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## Management of Chronic Pancreatic Pseudocyst

### When to Observe, When and How to Drain?

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### Introduction

In the United States, acute pancreatitis is the third most common gastrointestinal disorder, requiring more than 275 000 hospitalizations annually [1]. Pancreatic pseudocysts are a well-known consequence of acute and chronic pancreatitis [2]. Pseudocysts develop in 6–34% of cases of pancreatitis, but only a proportion are symptomatic with many resolving spontaneously [3–5]. Endoscopic drainage has become the standard of care at many centers, with similar efficacy, shorter length of hospital stay, fewer adverse events, better physical and mental well-being, and inexpensive compared to surgical cystogastrostomy [6,7]. This chapter highlights the strategies for management of pancreatic pseudocysts. It provides background into the current definition and the indications for and timing of intervention, and describes the various drainage techniques, adverse events, and postprocedure management.

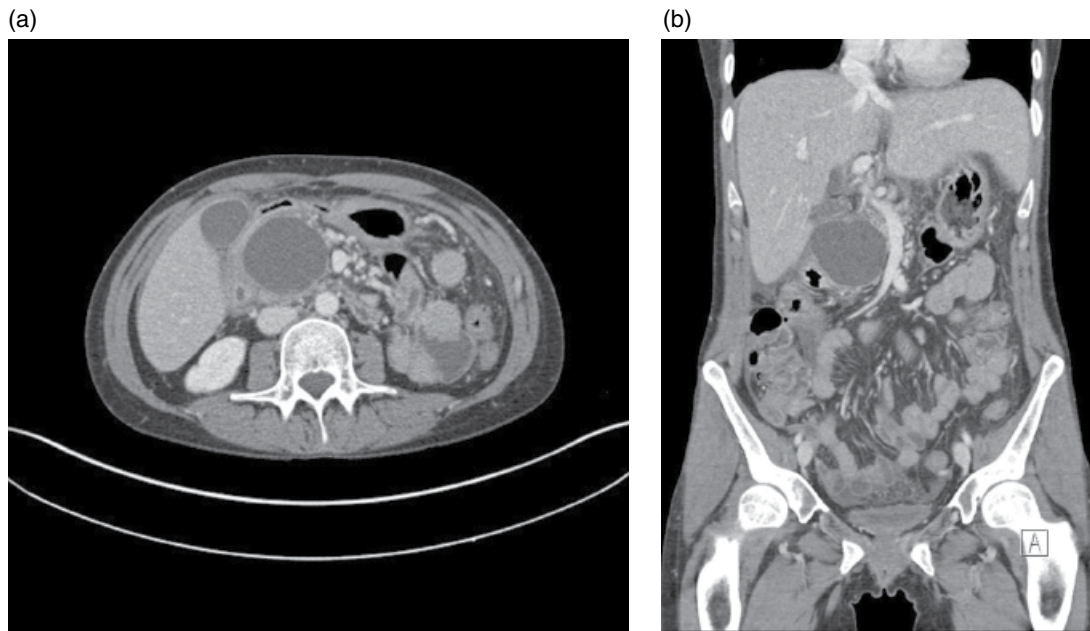
### Definition of Pseudocyst

The revised Atlanta classification system [8] defines an acute fluid collection with no necrosis and without a well-defined wall, developing within the first four weeks of interstitial edematous pancreatitis, as an acute peripancreatic fluid collection. This acute fluid collection can mature into a pseudocyst, generally after four weeks (Figure 40.1). Distinction of a pseudocyst from walled-off necrosis (WON) is important as the treatment outcome varies. While the majority of pseudocysts can be treated successfully by endoscopic transmural drainage alone in a single treatment session, WON requires multiple treatment sessions that may include endoscopic necrosectomy or

adjuvant interventions such as percutaneous drain placement or video-assisted retroperitoneal debridement [9]. The most common initial imaging modality for evaluation of a pancreatic fluid collection (PFC) is contrast-enhanced computed tomography (CT) of the abdomen, because it is readily available, relatively inexpensive, and can determine the presence of necrosis. Magnetic resonance imaging (MRI) may be more sensitive for characterizing the contents in a PFC and in determining pancreatic ductal integrity [10].

