Published online: 2019-09-26

Review Article

Endoscopic treatment for complex biliary and pancreatic duct injuries

Simon Bouchard, Jacques Devière

Department of Gastroenterology, Hepato-pancreatology and Digestive Oncology, Université Libre de Bruxelles, Erasme Hospital, Brussels, Belgium

Abstract Severe injuries of biliary or pancreatic ducts are associated with significant morbidity and mortality. Severe bile duct injuries such as major biliary leaks, complete transection, or complete occlusion of bile ducts can be grouped under the term complex bile duct injuries (CBDI). In the spectrum of pancreatic duct injuries, disconnected pancreatic duct syndrome (DPDS) represents the most severe form and most often occurs after a severe episode of acute pancreatitis. Treatment of these complex injuries is quite challenging and for many years surgical management has been considered the treatment of choice. However, in the past few years, some studies have reported the successful management of CBDI or DPDS using endoscopic procedures alone or in combination with a percutaneous approach. In this review, we detail the endoscopic or combined endoscopic/percutaneous treatment possibilities for CBDI and DPDS.

Key words Bile duct injuries, disconnected pancreatic duct syndrome, pancreatic duct rupture

Introduction

Iatrogenic bile duct injuries (BDI) are associated with increased morbidity, mortality, and financial burden. Most BDI is secondary to surgery, with laparoscopic cholecystectomy being the most frequently associated surgery.[1] In patients with minor BDI, such as peripheral bile duct leakages or non-severe bile duct strictures, endoscopic treatment has been shown to be effective.[2] In these cases, endoscopic treatment normally consists of a biliary sphincterotomy alone or in combination with nasobiliary drainage or temporary biliary stenting. A small proportion of patients will present with more severe iatrogenic BDI, such as major leaks, complete transection, or complete occlusion of the bile duct. These injuries are referred to as complex bile duct injuries (CBDI).[3] Traditionally, reconstructive surgery is necessary to recreate biliary continuity in these patients, but in the past few years, a limited number of patients have been successfully treated using endoscopy combined with a percutaneous approach.[3-8]

Access this article online	
Website: www.jdeonline.in	Quick Response Code
DOI: 10.4103/0976-5042.141926	

Pancreatic duct ruptures are most often secondary to an acute episode of pancreatitis or trauma.[9] These injuries are associated with the development of local complications such as pancreatic fluid collections (PFCs) and internal or external fistulas. Pancreatic duct ruptures can be either partial or complete. In the latter case, the patient is said to have disconnected pancreatic duct syndrome (DPDS). Endoscopic treatment has proven effective in patients with partial pancreatic duct rupture,[10] and there is increasing evidence that endoscopic treatment is a valuable alternative to surgery in selected patients with DPDS.[9,11-17]

This review article will focus on the endoscopic treatment possibilities for the two most severe biliary and pancreatic ductal injuries: CBDI and DPDS.

Complex Bile Duct Injuries

Bile duct injuries may be secondary to trauma but most often occurs after biliary surgeries, such as laparoscopic or open cholecystectomy, partial liver resection, or liver

Address for correspondence:
Dr. Simon Bouchard, Department of Gastroenterology, Hepato-pancreatology and Digestive Oncology, Université Libre de Bruxelles, Erasme Hospital, Brussels, Belgium. E-mail: simon.bouchard@umontreal.ca

transplantation.[1,6,7] A review of 1.6 million cholecystectomies in the 1990's reported an incidence of BDI of 0.5% after laparoscopic cholecystectomy.[1] The risk of biliary injury is higher in patients undergoing laparoscopic cholecystectomy compared to open cholecystectomy. Possible risk factors for iatrogenic BDI include older age and male sex.[18] BDI can be either secondary to direct biliary injury or thermal injury or due to misplacement of surgical clips.[19] When biliary injuries are recognized during surgery, which is the case in only 25-32.4% of patients, immediate repair is preferable if an experienced hepatobiliary surgeon is available.[20] If not, after adequate drainage, patients should be transferred to an experienced multidisciplinary team.

Initial symptoms associated with BDI can be non-specific (vomiting, nausea, abdominal pain) and vary depending on the level and the severity of the injury. Clinical presentation of patients with CBDI may include obstructive jaundice, cholangitis, abnormal liver function tests, visualization of bile in surgical drains, or the development of bile collection (biloma) or of bile peritonitis.[4,20] In patients with complete obstruction of the bile duct, bilirubin will most often be elevated, as opposed to patients with severe bile leaks who can present with a normal bilirubin level.

Computed tomography (CT) scan or abdominal ultrasound examination can reveal either the presence of fluid collection in patients with bile leak or dilate bile ducts in cases of biliary obstruction. If CBDI is suspected clinically, confirmation of the diagnosis is done either by endoscopic retrograde cholangio-pancreatography (ERCP) [Figure 1], percutaneous transhepatic cholangiography (PTC) or by magnetic resonance cholangio-pancreatography (MRCP), which has become the key exam for therapeutic planning. These methods of investigation can precisely indicate the level, type, and the extent of BDI.

