5 The Endoscopic Management of Biliary and Pancreatic Injury

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Pancreaticobiliary injuries are frequently encountered by interventional endoscopists and are a common cause of morbidity and even mortality. They are seen postoperatively after cholecystectomy, liver transplantation, pancreatectomy, and splenectomy. They may also result from blunt and penetrating trauma, and may even be related to gastrointestinal interventions like ERCP or liver biopsy. Early recognition and a multidisciplinary approach to treatment are crucial to limit systemic effects of the injury and prevent associated morbidity. Principles of therapy are often similar whether the injury is iatrogenic or traumatic. This chapter focuses on the endoscopic management of these biliary and pancreatic injuries rather than stone disease or neoplastic processes.

Bile Leak

Bile leaks (BL) can occur after any procedure in which the hepatobiliary system is manipulated, and may also result from blunt or penetrating trauma. The typical signs and symptoms include abdominal pain and the accumulation of bile rich fluid in the peritoneal cavity or external drains. It is important to note that liver function tests may be normal with BL because bile flow is typically not obstructed. If a leak is identified during surgery, surgical repair is warranted at that time. Bile leaks identified postoperatively are optimally managed with percutaneous drainage and/or ERCP. Repeat surgical intervention is generally deferred unless mandated by a deteriorating patient condition or presence of a completely disconnected duct. This section addresses the utility of ERCP in diagnosing and managing BL.

Historically, the definition of a bile leak has lacked standardization. Past definitions have been based on the volume (20–50 mL) of fluid accumulating postoperatively, the bilirubin concentration (5–20 mg/dL) of the fluid, and timing of the leak. More recently, the International Study Group of Liver Surgery proposed a consensus definition [1] in which bile leakage was defined as:

- Increased bilirubin concentration in the abdominal drain or in the intra-abdominal fluid (define as three times greater than the serum bilirubin concentration).
- Leak occurrence on or after postoperative day 3.
- Leak requiring radiologic intervention (i.e., interventional drainage) or re-laparotomy resulting from bile peritonitis.

Because up to 24 % of patients have some degree of fluid collection in the gallbladder fossa after resection, these criteria help to delineate a clinically significant bile leak from clinically inconsequential fluid accumulation [2]. A grading system for bile leaks has also been proposed to determine the severity of leaks:

- *Bile leakage grade A*: BL characterized by clinical stability in the patient and adequate leakage control by an intra-abdominal drain. Leakage should decrease and resolve by 7 days.
- *Bile leakage grade B*: Clinical deterioration of the patient is seen due to the leak (sepsis, abscess formation, pain,

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etc.). Grade A leaks that persist for greater than 7 days are included as well. Intra-abdominal drainage alone is inadequate, and these require additional radiologic or endoscopic intervention. Surgery may be avoidable.

- *Bile leakage grade C*: Require repeat surgical intervention to control the complication. The postoperative course of the patients is prolonged, and secondary postoperative complications (e.g., abdominal wound infection) may result.

Technique

The goal of endoscopic management of BL is to reduce the transpapillary pressure gradient between the bile duct and duodenum via sphincterotomy and/or endoprosthesis placement. This results in a preferential flow of bile into the duodenum rather than through the leak site. The placement of a stent can also bridge the lesion, further protecting the leak site.

It is worthwhile to understand certain endoscopic principles when managing patients with BL. Guidewire cannulation is preferential, with recognition that cannulation may be more difficult in patients with BL due to the upstream decompression of the ducts that results from the leak. After cannulation, a complete cholangiogram should be performed to identify the leak and determine its size. A *large bile leak* is one in which the leak is identified prior to filling the intrahepatic branches (Fig. 5.1a, b). A *small bile leak*, conversely, is a BL that is seen after filling of the intrahepatic biliary tree (Fig. 5.2a, b). The cholangiogram can also be utilized to identify retained intraductal stones or areas of stenosis that may be contributing to the BL. These are then treated as indicated.

While sphincterotomy alone may be considered for small leaks, data suggests a greater likelihood of leak resolution with the use of stents, with or without sphincterotomy, than biliary sphincterotomy alone [3]. Sphincterotomy can be deferred in patients with coagulopathies or other adverse risk for bleeding. After sphincterotomy, a stent is deployed into the biliary tree (Fig. 5.3a, b). In general, 10 F plastic biliary stents are preferred over 7 or 8.5 F stents as they have a more durable patency profile and improve downstream flow. While bridging the lesion is not essential, it should be considered if technically feasible. For hepatic, intrahepatic, and subvesical bile duct (duct of Luschka) leaks, placement of the proximal aspect of the stent into the affected system involved should be attempted as possible.

Ninety-five percent of BL resolve within 2 weeks utilizing stent therapy as described [4–6]. Therefore, stents should be maintained for at least 14 days and up to 6 weeks, at which time they should be removed. Many endoscopists perform cholangiography at the time of stent removal to document leak resolution, although this is not mandated if the BL is felt to have resolved at the time of stent removal (Fig. 5.3c). If contrast dye is injected, it is important not to overfill the biliary tree, as too much pressure can reopen the leak. Occlusion cholangiography is thus discouraged. For persistent leaks, a stent may need to be replaced and exchanged until resolution is confirmed. For persistent large bile leaks, a covered self-expanding metal stent (SEMS) may be considered to provide a greater decrease in pressure gradient across the ampulla and better facilitate "bridging" over the injury. While upfront costs may be more, early use of covered SEMS for BL may decrease the need for reintervention and thus may make this a cost-effective approach.

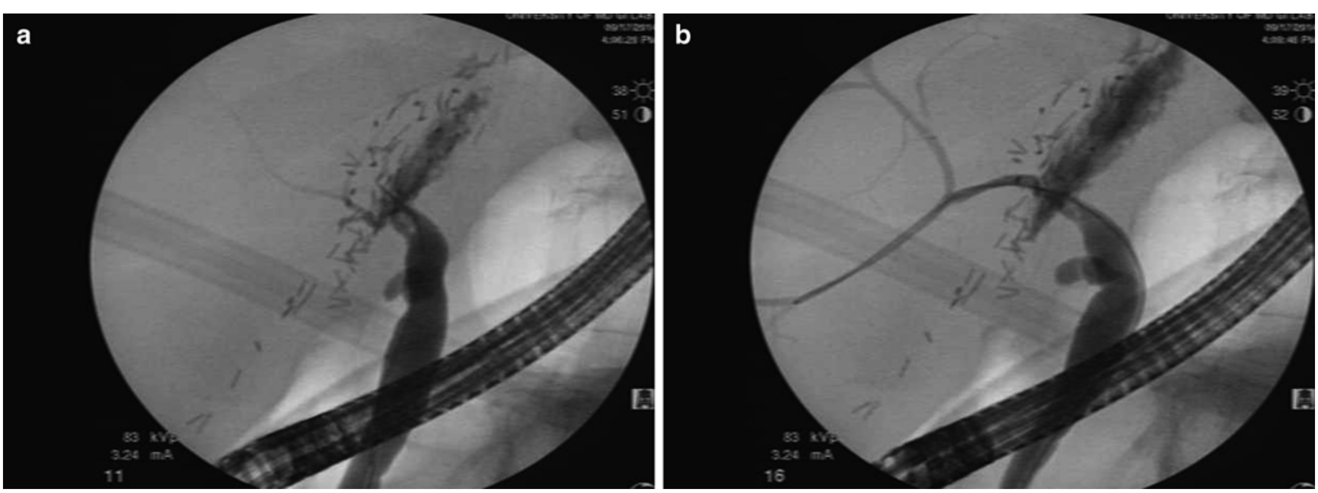

Fig. 5.1 Large anastomotic bile leak after living donor liver transplantation (**a**). The leak is seen prior to complete filling of the intrahepatic ducts (**b**)

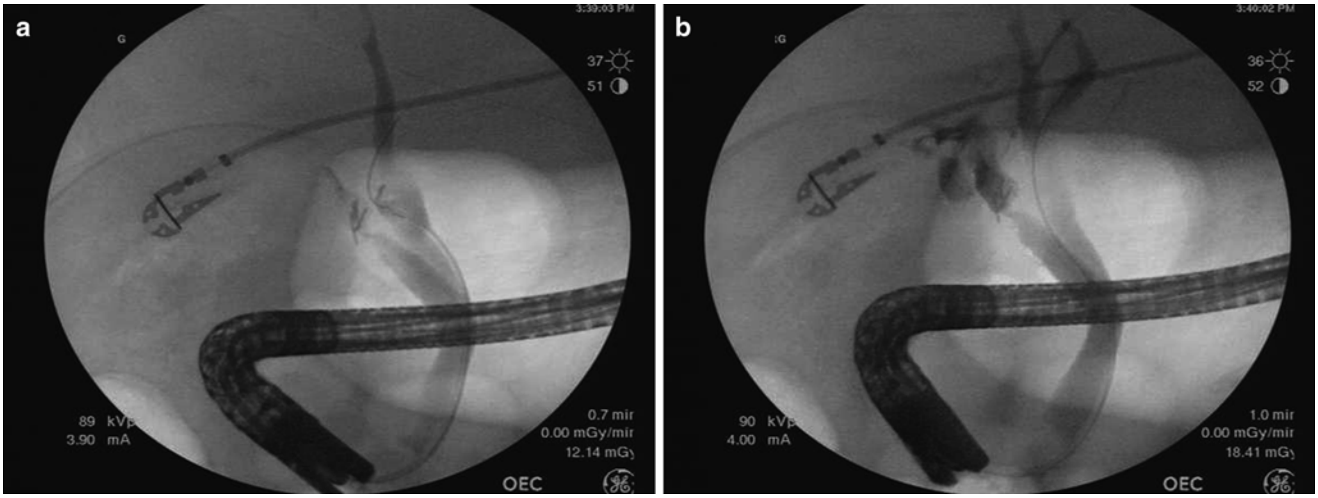

Fig. 5.2 No bile leak is seen initially in a patient after cholecystectomy (**a**). A small bile leak at the cystic duct remnant is seen only after filling of the intrahepatic ducts (**b**)

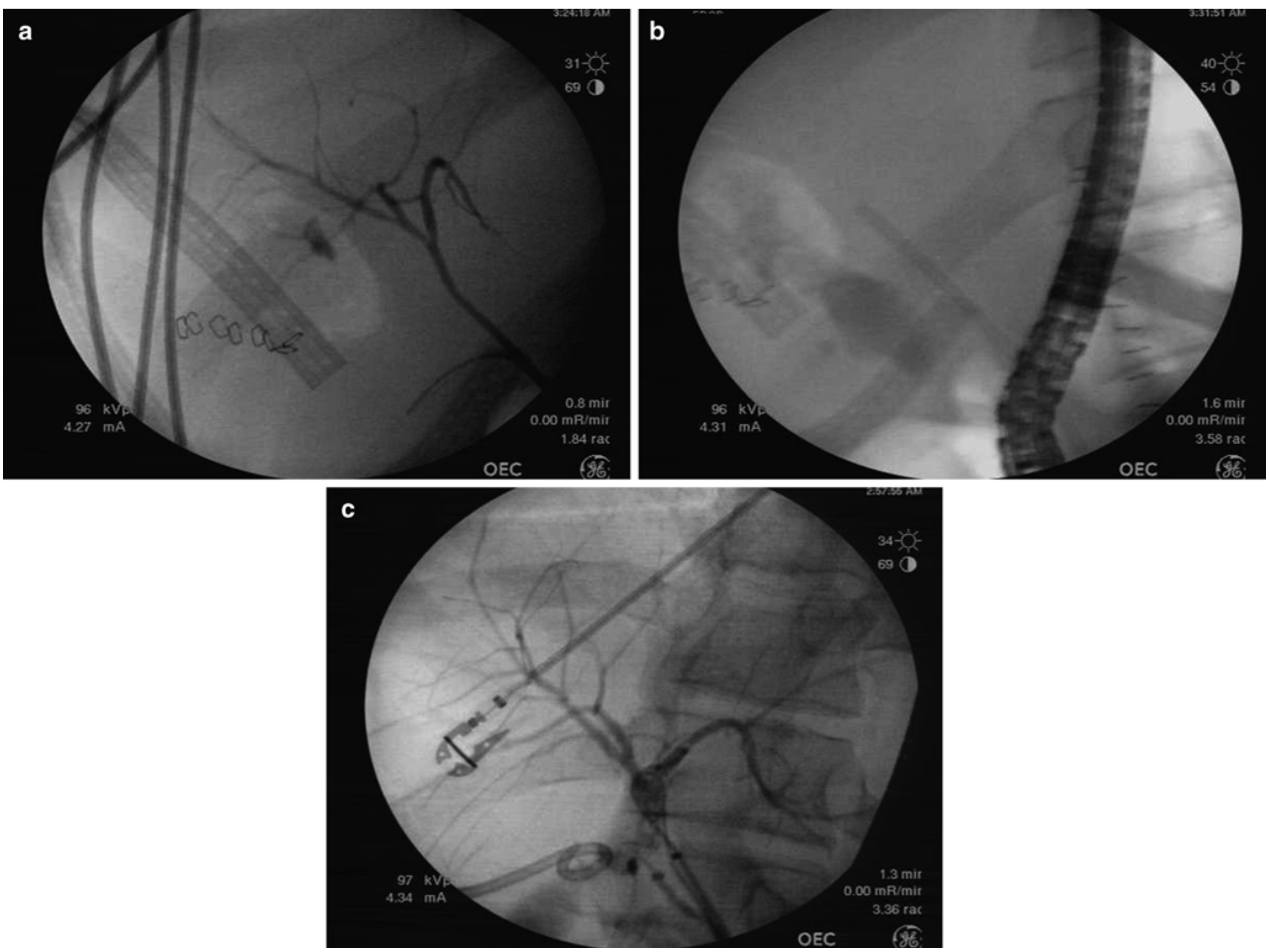

Fig. 5.3 A bile leak is seen at the resected gallbladder bed (**a**). A plastic biliary stent is places after sphincterotomy (**b**). The leak is resolved after 4 weeks of stent dwell time (**c**)