### When to Observe or Drain

Drainage is indicated only for patients who are symptomatic, have rapidly enlarging pseudocysts, or have systemic illness as a result of an infected pseudocyst that does not improve with medical management [11]. If patients meet criteria for drainage, the next question is the timing of intervention. Within the first four weeks after an attack of pancreatitis, the wall of the PFC is immature and so treatment should be temporized if possible [12,13], with analgesics, enteral nutrition, and antibiotics when indicated. The most common reason for failure of conservative measures during this early period is infection, which can be managed by placement of a percutaneous drainage catheter. Occasionally, smaller-sized fluid collections can be treated by placement of a transpapillary stent at endoscopic retrograde cholangiopancreatography (ERCP) if a ductal leak is evident on pancreatogram [14]. Beyond the three- to four-week period, most immature PFCs become encapsulated and prime for endoscopic drainage provided they are adherent or adjacent to the wall of the stomach or duodenum.



**Figure 40.1** CT of the abdomen on (a) anteroposterior and (b) coronal views revealing a large fluid-filled pseudocyst with no surrounding necrosis or peripancreatic inflammation. *Source:* courtesy of Shyam Varadarajulu.

### Important Preprocedure Considerations

Prior to embarking on an intervention, clinical history, cross-sectional imaging studies, and laboratory results should be reviewed, and a thorough endoscopic ultrasound (EUS) examination of the pancreas should be undertaken to confirm appropriateness of indication and to optimize safety. The international normalized ratio and platelet counts should be corrected if abnormal to, respectively, less than 1.5 and above  $50 \times 10^9/l$  [15]. Perioperative management of anticoagulant and antiplatelet agents are similar to that for other high-risk endoscopic procedures, such as mucosal resection and biliary sphincterotomy [16]. The procedure is usually performed with the patient under general anesthesia to minimize the risk of aspiration [17]. Prophylactic broad-spectrum antibiotics are administered to minimize the risk of infection [18]; we recommend administration of a one-time dose of ciprofloxacin 400 mg intravenously before the procedure and continue oral antibiotics for three to five days [19]. On cross-sectional imaging studies, assessing the relationship of the pseudocyst to the gastrointestinal lumen, the presence and location of collateral vasculature, and assessing from where in the pancreas the collection arises identifies potential areas for endoscopic drainage. An immature pseudocyst wall is thin and poorly adherent to the gastrointestinal lumen, and drainage should be avoided to minimize the risk of perforation. Excluding vasculature between the EUS transducer and pseudocyst reduces the possibility of bleeding; also, it