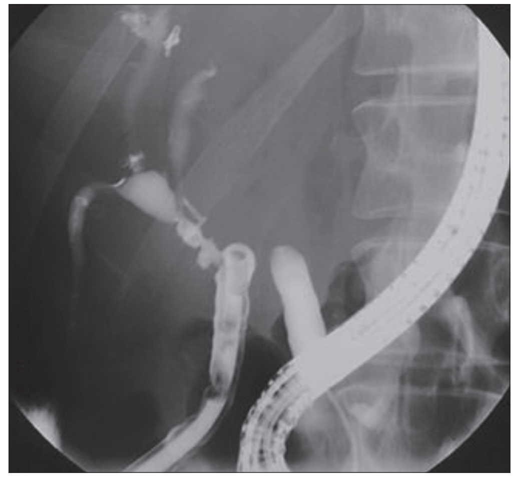

Figure 1: Post-operative complex bile duct injury. At endoscopic retrograde cholangio-pancreatography, a complete biliary stop is visualized at the level of the common bile duct. Injection of contrast medium through a percutaneous drain demonstrates exclusion of biliary segments and a biliary leak

Table 1: Amsterdam Academic Medical Center's classification

Type	Criteria
A	Cystic duct leaks or leakage from aberrant or peripheral hepatic radicles
B	Major bile duct leaks with or without concomitant biliary strictures
C	Bile duct strictures without bile leakage
D	Complete transection of the duct with or without excision of some portion of the biliary tree

Classification of iatrogenic bile duct injuries

Different classifications for BDI have been published, although no single classification has been universally accepted. The Bismuth classification has traditionally been used to assist surgeons in choosing the most appropriate method for biliary repair with open surgery. This classification is based on identification of the level of the biliary tract where healthy biliary mucosa is available for a surgical anastomosis.[21] However, the Bismuth classification does not cover the whole spectrum of possible iatrogenic BDI. More detailed classification systems have since been developed such as Strasberg's classification, Amsterdam Academic Medical Center's classification [Table 1],[23] Neuhaus' classification, Csendes' classification, Stewart-Way's classification, and the CUHK classification.[22-26]

Surgical and Percutaneous Treatment of Complex Bile Duct Injuries

Traditionally, CBDI have been treated by surgical reconstruction of biliary continuity. Depending on the level and extension of the BDI, a choledocho-choledochostomy bile duct reconstruction or a Roux-en-Y bilioenteric anastomosis is usually performed. In a few patients, especially if an associated vascular injury is present, a partial liver resection may be necessary.[27] In rare cases of end-stage liver disease secondary to CBDI, liver transplantation is sometimes required.[28]

Many factors can influence the success of surgical reconstruction for CBDI including the surgeon's experience, the level and type of biliary injury, and the presence of local inflammation during surgery.[3] After surgery, as many as 25% of patients develop symptomatic anastomotic complications that require further treatment (endoscopic, percutaneous, surgical). Surgical treatment for CBDI is also associated with significant morbidity and mortality.[29] This high rate of immediate and late complications has justified the development of alternative treatments, mainly based on biliary decompression by the endoscopic route for leaks and endoscopic stenting for postoperative biliary stenosis. The role of endoscopy in specialized referral centers for these indications is now widely accepted as well as the need for attempting or considering this less invasive treatment before any decision to redo surgery. However, the use of a transpapillary endoscopic approach remains limited in major BDI where the continuity of anatomy has been disrupted.

In selected patients, percutaneous treatment of iatrogenic BDI is an additional management option and has been associated with good long-term results.[30] In patients without biliary-enteric continuity, such as patients with complete transection of the bile duct, definitive treatment using only a percutaneous approach is not possible. However, PTC can be useful to decompress the dilated proximal ducts initially in cases of biliary obstruction or to limit bile flow into a biloma in patients with bile leaks.

Endoscopic Management of Complex Bile Duct Injuries

Combined endoscopic and percutaneous procedures for treatment of complex bile duct injuries

Non-surgical repair of CBDI, including complete transection of the bile duct, using a rendezvous procedure (combining an endoscopic and percutaneous approach) has been reported in a limited number of case-reports or case-series.[3-8]

In 2000, we reported a combined percutaneous-endoscopic approach using a TIPSS-200 set (Cook) to successfully treat a patient who presented with excision of the common hepatic duct after a cholecystectomy. Initial ERCP revealed complete obstruction at the level of excision. Both the endoscopic and percutaneous procedures were performed under general anesthesia by experienced therapeutic endoscopists. The TIPSS-200 is normally used for the placement of transjugular intrahepatic portosystemic shunts (TIPS). After a percutaneous cholangiogram had been done using a 6F needle and catheter, a 0.035-inch Amplatz Super Stiff guidewire (Cook) was advanced to the level of biliary transection. The 6F catheter was exchanged using the guidewire for a 5F catheter mounted in a 10F curved sheath (TIPSS-200 set, Cook). The guidewire was then exchanged for the needle of the TIPSS-200 set. The metallic sheath has an angulated tip that allows for optimal orientation before doing a puncture. With the distal biliary stump distended endoscopically by a second endoscopist, the TIPSS-200 set was maneuvered until clear contact with the biliary stump was visualized fluoroscopically. The biliary stump was then punctured to recreate biliary continuity. An 8.5F Ring catheter was left in place for biliary drainage, and within a few days, the drainage catheter was exchanged for plastic stents by a standard rendezvous procedure. This successful technique was not associated with any short- or long-term complications.[8]