Bile Leak After Cholecystectomy

Significant post-cholecystectomy (post-CCY) bile leaks occur in 0.2–2 % of cases, with rates being higher when laparoscopic approaches are utilized over open cholecystectomy [6, 7]. ERCP serves as a good diagnostic value for evaluating BL after CCY, with sensitivities ranging between 83 and 98 % and technical success rates higher than 95 % [5, 6, 8]. After cholecystectomy, leaks typically occur at the cystic duct or the subvesicular bile ducts (ducts of Luschka), with these sites representing 54–78 % and 13–24 % of post-cholecystectomy leaks, respectively [3, 6, 8] (Fig. 5.4a). In cases of complicated cholecystitis, limited visibility may result in incomplete gallbladder resection and subsequent large bile leaks (Fig. 5.4b). Leaks can also be seen from the common bile duct, common hepatic duct, or branching hepatic ducts, but these are less common after cholecystectomy than they are after liver resection. Complete disruption of the main bile duct, including inadvertent bile duct ligation, is rare, but can be identified readily with ERCP [9]. In up to a third of cases, retained bile duct stones of strictures may be contributing to post-cholecystectomy leaks and are identified on initial cholangiogram.

ERCP with sphincterotomy and stent placement have historically shown leak resolution rates of 70–100 % for post-cholecystectomy BL [4–6] (Fig. 5.5a, b). Sandha et al. showed a resolution rate of 91 % and 100 % amongst 207 patients with high-grade and low-grade bile leaks, respectively, while Kaffes and colleagues showed a resolution rate of 92 % in 100 patients with leaks after gallbladder resection [3, 6]. In another study of 127 patients, a single ERCP led to a 91 % resolution that improved to 95 % when additional endoscopic interventions were

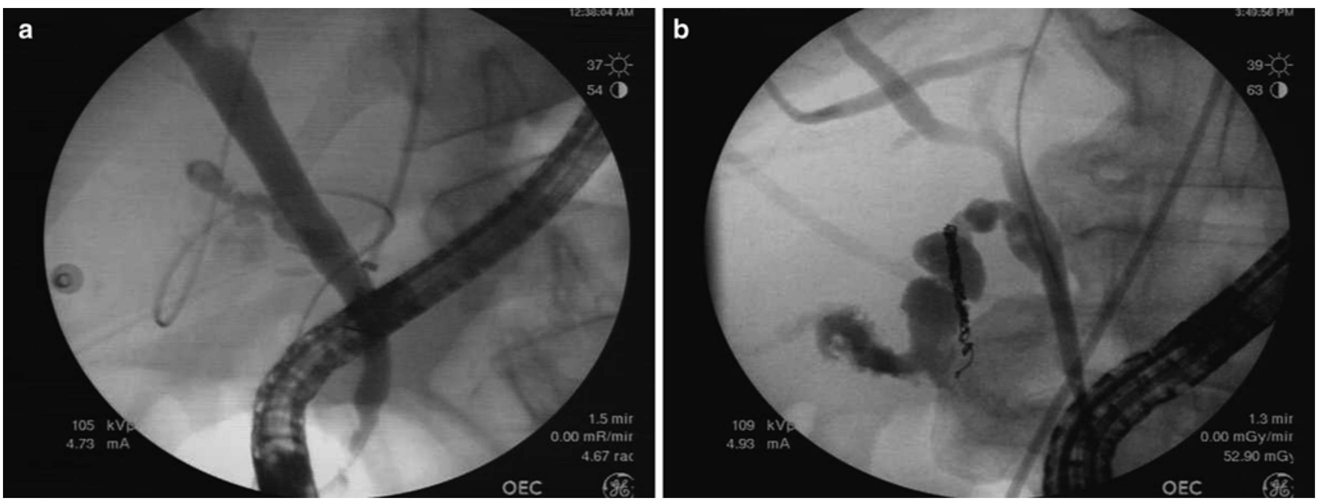

Fig. 5.4 Cystic duct stump leak (**a**). Leak from retained gallbladder remnant (**b**)

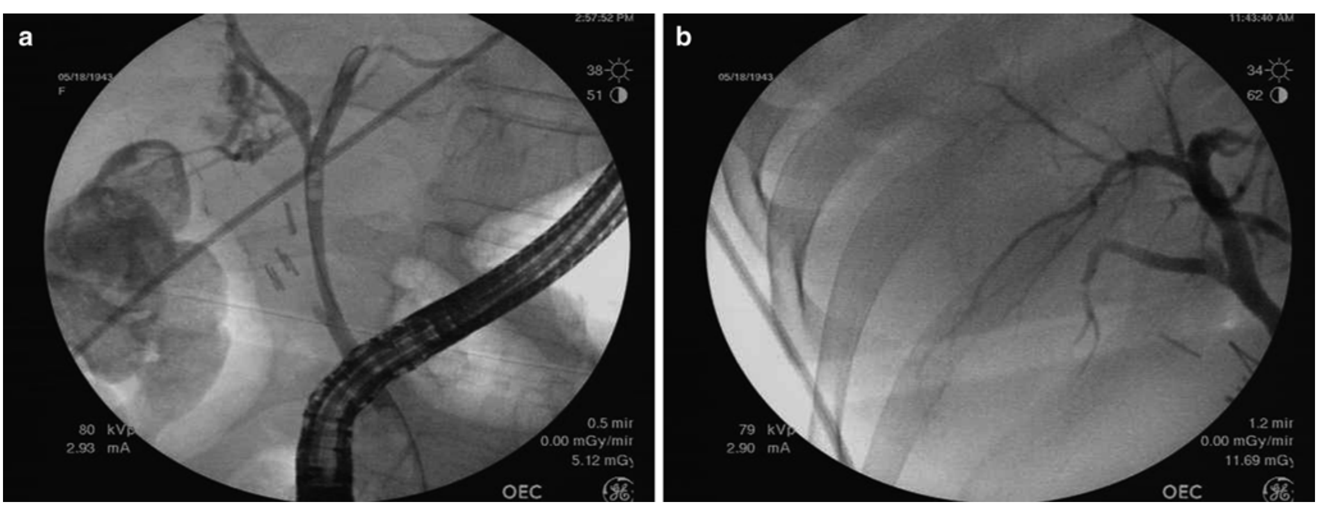

Fig. 5.5 A leak is seen within a segmental branch of the right hepatic ductal system (**a**). The leak is resolved after endoscopic sphincterotomy and a period of transpapillary stenting (**b**)

permitted [8]. While two studies suggest that biliary sphincterotomy alone may be adequate for low-grade leaks (leak resolution rates of 87–91 %), several other studies have shown sphincterotomy alone is significantly associated with treatment failure when compared to biliary stent placement alone or endoscopic sphincterotomy and stent placement as combined therapy [3, 8]. Stent placement is thus generally recommended for managing leaks after cholecystectomy where technically feasible.

Resolution of leak after cholecystectomy is typically reported within 7–14 days after stent placement [3, 10]. Median time to stent removal has been variable, but stents are generally removed at 4–6 weeks. A longer duration of stent placement is required if BL are associated with strictures. Performance of ERCP for post-CCY bile leaks has a complication rate if 1–4 %, a rate similar to other non-high risk ERCPS [6].

Bile Leak After Liver Resection

Liver resection (LR) is a well-established means of treating both benign and malignant liver diseases. While technical expertise has been improving as utilization increases, LR continues to be complicated by bile leak in approximately 15 % of cases [11–13]. Given the morbidity and mortality associated with such leaks, early recognition and management becomes imperative.

Postoperative BL following LR can be categorized as central bile leaks from the hilum or common hepatic duct, or peripheral bile leaks from the resection surface (Fig. 5.6a). Risk factors for bile leak after LR are generally related to technical aspects of the surgery, including longer operative time, left hemi-hepatectomy, and segment IV resection [12–14]. Central bile leaks after LR tend to manifest as larger volumes of bile spillage into the peritoneum, and have been associated with a worse prognosis than peripheral leaks. Options for managing post-LR leaks include surgical repair, percutaneous drainage, and endoscopic therapy. While timing is not well-defined, current literature suggests that it may be safe to wait up to 2 weeks after surgery for spontaneous resolution as long as percutaneous drainage is established and output is closely monitored [15]. Careful attention should be made toward the patient's PO intake to prevent dehydration from fluid losses in the bile in the case of large leaks, with IV hydration when needed.

All patients with LR leaks should have an endoprosthesis placed via ERCP. As a general rule, spanning the area of leak is preferential for central leaks. For peripheral leaks after LR bridging the leak is often difficult. Generally 7 or 10 F stents are utilized, with 10 F being preferred. After 2–6 weeks, endoscopic cholangiography is repeated and the stents replaced if the leak persists (Fig. 5.6b).

Success rates of ERCP for post-LR bile leaks have been reported to be between 59 and 100 % [15]. In one study, use of a bile duct endoprosthesis was associated with a better response rate than sphincterotomy alone. Central leaks have been shown to be less responsive than peripheral leaks in this context, but success rates of 59–72 % have been reported for central BL after LR [15]. The number of interventions are variable, but one study showed more ERCPs were required for leaks after hepatobiliary surgery than for those following cholecystectomy (1.4 versus 1.1) [8].

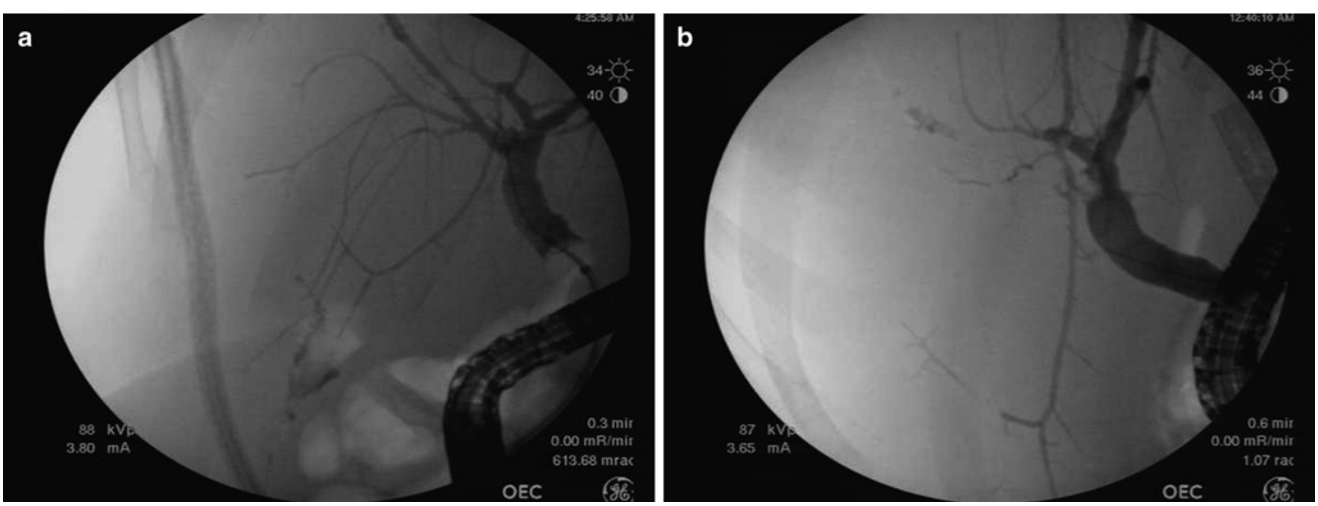

Fig. 5.6 A bile leak is seen at a subvesical duct along the resected gallbladder bed (**a**). This leak is resolved after a month of transpapillary biliary stent placement (**b**)

Traumatic Bile Leak

A prolonged bile leak as a consequence of hepatic trauma has been reported to occur in as few as 0.5 % and as many as 20 % of patients after their presenting injury [16]. When they do occur, patients with post-traumatic BL require more therapeutic procedures, have longer hospital courses, and require higher hospital charges than those without BL [17–19]. Given that up to 97 % of traumatic bile duct injuries occur in the context of trauma to other intra-abdominal organs or vascular structures, most are managed surgically if identified during initial injury screening or during initial laparotomy. When identification is delayed, endoscopic therapy has been shown to be successful in cases where repeat surgery is not appropriate or deemed too high risk for the patient.