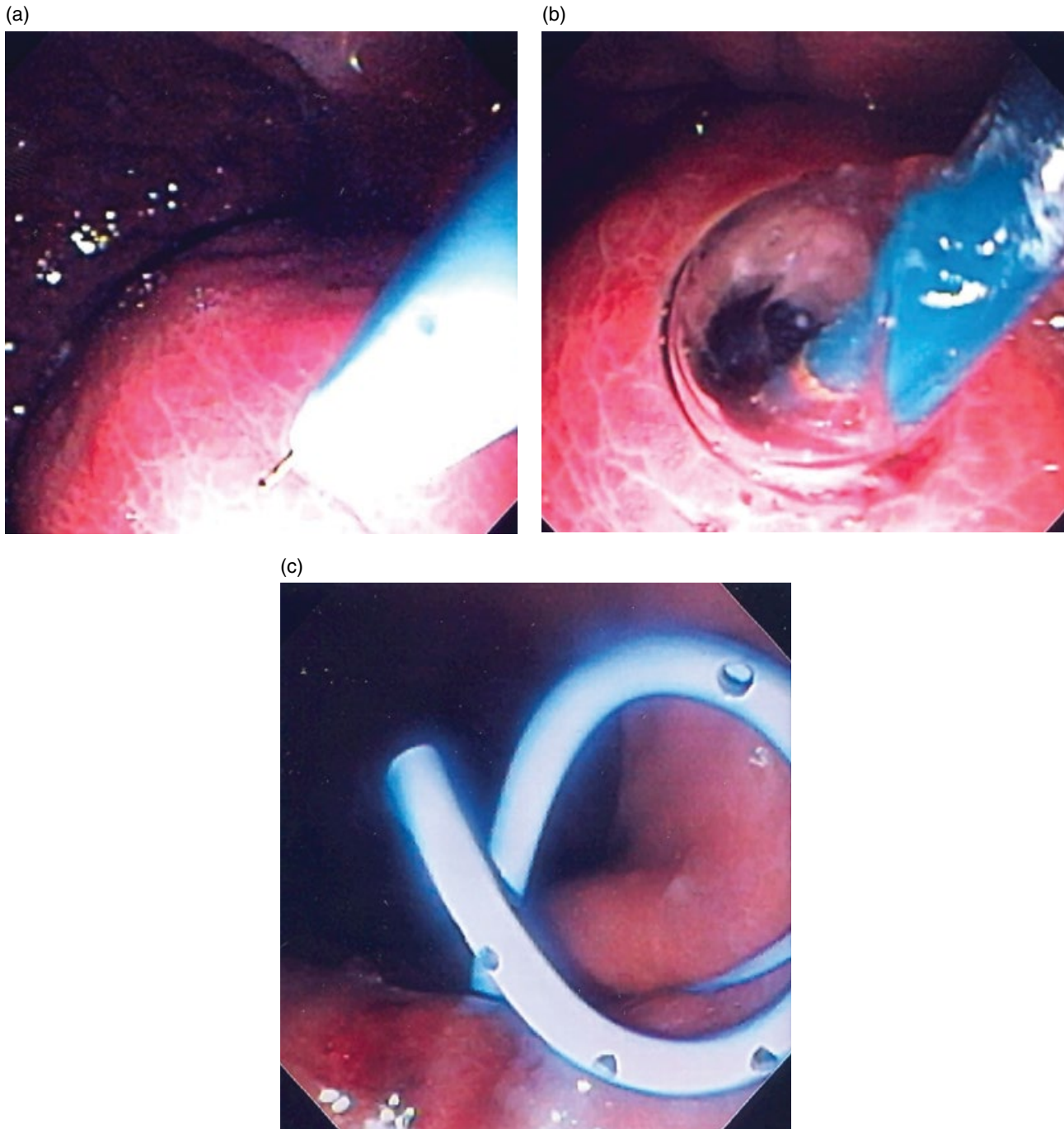
is important to access the pseudocyst from a vantage point that is as close to the transducer as possible, preferably less than 10 mm, to minimize the risk of perforation or leakage. Some pseudocysts may extend to the lower abdomen or pelvis and may require dual-modality (endoscopic plus percutaneous) drainage to achieve treatment success. Finally, cystic pancreatic neoplasms, duplication cysts, and solid necrotic tumors can mimic a pseudocyst on cross-sectional imaging, and therefore need to be excluded by EUS. Pseudocysts may also develop secondary to an underlying solid pancreatic neoplasm or intraductal papillary mucinous neoplasm [20,21]; these diseases may require adjunctive therapy, and a diagnosis and treatment plan should be made prospectively where possible.

### Procedural Technique: How to Drain

Pseudocysts can be drained under EUS guidance or by using a forward- or side-viewing endoscope without EUS, which is termed conventional transmural drainage (CTD).

#### Conventional Transmural Drainage

CTD is safe and effective technique to perform in the presence of a visible endoscopic bulge and no obvious vasculature at the point of needle entry. In a prospective comparative study of 99 patients, in which those with bulging pseudocysts had CTD and those without underwent EUS-guided transmural drainage, there was no significant



**Figure 40.2** Conventional transmural drainage of a pancreatic pseudocyst as demonstrated by access via (a) needle-knife cautery, (b) transmural dilation, and (c) plastic stent placement. *Source:* courtesy of Shyam Varadarajulu.