Our group has since successfully used this technique in four patients with symptomatic biliary exclusion secondary to biliary surgery or trauma (unpublished data). The main theoretical risk of this technique is hemorrhage from the accidental puncture of blood vessels in proximity to the common bile duct (CBD). This risk can be limited by identifying clear contact of the needle with the biliary stump before doing the puncture and by aiming at the right side of the biliary stump since the vessels follow the left wall of the CBD. However, this complication has not occurred in our limited experience.

In a recent study by Donatelli *et al.*, 21 patients with CBDI (including complete transection or stenosis) after hepatobiliary surgery were treated using a different type of combined endoscopic and percutaneous approach. In this study, cholangiograms were performed by experienced therapeutic endoscopists, and the percutaneous approach was performed by interventional radiologists. After performing a biliary sphincterotomy, a 7F catheter mounted on a guidewire was advanced against the distal stump of the CBD. Using a catheter, the distal stump was punctured, allowing the guidewire to advance into the subhepatic space. Using a percutaneous approach, the excluded intra-hepatic biliary ducts were punctured. A guidewire was then advanced directly into the subhepatic space in patients with biliary leaks, or after performing a puncture of the proximal biliary stump in cases of complete biliary stop. Under fluoroscopic guidance, a Dormia basket was advanced either percutaneously or endoscopically into the subhepatic space to catch the opposite guidewire. This allowed the recreation of biliary continuity between the excluded proximal ducts and the distal bile duct. With the Dormia basket and the opposite guidewire pulled out, the remaining guidewire was used to dilate the tract to a maximum diameter of 8 mm and one or more biliary stents were left in place using a classic rendezvous technique. Biliary stents were exchanged routinely every 3 months for calibration of biliary stenosis.[3]

In this study, patients were stented for a mean duration of 14.5 months. The procedure was possible in 20. Five patients with isolated right and left biliary ducts required separate rendezvous procedures. An average of seven combined procedures was necessary per patient. At long-term follow-up, 14/20 patients had complete resolution of their biliary complication. Twenty percent of patients are still treated with biliary stents. This treatment approach was not associated with serious complications.[3]

In a study by Fiocca *et al.*, 22 patients with complete transection of the bile duct secondary to cholecystectomy were also treated with a combined endoscopic and percutaneous approach. While a guidewire was advanced endoscopically through the papilla into the subhepatic space, a percutaneous approach in the right intra-hepatic biliary ducts allowed the advancement of a snare loop into the subhepatic space. The guidewire was caught by the snare loop and pulled through the percutaneous access. After dilation of the tract, a drainage catheter was left in place for 1 or 2 weeks. With a rendezvous procedure, the drainage catheter was eventually exchanged for two 10F biliary stents with the proximal ends in the right hepatic ducts. The left hepatic ducts were also punctured percutaneously during a separate procedure with two additional 10F biliary plastic stents also left in place. The plastic biliary stents were left in place for a total of 12 months.[4]

This combined treatment approach was possible in all patients. At long-term follow-up, 18 patients had a complete resolution of the BDI, two patients still had plastic stents and three patients presented with biliary stones after removing biliary stents. This treatment approach was also considered safe, although one patient required angioembolization due to the development of hemobilia after a left PTC.[4]

Other case-reports have also reported successful experiences in the restoration of biliary continuity in patients with CBDI using a combined approach, either using a biopsy forceps advanced through the papilla to grasp a guidewire in the subhepatic space,[5] or a snare loop advanced percutaneously into a biloma to catch a naso-biliary catheter already located in the biloma.[6] Finally, Nasr *et al*. have reported the successful treatment of two patients with CBDI after segmental hepatectomy using a rendezvous procedure.[7]

Endoscopic treatment of complex bile duct injuries using endoscopic ultrasound

Internal drainage of excluded biliary ducts can also be performed using endoscopic ultrasound (EUS). This approach does not allow repermeabilization of normal biliary continuity but rather the creation of an alternative internal bilio-digestive drainage path. EUS-guided choledochoduodenostomy (CD) is a possible drainage method in patients with loss of continuity at the level of the distal CBD.[31] For patients with excluded left intrahepatic ducts, EUS-guided hepaticogastrostomy could also be considered.[32] In patients with isolated right intrahepatic duct obstruction, biliary drainage by EUS-guided hepaticoduodenostomy has also been shown to be feasible.[33] However, these techniques have not specifically been evaluated in patients with iatrogenic CBDI and may be more difficult in the absence of BD dilatation. In patients having had surgical repair with further stenosis of an hepaticojejunal anastomosis, the EUS-guided approach might, however, have an advantage over PTC by allowing calibration of the stricture and stent exchanges without the need for maintaining a percutaneous access.

