges from 0% to 24% with an average fistula rate of 12.9% following pancreaticoduodenectomy [19] and 5–28% after distal pancreatectomy [20].

The risk of developing a postoperative pancreatic fistula varies according to the underlying pancreatic pathology and the consistency of the pancreatic parenchyma. A fibrotic pancreatic remnant in patients with chronic pancreatitis facilitates the creation of an uncomplicated pancreatico-enteric anastomosis, whereas soft and friable pancreatic parenchyma makes the anastomosis more difficult to perform and is associated with a higher risk of pancreatic fistulas as is the absence of duct dilation (< 4 mm). The presence of diabetes mellitus, previous laparotomy, longer operating time, and non-stapler stump closure constitute additional risk factors for the development of pancreatic fistulas [21].

The International Study Group on Pancreatic Fistula (ISGPF) [18] consensus paper defined a postoperative pancreatic fistula (POPF) as the existence of any fluid output via an intraoperatively placed or postoperatively inserted drain on or after postoperative day 3 with amylase content greater than three times the upper normal serum value [18]. 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 postoperative pancreatic fistula, listed in Table 33.2.

Investigations

Laboratory Tests

In patients with an external fistula, the effluent should be collected for fluid analysis. Although there is no established cutoff, a pancreatic fluid amylase level greater than three times the serum amylase is supportive of a diagnosis of a pancreatic fistula. In patients with ascites, diagnostic paracentesis should be performed. Ascitic fluid should be sent for cell count, Gram stain, culture, amylase, albumin, total protein, and cytology. The combination of a serum-albumin ascites gradient below 1.1 g/dl, a total protein level > 3 g/L, and ascitic amylase greater than serum amylase is suggestive of pancreatic ascites. Often fluid amylase levels are 4000 units/L or higher. In some cases, the white cell count may be elevated due to a concomitant infection [22].

Endoscopic ultrasound facilitates fine-needle aspiration to sample cyst fluid for amylase, CEA, and cytology which

Table 33.2 Grading of postoperative fistula (POPF) according to the International Study Group on Pancreatic Fistula (ISGPF) [18]

Grade	A	B	C
Clinical conditions	Well	Often well	Ill appearing/bad
Specific treatment Partial (peripheral) or total parenteral nutrition, antibiotics, enteral nutrition, somatostatin analogue, and/or minimal invasive drainage	No	Yes/no	Yes
US/CT (if obtained)	Negative	Negative/positive	Positive
Persistent drainage (after 3 weeks)	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

can help differentiate pseudocysts from cystic neoplasms. Pancreatic fluid collections and pseudocysts will typically have high amylase levels, low CEA levels, and inflammatory cells or acellularity on cytological evaluation. Thoracentesis should be performed in patients with a pleural effusion. Effusions associated with pancreaticopleural fistulas are exudative and amylase-rich with pleural fluid amylase greater than the upper limits of normal for serum amylase or a pleural fluid to serum amylase ratio greater than 1.0. Pleural effusions due to a pancreaticopleural fistula can be distinguished from a symptomatic pleural effusion that occurs following acute pancreatitis by a therapeutic thoracocentesis. Pancreaticopleural effluents have high amylase content and tend to re-accumulate after therapeutic thoracentesis, whereas sympathetic pleural effusions do not have an elevated amylase and do not recur.

Chest Radiograph

A chest x-ray should be obtained in patients with symptoms of cough, shortness of breath, and dysphagia. It can show unilateral or bilateral pleural effusion in patients with pancreaticopleural fistula.

Abdominal CT Scan

An abdominal computerized tomography (CT) primarily serves to rule out other causes of abdominal pain. In patients with a pancreatic fistula, an abdominal CT scan may demonstrate free and walled-off fluid collections in the abdominal and thoracic cavities and changes of acute or chronic pancreatitis including focal pancreatic enlargement, parenchymal atrophy, pancreatic ductal dilatation, and calcification. Contrast enhanced CT scan has been shown to be a useful technique in particular to identify the presence of (infected) pancreatic necrosis. The location of the fluid collections seen on CECT can be suggestive of the site of pancreatic duct disruption [23]. Newer computed tomography (CT) technology with thinner collimation and multirow detector CT (MDCT) with post-processing techniques, such as multiplanar reformations, has led to improved visualization of the PD [24].

Magnetic Resonance Cholangiopancreatography (MRCP)

With MRCP one can noninvasively evaluate the pancreatic parenchyma and also delineate pancreatic duct morphology. MRCP has been shown to be particularly useful for detecting pancreatic duct disruptions [25, 26]. A recent study in 31 patients with suspected PD disruptions reported MRCP could correctly diagnose an intact pancreatic duct in 8 patients (100%) and localize the site of disruption in 21 of 23 patients with ductal leak (91%) [25]. One of the limitations of MRCP is the absence of visualization of ductal filling and extravasation in real time, as seen on ERCP, thus giving rise to the possibility of missed diagnosis of pancreatic duct injury in non-dilated ducts [27]. To overcome this limitation, dynamic secretin-stimulated MRCP was studied in 17 patients with suspected pancreatic duct disruption [28]. After secretin administration, changes in the duodenal and jejunal fluid content were evaluated as well as the size or signal intensity of pancreatic fluid collection recorded. In healthy individuals with no pancreatic duct disruption, secretin administration increases the duodenal and jejunal fluid content, with less than 1 mm transient increase in pancreatic duct diameter. Any increase in fluid outside these anatomic regions is suggestive of a pancreatic duct disruption. Dynamic MRCP was able to identify pancreatic duct disruption in 10 of 17 patients (59%), and the investigators concluded that this is a safe and noninvasive technique, providing additional information about pancreatic duct integrity and anatomy, thus facilitating appropriate management. A further advantage of MRCP over ERCP is its ability to characterize the pancreatic duct upstream of the site of complete disruption, an area that is not visualized on ERCP [25]. Though often helpful in the diagnosis, a limitation of MRCP is the obvious inability to intervene therapeutically at the time of diagnosis.

Endoscopic Retrograde Cholangiopancreatography (ERCP)

Endoscopic retrograde cholangiopancreatography (ERCP) provides direct proof of a pancreatic leak or fistula and is the test of choice if therapeutic pancreatic stenting is planned. It has the highest accuracy in diagnosing a pancreatic disruption. It enables direct and dynamic visualization of the pancreatic anatomy as well as the ability to precisely identify the location (head, neck, body, or tail of pancreas) and extent of the disruption [2, 3, 29, 30]. On ERCP, pancreatic disruption is defined as extravasation of contrast medium from the ductal system and can be further defined as partial (opacification of the proximal PD upstream to the site of disruption) or complete (no visualization of the pancreatic upstream to the leak) [2, 3, 29, 30]. It can also provide information about the presence of stricture or calculi in the downstream portion of the duct. Although being the most sensitive technique to detect a PD disruption, ERCP is invasive and requires expertise, and the rates of cannulation of the pancreatic are operator dependent, with failed cannulation or inadequate pancreatography observed in up

Table 33.3 Classification of pancreatic injuries by endoscopic retrograde cholangiopancreatography [34]

Grade	Description
I	Normal main pancreatic duct on MRCP
IIa	Injury to branches of main pancreatic duct on ERCP with contrast extravasation inside the parenchyma
IIb	Injury to branches of main pancreatic duct on ERP with contrast extravasation into the retroperitoneal space
IIIa	Injury to the main pancreatic duct on ERCP at the body or tail of the pancreas
IIIb	Injury to the main pancreatic duct on ERCP at the head of the pancreas

Table 33.4 Management strategies for pancreatic fistula and leak

1. Medical management
2. Interventional therapy
Endoscopic therapy
Transmural drainage
Transpapillary drainage
EUS-guided pancreaticoduodenostomy/ pancreaticogastrostomy
Combination of above procedures
Radiological interventions
Surgical interventions

to 10% of patients [31–33]. It also carries the disadvantage of requiring sedation and is associated with risks of post-procedure pancreatitis and subsequent infection of sterile pancreatic fluid collections. Table 33.3 shows the pancreatographic classification of pancreatic duct injuries caused by blunt trauma in the pancreas [34].