difference in rates of treatment success and adverse events [22]. Two prospective randomized trials of EUS versus CTD determined equivalency for bulging pseudocysts, but EUS was required for those without a visible bulge because access by conventional drainage was not feasible [19,23]. Also, smaller pseudocysts and those located in the tail of the pancreas require EUS guidance for drainage because they rarely cause luminal compression [20]. CTD

is performed with either a forward-viewing therapeutic endoscope or a side-viewing duodenoscope (Figure 40.2). The point of entry is chosen visually over the endoscopic bulge and the pseudocyst is entered by using a needle-knife catheter. Once successful cyst entry is visually confirmed, either by drainage of cyst contents into the gastrointestinal lumen or by cyst aspiration via the catheter, a guidewire is coiled within the pseudocyst cavity. The transmural tract is

then dilated to 10–15 mm using balloon catheters and one or two double-pigtail plastic endoprotheses are deployed. The main advantages of CTD include the larger working channel diameter of a therapeutic gastroscope or duodenoscope, increased suction capacity, increased endoscope flexibility, and better endoscopic visualization than when using an echoendoscope.

### EUS-guided Drainage

EUS provides visualization and access to the pseudocyst even in the absence of a visible endoscopic bulge. Additionally, the ability to perform the entire procedure under real-time sonographic guidance improves the technical success and safety profile of the technique. There are two methods currently being adopted for EUS-guided pseudocyst drainage: the multistep technique using plastic stents and the single-step technique using lumen-apposing metal stents (LAMS).

#### Multistep Technique Using Plastic Stents

##### **Step I: Access**

Under EUS guidance, a 19-gauge FNA needle is used to puncture the pseudocyst wall. Suction is applied to sample the fluid to exclude infection (cultures, Gram stain) and for confirmation of diagnosis (tumor markers, cytology, chemistry). A 0.025- or 0.035-inch (0.635 or 0.889 mm) guidewire is passed through the needle and coiled within the cyst cavity. Minimal endoscopic visualization is used with EUS, and fluoroscopy guidance aids in assessing the length, direction, and coiling of the wire within the cyst cavity.

**Step II: Transmural Tract Dilatation** Initial transmural tract dilation is performed mechanically or with the aid of electrocautery. Graded dilation (without cautery) requires use of ERCP cannulas to sequentially enlarge the tract to between 4.5 and 10 Fr, until it is wide enough for passage of a dilating balloon. Tract dilation with electrocautery uses either a needle-knife catheter or a 6–10 Fr cystotome. After initial tract dilation, further dilation to between 6 and 15 mm is performed using radial dilation balloons. While the effect of larger balloon inflation on drainage efficacy or adverse events has not been formally studied, pseudocysts in general do not require dilation above 10 mm.

**Step III: Stent Placement** Given the thin density of cyst contents, pseudocyst drainage can usually be accomplished by placement of one or more 7 or 10 Fr double-pigtail plastic stents through a single transmural tract (Figure 40.3). In a study of 117 patients who underwent EUS-guided drainage of uncomplicated pseudocysts by using plastic stents, the overall treatment success rate was 98.3%. One intervention was required by 87.2% of patients, 11.1%

required more than one intervention, and 1.7% failed treatment [24]. The median number of interventions required for treatment success was similar in patients receiving 7 or 10 Fr stents, and in those having one stent or more than one stent. On multivariate analysis, the size and number of stents were not associated with the number of interventions required for treatment success when adjusted for pseudocyst size, location, drainage modality, presence or absence of pancreatic duct stent insertion, and luminal compression.

#### Single-step Technique Using LAMS

There has been growing interest in placing LAMS for pseudocyst drainage as the technique is much easier than the placement of multiple plastic stents. LAMS are fully covered with a wide lumen (8–16 mm diameter) to expedite the drainage of cyst contents and possess bilateral flanges at both ends to minimize the risk of stent migration. LAMS can be equipped with or without an electrocautery-enhanced delivery system.