In patients with bilomas secondary to CBDI, successful EUS-guided transmural drainage of the bile collection has been described in a small series of five patients, including one patient with a traumatic transection of the bile duct.[34]

In a recent case-report presented in abstract form, Perez-Miranda *et al*. have reported the use of magnets to recreate biliary continuity in a patient with a disconnected choledochocholedochostomy after liver transplantation. A EUS-guided CD with placement of a self-expandable metallic stent (SEMS) had been performed 3 weeks earlier to provide internal biliary drainage. A proximal magnet was then advanced through the CD tract, and a distal magnet was advanced through a transpapillary SEMS, which resulted in the recreation of biliary continuity after 10 days. This is the only reported case of restoration of biliary drainage using magnets after the creation of a EUS-guided biliary drainage tract.[35]

Disconnected Pancreatic Duct Syndrome

Clinical and diagnostic aspects

Rupture of the main pancreatic duct (MPD) is most often secondary to severe episodes of acute pancreatitis but may also result from chronic pancreatitis, trauma, or malignancy, or be secondary to pancreatic or non-pancreatic surgery.[9,36,37]

Main pancreatic duct rupture can be either partial or complete, in which case the term DPDS is used. In DPDS, a segment of the pancreas upstream from the area of complete rupture is isolated from the distal pancreas. The disconnected pancreatic gland upstream from the site of rupture continues to secrete pancreatic secretions that cannot reach the duodenum through the distal MPD. This can result in the formation of PFCs and internal or external pancreatic fistulas. Persistent PFCs or fistulas despite medical treatment should raise the suspicion of underlying DPDS.[17] Rupture occurs in the area of the neck of the pancreas in 58% of the cases, this region being potentially more susceptible to ischemia during severe episodes of acute pancreatitis.[11]

Contrast-enhanced CT is often used as the initial imaging modality for evaluation of severe acute pancreatitis and its complications.[38] Findings that evoke a diagnosis of DPDS are the presence of fluid collection along the expected course of the MPD associated with visualization of enhancing upstream pancreatic parenchyma.[25] If a diagnosis of DPDS is suspected on the basis of CT imaging findings, evaluation of pancreatic ductal anatomy by ERCP or secretin-enhanced MRCP is mandatory to confirm the diagnosis.

If ERCP is performed, a cutoff of the MPD is observed with possible contrast medium extravasation at the site of ductal disconnection.[25] ERCP does not allow opacification of the MPD upstream from the site of disconnection. MPD obstruction secondary to obstructive calcifications or strictures may falsely suggest a diagnosis of DPDS. ERCP has the disadvantage of being invasive with a risk of complications such as post-ERCP pancreatitis and infection of pancreatic collections. For these reasons, it has been largely replaced by magnetic resonance imaging for diagnosis.

Secretin-stimulated MRCP (sMRCP) is now preferred as the initial diagnostic imaging modality and for therapeutic planning in patients with suspected DPDS. Intravenous administration of secretin allows accurate outlining of the pancreatic ductal anatomy. sMRCP is a safe and non-invasive test that allows visualization of pancreatic parenchyma and can identify pancreatic duct disruption, fistulas, and associated fluid collections.[39-42]

Surgical Treatment of Disconnected Pancreatic Duct Syndrome

A surgical approach has traditionally been considered as the preferred approach for patients with DPDS, at least in the last century. The surgical procedure normally consists of either a resection of the isolated distal pancreatic segment or a reconnection of the isolated pancreatic duct or pancreatic fistula to a Roux-en-Y small intestinal loop.[43] Different factors such as the size of the isolated pancreatic segment and underlying pancreatic function can influence the choice of the type of surgical procedure.[44] However, surgical treatment of DPDS is often difficult due to the presence of peripancreatic inflammation, adhesions, or collateral circulation secondary to segmental portal hypertension. Surgical treatment is associated with high morbidity and mortality rates.[45]

Endoscopic Treatment of Disconnected Pancreatic Duct Syndrome

Certain clinical consequences of DPDS including PFCs, external fistulas, and recurrent pancreatic type pain due to the ductal hypertension are amenable to different endoscopic treatments, which are detailed in Figure 2.

Pancreatic fluid collections

In patients with PFCs secondary to DPDS, the main goal of therapy is to drain the fluid collection that communicates with the proximal pancreatic duct. Endoscopic drainage of the PFC is done by performing a cystenterostomy, which creates a path of low resistance between the PFC and the GI lumen, and ensures drainage of the pancreatic secretions produced from the isolated pancreatic gland. The site of cystenterostomy is usually chosen by identifying, with the use of predrainage abdominal imaging, an area where the PFC is in closest proximity to the adjacent digestive lumen.