Fistulography

Fistulography should be reserved to determine the site of internal communication of an external pancreatic fistula only if it is not evident on ERCP or MRCP. For pancreatic fistula occurring after pancreatic resection, fistulography is done via ERCP. In patients with operative or percutaneously placed pancreatic drainage catheters, a fistulogram can easily be performed using fluoroscopy, CT, or MRCP. It allows visualization of the fistula tract course, locating the origin from the pancreatic duct, delineation of any fluid collection that is in communication with the fistulous tract, and guiding repositioning of catheters to optimize drainage.

Management

As pancreatic duct leaks are not common, the current scientific evidence regarding clinical management of pancreatic duct leaks and disruptions is largely based on case reports, case series, and expert opinion. There are no randomized controlled trials that have compared the efficacy of medical, endoscopic, radiologic, or surgical treatment modalities. Because of their complexity, pancreatic duct leak patients are best managed by a multidisciplinary team comprised of therapeutic endoscopists, interventional radiologists, and surgeons. The management of pancreatic fistula depends on the presence and severity of symptoms, the characteristics and location of the ductal disruption (presence of a downstream pancreatic duct obstruction, presence of a confined fluid collection, and presence of pancreatic necrosis), and the presence of associated complications such as infection. Early surgical intervention should be considered whenever there is a leak in the pancreatic tail, when the site of ductal disruption cannot be bridged by a stent, or whenever a downstream stricture cannot be stented. Careful attention to an optimal maintenance of hydration, nutrition, and electrolyte balance through the management of the disease process is of prime importance for a successful clinical outcome. Table 33.4 outlines the management of pancreatic fistula and leak.

Medical Management

Patients with a pancreatic fistula are at risk for developing significant nutritional and electrolyte imbalances. Due to the diversion of pancreatic exocrine secretions, excessive loss of sodium and bicarbonate may occur. Patients often present with significant nausea, anorexia, and an inability to tolerate oral intake. In addition, depending on the relative absence of pancreatic enzymes in the duodenum, patients often have poor nutritional absorption, particularly of protein and fat [35]. In the absence of significant symptoms or coexisting infected pancreatic necrosis, initial management of pancreatic fistula consists of supportive care.

Cornerstone of medical management is the inhibition of pancreatic stimulation by maintaining patients nil by mouth (NPO). Nutrition is provided via nasojejunal feeding or by total parenteral nutrition (TPN). Enteral nutrition is associated with a lower incidence of infection, higher 30-day fistula closure rates, and shorter time to closure of postoperative pancreatic fistula as compared with TPN [36, 37]. Enteral feeding therefore should be favored whenever possible because it maintains the mucosal barrier, is relatively simple to administer, and is less costly than TPN. Theoretically, post-pyloric and even post-duodenal feeding seems desirable to minimize stimulation of secretions and maximize pancreatic rest, but there is no scientific evidence that this approach is to be favored over gastric feeding [38]. TPN should be administered to patients who are unable to receive enteral feeding but is not without risks including the occurrence of line sepsis and cholestatic injury to the liver. Somatostatin preparations

may be effective in the reduction of fistula output and help to correct electrolyte imbalances but do not improve the rate of fistula closure. In a 2012 meta-analysis of seven randomized trials that included 297 patients of which 102 had pancreatic fistula, closure rates were not significantly higher in patients treated with somatostatin analogues as compared with controls [39]. Special attention should be directed to optimal care of the external fistula opening as pancreatic juice may cause painful and difficult to treat skin excoriation.

The abovementioned treatment approach is based on the rationale that reduction of the pancreatic secretion decreases the flow of the pancreatic juice through the pancreatic duct and thus expedites healing of the pancreatic fistula. This conservative approach of prolonged pancreatic rest may be sufficient to heal the ductal disruption but occurs at the cost of prolonged hospitalization with a concomitant increase in the cost of treatment and an increased risk of hospital-acquired infections. Moreover, conservative therapy fails in a significant proportion of patients with large disruptions or ductal obstruction downstream of the disruption. Case series have reported fistula closure in approximately 80 percent of external and 50 to 65 percent of internal fistula over 4–6 weeks following supportive care [19]. Follow-up abdominal imaging with an abdominal CT scan or MRCP should be obtained after 6–8 weeks to evaluate the pancreatic fistula and presence of persistent peripancreatic fluid collections. Imaging should be repeated sooner if the patient develops abdominal pain, fever, chills, jaundice, or early satiety. In patients with clinical symptoms and signs suggestive of sepsis, or increasing white blood cell count, pancreatic fluid should be sent for Gram stain and culture to rule out an infection. Systemic antibiotics should be administered in patients with evidence of infected pancreatic fluid collections.

In patients with pancreaticopleural fistula and mediastinal fistula, prolonged conservative therapy involving fasting, parenteral nutrition, somatostatin or its analogues, and attempts to appose leaking mucosa (serosal apposition) have been recommended. The latter includes multiple paracentesis or thoracentesis or even placement of an indwelling chest tube. Usually, medical therapy is continued for 2–3 weeks before another intervention is believed to be warranted [40].

Conservative management for external pancreatic fistula often leads to a reduction in fistula output, but closure rates of external pancreatic fistula vary from 44% to 85% [41]. In patients with persistent external pancreatic fistula despite conservative treatment, endoscopic or surgical alternatives must be considered [42]. In patients with pancreatic fistula unresponsive to medical management, additional interventional treatments are warranted.

Endoscopic Management

In the last two decades, considerable advancements have been made in therapeutic pancreatic endoscopy, and over the years, endoscopic drainage has been used to treat pancreatic duct disruptions with encouraging results.

Transpapillary Drainage

Before considering endoscopic therapy, complete assessment should be done for the site and type of pancreatic duct disruption; anatomy of the pancreatic duct, especially the duct downstream of the disruption; and presence or absence of associated pancreatic fluid collections. A clinically useful investigation that demonstrates the relationship of external pancreatic fistula with the pancreatic duct is a fistulogram which can provide important information and clearly delineate the fistulous tract [23].