There are limited reports about the endoscopic management and outcomes of biliary injury after blunt or penetrating abdominal trauma. This is in part due to a low frequency of presentation, with traumatic bile duct injuries representing only 0.1–2 % of all trauma admissions [20–22]. Intrahepatic duct injuries typically occur in the small sub-segmental ducts following blunt hepatic trauma, and generally are self-limiting. When they do not resolve, percutaneous drainage, endoscopic therapy, or surgery are required. Simple drainage remains the most common management option for a biliary leak from the intrahepatic biliary tree, and the majority will close without further intervention. Extra-hepatic bile duct injury generally occurs in the context of injury to other intra-abdominal organs, typically following blunt trauma. Concomitant duodenal, pancreatic, or vascular injuries are typically seen. While repair can be attempted during peritoneal exploration, this is not always possible, or biliary injury may be overlooked at initial laparotomy. In circumstances such as these, or when control of posttraumatic BL is incomplete, management of BL with intra-abdominal drains and concomitant ERCP should be considered.

Several small retrospective studies have shown that ERCP yields a treatment success of 89–100 % for traumatic bile duct injuries manifesting as BL. Bridges and colleagues achieved a resolution in nine of ten patients with penetrating or blunt liver injury after endoprosthesis placement alone, including eight patients with severe (grade 4 or 5) injury. An Israeli study noted resolution in all 11 patients with BL after hepatic trauma when treated with both endoscopic sphincterotomy and stent placement [23]. Bajaj et al. similarly showed BL resolution after ERCP in eight of nine (89 %) of patients, seven of whom received stents in addition to sphincterotomy [24]. Earlier studies also showed resolution rates of 100 % in studies including five to eight patients [25–28].

One special clinical situation deserving attention is that in which duodenal or small intestinal injury mimics a traumatic bile duct injury. In this circumstance, an ERCP is requested on account of bile-rich fluid accumulation in the peritoneum or external drain. If the cholangiogram is negative for a leak, a bowel perforation should be considered. Oral contrast-enhanced imaging should be performed when the diagnosis remains in doubt.

Endoscopic treatment protocols for traumatic biliary injuries are similar to those for iatrogenic bile duct injuries (Video 5.1). In general, a 7 to 10 F stent is placed, with the latter favored if a dilated ductal system is seen. While bridging the ductal system is not mandated, attempts should be made to place a stent within the left or right ductal system that suffered the injury. For peripheral leaks, a smaller stent may be preferred to approximate the leak more easily within the segmental branches of the intrahepatic biliary systems [19]. Anecdotal experience at the University of Maryland's Shock Trauma Center suggests traumatic bile duct injuries may take longer to resolve and often require multiple stent exchanges. Larger stents (10 F) are favored to facilitate leak resolution.

Postoperative Biliary Strictures

Benign biliary strictures result from a number of processes, including chronic pancreatitis, PSC, and postoperative biliary strictures (POBS). POBS will be the focus of this section.

POBS are most often associated with cholecystectomy or liver transplantation, although any surgery in which trauma or ischemia to the biliary tree result may be implicated in stricture formation. Biliary decompression is required in instances in which clinically significant obstruction occurs (i.e., jaundice, cholangitis, secondary biliary cirrhosis, hepatic graft dysfunction). ERCP with endoprosthesis placement is the primary treatment modality for POBS where technically possible. For refractory strictures surgical diversion via hepatico- or choledochoenterostomy may be required.

Laparoscopic Cholecystectomy

Introduction and Pathogenesis

While the evolution of laparoscopic cholecystectomy has led to shorter hospital stays and other improvements, these have come at a cost of higher rates of bile duct injury compared with open cholecystectomy (1–2 % versus 0.15 %) [6, 7]. This is in part due to the fact that laparoscopic cholecystectomy allows less complete traction of the gallbladder and cystic duct than open surgery, leading to incomplete isolation of anatomical structures and the potential for traction, thermal or penetrating injury to the bile ducts. When the degree of injury is substantial enough, biliary stricturing may occur, leading to obstructive signs or symptoms in the postoperative period. Incorrect placed clips or ligatures are less common but do occur, and typically manifest much earlier than strictures developing from healing tissue injuries along the biliary tract.

Diagnosis

Clinically significant biliary strictures after cholecystectomy typically demonstrate signs of obstruction. These include jaundice, pain, and signs of sepsis. Elevated alkaline phosphatase or bilirubin may also be seen and should raise suspicion of a bile duct injury in someone with a prior biliary surgery. Cross-sectional imaging usually demonstrates ductal dilation proximal to the stricture unless there is associated leak. MRCP has been shown to have particularly good accuracy for postoperative biliary strictures, which appear as a smooth tapering of the luminal signal. Multislice technique can help to avoid overestimation of stricture length so that proper endoscopic or surgical planning can be made [29].

Management

Technical success rates for the endoscopic treatment of benign post-cholecystectomy strictures with ERCP are greater than 90 %. While balloon dilation alone achieves suboptimal stricture resolution rates of only 25–38 %, endoscopic therapy utilizing stents with or without dilation yields clinical success rates of 80–95 % [30–37]. It is thus recommended that stents be utilized when possible for postoperative strictures. Complications have been reported in 22–33 % of patients and are usually related to stent migration or stent obstruction.

Endoscopic Technique

Standard wire-guided cannulation is performed and identification of the area of stenosis is made with cholangiography (Fig. 5.7a). While a sphincterotomy is not mandatory, it facilitates placement of multiple stents when required. Cytologic brushings should be obtained at least one time, as malignancy is sometimes misdiagnosed as a post-cholecystectomy stricture. Balloon dilation (4–10 mm) is then employed to open up the stricture. The use of contrast to inflate the dilation balloon permits visualization of the balloon fluoroscopically, and the waist of the balloon can be visualized to ensure obliteration of the stenotic area. For tight strictures, a Soehendra biliary dilation device (4–7 F) may be employed, followed by balloon dilation of the stenosis. For very tight strictures, an angioplasty balloon may be required to permit the initial dilation. After dilation, a single plastic stent (7 F, 8.5 F, 10 F) or multiple plastic biliary stents are then placed across the stricture (Fig. 5.7b). Treatment generally consists of sequential ERCP and stent exchange every 3 months, with increasing stent numbers sequentially placed during a 12-month treatment period until stricture resolution [36].

When utilizing a multiple stent strategy, stricture resolution is achieved in 80–95 % of patients with postsurgical strictures [33, 35, 38, 39]. Use of multiple, side-by-side plastic stents may lead to improved success rates when compared to single plastic stents alone. A review of 47 studies in which extrahepatic POBS of varying etiologies were treated, clinical success rates were achieved in 94 % with multiple plastic stents versus 59 % with single stent use. For benign POBS other than OLT, clinical success rates with multiple plastic stents were reported in 81 % [40]. Complication rates were also lower when multiple stents are placed compared to single stent use.

Several small series have demonstrated the successful use of covered self-expanding metal stents (SEMS) for benign POBS of varying etiologies (Fig. 5.8a, b). Technical success rates have exceeded 98 %. When fully or partially covered 10-mm SEMS were used for benign POBS after cholecystectomy, clinical success rates of 62.3 % were reported in a 2009 systematic review. This was lower than that seen with multiple plastic stents (81.3 %) and may support the former as the first line option for POBS management [40]. However, formal comparisons between multiple plastic stents and SEMS are lacking at present. A more recent prospective study has shown stricture resolution rates of 72 % for post-

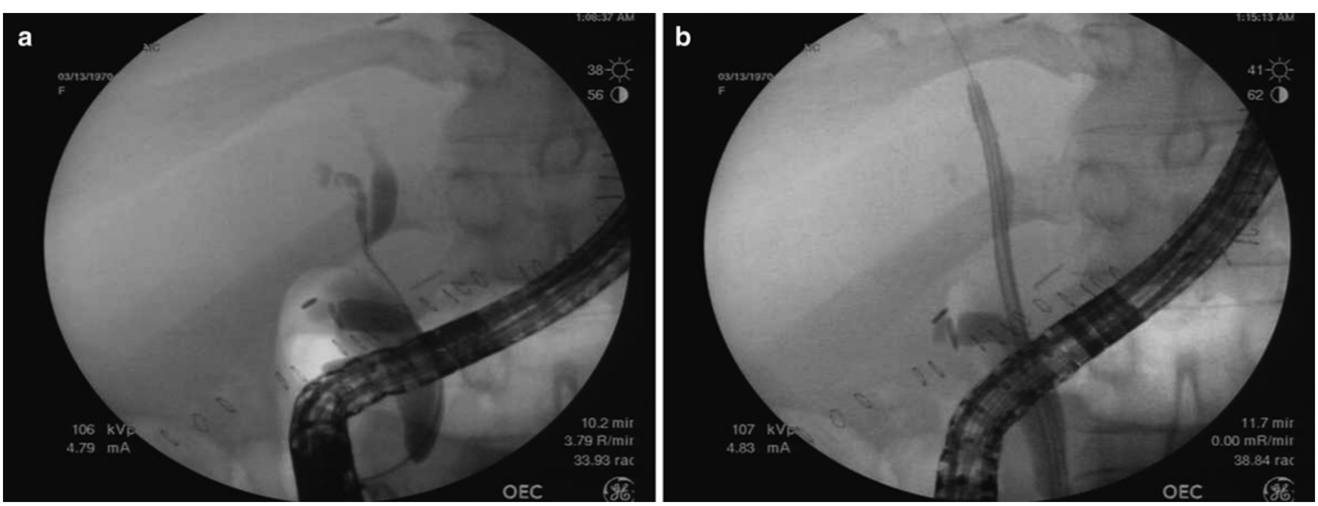

Fig. 5.7 A guide wire traverses a post-cholecystectomy biliary stricture (**a**). A stent is placed across the biliary stricture after dilation (**b**)

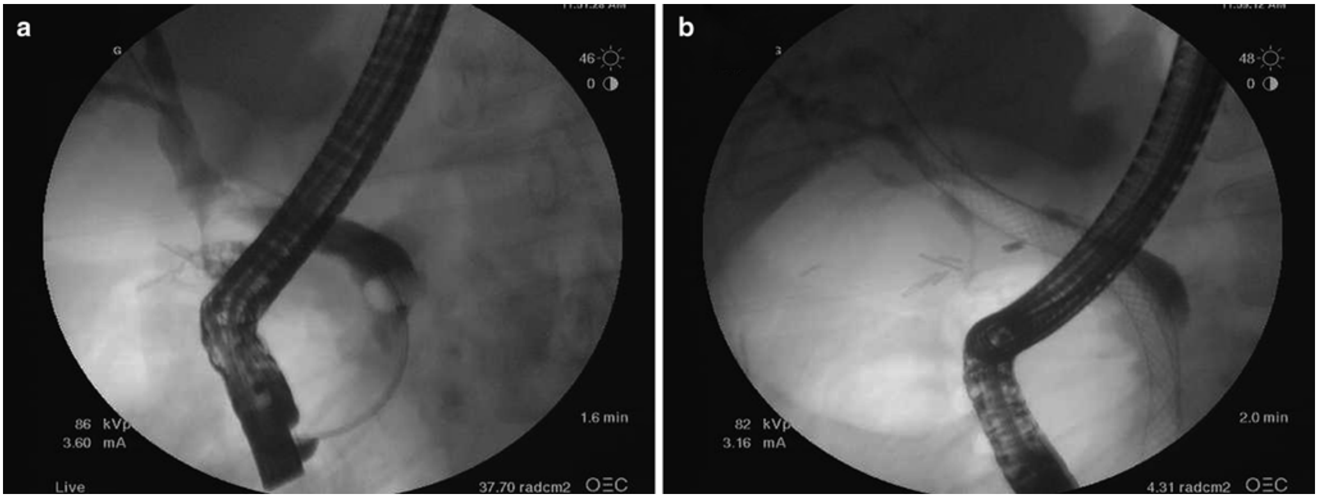

Fig. 5.8 A benign biliary stricture and bile leak are seen post-cholecystectomy and prior self-expanding metal stent (SEMS) placement (**a**). Both the leak and stricture are treated with another SEMS (**b**)

cholecystectomy strictures when SEMSs are used with a dwell of 10–12 months [41]. Stent migration remains a concern with covered SEMS, however, and appears to increase with stent indwell duration. Migration rates of 16.7, 22.2, and 66.7 % reported at 3-, 6- and 12 months have been reported [41]. Generally, SEMSs should not be used for longer than 12 month, and a change after 3–6 months should be considered. Because of the difficulty in removing uncovered SEMSs, their use for benign POBS is not recommended [36].