The role of ERCP in the endoscopic management of patients with PFCs and DPDS is questionable. While the efficacy of transpapillary drainage with stenting has been shown in partial MPD ruptures,[10] its role is more limited in DPDS.[16] Transpapillary stent placement to bridge the rupture site is most often not possible since there is complete disruption of the MPD. In patients with an MPD stricture or stone distal to the disconnection site, transpapillary drainage with sphincterotomy and stenting may be useful to reduce ductal pressure in the distal segment of the pancreas. If transpapillary drainage is performed in patients with DPDS and PFCs, combination with other endoscopic techniques is necessary.[13] Moreover, if the proximal part of the pancreas communicates with a collection, it is probable that transmural drainage would still be preferred to transpapillary drainage because in the former, persistence of drainage is independent of stent patency.

Transmural drainage of persistent pancreatic fluid collections

Cystenterostomy without the use of EUS is possible if the PFC produces a bulge in the gastric or duodenal wall.[46] EUS-guided transmural drainage allows treatment of fluid collections that are smaller or that are not in intimate contact with the gastric or duodenal wall and improves the safety of the cystenterostomy by helping avoid blood vessels that can be located between the PFC and the GI lumen. Currently, transmural PFC drainages should always be EUS guided both for safety and efficacy.[15]

Depending on the location of the PFC, a cystenterostomy can either be performed through the gastric wall or the duodenal wall. In rare cases, it can also be done from the fourth portion of the duodenum. It is believed that drainage through the duodenum, possibly due to its thin wall, might create a long-term patent fistula, even after the removal or migration of transmural stents.[47,48]

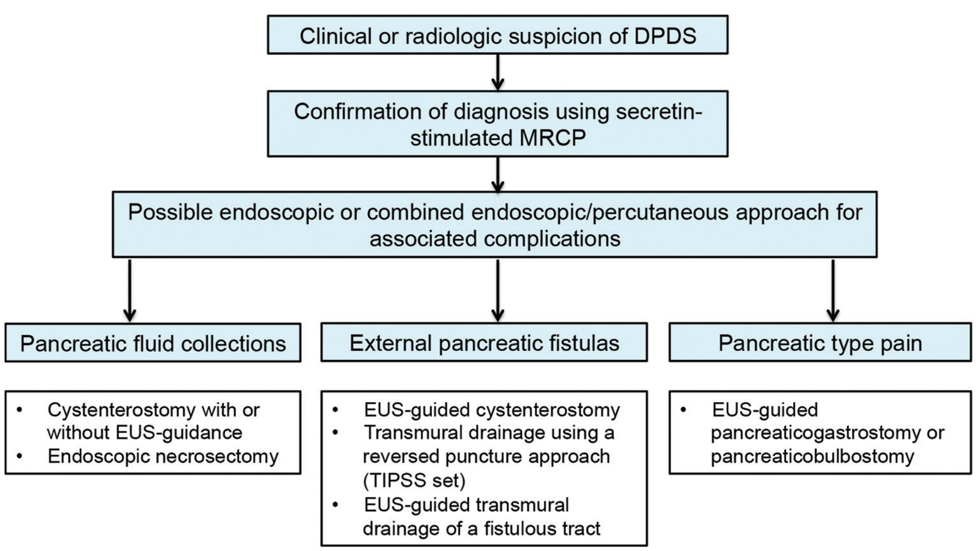

Figure 2: Proposed algorithm for endoscopic management of disconnected pancreatic duct syndrome

The technique of cystenterostomy can vary slightly from one center to another. Here, we describe our usual approach [Figure 3]. Once the fluid collection has been visualized, either endoscopically or with the use of EUS, it is punctured with an electrosurgical needle followed by the advancement of a 0.035-in guidewire into the collection. The puncture tract is then enlarged using a cystenterostome (Cystotome, Cook endoscopy). A second guidewire can be advanced into the cystenterostome sleeve if insertion of more than one transmural stent or a nasocystic catheter is planned. The cystenterostome is then removed and with the guidewires still in place, transmural stents and/or a nasocystic catheter are advanced into the collection. If more than one stent is inserted, the tract is also dilated using a dilation balloon.[46]

In 1995, we reported our center's experience with the endoscopic management of 12 patients with DPDS and cyst formation. In nine patients, DPDS was secondary to an episode of acute pancreatitis. All patients but one had an endoscopic sphincterotomy, seven patients had transpapillary drainage, and 9 out of 12 patients were treated by cystenterostomy with one or multiple transmural stents left in place for different durations (range of 1 day to 1 year). Cyst resolution and clinical recovery was observed in 11 patients and there were no recurrent fluid collections at long-term follow-up.[13]

In recent years, different groups have also reported good long-term results after transmural drainage of PFCs in patients with DPDS. In one study of 22 patients successfully treated with permanent transmural stenting, there was no recurrence of PFCs at long-term follow-up (median of 1026 days).[14]

In a recent retrospective study by Rana *et al.*, 30 patients with DPDS underwent transmural drainage of walled-off pancreatic necrosis. All patients had long-term placement of two or three double pigtail transmural stents. After a mean follow-up of 20 months, one patient developed a recurrent symptomatic collection. Stent migration occurred in 16.6% of patients, including in the patient with the recurrent collection.[49] In a study by Shrode *et al.*, 33 patients with complete pancreatic duct disruption were treated by permanent transmural drainage. The resolution rate at 12 months was 73%. This rate was not improved by the addition of transpapillary stenting.[16]