The Procedure

Transpapillary drainage involves insertion of an endoprosthesis through the major or minor papilla into the pancreatic duct, creating a path of lesser resistance that directs drainage of pancreatic secretions through the papillary orifice into the duodenum rather than through the pancreatic duct disruption. The sphincter of Oddi and any ductal strictures/calculi in the downstream duct are the sites of resistance impeding the flow of pancreatic juices into the duodenum. These

Practical Considerations in the Medical Management of Pancreatic fistula

- Nil by mouth (NPO)
- Nutrition via nasojejunal feeding or total parenteral nutrition
- Administration of somatostatin or its analogues, preferably its long-acting form Sandostatin LAR (Novartis) 50–200 mcg subcutaneous 4 times daily for prolonged periods of time
- Daily care of the percutaneous fistula opening to avoid and treat skin erosions

Instruments and Accessories

- Standard pull-type sphincterotome or a needle knife
- Guidewire
- Dilation balloon (4, 6, and 8 mm)
- Dilating catheters (3–10 Fr)
- 8.5 Fr Soehendra stent retriever
- Pancreatic stents in various width and sizes (with or without pigtail)
- Brush cytology catheter and biopsy forceps (to exclude malignant strictures)
- Nasopancreatic drain

obstacles can be tackled by pancreatic sphincterotomy, stricture dilation, stone removal, and stent/nasopancreatic drainage insertion.

Pancreatic sphincterotomy increases the size of the pancreatic duct orifice and removes a source of resistance to transpapillary flow of pancreatic secretions. Pancreatic sphincterotomy can be performed using a standard pull-type sphincterotome or a needle knife [43]. When using a pull-type sphincterotome, pancreatic sphincter can be cannulated either in a single step or the biliary duct is cannulated first and a biliary sphincterotomy is performed to expose the pancreaticobiliary septum. This septum covers the intramural portion of the pancreatic duct. The pancreatic orifice can be found at the 3–6 o'clock margin of the biliary sphincterotomy. After cannulation of the pancreatic duct with the pull-type sphincterotome, a pancreatic sphincterotomy is performed in the 12 o'clock position along the full length of the pancreaticobiliary septum. Needle-knife pancreatic sphincterotomy necessitates the initial placement of a pancreatic duct stent. The pancreatic duct stent serves as a guide for the direction and extent of the needle-knife incision and provides prophylaxis against the development of post-ERCP pancreatitis. The needle-knife incision should be started at the papillary orifice and extended along the intramural portion of the pancreatic duct by following the course of the stent. Occasionally, this technique cannot be used when strictures or stones in pancreatic head impede initial placement of the stent [43].

Pancreatic duct strictures or stones can impede transpapillary flow of pancreatic secretions, forcing this flow to exit the pancreatic duct through a duct leak. This ongoing extravasation perpetuates the presence of a fistula tract. Eradication of such obstructive lesions can lead to the resolution of fistulas. Endoscopic therapy of pancreatic duct strictures involves progressive dilation and stenting. Dilation balloons are available in 4-, 6-, and 8-mm diameters [43]. The diameter of the stricture and the adjacent pancreatic duct dictates the size of balloon to be used. After passing a guidewire across the stricture site, the dilation balloon is passed over the guidewire and positioned at the area of narrowing. Radiopaque markers at the distal and proximal ends of the balloon facilitate accurate positioning. The balloon is inflated to a predetermined pressure until there is obliteration of the balloon waist at the site of narrowing. Rarely, tight strictures cannot be traversed with a balloon catheter and must initially be dilated by passing graduated dilating catheters across the stricture. These catheters are passed over a guidewire and range from 3 Fr to 10 Fr in size [43]. In very tight strictures, the use of the 8.5 Fr Soehendra stent retriever may be necessary to facilitate passage of dilation balloons or stents.

Pancreatic stent placement serves several purposes. It bridges the sphincter of Oddi and eliminates any resistance to transpapillary flow caused by the sphincter. Stenting also maintains the patency of strictures that have been dilated. Ideally, the stent should bridge the site of disruption [44]. Bridging pancreatic stents helps to close the fistula rapidly by decreasing the ductal pressure and abolition of pancreatic pressure gradient, achieved by bypassing the sphincter of Oddi and stricture and by mechanically blocking the fistula lumen. The technique for placing a stent in the pancreatic duct is similar to that used for placing a biliary stent. Stents can be placed with or without pancreatic sphincterotomy. Stent diameter, which ranges from 3 Fr to 10 Fr, is determined by the diameter of the pancreatic duct. In general, the stent diameter should not exceed the upstream duct diameter. Flaps located on both ends of the stent prevent stent migration. Stent length should be chosen such that one flap is located just outside the papilla and the other flap is positioned proximal to the area of ductal disruption. In cases where attempts to advance a guidewire into the upstream portion of the duct are unsuccessful, a shorter stent can be placed that does not traverse the site of ductal disruption but only the pancreatic sphincter.

The important factors associated with successful and poor outcome of transpapillary drainage are listed in Table 33.5 [3, 29].

The current evidence suggests that transpapillary drainage alone is safe and effective for patients with communicating small pseudocysts (<6 cm) and has best results if the pancreatic duct disruption is partial and is bridged by the endoprosthesis [45, 46]. The optimal duration of stent therapy is not clear, as shorter duration is associated with a lack of resolution of pancreatic duct disruption and, thus, increased risk of recurrences, whereas longer duration of stenting is associated with stent occlusions and stent-induced ductal changes [3, 29, 47, 48]. In the majority of case series, stents were left in place for 4–6 weeks, and it has been observed that even with this small duration, noticeable ductal changes appear in patients with acute pancreatitis who otherwise have a normal pancreatic duct. Biodegradable stents or recently designed stents that cause less ductal damage may have an increasing role in these clinical situations [49, 50].

Table 33.5 Factors associated with successful and poor outcome of transpapillary drainage [3, 29]

Factors associated with successful outcome of transpapillary drainage:
1. Partially disrupted pancreatic duct
2. Disruption in the body of pancreas
3. A bridging stent
4. A longer duration of stent therapy
Factors associated with poor outcome of transpapillary drainage
1. Female gender
2. Patients with acute pancreatitis
3. Stents not bridging the disruption
4. Shorter duration of stent therapy