Exceptional Circumstances After Cholecystectomy

Complete transection of the bile duct is a rare complication of laparoscopic cholecystectomy in which traction applied to the gallbladder gulf leads to distortion and inadvertent ligation of the choledochus (Fig. 5.9). If discovered intraoperatively, an end-to-end choledochocholedochostomy or a hepaticojejunostomy is performed. When not identified during surgery, ductal transection is usually identified by ERCP carried out for the presence of a bile collection by imaging or drain output.

When identified postoperatively, a minimally invasive treatment utilizing a rendezvous between ERCP and percutaneous transhepatic cholangiography has become a preferred management option. A multidisciplinary team consisting of an endoscopist and an interventional radiologist is needed [42]. A guidewire is advanced across the papilla, into the bile duct, and into the subhepatic space. At the same time, the radiologist performs a percutaneous transhepatic cholangiography of the hepatic ducts, typically dilating them to 10 F in order to introduce a snare loop. The snare is advanced to the subhepatic space to catch the guidewire, which is externally advanced across the percutaneous entry point. Balloon dilation of the transected region is performed from both the

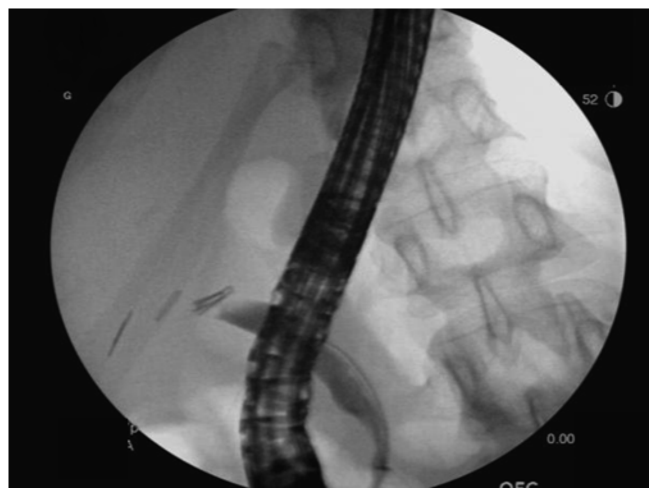

Fig. 5.9 Inadvertent placement of clips is noted across the common bile duct. The duct disruption was treated with endoscopic balloon dilation followed by transpapillary stent placement. In some circumstances, a rendezvous procedure utilizing percutaneous transhepatic cholangiography may also be required

percutaneous and transpapillary approaches in order to open the clips and permit the percutaneous insertion of an internal–external biliary drain. This drain is left in placed to avoid bile spillage into the abdomen. A percutaneous abdominal drainage may also be placed if necessary based on imaging or suspicion on ongoing leak despite ductal drainage. After 2–4 weeks, multiple 10 F plastic stents are placed, and are left in for at least 3 months, with stent changes as required. In their series, Fiocca et al. utilized and initial right hepatic approach followed by an additional left hepatic approach at 2–3 weeks to ultimately place four 10 F stents across the transected region (two in the left hepatic system and two in the right). With this method, 16 patients of the 22 patients who had completed treatment were asymptomatic 4 years after first endoscopic intervention [43].

Liver Transplantation

Introduction

There are several potential causes of cholestatic liver injury after liver transplantation, including reperfusion injury, delayed graft function, vascular complications, bile leaks, functional ampullary obstruction, and biliary stricture. Biliary stenosis can be difficult to distinguish clinically from the other causes, and radiographic tools like HIDA scan or MRCP may have a limited ability to effectively rule out an obstruction in the immediate and long-term postoperative period. Cholangiography remains the gold standard for diagnosing both anastomotic and non-anastomotic strictures after liver transplantation. While ERCP is the first line therapy for anastomotic strictures, its role for non-anastomotic strictures is more limited.

Considerations Before Cholangiography

Biliary strictures occur between 4 and 13 % of patients after orthotopic liver transplant (OLT) and in up to 19–32 % of living-donor liver transplant (LDLT) recipients [44–50]. Retrospective studies show that most strictures will present within 6 months of transplantation [51]. Strictures may come to clinical attention in a variety of ways: elevated conjugated bilirubin and alkaline phosphatase, abnormal imaging, jaundice, or evidence of cholangitis or other biliary complications. It is important to note that due to the denervation of the donor liver, the typical symptoms of biliary obstruction may be lacking. As such, serologies testing, and imaging should be performed prior to considering ERCP. Supplementary information from liver biopsy may be necessary to exclude non-stricturing causes of the laboratory abnormalities, including rejection, recurrent hepatitis, or infectious (viral) etiologies.

Radiography has a limited role for evaluating for biliary strictures after both OLT and LDLT. Less than 40–50 % of transplant recipients with anastomotic strictures show upstream biliary dilation, a limitation attributed to the denervation of the transplanted liver and fibrosis of the donor biliary system that occurs after transplantation [52–55]. HIDA scans are of limited benefit because of post-transplant graft dysfunction, medication effects, postoperative edema at the anastomosis and other confounding factors affecting the sensitivity. While one study showed HIDA scan had a negative predictive value of greater than 90 % in patients in the immediate postoperative period, other studies have shown a limited role for HIDA scan for the workup of post-transplantation strictures [56–58]. Similarly, while MRCP has been shown to have a sensitivity and sensitivity as high as 94–97 % for detecting biliary stenosis after transplant, this pooled data comes from small studies which have variable radiographic standards and which lack correlation with cholangiographic and clinical endpoints. As a whole, radiographic modalities are still considered less reliable for detecting biliary obstruction in the post-transplant population than they are for benign strictures from other etiologies.

Thus, when the suspicion for a biliary stenosis is high enough, ERCP remains the preferred diagnostic and therapeutic modality.

Classification of Biliary Strictures After Liver Transplantation

Most classification systems for post-liver transplantation strictures take into account the location of the stricture in relation to the surgical anastomosis. Most biliary strictures after transplant are anastomotic strictures (AS) and involve the choledochocholedochostomy. This is compared to those at site other than the anastomosis, or non-anastomotic strictures (NAS) (Fig. 5.10a–d). The clinical outcomes for AS versus NAS are significantly different, as are their respective responses to endoscopic therapy [59].

Pathogenesis

Technical problems remain the main cause of up to 80 % of post-OLT anastomotic strictures. These include fibrosis and ischemia resulting from donor-to-recipient duct mismatch, small-sized bile ducts, tension at the anastomosis, electrocautery or suture effect, or local infection [60–62]. Preceding bile leak is associated with late-onset AS, as is ischemic injury at the terminus of the donor duct over time [30, 59]. Studies have shown that AS tend to occur more often in LDLT than after OLT, in hepaticojejunostomy rather than duct-to-duct anastomosis, and that the use of T-tube in duct-to-duct anastomoses is generally protective when compared to those made without T-tubes [30, 63–65]. Other risk factors for AS include a BMI > 25 and recurrent HCV in the donor graft, the latter of which tends to lead to later onset AS.

Non-anastomotic strictures are typically due to ischemic complications inherent to OLT, including those related to hepatic artery thrombosis and prolonged cold ischemia time of the graft. NAS are also attributed to recurrent liver disease, chronic rejection, blood-type mismatch incompatibility, older age of donors (>60) and CMV infection [59, 66, 67]. Ischemia-associated NAS tends to present within 1 year of transplant, while immunogenic causes are more delayed in onset [30, 61]. NAS have been shown to occur earlier than AS, with a occurrences generally seen in the 3–6 month range [68, 69].

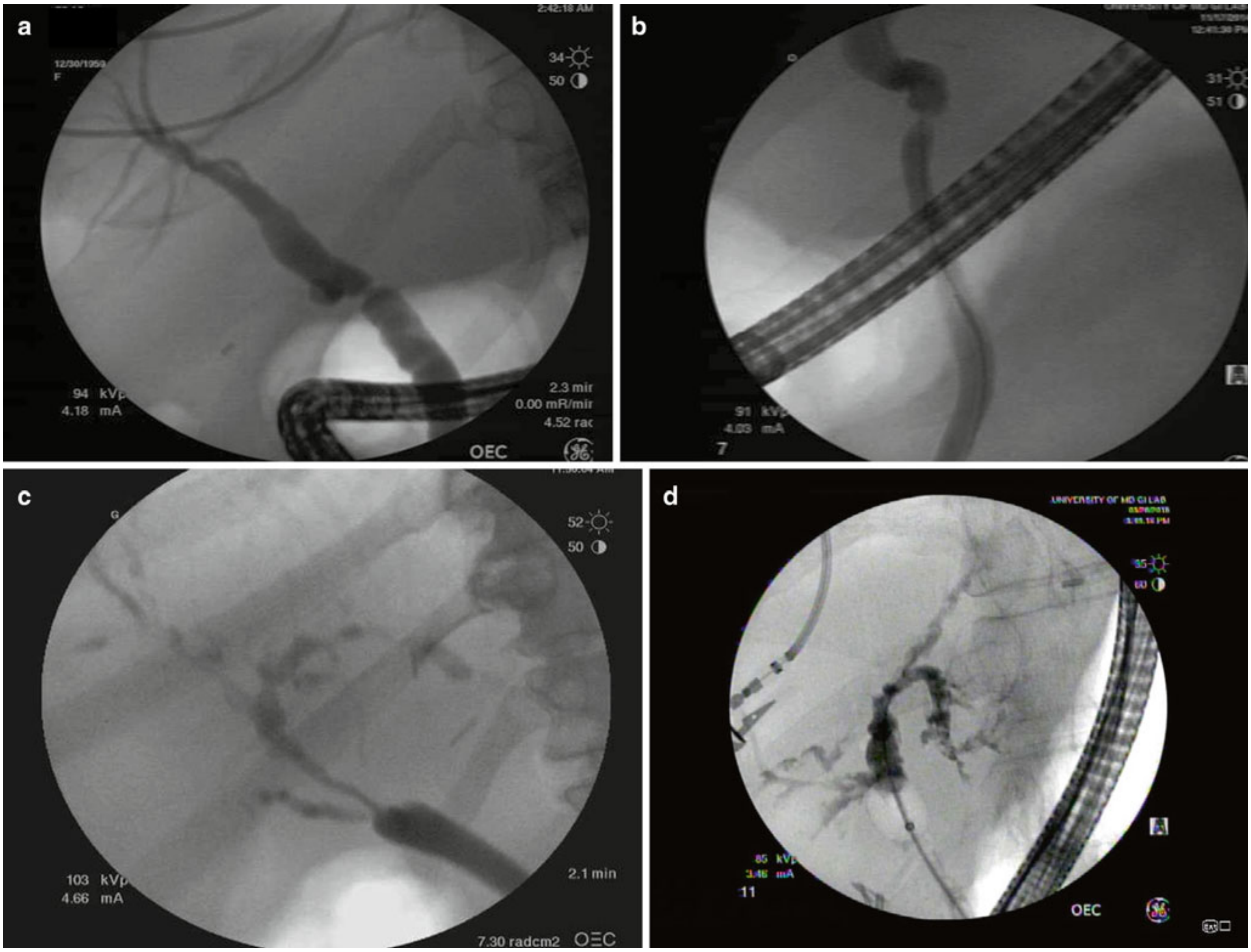

Fig. 5.10 An anastomotic stricture is identified after orthotopic liver transplantation (**a**). This stricture is patent after 6 weeks of therapy with a plastic biliary stent (**b**). Non-anastomotic strictures are seen in the secondary and tertiary branches of the donor intrahepatic system after orthotopic liver transplantation (**c** and **d**)

Management

Early reports from the transplant literature favored surgery and PTC as treatment modalities for post-liver transplantation biliary strictures. Percutaneous trans-hepatic management had been considered the preferred nonoperative treatment modality, with success rates of greater than 85 %. Both modalities are limited in terms of desirability, however, as they are invasive, and each carries its own significant morbidities. Recent advances in endoscopic techniques have been such that ERCP has now supplanted both surgery and percutaneous cholangiography as the preferred diagnostic and therapeutic modality.

Anastomotic Strictures (OLT)

The first challenge of AS is gaining wire access across the stricture. Anastomoses may be tortuous or kinked with multiple cystic duct remnants (both recipient and donor) across which to navigate. Care should be taken with wire passage, especially in the early postoperative period (within 30 days). Once access is obtained, a combination of dilation and stenting should be attempted (Fig. 5.11a–c). (NOTE: dilation should be avoided in early anastomoses due to a concern for dehiscence at this site). While balloon dilation with a 4-, 6-, or 10-mm balloon alone can be considered, success rates of only 25–38 % have been reported with this technique [70, 71]. The use of endoprosthesis after dilation appears to offer a more durable stricture response rate, with stricture resolution reported in 64–100 % of post-OLT patients when a strategy of increasing plastic stents or SEMS is utilized [72–82].