Pelaez-Luna *et al*. have reported long-term outcomes in 26 patients treated endoscopically (22 transmural drainages) for PFCs associated with DPDS. Short-term resolution or improvement of the collection was observed in 61% of patients, seven patients went to surgery after failure of endoscopic therapy. Development of chronic pancreatitis and diabetes mellitus was also observed in 26% and 16%, respectively, of patients at follow-up.[11]

Duration of transmural stenting

When transmural stents are removed endoscopically, the risk of PFC recurrence increases. In one study including 11 patients with DPDS and PFCs successfully treated with transmural drainage, the stents were removed after resolution of the

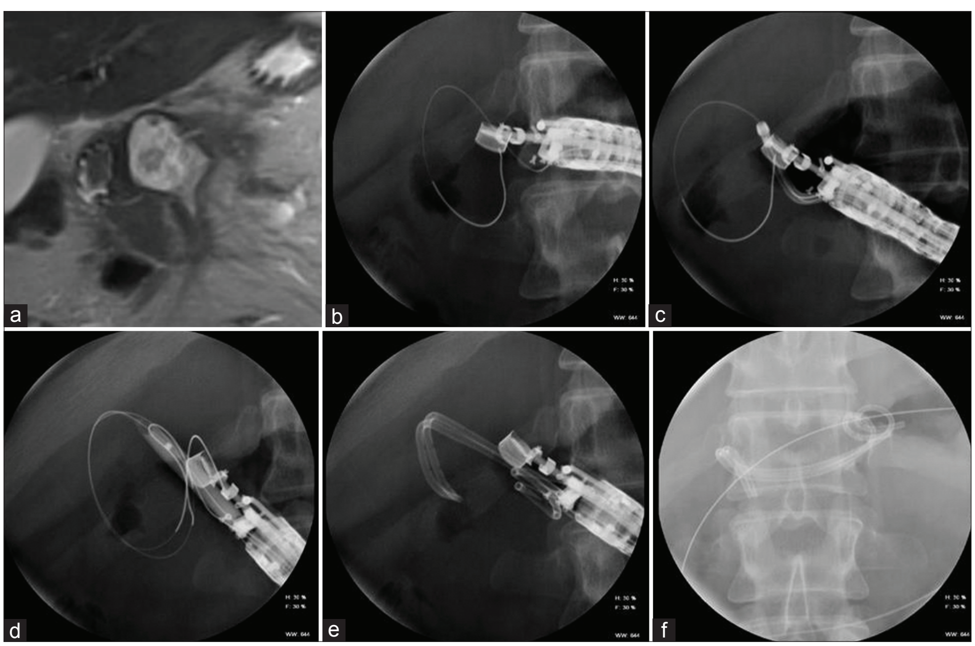

Figure 3: (a) A secretin-stimulated magnetic resonance cholangio-pancreatography showing a pancreatic fluid collection associated with a complete pancreatic duct disruption. (b) Using endoscopic ultrasound guidance, the pancreatic fluid collection (PFC) is punctured with an electrosurgical needle and a 0.035-inch guidewire is advanced into the collection. (c) The puncture tract is then enlarged using a cystenterostome. (d) After a second 0.035-inch guidewire has been advanced, the puncture tract is dilated using an 8 mm balloon dilator. (e) Using the guidewires, two double pigtail stents are advanced into the PFC to keep the fistula tract open. (f) After removal of the endoscope, the two double pigtail stents are seen side-by-side

collection. This strategy was associated with a recurrence of PFC in 45% of patients.[15]

Although prolonged stenting is associated with better outcomes,[50] most data is derived from retrospective studies and the optimal duration of transmural stenting is still debated. A randomized controlled trial was performed in our center to evaluate if patients that previously had drainage of PFCs were at higher risk of recurrence if the transmural stents had been retrieved. Twenty-eight patients were either assigned to a group where stents were retrieved after resolution of the fluid collection or to a group where the stents were left in place. Higher recurrence rates were observed in patients that had their stents retrieved (5 patients vs. 0 patients, $P = 0.013$). Of the five patients with recurrence, four had a DPDS.[51]

In patients with DPDS, 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 our center 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.[12]

Although many fear that long-term transmural stents may lead to complications such as recurrence of PFC due to stent occlusion or infection of fluid collections, this has not been demonstrated in recent studies with long follow-up.[14,49,51] Large cohort studies with longer follow-up periods may be necessary to clarify these concerns, although in our experience, we have never observed a recurrence due to stent occlusion.

Spontaneous migration of transmural stents occurs in 13.6-33% of patients.[14,16,49,51] The exact rate of stent migration is often unknown since most studies have not performed follow-up abdominal imaging in all patients. In a study by Arvanitakis *et al.*, patients were prospectively followed with abdominal imaging and a third of the patients had spontaneous migration of transmural stents.[51] The risk of migration was not influenced by the number or the diameter of the stents. Interestingly, migration of transmural stents was not associated with PFC recurrence. It is hypothesized that with PFC resolution, the walls of the collection slowly join together which can lead to gradual stent migration.