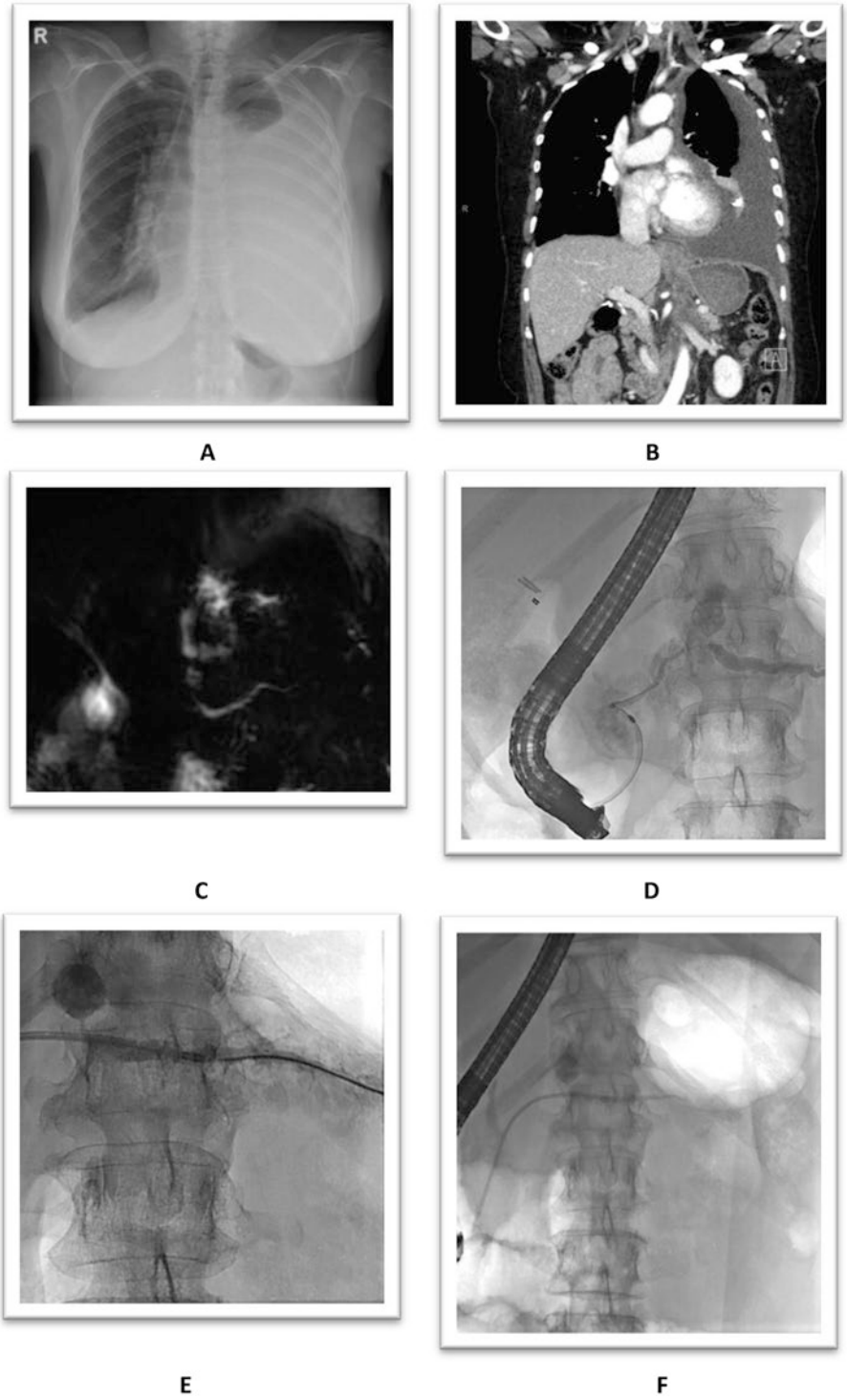

Fig. 33.1 A patient with previous history of acute severe biliary pancreatitis, presented with shortness of breath: (**a**) chest x-ray showing massive left-sided pleural effusion, (**b**) CT scan of thorax, (**c**) MRCP showing presence of peripancreatic fluid collection without any obvious leak, (**d**) ERCP showing a leakage cranial to stricture in the body of pancreas with proximal ductal dilatation, (**e**) a 6 Fr cystotome with the help of electrocautery was used to negotiate the stricture, (**f**) a 12 Fr 5 cm plastic stent placed with the proximal tip proximal of the stricture and site of leakage

Experience with transpapillary drainage for pancreatic ascites and effusions are limited to case reports and series [51–56]. Saeed and colleagues had the first report on a case of successful resolution of percutaneous pancreatic fistula after pancreatic stent placement [44]. Since then, several reports have been demonstrated the efficacy of the endoscopically placed pancreatic stents in facilitating fistula closure [57–62]. Telford and colleagues reported successful resolution of pancreatic ascites in six of seven patients (86%) after endoscopic PD stent placement with a median duration to resolution of 6 weeks [29]. Figure 33.1 below clearly demonstrates the role of pancreatic stent in the management of internal pancreatic fistula with massive left-sided pleural effusion secondary to pancreatic duct stricture and leak.

In the above-described patient, at follow-up ERCP 2 months later, no more leakage was seen, and the stricture was less pronounced. The 5 Fr stents was exchanged for a single 7 Fr stent. Brush cytology showed no signs of malignancy. Due to a poor neurological condition, the decision was made to remove the stent 2 months later via gastroscopy and only repeat exams and investigations in the case of recurrent pleural effusion. No recurrence of pleural effusion was seen during 4 years of follow-up.

Like a stent, the placement of transpapillary nasopancreatic drain can also facilitate healing of ductal disruptions by partially occluding the leaking duct or by traversing the pancreatic sphincter, thereby converting the high-pressure pancreatic duct system to a low-pressure system with preferential flow through the nasopancreatic drain. Downsides of a nasopancreatic drain are that they are uncomfortable to patients and there is a risk that the nasopancreatic drain may accidentally dislodge. A benefit of a nasopancreatic drain is the ability to easily obtain repeated pancreatograms to monitor the healing of ductal disruption without having to repeat ERCP. Moreover, a blocked nasopancreatic drain is opened up through flushing and aspiration, thus obviating the need for repeat ERCP and stent replacement as in the case of a blocked stent. Also, after demonstrating healing of duct disruption, a nasopancreatic drain can be easily removed without necessitating an endoscopy. Bhasin and colleagues [51] described the usefulness of endoscopic transpapillary nasopancreatic drain placement in ten patients with pancreatic ascites and effusion. Following placement of a nasopancreatic drain, the ascites and/or pleural effusion resolved in all patients within 4 weeks. All patients had partial pancreatic duct disruption, and the nasopancreatic drain bridged the disruption in eight of the ten (80%) patients.

Kozarek and colleague [63] investigated the role of endoscopic transpapillary pancreatic duct stent placement in nine patients with an external pancreatic fistula. The stents bridged the disruption in three patients, and fistulas successfully healed in eight (89%). Costamagna and colleagues [64] reported on 16 patients with postsurgical external pancreatic fistula using endoscopic transpapillary nasopancreatic drainage. Successful outcomes were achieved in 12 (75%) patients, and fistulas healed in 11 of these 12 patients with a mean time to closure of external pancreatic fistula of 8.8 days (range: 2–33 days. These studies suggest that external pancreatic fistula can be effectively treated by transpapillary stent and nasopancreatic drain placement, with the best results being obtained in patients with a partial pancreatic duct disruption that can be bridged. Figure 33.2 shows the management algorithm of internal pancreatic fistulas (pancreatic ascites and pleural effusion) [53].