For a strategy using multiple plastic stents, one to two 7 or 10 F stents are initially placed (Video 5.2). Subsequent ERCP with balloon dilation and stent insertion occurs every 8–12 weeks with increasing numbers of stents placed as possible until the stricture resolves. While some studies utilized time intervals as short as 2-week intervals between ERCP, intervals of 8–12 weeks are typically performed in clinical

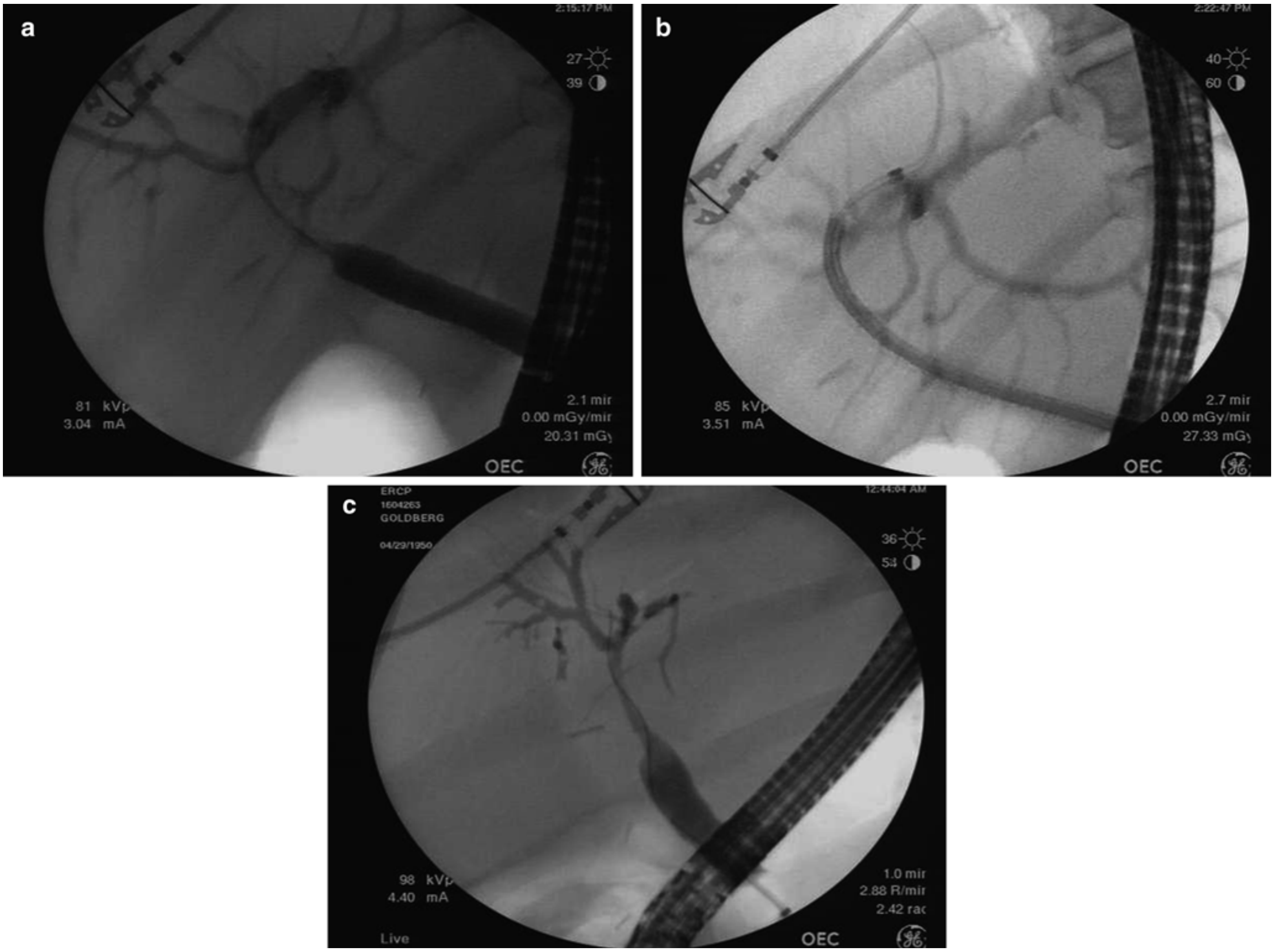

Fig. 5.11 A guide wire is placed across an anastomotic stricture and balloon dilation is performed (**a**). This is followed by a period of stent placement across the anastomosis (**b**). The stenosed area is improved after stent removal (**c**)

settings [72, 74, 83, 84]. In a review of eight studies and 440 patients, an average of two to three stents were placed per ERCP, with stent duration of 3.6–15 months. Using such a strategy, clinical success rates of 84 % and 86 % were reported for early- and late-onset AS, respectively [51]. Stent duration for greater than 12 months was associated with higher stricture resolution rates and lower stricture recurrence rates than stents placed for less than a year (97 % versus 78.3 % and 1.5 % versus 14.2 %, respectively) [51].

When plastic stents fail to yield adequate stricture resolution, the use of partially or fully covered biliary SEMS can be considered. Some small studies have also used SEMS as the primary therapy for AS when feasible. Most studies using SEMS exchanged or removed the stents at intervals of 2–3 months [76–81]. In a review of ten studies and 200 patients, a stricture resolution rate of 78–82 % was reported. Stent duration of greater than 3 months was associated with higher stricture resolution rates and lower stricture recurrence rates than stents placed for less than 3 months (89.5 % versus 71.8 % and 8 % versus 15.3 %, respectively) [51].

There are no trials directly comparing using multiple plastic stents and SEMS, and the former are generally the preferred initial strategy in most institutions. A stent migration rate of 16 % SEMS further supports the use of plastic stents initially where possible [51]. Anecdotal reports of anastomotic dehiscence with SEMS are also available.

Non-anastomotic Strictures

NAS are more difficult to treat and are generally less responsive to endoscopic therapies than AS. Success rates in the vicinity of 60 % have been reported after OLT, but rates are lower in the context of LDLT (25–33 %) [48]. Furthermore, stent patency is limited by biliary sludge accumulation. Therefore, patients with complex NAS often require retransplantation, and the role of ERCP becomes one of a bridge to surgery rather than a definitive treatment modality in itself [48].

Endoscopic therapy of NAS typically consists of balloon dilation of all accessible strictures and extraction of biliary sludge and casts proximal to the lesions. This may be followed by the placement of plastic stents with replacement every 3 months until strictures are deemed adequately patent. Given their refractory character, NAS typically require multiple treatments. In one study, a median of six treatments were done every 8–10 weeks [85]. In cases in which obstruction does not improve or does so for only a short duration, multidisciplinary discussions with the surgeon are thus warranted, as early retransplantation may be indicated to prevent cholangitis, abscess formation, and progressive graft loss.

Endoscopic success as defined by improvement of cholestatic parameters and cholangiographic patency occur in 6–91 %, although the proximal location of NAS may permit stent placement in a few as 31 % of patients [68, 85]. In a study of 72 patients with NAS, of whom 85 % were treated, 68 (94.4 %) had persistent strictures and 22 (31 %) required retransplantation. Only 25 % received stents [68].

Living-Donor Related Transplantation (LDLT)

Biliary complications, including stricture formation and leak, occur in approximately one-third of living donor liver transplantation recipients [48, 86] (Fig. 5.12). Furthermore, studies show these complications are more refractory to treatment than those after orthotopic liver transplantation. For anastomotic strictures arising after LDLT, the treatment success rates of 31–100 % have been reported [30, 48, 86, 87]. Multiple treatments are generally required, with studies showing an average of 2.7–4 procedures required to meet success endpoints [51].

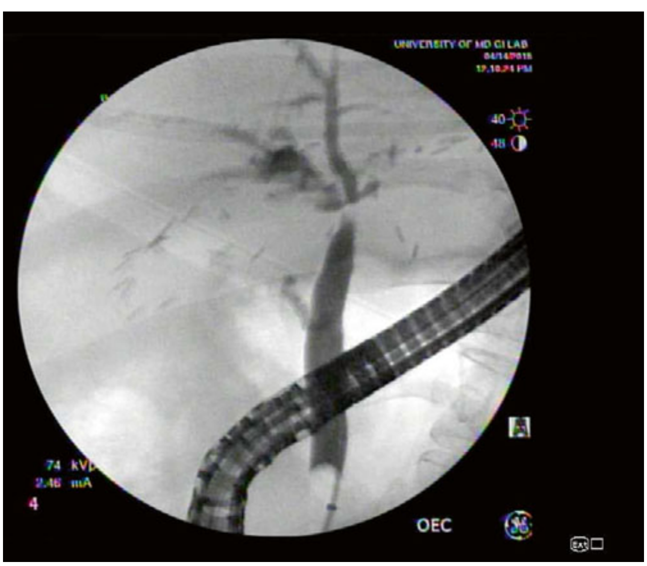

Fig. 5.12 An anastomotic stricture is seen after living donor liver transplantation

Complications

Complications rates for ERCP after OLT are generally low, with most reports showing complication rates of 2–6 % [75]. These complications include pancreatitis, bleeding, stent migration, infection, and dehiscence of the anastomosis. Management varies depending on the nature and location of injury or complication.

Pancreatic Duct Leaks

Pancreatic duct (PD) injury may result from acute or chronic pancreatitis, pancreatic and splenic surgery, pancreatic malignancy, guidewire injuries during ERCP, or abdominal trauma. Persistent PD disruption may lead to pancreatic ascites, pancreatic and peripancreatic fluid collections, or fistula formation. The clinical sequelae of PD disruption depend on a number of factors including the etiology of the disruption, the location and extent of the disruption, the presence of downstream obstruction, and the rate of pancreatic secretion.

Epidemiology

Up to 40 % of patients with acute pancreatitis will develop some type of acute fluid collection [88]. Recently, the revised Atlanta classification 2012 [89] recategorized the various types of pancreatic collections. In acute interstitial edematous pancreatitis, collections that do not have an enhancing capsule are called acute peripancreatic fluid collections (APFC); after development of a capsule, they are referred to as pancreatic pseudocysts (PP; usually after the first 4 weeks). In necrotizing pancreatitis, a collection without an enhancing capsule is called an acute necrotic collection (ANC; usually in the first 4 weeks) and once an enhancing capsule has developed, they are referred to as walled-off necrosis (WON, usually after 4 weeks). Fortunately, only a small percentage of acute fluid collections will go on to develop PP or WON. Persistent or enlarging PP suggests an ongoing ductal injury. Similarly, WON frequently involves a ductal leak. WON patients have been shown to have disconnected duct syndrome (DDS) in 35–70 % of cases [90].

Clinical Manifestations

The manifestations of PD disruption include pseudocysts, WON, pancreatic ascites, pancreatic fistula (pancreatic-cutaneous fistula, pancreatic-pleural fistula) and disconnected duct syndrome. The ductal disruption can be identified in the head, body, genu, tail and sometimes at multiple sites.

Ductal disruption can be complete or partial. Signs and symptoms are variable, but can include nausea, pain, tachycardia, ileus and hypotension. Obstruction of the biliary tree, gastric outlet and small intestine may also be seen.

Diagnosis

Computed Tomography (CT)

Cross sectional imaging with a pancreatic protocol CT is typically the best initial diagnostic test for patients with smoldering or severe pancreatitis who may have a pancreatic duct leak [90]. CT can identify the size, location, and content of fluid collections, and also determine whether there may be compression on vital organs such as the stomach, small intestine or biliary tree. CT can also help to determine the maturity of the capsule (aka rind) and whether a mature fluid collection may be amenable to endoscopic drainage. Importantly, serial CT scans can be used to date the age of a collection, an important determinant in deciding when a collection is mature enough to drain.

Endoscopic Retrograde Pancreatography (ERP)

ERP is the gold standard for the diagnosis of ductal injuries as it can provide detailed images of the pancreatic duct and define the location and nature of the injury [91]. It can be performed preoperatively, intraoperatively or postoperatively in patients with pancreatic injury, and it is also offers the potential for therapy. ERP should be considered in any patient who has evidence of a persistent or symptomatic leak. Since many acute pancreatic fluid collections related to acute pancreatitis resolve on their own, it is reasonable to defer ERP in this setting. For patients with persistent or enlarging fluid collections related to pancreatitis (ex PP or WON), ERP should be performed. Similarly, patients with evidence of persistent leaks after surgery or trauma should undergo ERP for potential diagnosis and therapy. Because of the potential of infecting sterile pancreatic fluid collections, patients with evidence of leak by ERP should be given prophylactic antibiotic therapy. A quality pancreatogram should be obtained to identify the size and location of the leak as well as any factors that may be contributing to its persistence, such as a stone or a stricture.

Magnetic Resonance Pancreatography (MRCP)

MRCP is a useful noninvasive modality that can be used as a diagnostic complement to therapeutic ERCP. Secretin-enhanced MRCP can characterize an active leak and minimizes the potential complications associated with ERCP [92]. MRCP has an added advantage of delineating the pancreatic duct upstream to complete disruption, an area not visualized on ERP. The most important limitation of MRCP is that therapeutic procedures cannot be performed [93]. Similar to cross sectional imaging with CT, MRI images can provide important information about the size, location and content of a fluid collection and whether there is impingement on important adjacent structures.