Safety issues

Complications directly related to EUS-guided PFC drainage can occur in approximately 10% of patients and include bleeding at the site of cystenterostomy, pneumoperitoneum, and systemic infection.[46] Small-bowel obstruction secondary to migration of transmural double pigtail stents has also been reported in two patients, with one patient requiring surgery.[14]

Persistent pancreatic fluid collections despite transmural drainage

In certain patients with DPDS, unresolved PFCs might be due to the presence of infected organized pancreatic necrosis. A more aggressive approach with endoscopic debridement of the organized necrosis is required in these patients. After performing a balloon dilation of the cystenterostomy tract, the endoscope is advanced into the collection and endoscopic debridement of the necrotic material is performed under direct endoscopic control. Repeated endoscopic necrosectomy sessions are most often required. Transmural stents are also left in place to maintain a patent fistula.[12,52,53]

External percutaneous fistulas secondary to disconnected pancreatic duct syndrome

Disconnected pancreatic duct syndrome can be associated with external percutaneous fistulas (EPFs), also known as pancreaticocutaneous fistulas. EPFs can occur after pancreatic surgery such as surgical necrosectomy,[54] after percutaneous drainage of PFCs,[55] or following abdominal surgery in an area adjacent to the pancreas.[56] In patients undergoing surgical necrosectomy for infected necrosis, it is preferable to avoid leaving a percutaneous drain in place because of the subsequent risk of persistent EPFs. To limit the risk of developing EPFs, endoscopic drainage is considered the preferred option for post-operative fluid collections.[12,53]

Conservative management for EPFs consists of fasting, nutritional support, and administration of somatostatin or its analogues to inhibit pancreatic secretions. This medical approach is associated with a reduction in fistula output, but closure rates of EPFs vary from 44% to 85%.[57] Thus, efficacy is limited and additional treatment methods are often necessary.

In patients with persistent EPF despite conservative treatment, surgery is an option but is associated with elevated morbidity and mortality rates.[58] Surgical treatment consists of initial drainage of PFCs, followed by resection of the isolated pancreatic gland or by the creation of a low pressure path between the isolated pancreatic duct and the GI lumen.[59]

Endoscopic (and combined percutaneous) approach to external percutaneous fistulas

The goal of endoscopic or combined percutaneous and endoscopic treatment is to transform an external fistula into an internal fistula by creating a path of lower resistance for pancreatic fluid drainage.

Transpapillary drainage with stenting for pancreaticocutaneous fistulas is often useful in the setting of a partial MPD rupture,[60-64] but limited in a setting of DPDS.

In patients with an EPF associated with a PFC upstream from the site of MPD disconnection, drainage of the PFC by EUS-guided cystenterostomy, as previously described, is the treatment of choice. Long-term placement of one or more double pigtail transmural stents will keep the cystenterostomy tract open. This will create a long-term internal fistula that drains pancreatic fluid upstream from the site of MPD disconnection and allows EPF closure. In six patients treated by this method, the EPF closure rate was 100%.[65]

Novel drainage technique for external percutaneous fistulas without associated fluid collections

Endoscopic management of EPF without an associated PFC can be quite challenging. In a study by Arvanitakis *et al*.,[65] endoscopic or combined percutaneous and endoscopic treatment was performed in 16 patients with persistent EPF after previous unsuccessful conservative treatment. Ten of the 16 patients had DPDS. The goal of these new drainage techniques was to create a pathway between the EPF tract and the duodenal or gastric cavity.

Mainly two techniques were described. 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 reinternalization of the fistula and closure of the external path [Figure 4].

The other technique, still performed under fluoroscopic control, used a TIPSS set (TIPSS-200 set, Cook) inserted over a guidewire into the EPF tract and maneuvered to puncture the GI tract under endoscopic and fluoroscopic control, thus creating a transmural drainage path. Both endoscopic and percutaneous procedures were performed by experienced endoscopists.[65]

Irani *et al*. also used this combined procedure using a TIPSS-200 set in 10 patients with DPDS and EPF, 70% of patients were successfully treated after a mean follow-up of 25 months.[66]

Endoscopic ultrasound-guided treatment of external percutaneous fistulas in the absence of fluid collections

In patients with an EPF and the absence of a PFC, EUS-guided transmural drainage of the fistulous tract has also been described. This method can be an alternative to the previously described outside-in puncture technique, especially in patients with varices in the puncture tract or fistula tract at a distance from the upper GI tract. As previously described, if a percutaneous catheter or a surgical drain is already placed in the fistulous tract with its distal end close to the GI lumen, injection of water or contrast under EUS guidance can allow visualization of a fluid collection.[65] EUS-guided transmural drainage of this transient collection that communicates with the EPF is then possible.[65] EUS-guided transmural puncture of the fistula without previous injection of fluid to create a collection has also been described. The EUS-guided transmural puncture is performed by aiming the percutaneous catheter located in the fistula tract adjacent to the GI lumen[66] or by aiming at a dilated pancreatic duct.[64,67] Drainage is maintained by placement of one or more transmural stents.