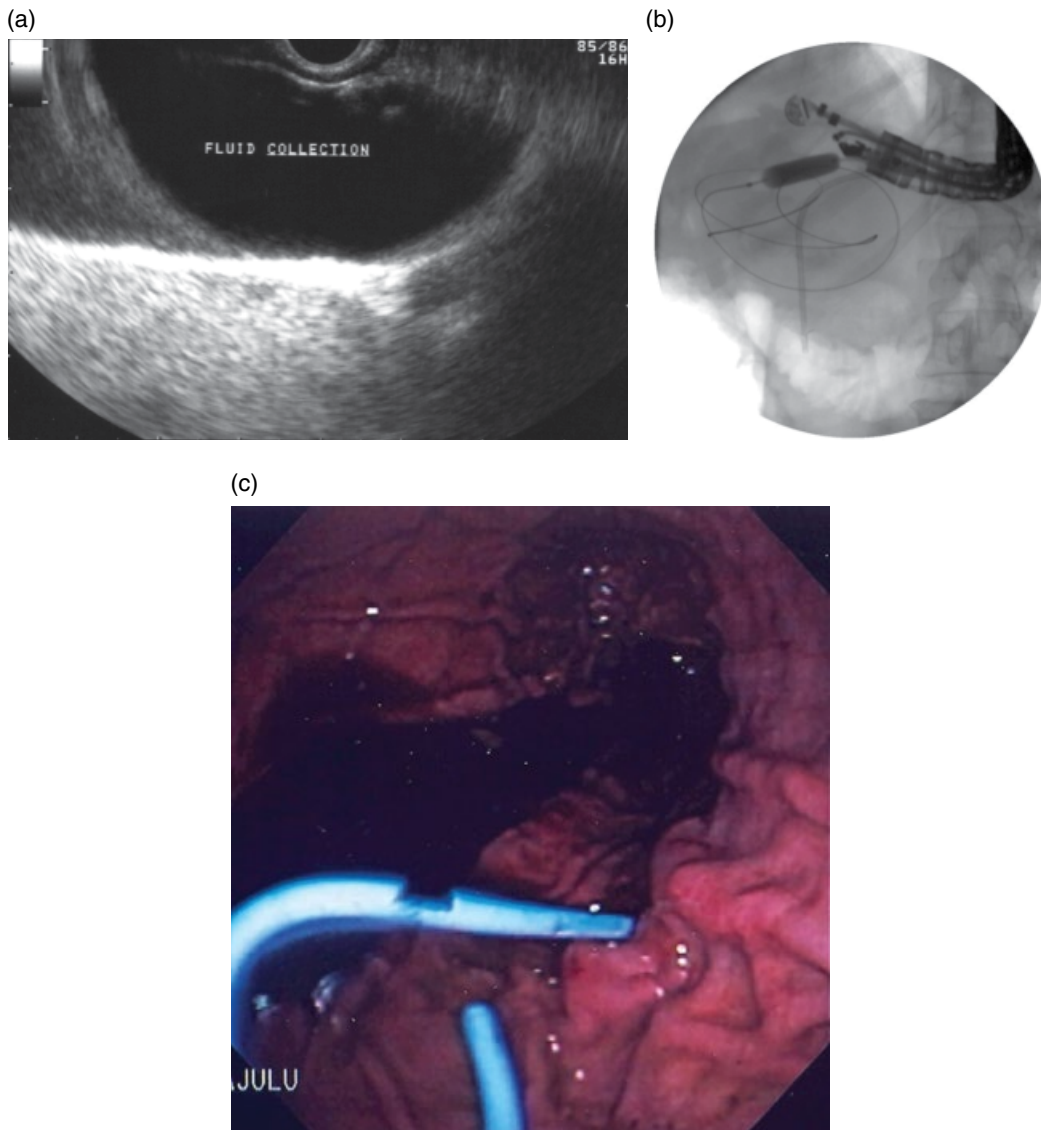
**Non-electrocautery-enhanced Delivery System** The pseudocyst is punctured under endosonographic guidance using a 19-gauge FNA needle, followed by insertion of a guidewire through the needle, which is looped inside the cavity. The transmural tract is then sequentially dilated over the guidewire using first an ERCP cannula, needle-knife catheter, or a cystotome, followed by a 4–6 mm dilating balloon. LAMS on a delivery system is then inserted over the guidewire into the pseudocyst cavity. The distal flange is deployed first under endosonographic guidance, followed by deployment of the proximal flange under either endosonographic or endoscopic view.