In case of a postoperative pancreatic fistula, the timing of ERCP is controversial, but there is evidence that extending the period of conservative therapy beyond 3 weeks increases

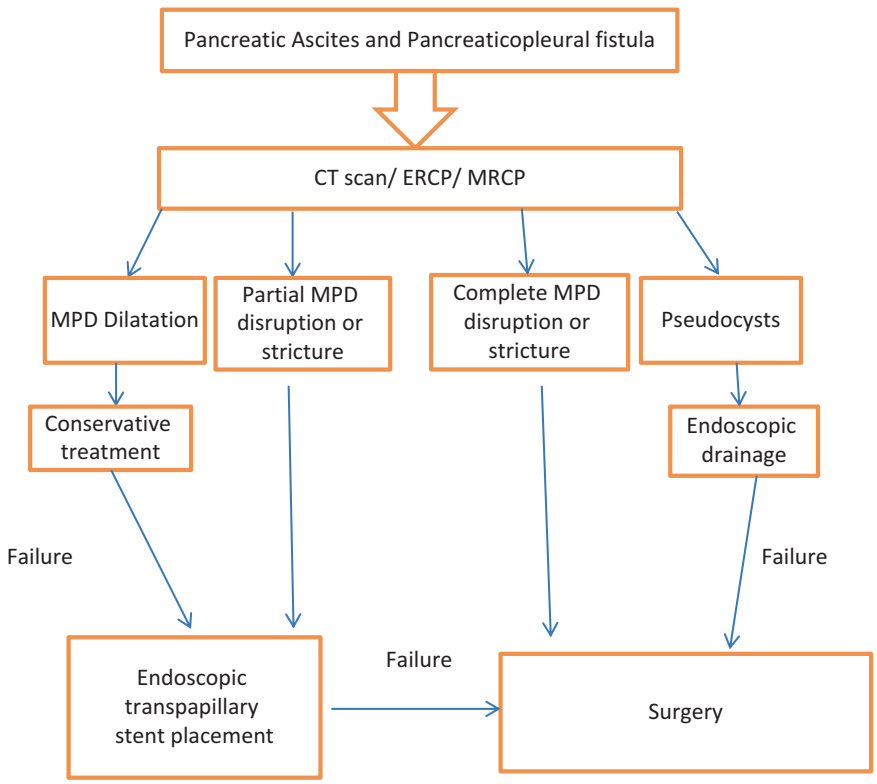

Fig. 33.2 Algorithm for the management of internal pancreatic fistula [53]

Table 33.6 Success rate of transpapillary drainage in patients with POPF

Study	Patients	Method	Success Rate
Costamagna [64]	16	Nasopancreatic drain	12/16 (75%)
Boerma [67]	15	Pancreatic duct stent	13/15 (87%)
Howard [65]	7	Pancreatic duct stent	7/7 (100%)
Kozarek [63]	9	Pancreatic duct stent	8/9 (89%)

the mortality rate [65, 66]. Most experts recommend ERCP when a fistula persists for at least 2 weeks. The first report on the use of pancreatic stents in the treatment of internal and external postoperative pancreatic fistula was published in 1993 [44]. The success rate of endoscopic pancreatic stenting in more recent series has been 75–100% with an average clinical success rate of 85% in a total of 47 patients [19]. The technique comprises of placing a 5–7 Fr diameter stent of variable length and preferably across the site of ductal disruption [63–65, 67]. Table 33.6 summarizes studies, which have used stents to treat postoperative pancreatic fistula with success rates.

A management algorithm for postoperative pancreatic fistula is shown in Fig. 33.3 [9].

Prophylactic endoscopic pancreatic stenting has been considered as a measure aimed to reduce the development of postoperative pancreatic fistula following distal pancreatectomy [68]. A pancreatic stent reduces the secretory pressure on the surgical closure [68, 69]. Prophylactic endoscopic pancreatic stenting is usually performed approximately 6 days before the distal pancreatectomy. The stent should be removed 1–2 weeks after the distal pancreatectomy to prevent any alterations to the pancreatic duct [70–72]. Abe and colleagues reported that routine preoperative pancreatic stenting was effective in preventing postoperative pancreatic fistula; of the nine patients who underwent this endoscopic procedure and subsequently underwent a distal pancreatectomy, none developed a postoperative pancreatic fistula [68]. At present, the available evidence is too scarce to routinely recommend the use of prophylactic endoscopic pancreatic stenting in this setting.

Complications

Several observational case studies have demonstrated that transpapillary drainage is safe and effective in patients with communicating pancreatic pseudocysts [3, 26, 29, 73, 74]. This route of drainage is physiologic, as it depends on the normal anatomic route of drainage of pancreatic juice and does not involve creation of an alternative non-physiological route of drainage such as in transmural drainage. The advantage of the transpapillary approach over the transmural drainage is the reduced risk of bleeding or perforation associated with transmural drainage. Transpapillary drainage however, carries risks associated with ERCP including post-ERCP pancreatitis, bleeding, and retroperitoneal perforation after sphincterotomy and also raises the risk of infection and stent-induced ductal changes mimicking chronic pancreatitis, especially in patients with acute pancreatitis or trauma and normal pancreatic duct [45, 47, 48, 75].

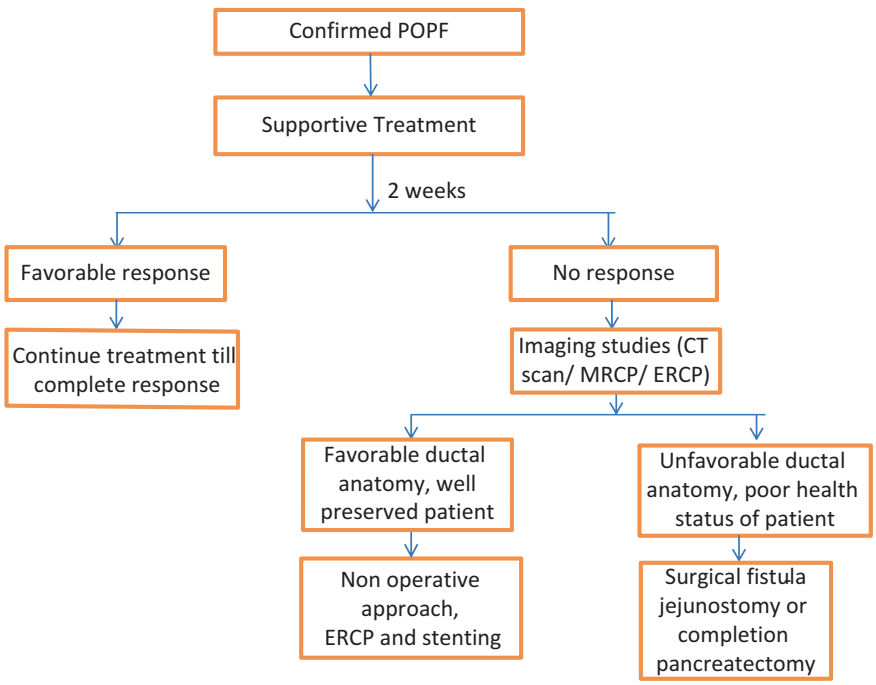

Fig. 33.3 Algorithm for the management of POPF [9]

Complications of Transpapillary Drainage
- Bleeding after sphincterotomy
- Post-ERCP pancreatitis
- Retroperitoneal perforation after sphincterotomy
- Secondary stent-induced changes and strictures in the part of the pancreatic duct that has been stented in particular at the proximal stent tip
- In- or outward plastic stent migration

Instruments and Accessories
- Ultrasound processor and linear echo endoscope
- 19 G EUS fine-needle device
- Long guidewire(s)
- Oasis 8 Fr stent pusher (to facilitate the introduction of a second guidewire)
- Cystotome (6 or 10 Fr)
- Dilation balloon (8 mm)
- Plastic double-sided pigtail pancreatic stents or fully covered metal expandable stents specifically designed for the drainage of fluid collections (lumen-opposing stents, e.g., Hot AXIOS stent, Boston, Scientific)

Transmural Drainage

Pseudocysts are the most common presentation of a pancreatic duct leak. Pseudocysts developing as a consequence of pancreatic duct disruption may be drained via the transpapillary or transmural route, or a combination of both. The transmural drainage of pseudocysts is achieved by placing one or, preferably, more stents through an endoscopically created fistulous tract between the pseudocyst and the gastroduodenal lumen. Internal drainage of pseudocyst contents leads to the collapse and resolution of the fluid-filled cavity, which eventually results in closure of the pancreatic fistula. Consideration of endoscopic pseudocyst drainage depends on several factors including the position of the fluid collection relative to the gastric or duodenal wall, the location of surrounding vascular structures, and the physical consistency of the cyst contents (solid components versus liquid only).