Fluid Amylase

Patients with persistent output from a JP drain after pancreatic surgery, or variable output of clear fluid following percutaneous drainage of a fluid collection may have a pancreatic duct leak. These patients should have the fluid checked for amylase levels which will be markedly elevated in the setting of a pancreatic leak [94, 95].

Management

Pseudocysts (PP)

A pancreatic pseudocyst is surrounded by a well-defined wall and contains essentially no solid material. If aspiration of cyst content is performed, there is usually a markedly increased amylase level. A low amylase content and high CEA level in the cyst may suggest an underlying mucinous neoplasm of the pancreas [96, 97]. A pancreatic pseudocyst is thought to arise from disruption of the main pancreatic duct or its intra-pancreatic branches without any recognizable pancreatic parenchymal necrosis [89].

Indications for Drainage

The indications for drainage of pancreatic pseudocysts have changed overtime. Initially, it was thought that size of pseudocyst (>6 cm) and duration of presence of pseudocyst (>6 weeks) were important indicators for pseudocyst drainage. These criteria are now obsolete [98–101]. Presently, the development of persistent symptoms thought to be related to the presence of the pseudocysts or development of a complications related to the pseudocyst such as infection, bleeding, biliary, or gastric outlet obstruction are indications for drainage.

Patient Selection for Endoscopic Drainage

The first step of determining whether the pseudocyst is endoscopically drainable is to differentiate a pseudocyst from any other types of pancreatic cysts.

Imaging

Pancreatic pseudocysts typically appear as unilocular cysts with thin walls and without internal septa, a solid component, or central cyst wall calcification (Fig. 5.13). The patient nearly always presents with a clinical history of pancreatitis. The diagnosis is supported by imaging findings of inflammation, atrophy, or calcification of pancreatic parenchyma, and dilatation of the pancreatic

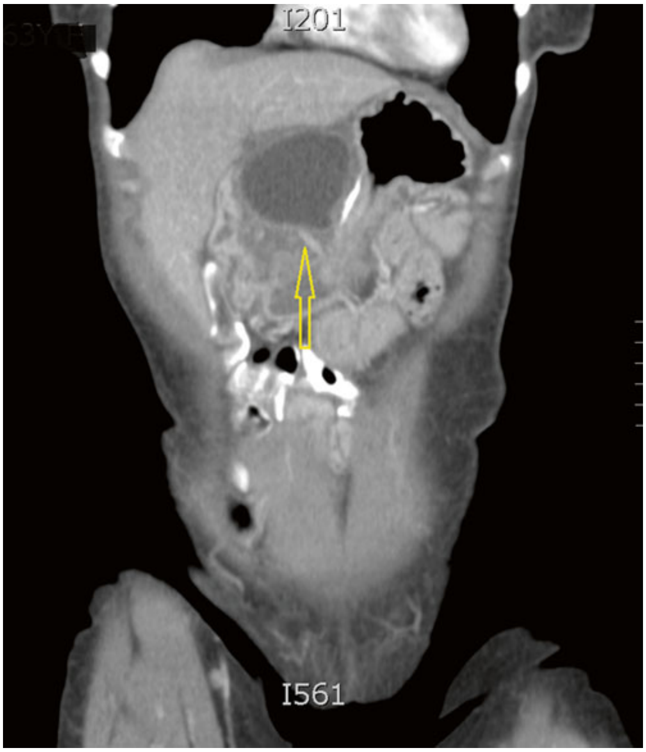

Fig. 5.13 CT scan of the abdomen showing thin walled pseudocyst compressing the stomach. Note the homogenous fluid and lack of internal septae

duct [96]. Noninvasive imaging does have limitations in distinguishing pseudocysts from cystic neoplasms, especially when there are no morphologic signs of pancreatitis and no clear communication with the duct [101, 102].

Cyst Fluid Analysis

When cross-sectional imaging does not provide a definitive diagnosis, additional information aspiration of the contents of a cyst may help the diagnosis [102]. CEA has been shown to be the most accurate marker to distinguish non-mucinous from mucinous cysts [96]. CEA does not, however, distinguish benign from malignant mucinous neoplasms [96]. Amylase is also a helpful marker, as amylase is typically very high, usually in the thousands and almost never <250 ng/mL in pseudocysts [97], but is low in serous cysts [97]. It should be understood, however, that measurement of CEA or amylase in cyst fluid has not been approved by the US Food and Drug Administration (FDA) and has never been formally validated or approved by the FDA [96].

Contraindications

Contraindications to cyst drainage include a cyst to gastrointestinal wall distance of greater than 1 cm, presence of vascular structures in the projected needle path that can't be circumvented with the aid of EUS, and pseudoaneurysms [103, 104]. The presence of debris is a cyst increased the risk of infection and is a relative contraindication for simple drainage. In these circumstances, more extensive procedures such as endoscopic necrosectomy (see below) should be considered.

EUS Guided Transmural Drainage (EUD) Versus Conventional Direct Transluminal Drainage by Forward-Viewing Endoscopy (CTD)

A prospective randomized controlled trial by Park et al. [105] studying CTD versus EUD revealed no significant difference in clinical outcomes between CTD and EUD [105]. However, the rate of technical success was higher for EUD (94 %) than for CTD (72 % $P = 0.039$). Most of the difference in technical success was secondary to the inability of CTD to drain non-bulging cysts. A meta-analysis by Panamonta et al. comparing the technical success and clinical outcomes of EUD and CTD for bulging PPs showed EUD was not superior to CTD in terms of short-term or long-term success and the overall complications were similar in both groups [106]. EUD of PP is a preferred endoscopic option in patients who have non-bulging cysts, a small portal of entry based on computed tomography (CT), intervening vessels seen by CT, unusual locations of PPs, or coagulopathy. In cases of failed CTD, EUD should also be considered.

Endoscopic Transmural Drainage Versus Percutaneous Drainage

Retrospective studies reveal no significant differences in clinical success rates when comparing endoscopic transmural drainage to percutaneous drainage [103]. However, percutaneous transmural drainage was associated with a higher reintervention rate, longer hospital stays, and increased number of follow-up abdominal imaging studies [103]. Furthermore, percutaneous drainage of PPs may lead to pancreatico-cutaneous fistulae. Therefore, endoscopic transmural drainage is the preferred modality for the drainage of symptomatic PP compared with percutaneous drainage.

Endoscopic Transmural Drainage (ETD) Versus Surgical Drainage

A prospective randomized controlled trial by Akshintala et al. regarding surgical drainage versus ETD for symptomatic PP revealed no difference in treatment success, complications, or reinterventions between the surgical and endoscopic transmural drainage groups. However, the length of hospital stays was shorter, the physical and mental health scores were better, and the total mean costs were lower for the ETD group [104]. Surgical treatment still has an important role in terms of adjunctive or salvage therapy, if endoscopic or percutaneous intervention fails.

Transpapillary Drainage

Transpapillary drainage requires that the PP communicate with the main pancreatic duct and that it has few septations to permit complete drainage. It should be considered for small pseudocysts (typically <6 cm) that are symptomatic. An advantage of transpapillary drainage is that associated ductal pathology such as stones, strictures or fistulae can be identified and treated.

Multimodality Endoscopic Treatment of Pancreatic Duct Disruption with Stenting and Pseudocyst Drainage

Older retrospective studies have recommended assessing the main pancreatic duct at the time of PP drainage with endoscopic retrograde cholangiopancreatography (ERCP) as patients with major main pancreatic duct leaks may require stent placement to bridge the leak [107, 108]. A retrospective study by Shrode et al. [109] also demonstrated the pancreatic duct disruptions require multimodality treatment, addressing not only the integrity of the pancreatic duct but also any associated fluid collections. Based upon their results, they recommended partial ductal disruptions be managed with a bridging stent. However, complete ductal disruptions did worse with a combination of cystgastrostomy/enterostomy and transpapillary stenting than disruptions treated with cystgastrostomy/enterostomy alone [109].

Technique of Drainage

Conventional Transmural Drainage (CTD)

Either a side viewing duodenoscope or a therapeutic upper endoscope can be used for CTD. The authors prefer a duodenoscope as the elevator makes stent insertion easier. The stomach is insufflated and the area of extrinsic compression of the stomach is located. A needle knife sphincterotome is then utilized to puncture directly into the bulge created by the cyst. Blended current is utilized for the puncture. Entry into the cyst is confirmed by injecting contrast under fluoroscopy which demonstrates laminar flow. In addition, cyst fluid is aspirated and typically has a “dishwater” appearance. The fluid should be sent for amylase and culture. A guidewire is then looped inside the pseudocyst. Next, a 10–15 mm through the scope balloon is used to dilate the transmural tract. A short (5–7 cm) double pigtail 7 to 10 F plastic stent is then advanced over the guidewire and deployed with the proximal end in the gastric lumen and the distal end within the pseudocyst cavity. The steps of wire placement and stent placement can be repeated until multiple (two to four) double pigtail stents are in place.

EUS Guided Transmural Drainage (EUD)

Two-Step Approach [110]

The pseudocyst is localized using an echoendoscope. An ultrasonography examination is performed to determine characteristics and contents of the cyst and to ensure the absence of pseudoaneurysms or vascular structures within the expected trajectory of the needle. A 19-gauge needle is then used to puncture the pseudocyst. Once inside the pseudocyst, the needle is replaced with a 0.035-in. guidewire, which is looped inside the cyst. Next, the echoendoscope is withdrawn, with the wire secured in place within the pseudocyst, and the echoendoscope is replaced with a side-viewing duodenoscope. The transmural tract is then dilated and stented as described for CTD above.

One-Step Approach [110]

In this technique, the echoendoscope is used to perform the entire drainage. After identifying the pseudocyst, a needle is passed into the pseudocyst and the needle is exchanged for a guidewire (Fig. 5.14). Then, a through-the-scope balloon is used to dilate the cystogastrostomy tract. Balloon dilation of the tract is usually performed to a size that would be acceptable for delivery of either two 10 F plastic stents or a covered metal biliary stent. Typically, 8–12 mm dilating balloons suffice. After dilation of the tract, the endoprosthesis is delivered through the echoendoscope across the cystogastrostomy or cystenterostomy. The advantage of this technique over the two-step approach is that it avoids exchange of the entire

Fig. 5.14 EUS of walled off necrosis (WON) demonstrating needle puncture access. Note the heterogenous material suggesting necrotic debris

endoscope over the guidewire, and thus decreases the risk of guidewire displacement.

After performance of the endoscopic cystogastrostomy or cystenterostomy, patients are usually placed on 5–7 days of antibiotics to avoid cyst infection. Reassessment with CT abdomen in 2–4 weeks is performed to determine if the cyst has collapsed/resolved. Once the cyst has collapsed, stents may be removed.

Walled Off Necrosis (WON) and Infected Pancreatic Necrosis

WON consists of necrotic pancreatic and/or peripancreatic tissue contained within an enhancing wall of reactive tissue. By definition, it is mature, encapsulated and typically occurs ≥4 weeks after onset of necrotizing pancreatitis [89]. WON may be sterile or may become infected. Infected pancreatic necrosis has varying amounts of necrotic material and pus, and the amount of pus may increase with liquefaction of the necrosis. Clues to the presence of infected necrosis may be the development of late-onset fever, sepsis or clinical deterioration of the patient. While the presence of gas in the collection seen by cross-sectional imaging suggests infection, the diagnosis of infected necrosis requires fine needle aspiration. Infection of pancreatic necrosis develops in approximately 30 % of patients with necrosis [111]. It is important to determine whether infected necrosis is present because infected pancreatic necrosis is associated with higher mortality rate from sepsis and multiorgan failure. Historically, management of infected pancreatic necrosis required prompt surgical debridement. However this concept has been challenged by multiple reports and case series showing that antibiotics alone can lead to resolution of infection and, in select patients, avoid surgery altogether [112]. Also there is growing evidence suggesting endoscopic transmural drainage and necrosectomy is a viable alternative to percutaneous drainage and surgical intervention in the treatment of infected walled-off pancreatic and peripancreatic necrosis [113].

Endoscopic Drainage/Necrosectomy Versus Surgical Management

A prospective randomized controlled trial by Bakker et al. [114] comparing direct endoscopic drainage/necrosectomy of WON or infected WON versus surgical management demonstrated significant advantages to an endoscopic approach. These advantages included reduction of the pro-inflammatory response (serum interleukin-6), reduction in the incidence of new-onset multiple organ failure, less intra-abdominal bleeding, decreased pancreatic and enterocutaneous fistula formation, and a reduction in the incidence of iatrogenic perforation of a visceral organ.