**Electrocautery-enhanced Delivery System** The pseudocyst is directly punctured using the electrocautery-enhanced tip of the stent delivery system under endosonographic guidance, without the need for a guidewire. The delivery system is then advanced into the PFC and the distal flange is deployed first under endosonographic guidance, followed by deployment of the proximal flange under endosonographic or endoscopic view (Figure 40.4).

### Special Considerations

#### Disconnected Pancreatic Duct Syndrome

Disconnected pancreatic duct syndrome (DPDS) is defined as the complete disruption of the main pancreatic duct with resultant disconnection of the viable upstream distal pancreatic gland from the main pancreatic duct downstream. Consequently, a symptomatic pseudocyst can form in the disconnected gland. Transmural pseudocyst drainage allows the disconnected pancreatic segment to drain via an enteral



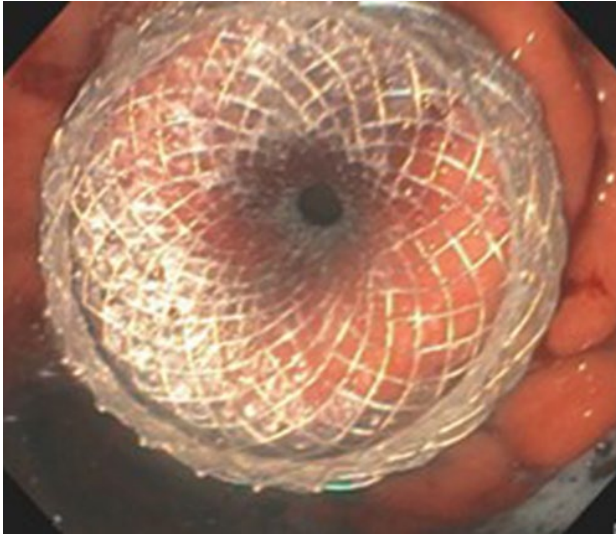
**Figure 40.3** EUS-guided drainage of a pancreatic pseudocyst as demonstrated by anechoic fluid collection without debris (a), followed by passage of a guidewire and transmurals balloon dilation (b) and placement of the first 7 Fr double-pigtail plastic stent. *Source:* courtesy of Shyam Varadarajulu.

bypass into the gastrointestinal lumen. In a randomized controlled trial of 46 patients who had successful transmural drainage, stent retrieval was associated with higher recurrence rates compared with leaving the transmural stents *in situ* (38.4% vs. 0%) [25]. This suggests that the transmural stents serve as a conduit between the disrupted pancreatic duct and the digestive tract, even after the pseudocyst has resolved. We therefore recommend the placement of indwelling plastic stents for pseudocyst drainage to minimize the chances of long-term recurrence.

#### Ductal Communication with Pseudocyst

If the pseudocyst communicates with the main pancreatic duct, an endoprosthesis can be placed through the major or minor papilla, creating a path of least resistance, to facilitate

drainage of secretions through the papillary orifice (Figure 40.5). Current evidence suggests that transpapillary drainage alone is safe and effective for communicating small pseudocysts that measure less than 6 cm and has best results if the ductal disruption is partial and is bridged by the endoprosthesis [26]. The optimal duration of pancreatic stenting is unclear, because shorter duration is associated with non-healing of the ductal injury and thus increased risk of recurrences, whereas longer duration of stenting is associated with stent dysfunction and stent-induced ductal strictures. An additional consideration is the risk of pseudocyst superinfection with transpapillary stenting. A suggested approach involves placement of a bridging stent if a leak is identified, in addition to transmural stenting [14]. Ductal stenting is not indicated if the pancreatic duct is intact or in the