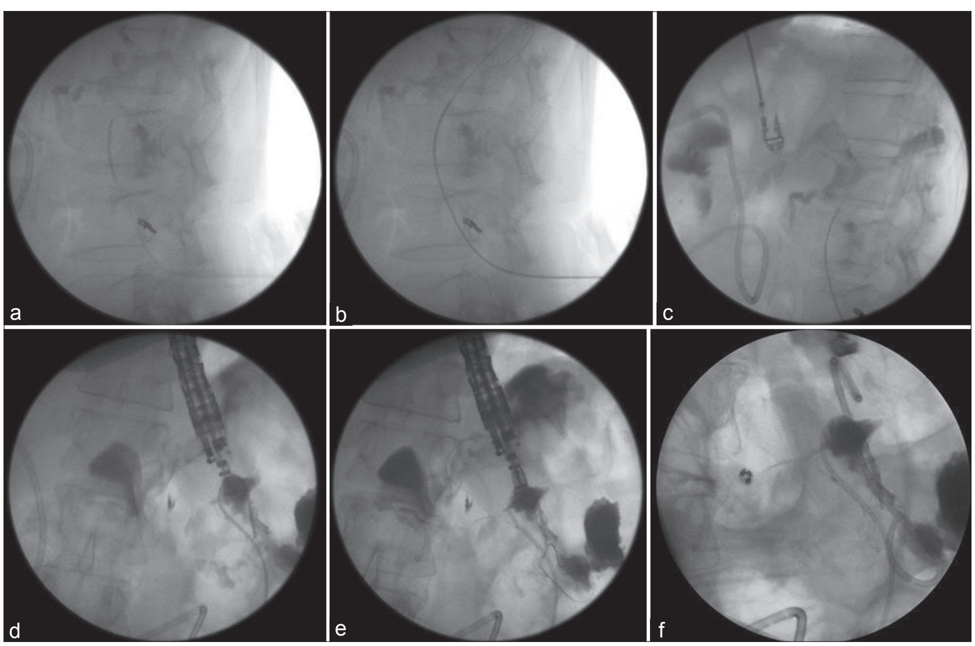

Figure 4: Internalization of an external pancreatic fistula (EPF) in the absence of a fluid collection. (a) Under fluoroscopic guidance, a small 5F catheter is advanced in the fistula tract. (b and c) A guidewire is advanced through the catheter and maneuvered further in the fistula tract until it reaches the virtual cavity adjacent to the gastrointestinal lumen. (d) The catheter is advanced in the virtual cavity. The cavity is then transiently filled by injecting contrast through the catheter, which allows visualization of the cavity by endoscopic ultrasound (EUS). (e and f) An EUS-guided puncture of the transiently filled cavity is performed. After advancing a 0.035-inch guidewire in the cavity, the tract is enlarged using a cystenterostome, and a transmural double pig tail stent is left in place

Internal fistulas

The most clinically problematic internal fistulas are those communicating with the pleura. These pancreaticopleural fistulas often require pleural drainage. Surgery is considered in patients who do not improve with conservative treatment.[68] In selected cases, internal fistulas could possibly be approached endoscopically as EPFs.

Pain secondary to ductal obstruction

Even in the absence of fluid collections or fistulas, some patients with DPDS have abdominal pain or recurrent episodes of pancreatitis secondary to the obstruction of the MPD. In selected patients with a dilated pancreatic duct upstream from the area rupture, endoscopic drainage by EUS-guided pancreaticogastrostomy or pancreaticobulbostomy might be a valuable alternative to surgery.[12] This allows drainage of the pancreatic secretions from the isolated pancreatic gland and lowers ductal pressure which is thought to contribute to pancreatic pain. Transmural plastic stents are left in place to keep the fistula tract open. A few studies including small numbers of patients with DPDS have shown that this technique is relatively safe and can be effective in relieving abdominal pain.[69,70] However, this is a challenging endoscopic procedure that is associated with an 8% rate of technical failure, even in expert hands.[69]

Conclusion

Patients with CBDI or DPDS have severe duct injuries that most often require referral to a specialized center for optimal management. For both types of injuries, surgical reconstruction was traditionally considered the optimal approach to treat these patients. However, as illustrated in this review, a growing number of studies in the recent medical literature suggest that endoscopic treatment alone or in combination with a percutaneous approach can be effective and safe in selected patients. Due to the complexity of these procedures and because of the potential risk of complications, these advanced techniques must be performed by experienced therapeutic endoscopists or interventional radiologists in the proper setting. Additional studies are still necessary to further clarify the exact role of endoscopy in the management of CBDI and DPDS.

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How to cite this article: Bouchard S, Devie`re J. Endoscopic treatment for complex biliary and pancreatic duct injuries. J Dig Endosc 2014;5:2-12.

Source of Support: Nil, **Conflict of Interest:** None declared.