In general, pseudocysts that are adherent to the gastroduodenal wall, predominantly fluid filled, and without intervening blood vessels are amenable to endoscopic drainage. EUS provides detailed imaging of the pseudocyst wall and content that may not be possible to appreciate with alternative methods like transabdominal ultrasound or CT scan. Varices or retroperitoneal vessels situated between the gastroduodenal wall and the pseudocyst wall can be easily detected with EUS imaging. EUS can accurately identify intracystic solid debris and allows appropriate measures to be taken to avoid infection after drainage procedures. It also offers the advantage of excellent visualization of pancreas and peripancreatic areas and provides real-time guidance to advance the needle safely into the pseudocyst cavity without inadvertent puncture of any intervening blood vessels. Therefore, EUS-guided drainage should be considered in patients with non-bulging fluid collections, patients at high risk of bleeding complications, prior failed transmural attempt without EUS guidance, and collections inaccessible by standard endoscopic techniques (e.g., pseudocysts located at the tail end of the pancreas) [76, 77].

The Procedure

A linear echo endoscope is used, preferably with a large working channel, to search for the most optimal localization for draining the fluid collection. A puncture spot is chosen where the fluid collection is closest to the gastrointestinal wall while avoiding interposing blood vessels. The actual puncture of the fluid collection is done with either a 19 G EUS puncture needle or as a one-step procedure using the cystotome. The former approach has some advantage in certain situations in which it is more challenging to enter the collection, for example, in the case of infected necrosis with solid material and air. In such case, fluid can be aspirated to confirm the appropriate position of the needle, or contrast can be injected to delineate the fluid collection. Next, a long guidewire is introduced through the needle or the cystotome into the fluid collection letting it curl one or two times to secure its position. When a needle was used to enter the fluid cavity, it is now removed. In case the inner cystotome catheter was used to enter the fluid collection, the outer catheter is advanced into the cyst to widen the fistula, again using electrocautery. For this, the plug on the handle of the cystotome connecting it to the electrocautery device is disconnected from the inner and moved to the connector of the outer catheter. If a EUS needle was used to puncture the fluid collection, the puncture channel can be dilated immediately with an 8 mm dilation balloon that is inserted over the guidewire into the fluid collection. Many prefer to use the outer catheter of the cystotome (10 Fr) for this purpose using electrocautery because it may prove very difficult to pass the dilation catheter into the fluid collection when, for example, the wall of the fluid collection is well developed such as, for example, in the case of a pseudocyst. An added advantage of using the outer catheter of cystotome is that a second guidewire can be introduced into the fluid collection easily which greatly facilitates the placement of multiple plastic stents. Depending on indication and personal preference, either (multiple) plastic stents, usually double-pigtail 5–7 cm 8.5 Fr stents, are placed under fluoroscopic and endoscopic guidance. In case of an infected fluid collection, often also a nasocystic drain is inserted. Lately, the placement of lumen

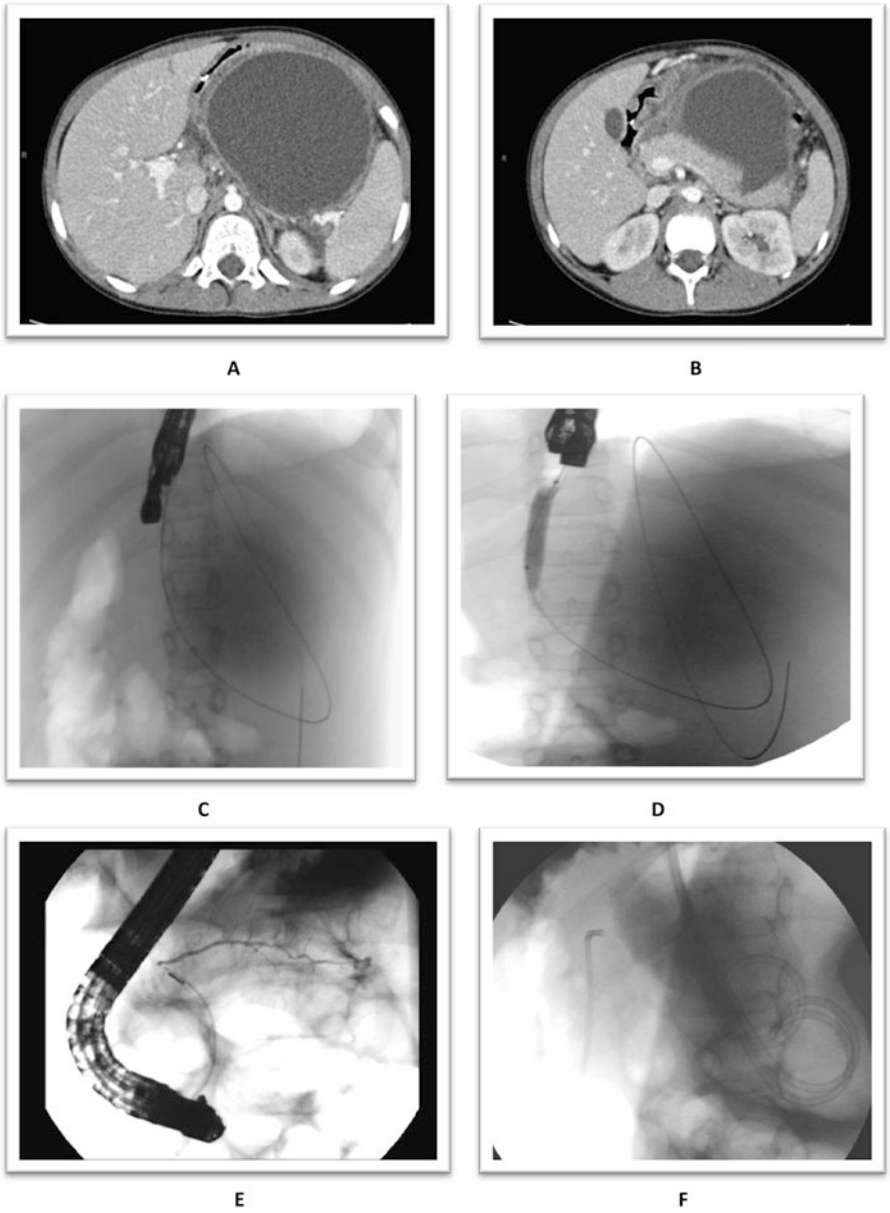

Fig. 33.4 A young female presented with a large pancreatic pseudocyst secondary to pancreatic trauma: (**a**) CT scan showing a large homogenous fluid collection; (**b**) partial rupture of pancreatic parenchyma in the tail area with communication with the cyst; (**c**, **d**) EUS-guided transmural drainage of the cyst; (**e**) ERCP, a leak in pancreatic tail clearly seen; (**f**) a 5 Fr 5 cm plastic stent placed transpapillary, three 7 Fr 7 cm double-pigtail plastic stents in pseudocyst

apposing metallic expandable stents has become more popular (see further).