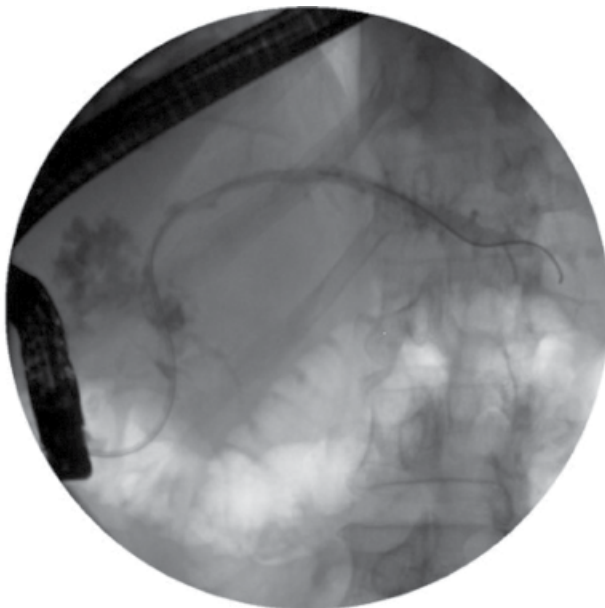
**Figure 40.4** Endoscopic view of a lumen-apposing metal stent when deployed via the stomach for pseudocyst drainage. *Source:* courtesy of Shyam Varadarajulu.

presence of DPDS with no communication between the downstream pancreatic duct and pseudocyst.

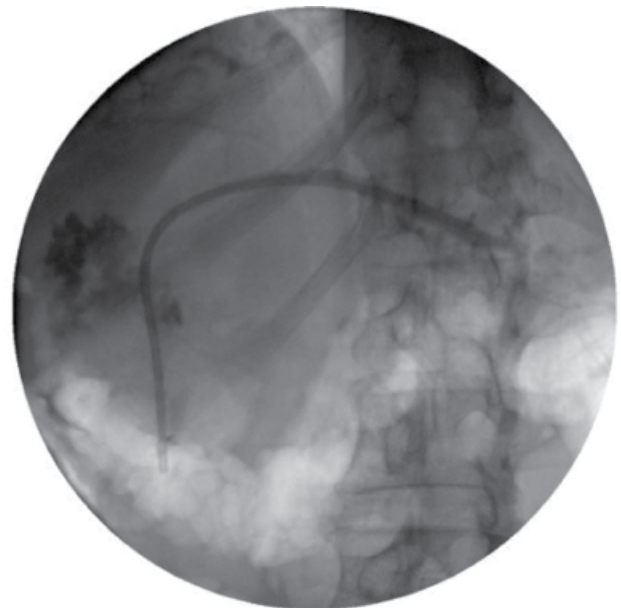
#### Multiple Pseudocysts

Multiple large pseudocysts may be drained concurrently to minimize the possibility of superinfection. Additionally, if the cysts are large and located in the lower abdomen or pelvis without endoscopic access, then placement of adjunctive percutaneous drainage catheters must be considered to expedite treatment and recovery time.

(a)



(b)



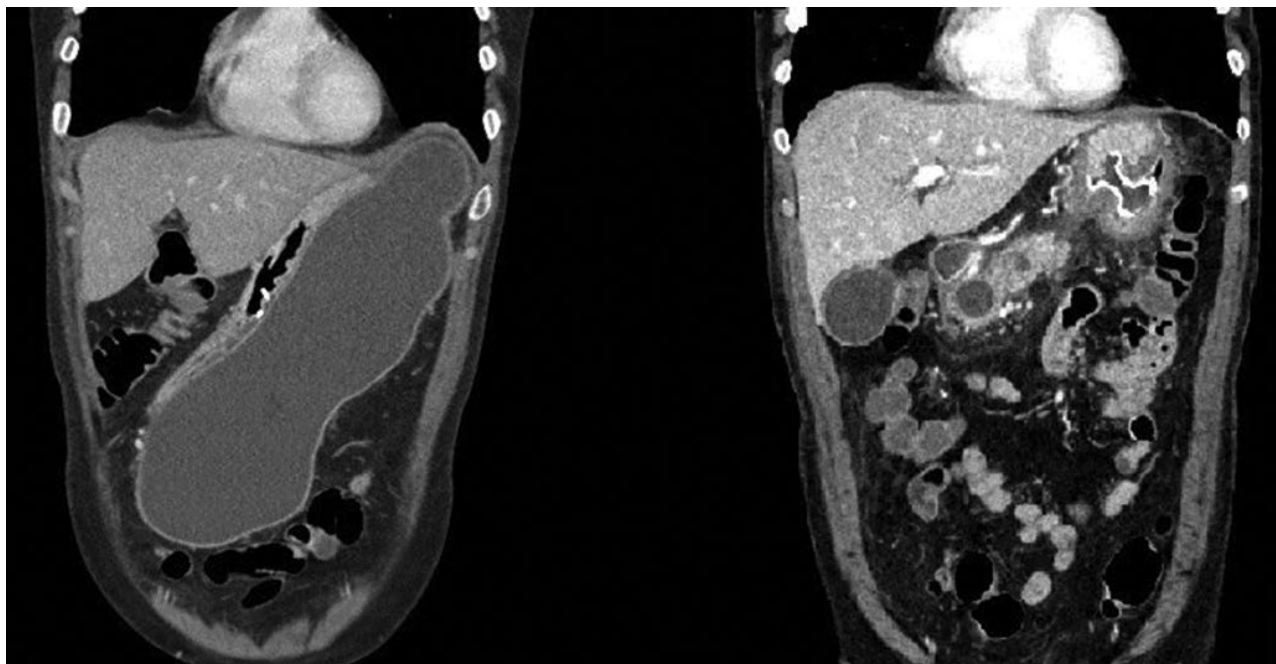
**Figure 40.5** Pancreatogram revealing a ductal leak (a) that is managed by transpapillary bridging stent placement (b). *Source:* courtesy of Shyam Varadarajulu.