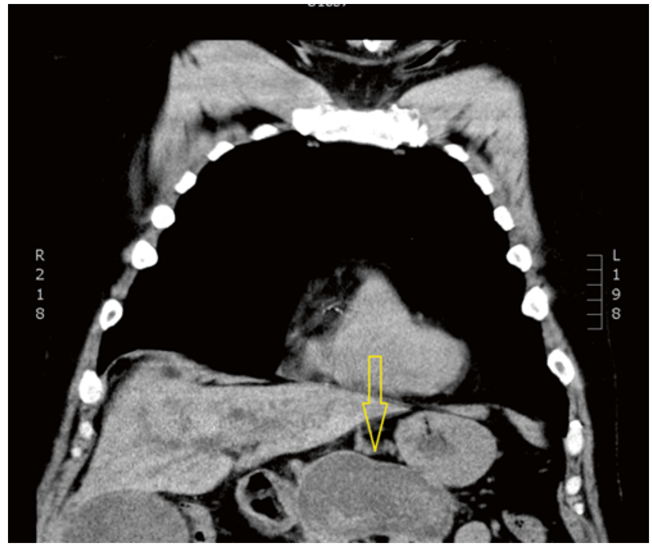

Fig. 5.15 CT scan of the abdomen showing heterogenous material within the pancreatic walled off necrosis

Endoscopic Necrosectomy

Indications

In collections with necrotic debris (Fig. 5.15), clinical success rate is poor with simple endoscopic or percutaneous drainage methods alone. The practice of utilizing a nasocystic tube to flush the necrotic debris from WON can be considered, but frequently fails and is poorly tolerated by patients. Over the last decade, endoscopic necrosectomy has emerged as a viable alternative to surgery for WON with and without infection.

A direct endoscopic necrosectomy should be considered under the following conditions [111]:

1. Necrotizing pancreatitis is present.
2. US, EUS, CT, or MRI show solid components in the fluid collection.
3. Acute inflammation suggesting an infected WON is present.

Technique

Non EUS Guided Necrosectomy

A therapeutic upper endoscope or side viewing duodenoscope is passed into the stomach. The authors prefer a straight viewing upper endoscope for endoscopic necrosectomy as it is easier to pass into the necrotic cavity. Access to the WON is obtained similar to the method described above for CTD. A guidewire is advanced into the WON and a large volume through the scope balloon is used to dilate the transmural tract to 12–15 mm. More aggressive balloon dilation can be performed in a graduated approach up to 20 mm to ease the introduction of the therapeutic upper scope into the cavity for endoscopic debridement. Necrotic debris is removed utilizing snares, baskets and vigorous flushing. Once adequate debridement is performed, the WON is stented with multiple plastic double pigtail stents or a self-expandable metallic stent (SEMS). Serial procedures are performed every few days until all necrotic tissue is removed. Usually, the patients are placed on antibiotics to avoid WON cavity infection during the course of necrosectomy.

EUS Guided Necrosectomy with New Self-Expandable Metallic Stent (SEMS) [111]

One-step EUS-guided walled-off pancreatic necrosis drainage is performed transgastrically using a 19-gauge needle. After bougie using a 4-mm dilating balloon, a self-expandable metallic stent (SEMS) is deployed under fluoroscopic and endoscopic image guidance. In further sessions, a standard upper endoscope is inserted through the SEMS into the walled-off pancreatic necrosis and the necrotic tissue is removed. Stents can be removed once there is CT confirmation of cyst collapse/resolution.

Covered Self-Expandable Metallic Stents (CSEMSs)

The use of fully covered self-expandable metallic stents (CSEMSs) may further improve the clinical success of endoscopic drainage of WON and infected necrosis (Fig. 5.16a–c). Kawakami et al. have summarized reports of 56 patients with WON infected necrosis [91]. The technical success rate was 100 % and the complete resolution rate was 87.8 %. These numbers are comparable to simple transmural pseudocyst drainage.

Treatment of Partial Main Duct Disruptions and Side Branch Disruptions

Medical management of pancreatic duct leaks utilizes conservative management with bowel rest, total parenteral nutrition (TPN), or nasojejunal tube feedings. Somatostatin analogues such as Octreotide or Pasireotide may decrease pancreatic juice extravasation [115, 116]. Many patients with small pancreatic leaks can experience resolution of their leaks without any intervention [90]. In refractory cases,

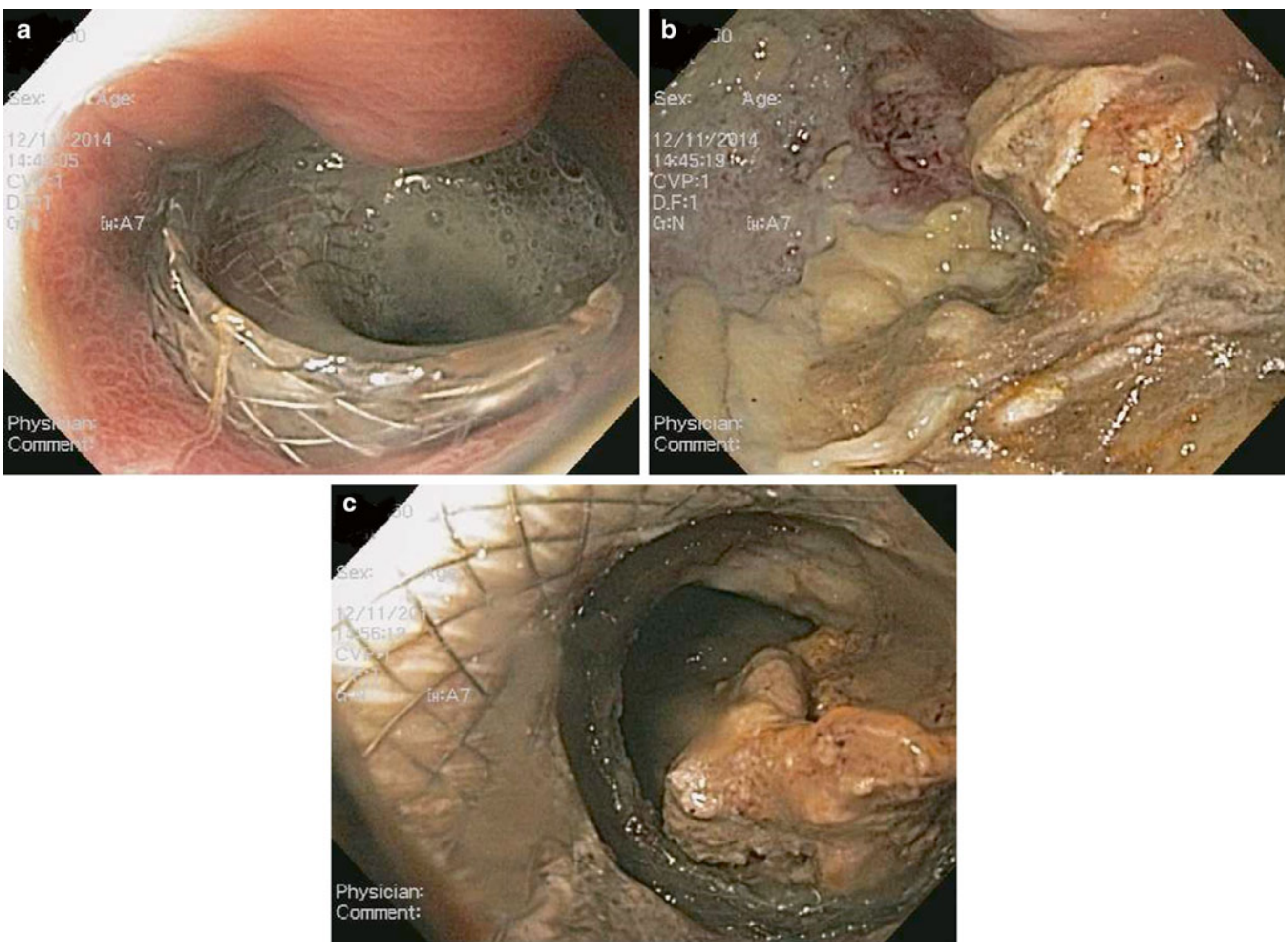

Fig. 5.16 (**a**) Self-expanding metal stent draining the walled off necrosis. (**b**) Contents of WON demonstrating necrotic material. (**c**) Necrotic debris being removed through the SEMS

ERCP with a transpapillary stent can facilitate the leak closure [117, 118]. Pancreatic stenting is effective in treating pancreatic leaks because the stent reduces the pancreatic ductal pressure [90, 117]. Stenting should aim to bridge the leak and is usually ineffective if the duct is completed disconnected and therefore unbridgeable [119, 120].

Pancreatic Cannulation

The main principles involved in pancreatic cannulation are similar to those of biliary cannulation. Guidewire cannulation, while often preferred for biliary cannulation, can sometimes be challenging for pancreatic cannulation in the setting of ductal injury. This is the result of an abnormal path the wire may take especially if there is a disruption in the head of the pancreas. Therefore, there should be a low threshold to inject contrast and identify the pertinent anatomy once the papilla is engaged. It is critical to understand ampullary anatomy for successful pancreatic duct cannulation. When ampulla is positioned in the middle of the endoscopic view, the pancreatic duct orients towards 1 o' clock whereas common bile duct orients towards 11 o' clock. Successful selective cannulation is facilitated by orienting the cannulating instrument in the proper orientation. If access to the main pancreatic duct is restricted by complete pancreas divisum or duct disruption in the head of the pancreas, it may be possible to access the main pancreatic duct through the minor papilla [121].

Conventional MRCP and secretin enhanced MRCP can be utilized to map out pancreatic ductal anatomy prior to ERCP. For example, its sensitivity for diagnosing divisum is 65–73 % [122, 123]. In difficult cannulation cases, IV Secretin injection can be used to facilitate cannulation of the either the major or minor papilla during endoscopic retrograde cholangiopancreatography (ERCP) [124, 125].

Pancreatic Sphincterotomy

Once successful cannulation of the pancreatic duct orifice is achieved, the guidewire is advanced into the main pancreatic duct and confirmation of position is usually obtained with contrast injection (Fig. 5.17). The sphincterotomy should be directed towards the 1 o'clock position with the very distal part of the cutting wire to prevent thermal injury to the duct. Pure cutting currents may decrease the risk of PD injury but increase the risk of bleeding compared to settings with more coagulation [126, 127]. The edema that ensues following a pancreatic sphincterotomy can cause ductal obstruction and eventual pancreatitis [128]. Therefore, following sphincterotomy, pancreatic stenting is crucial to prevent and/or decrease the severity of ERCP induced pancreatitis.

Endoscopic Transpapillary Stent Placement

The technique for placing pancreatic stents is similar to that used to place stents in the biliary tract. Once the pancreatic duct has been deeply cannulated, a hydrophilic 0.035″ guidewire is introduced into the duct and maneuvered if possible beyond the stricture or disruption. The stent is then introduced over the guidewire. Stents can be placed with or without pancreatic sphincterotomy. A sphincterotomy is usually preferred to facilitate drainage around the stent if it becomes clogged or dislodged, and to facilitate access in future procedures. Pancreatic stents are made primarily of polyethylene material. Pancreatic stent sizes range from 2 to 25 cm in length and 3 to 11.5 F in diameter [129] Choice of stent size depends on the caliber of the duct and the site of the disruption. Most of the pancreatic stents have side holes along their length to allow flow from side branches. In addition, most pancreatic stents have a mechanism (e.g., distal flange, pigtail) to prevent internal or external migration. If the there is a stricture in the pancreatic duct limiting the stent placement, the stricture can be dilated with a balloon or Soehendra dilator (5 or 8 F) to allow insertion.

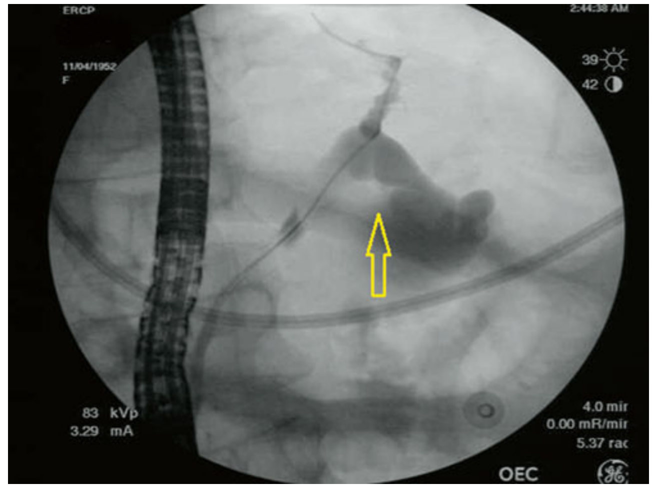

Fig. 5.17 Pancreatogram demonstrating wire extending across a partial pancreatic duct disruption. Extensive contrast extravasation is evident

Disconnected Pancreatic Duct Syndrome (DPDS)

Disconnected pancreatic duct syndrome (DPDS) is defined by complete discontinuity of the pancreatic duct such that a viable portion of the pancreas does not drain downstream into the duodenum [130] (Fig. 5.18). The severity of the syndrome depends on the location of the disruption. In cases where the disruption is in the head of the pancreas, the drainage of the entire pancreas is disturbed whereas disruptions in the tail affect a substantially smaller amount of pancreas. Patients may present with fluid collections, pancreatic ascites, pain and manifestations of exocrine and even endocrine insufficiency.