Figure 33.4 demonstrates a large pancreatic pseudocyst secondary to a leak in pancreatic tail, managed with transmural and transpapillary drainage. The patient had immediate relief of pain post-procedure. After 1 week, the fluid collection had disappeared completely as seen on abdominal ultrasound. The pancreatic stent was removed after 3 weeks and the double pigtails after 3 months. During 2 years of follow-up, the patient had no complaints, and no recurrence of a fluid collection occurred.

Conventional wisdom has been to remove the transmural stents in 6–8 weeks after resolution of the pancreatic fluid collection is confirmed on a follow-up CT scan. However, this strategy is associated with recurrence in 10–30% of patients, usually within 1 year after stent removal [19, 78]. Although prolonged stenting is associated with better outcomes, most data is derived from retrospective studies, and the optimal duration of transmural stenting is still debated [78]. In patients with disconnected pancreatic duct syndrome, prolonged transmural stenting seems particularly important, because drainage of the pancreatic secretions from the excluded pancreatic segment requires a patent fistula tract. The usual approach in most of the expert centers is to keep two transmural stents in place for long periods with elective stent replacement after 3–5 years. The stents are exchanged earlier if the patient presents with a recurrent collection [79, 80]. In a randomized controlled study, Arvanitakis

and colleagues compared the clinical outcomes of leaving transmural stents in place indefinitely following drainage with removal of stents after resolution of the pancreatic fluid collection [81]. Five of 13 patients in the stent-retrieval group had recurrence of the same pancreatic fluid collection, whereas in the group with indwelling stents, there was no recurrence noted in any patients. Most patients with recurrence had pancreatic duct disruption. The investigators suggested that long-term transmural stent placement should be considered in patients with complete pancreatic duct disruption or a communicating pancreatic fluid collection in the setting of chronic pancreatitis.

Complications

Complications directly related to EUS-guided pancreatic fluid collection drainage occur in approximately 10% of patients and include bleeding at the site of cystenterostomy, pneumoperitoneum, and local or systemic infection [82]. Small-bowel obstruction secondary to migration of transmural double-pigtail stents has also been reported [83].

Complications of EUS-Guided Transluminal Drainage

- Bleeding after upsizing gastroduodenal-cystostomy fistula with cystotome of dilation balloon
- Delayed bleeding due to mechanical friction between distal stent end and cyst wall (has been reported with metal lumen-opposing stents)
- Leakage of cyst fluid into the abdominal cavity with temporary peritonitis (can usually be managed conservatively with adequate analgesic therapy for 2 or 3 days)
- Secondary infection of the drained fluid collection, in particular in the case a necrotic collection containing solid parts necessitating endoscopic debridement
- Secondary infection of the drained fluid collection due to in- or outward migration of stent(s)

Endoscopic Pancreaticoduodenostomy or Pancreaticogastrostomy

This technique is designed for reconnecting a completely disconnected pancreatic duct to the gastrointestinal tract lumen [84]. The role of endoscopic management of patients with complete pancreatic duct disruption is still debated. While the efficacy of transpapillary drainage with stenting has been shown in incomplete main pancreatic duct ruptures, its role is much more limited in the disconnected pancreatic duct syndrome. Usually the upstream duct cannot be accessed by ERCP and transpapillary interventions are futile. There is no consensus on the optimal endoscopic approach to treatment of disconnected pancreatic duct syndrome, but the procedure entails the creation of an endoscopic pancreaticoduodenostomy or pancreaticogastrostomy. Most studies are from expert centers and include a small number of patients and have limited duration of follow-up. Importantly, the procedural adverse events are not trivial.

The Procedure

Instruments and Accessories

- Ultrasound processor and linear echo endoscope
- 19 G EUS fine-needle device, preferably the EchoTip access needle (Cook Medical) to prevent shearing of the guidewire
- Long guidewire
- Cystotome (6 Fr)
- Dilation balloon (4, 6 mm)
- 5 or 7 Fr plastic stents pancreatic stents

Procedural steps for endoscopic pancreaticoduodenostomy or pancreaticogastrostomy include the following. First, the dilated upstream pancreatic duct is punctured from the stomach or duodenum under EUS guidance using a 19 G aspiration needle, preferably the EchoTip® Ultra HD Ultrasound Access Needle (Cook Medical, USA) to prevent sheering of the wire. A small amount of contrast is injected in order to opacify the pancreatic duct. Next, a 0.035-inch or smaller-caliber guidewire is advanced into the ductal system. The transmural tract is then dilated by using dilation catheters, balloons, or preferably a cautery device such as a cystotome. Once proper access has been established with a wide-enough fistulous tract connecting the stomach lumen to the dilated disconnected pancreatic ductal system, a double-pigtail stent of suitable caliber is deployed to drain the disconnected main PD into the stomach or the duodenum [15]. A limiting factor for performing this challenging procedure is the lack of dedicated accessories facilitating easy, stable, and secure access into the pancreatic duct. Moreover, the plastic endoprostheses trend to migrate relatively frequent. More data with larger cohorts of patients are needed to validate the promising preliminary findings from a few expert centers [15]. Figure 33.5 shows an algorithm for the endoscopic management of DPDS [79].

Complications

Complications related to endoscopic pancreaticoduodenostomy or pancreaticogastrostomy largely resemble those of EUS-guided transluminal drainage. Frequent stent migration is of particular note as this is often a reason for recurrent symptoms. This then necessitates a new procedure as the fistulous tract may close off relatively quickly unless there is sufficient flow of pancreatic juice to maintain open communications with the stomach lumen.