## Postprocedure Care

Enteral nutrition should be initiated for patients with ongoing pancreatic inflammation, particularly in those with persistent anorexia, loss of weight, abdominal pain, or pyloric or duodenal stenosis after decompression [27]. A low-fat diet may be suitable in patients with minimal residual pancreatitis-related or pseudocyst-related symptoms. Cross-sectional imaging of the abdomen is obtained, at six to eight weeks in patients treated with plastic stents or at three to four weeks in patients treated with LAMS, to evaluate treatment response (Figure 40.6). If the collection has reduced to less than 2–3 cm, and the main pancreatic duct is intact, the transmural stents may be removed; in patients with DPDS, indwelling transmural plastic stents have been shown to decrease the rates of PFC recurrence [25].

## Adverse Events

The reported rate of adverse events for pseudocyst drainage is between 2.5 and 20%. These adverse events include bleeding, perforation, pseudocyst superinfection, and stent erosion, migration, and obstruction [28–30]. Bleeding at the transmural entry site can occur from inadvertent puncture through vessels or during transmural tract dilation. If the bleeding does not self-resolve or is large volume, the dilating balloon can be reinflated temporarily to tamponade the bleeding site or a metal stent may be placed for sustained tamponade. The sudden



**Figure 40.6** Preprocedure (*left*) and post-intervention (*right*) CT revealing a large 28 × 7 cm pseudocyst that resolved following lumen-apposing metal stent placement at three-week follow-up. *Source:* courtesy of Shyam Varadarajulu.

reduction in intracystic pressure on pseudocyst decompression can lead to bleeding from a friable vessel or pseudoaneurysm within the pseudocyst. Prospective studies have shown the occurrence of delayed bleeding if LAMS are not removed in a timely manner: we recommend their removal in three to four weeks after confirmation of pseudocyst resolution on follow-up CT [31]. The consequences of pseudocyst superinfection can be severe, and the risk must be limited through maximizing drainage and irrigation, particularly when the cavity contains debris. Free perforation can occur into the retroperitoneal or peritoneal space, and the risk is highest for poorly adherent collections. Management (surgery vs. endoscopy) depends on the estimated degree of peritoneal soiling and whether the pseudocyst has completely separated from the stomach.

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Air embolization is a rare but fatal adverse event, likely occurring secondary to a pressure gradient in an exposed uncompressed vein, and therefore procedures should ideally be performed with carbon dioxide insufflation to reduce the incidence and outcome severity.

## Conclusions

Endoscopic management is highly effective in the management of pancreatic pseudocysts and is therefore the current standard of care. However, outcomes are reliant on correct patient selection, procedural indication, risk stratification and, most importantly, a multidisciplinary team approach.

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