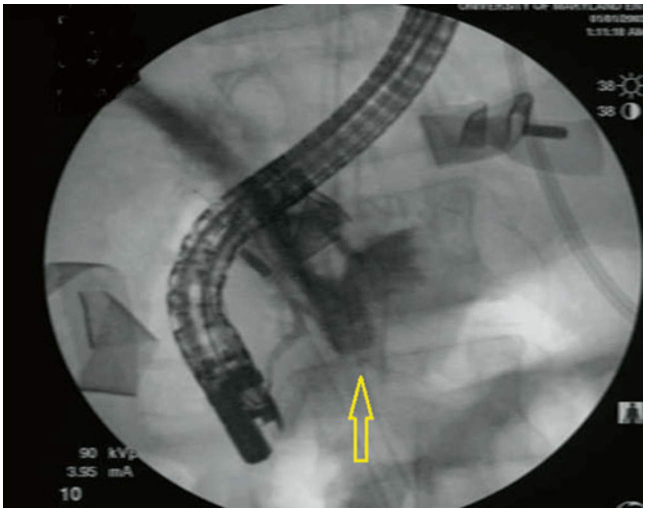

Fig. 5.18 Pancreatogram demonstrating complete disruption of the duct in the head with associated leak. Note the lack of filling of duct in the body and tail

Endoscopic Treatment

Transpapillary Stenting

Transpapillary stenting promotes drainage into the duodenum by decreasing the pressure gradient across the papilla [90, 117]. The predictors of success with this strategy depended largely on the degree of duct disruption and the ability to bridge the site of leak [120]. Because the disruption is complete in DPDS, transpapillary stenting is often unsuccessful [119]. In a study by Varadarajulu et al. of patients with complete disruption of the MPD who underwent insertion of a PD stent either to bridge the gap or into the collection, the outcome was successful in only 44 % and 26 % respectively [120]. The optimal duration of stent placement is unknown. Most endoscopists prefer stent removal and/or exchanges every 4–8 weeks [131]. A retrospective study of three patients by Telford et al. showed a longer duration of stent therapy ($P = 0.002$) was associated with a more successful outcome [118].

Transmural Drainage (EUS and Non-EUS Guided)

In DPDS, collections form from drainage of the disconnected segment of pancreas. Transmural drainage can indirectly drain the disconnected pancreatic segment into the gastrointestinal tract by forming a fistula between the collection and the stomach or small intestine. The decision to choose the trans-gastric or trans-duodenal approach is based on the relationship of the collection to the stomach or the duodenum. If the collection is amenable to either, then a trans-duodenal drainage is preferred because of the theoretic greater patency of the fistula after removing the stents [131]. Transmural stents are typically removed after resolution of the peripancreatic fluid collections. However, this approach has been associated with recurrence rates as high as 50 % [119, 126]. Leaving a stent permanently in place could prevent recurrence by creating a permanent fistula between the MPD and the gastrointestinal tract. In a study by Devière et al. of 13 patients with DPDS who underwent endoscopic transmural drainage, stents were left in place for a prolonged period, and no peripancreatic fluid collection recurred at a mean follow-up of 30 months [127]. A randomized control trail by Arvanitakis et al. also showed success with prolonged stent placement. None of the 15 patients in this trial developed recurrence of peripancreatic fluid collections when the stents were left in place compared with 5 of 13 patients in whom the stent was removed ($P = 0.013$) [132]. Stent occlusion of small caliber plastic stents is an obvious long-term concern. Placement of fully covered self-expandable metallic stents (e.g., Axios stents) for such forms of transmural drainage could be a more favorable alternative due to better patency rates. However, data regarding success of long term covered self-expandable metallic stents in this scenario is currently lacking.

Percutaneous Drainage

Ultrasound-guided or CT-guided percutaneous drainage of fluid collections is another option to indirectly drain a disconnected pancreatic segment. The major disadvantage of percutaneous drainage is the development of external pancreatico-cutaneous fistulae [133, 134].

Surgery

The two main surgical options for DPDS are: (1) reestablishment of drainage into the gastrointestinal tract (Roux-en-Y internal drainage by pancreaticojejunostomy, pancreaticogastrostomy, fistulojejunostomy, or cystojejunostomy) and (2) Resection of the disconnected segment (distal pancreatosplenectomy) [110].

Roux-en-Y internal drainage requires much less dissection and conserves the still functioning distal pancreas and the spleen. In a study by Howard et al. [135], a Roux-en-Y procedure was associated with a significant decrease in operative time, blood loss, transfusion requirement, and duration of hospital stay.

Trauma

Pancreatic injury is uncommon because the retroperitoneal location of the pancreas offers relative protection. However, the pancreas does overly the spine and blunt trauma can cause the pancreas to "break" as it smashes into the hard bony structure. These injuries classically involve the body of the pancreas. Common blunt injuries to the pancreas include crush injuries, seat belt injuries during motor vehicle collisions, handle-bar injuries from bicycle accidents and direct blows to the pancreas from assaults. Pancreatic injuries occur in approximately 5 % of patients with blunt abdominal trauma, and 8 % of patients with penetrating abdominal injuries [136, 137]. In the setting of blunt or penetrating trauma, pancreatic injuries may be suspected at the time of exploratory laparotomy. In these instances, intraoperative ERCP can provide valuable information to the surgeon contemplating the type of repair needed. More often, ductal injuries to the pancreas become evident postoperatively due to the accumulation of amylase rich fluids in the peritoneum, retroperitoneum or external drains. ERCP plays a crucial role in the diagnosis of the location and extent of the leak.

The American Association for the Surgery of Trauma (AAST) Organ Injury Scaling Committee has described a grading system that is widely used and can guide appropriate management [138].

Grades I injuries (Minor contusion or laceration without ductal injury) and Grade II injuries (Major contusion or laceration without ductal injury) are treated with nonoperative management techniques or simple drainage. Grade III injuries (Complete transection of distal pancreas or distal pancreatic parenchymal injury with pancreatic duct injury), Grade IV injuries (Proximal pancreatic transection or injury involving proximal duct or the ampulla), or Grade V injuries (Massive disruption involving the head of pancreas) often require resection with possible reconstruction and/or drainage procedures [139].

Endoscopic Treatment

Principles of endoscopic management of traumatic ductal injuries are similar to management of ductal disruptions described in previous sections. Early ERCP within a few days of the inciting trauma is essential to the potential success of endoscopic therapy. Endoscopic transpapillary drainage has been successfully used to heal duct disruptions in the early phase of pancreatic trauma and in the delayed phase to treat the complications of pancreatic duct injuries. However, in patients with type IV or V ductal injuries not amenable to transpapillary stents, morbidity and mortality greatly increase unless surgery is undertaken within the first 24 h. Most of the published experience in endoscopic treatment of pancreatic injury is in the form of case reports, and case series are retrospective and heterogeneous with small number of patients [115, 140, 141].

Pancreatic Strictures

Pancreatic strictures (Fig. 5.19a, b) are a common endpoint of various pancreatic injuries including chronic pancreatitis, acute pancreatitis, trauma, iatrogenic injuries from pancreatic stents and wires, and surgical anastomoses. Despite, the differing etiologies of pancreatic strictures, the presentation, evaluation and management are similar.

PD strictures typically present with pain and manifestations of exocrine insufficiency late in their course. CT can be helpful by showing ductal dilation upstream of the stricture. Depending on the cause of the stricture, parenchymal and ductal calcifications can also be seen. MRCP is very helpful in delineating the anatomy. Treatment is indicated in patients who are symptomatic. Asymptomatic pts do not necessarily require therapy.

Main pancreatic strictures should always be approached with suspicion since chronic pancreatitis patients have increased risk of pancreatic cancer. It is recommended that all pancreatic duct strictures be brushed for cytology. The absence of pancreatic calcifications, the presence of exocrine insufficiency and K-ras mutation on pancreatic duct brushing were identified as additional predictive factors for the development of pancreatic adenocarcinoma [142]. Physicians should have a low threshold to perform EUS to more closely examine the pancreatic parenchyma, with fine-needle aspiration of any areas felt to be suspicious for possible malignancy [36].

Symptomatic CP patients with a single MPD stricture located in the head of the pancreas are the ideal candidates for ERCP with pancreatic endotherapy while isolated strictures in the tail or multiple strictures with a chain of lake appearance are less amenable to endotherapy [143, 144]. A pancreatic sphincterotomy, by itself, is not effective for the treatment of pancreatic strictures. However, it facilitates instrumentation, drainage around stents, and access to the pancreatic duct during future treatment sessions. For isolated short PD strictures, dilation with a balloon is effective. (sizes 4–8 mm) For diffuse strictures, dilating catheters such as a Sohendra dilator are preferred (6–10 F). The size of dilation is dictated by the caliber of the stricture and the size of the remaining duct. Care must be taken not to overdilate a stricture and risk duct disruption. Following dilation therapy, stents that bridge the stricture are utilized. Typically, plastic stents are utilized with calibers ranging from 4 to 11.5 F. Size is again determined by caliber of the stricture and diameter of the remaining PD. Large-bore (8.5–11.5 F) stents have a longer patency [145]. Pain relief after single pancreatic stenting in chronic pancreatitis has been observed in 70–94 % of the patients [143, 146]. In the absence of early symptomatic improvement, stents should be removed [147]. If the stents are effective in improving symptoms, patients undergo serial pancreatic dilation and stenting procedures every 2–3 months for 6–24 months duration. It should be noted that pancreatic duct strictures often improve in their radiographic appearance, but rarely does the pancreatogram normalize. However, data suggest

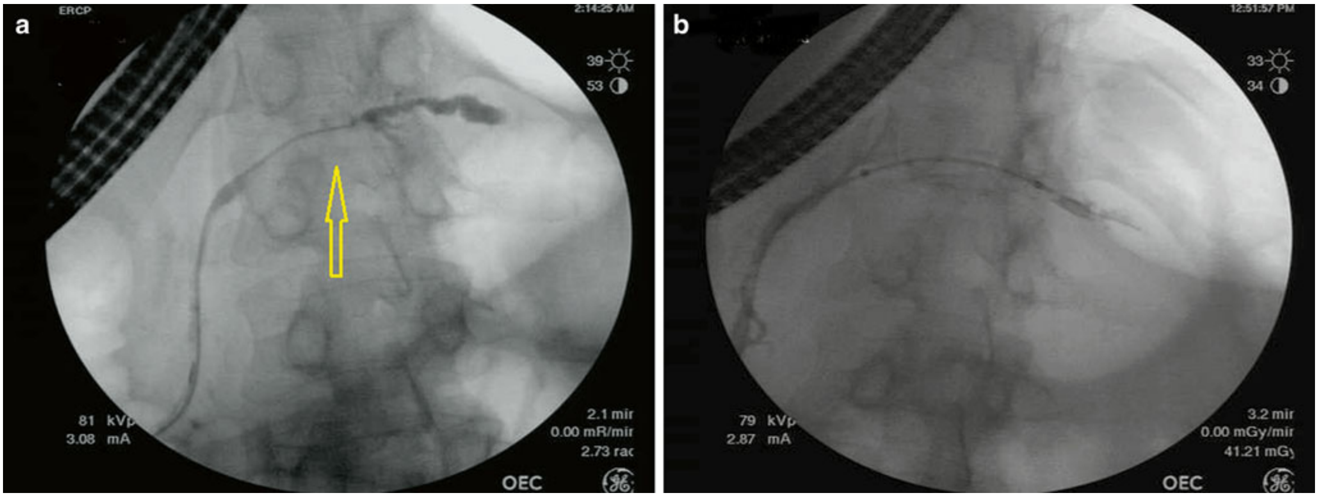

Fig. 5.19 (**a**) Pancreatogram showing stricture of the body of the pancreas that resulted from pancreatic trauma. Note the location of the stricture overlies the spine, a common spot for traumatic PD strictures. (**b**) Dilating balloon position across the PD stricture

that resolution of the stricture is not a prerequisite for symptomatic improvement since symptomatic improvement may persist after pancreatic stent removal despite persistence of the stricture [148]. After serial dilations and stenting sessions, a stent free trial should be considered. Recurrence of strictures requiring re-stenting was reported in 38 % of patients after 2 years follow-up [149]. The clinical results of pancreatic stenting are a good predictive factor for the outcome of drainage surgeries such as pancreaticojejunostomy.

Conclusions

Pancreatic and biliary injuries are commonly encountered by interventional endoscopists. A thorough understanding of the mechanisms of injury, pertinent anatomy, and patient presentation is vital for successful endotherapy. Patients with these injuries are often acutely ill and at risk for significant morbidity and mortality. ERCP can play a crucial role in treating these injuries and promoting patient recovery. Multidisciplinary approaches with surgeons and interventional radiologists are often necessary, especially in cases of complex injuries.

Video Legends

Video 5.1 Bile leak from the right intrahepatic bile system. The leak was treated with a biliary sphincterotomy and stent placement.

Video 5.2 Post liver transplant anastomotic stricture immediately distal to the bifurcation. The stricture was treated with balloon dilations and two traversing bile duct stents into the left and right hepatic ducts.

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