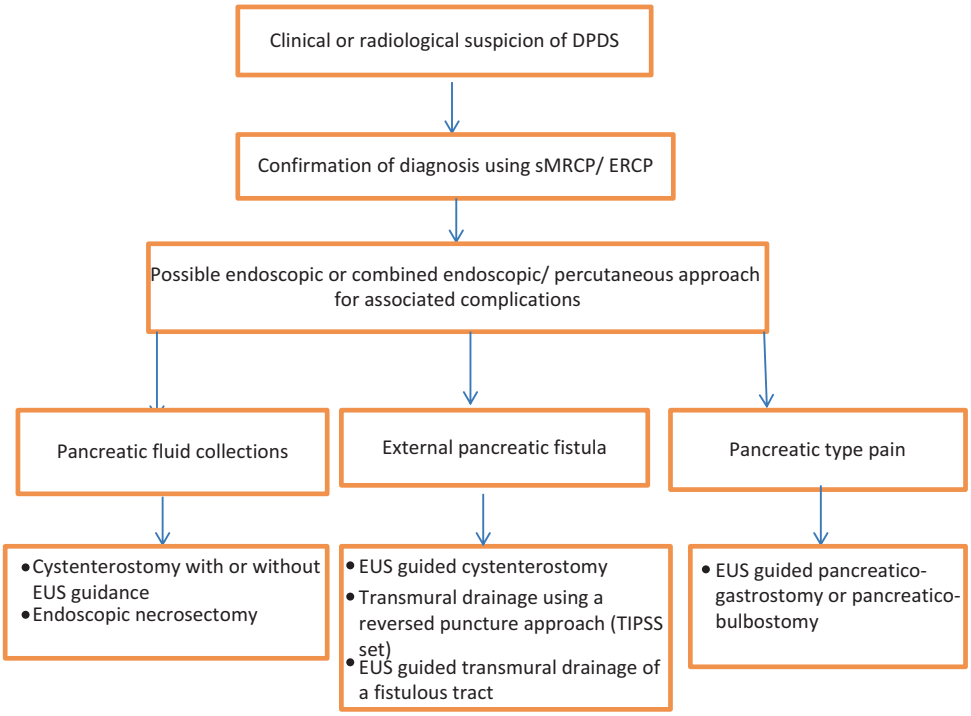

Fig. 33.5 Algorithm for endoscopic management of DPDS [80]

Complications of Endoscopic Pancreaticoduodenostomy or Pancreaticogastrostomy

- Bleeding during the creation of the gastropancreatostomy using the 6 Fr cystotome followed by balloon dilation
- Temporary leakage of cyst fluid into abdominal cavity with transient peritonitis (can usually be managed conservatively with adequate analgesic therapy for 2 or 3 days)
- Post-procedural pancreatitis
- Early partial stent migration, leakage, or occlusion leading to the formation of a peripancreatic fluid collection
- Early full stent migration leading to a clinical picture of a perforation with an acute abdomen and peritonitis necessitating endoscopic or surgical closure
- Late stent migration or occlusion with recurrence of symptoms
- Occurrence of secondary stent-induced changes and strictures in the part of the pancreatic duct that has been stented in particular at the distal stent tip and the entry point of the stent into the pancreatic duct

Novel Endoscopic Techniques and Approaches

Some patients have refractory fistulas that do not heal, even after optimal endoscopic management. Many patients with refractory pancreatic duct disruptions have large disruptions, disruptions located at the tail end of the pancreas, or complete pancreatic duct disruptions [15].

Patients with refractory fistulas may be treated with endoscopic glue or fibrin injection. Fibrin is a physiologic adhesive containing a combination of thrombin, fibrinogen, and calcium and does not promote foreign-body reaction or inflammation, but the exposure to pancreatic juice leads to rapid degradation, and, therefore, periodic injections are required to keep the fistula closed [85]. In contrast to fibrin, cyanoacrylate glue is a nonbiological compound that is more stable and is not degraded by pancreatic enzymes. Seewald and colleagues [86] assessed the safety and efficacy of endoscopic injection of N-butyl-2-cyanoacrylate into the fistulous tract combined with endoscopic transpapillary drainage in 12 patients with internal and external pancreatic fistula. The fistulas closed in eight (67%) patients, with a single injection in seven of these eight successfully treated patients. There were no complications, and none of the successfully treated patients had recurrence of the fistula. Fischer et al. [87] have shown successful closure of eight out of eight patients of postoperative pancreatic fistula with the use of fibrin glue. Advantages of N-butyl-2-cyanoacrylate are that it is possible to monitor the injection by mixing with lipiodol and it is more stable than fibrin glue. The potential complications are pancreatitis, pulmonary embolism, fever, and abscess formation. However, vascular embolization is less likely when being used for fistula closure. Another compound that has been used for closure of external pancreatic fistula is Glubran 2. This surgical glue

is composed of N-butyl-2-cyanoacrylate and methacryloxysulfolane and has lower toxicity and elicits lesser inflammatory response in comparison with N-butyl-2-cyanoacrylate glue. Mutignani and colleague [88] used endoscopic injection of Glubran 2 for closure of pancreatic fistula in four patients, three of whom had failed endoscopic drainage. The pancreatic duct disruption healed in three (75%) patients within 24 h of the procedure.

Endoscopic management of external pancreatic fistula without an associated pancreatic fluid collection can be extremely challenging. In a study by Arvanitakis et al., endoscopic or combined percutaneous and endoscopic treatment was performed in 16 patients with persistent external pancreatic fistula after previous unsuccessful conservative treatment [14]. Ten of the 16 patients had disconnected pancreatic duct syndrome. Two novel techniques were described by which a connection was established between the external pancreatic fistula tract and the duodenal or gastric cavity. The first one involved the transient filling of the fistula tract at the level of disconnection, rendering the virtual cavity transiently visible for EUS-guided drainage performed by a second operator. This resulted in a re-internalization of the fistula and closure of the external path [14, 79]. The other technique, performed under fluoroscopic control, used a TIPS (transjugular intrahepatic portosystemic shunt, TIPSS-200 set, Cook Medical) inserted over a guidewire into the external pancreatic fistula tract which was maneuvered to puncture the gastrointestinal tract under endoscopic and fluoroscopic control, thus creating a transmural drainage path. Both endoscopic and percutaneous procedures were performed by experienced endoscopists [14]. Irani et al. used this combined procedure using a TIPSS-200 set in ten patients with disconnected pancreatic duct syndrome and external pancreatic fistula; 70% of patients were successfully treated after a mean follow-up of 25 months [89].

There is also a report of sealing of an external pancreatic fistula by endoscopic deployment of coils (intravascular uses coil made of fibered platinum, 0.035 inches [0.89 mm] diameter, straight length 50 mm, coiled size 5 × 4 mm; Target Vascular, Boston Scientific, Ireland), but the safety and efficacy of this approach needs to be studied further [90]. An alternative approach to treating refractory pancreatic duct disruptions is placement of covered metallic stents. There have been case reports describing successful healing of refractory pancreatic fistulas by endoscopic insertion of self-expanding metallic stents [52, 91, 92]. Although placement of self-expandable metal stent appears to be an attractive option, stent-induced ductal and parenchymal changes limit its routine use; therefore, it should be used a last resort in difficult cases with no other feasible treatment options [93].

Conclusion

The current scientific evidence regarding clinical management of pancreatic duct leaks and disruptions is limited to case reports, case series, and expert opinion. Because of their complexity, pancreatic duct leak patients are best managed by a multidisciplinary hepato-pancreato-biliary team comprised of therapeutic endoscopists, interventional radiologists, and surgeons. The management of pancreatic fistula depends on the presence of symptoms, the characteristics and location of the ductal disruption, and the presence of associated complications such as infection. Distinct clinical manifestations must be recognized such as pancreatic ascites and pancreaticopleural fistula, disconnected pancreatic duct syndrome, and postoperative pancreatic fistula because all have their specifics and peculiarities with regard to medical, endoscopic, and surgical treatment. Careful attention to an optimal maintenance of hydration, nutrition, and electrolyte balance through the management of the disease process is of prime importance for a successful clinical outcome.

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