GUIDELINES

Guidelines for endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections

Recommendations of the Endoscopic Surgery Section of the Association of Polish Surgeons, the Endoscopy Section of the Polish Society of Gastroenterology, the Polish Pancreatic Club, the Laparoscopic and Robotic Surgery Section of the Association of Polish Surgeons, and the Pancreatic Surgery Section of the Association of Polish Surgeons; formulated by an expert panel led by Prof. Mateusz Jagielski, MD, PhD

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KEY WORDS

acute pancreatitis, drainage, endoscopy, endotherapy, minimally-invasive treatment, pancreatic fluid collections

ABSTRACT

This document presents a comprehensive overview of the management of postinflammatory pancreatic and peripancreatic fluid collections, with a particular emphasis on endoscopic treatment, developed by a team of experts based on the latest clinical and scientific evidence. The guidelines present a detailed scheme of treatment of patients with local complications of acute pancreatitis in the form of postinflammatory pancreatic and peripancreatic fluid collections.

List of abbreviations

ACS – abdominal compartment syndrome
ANC – acute necrotic collection
AP – acute pancreatitis
APFC – acute peripancreatic fluid collection
BFMS – biflanged metal stent
CEA – carcinoembryonic antigen
CECT – contrast-enhanced computed tomography
CP – chronic pancreatitis
CT – computed tomography
DPDS – disconnected pancreatic duct syndrome
ERCP – endoscopic retrograde cholangiopancreatography
Endo-VAC – endoluminal vacuum-assisted closure
EUS – endoscopic ultrasound
IAP – intra-abdominal pressure
ICU – intensive care unit
LAMS – lumen-apposing metal stent
MARPN – minimal-access retroperitoneal pancreatic necrosectomy
MIRPN – minimally-invasive retroperitoneal pancreatic necrosectomy
MRCP – magnetic resonance cholangiopancreatography
MRI – magnetic resonance imaging
MTGT – multiple transluminal gateway technique
NOTES – natural orifice transluminal endoscopic surgery
PEN – percutaneous endoscopic necrosectomy
PP – pancreatic pseudocyst
PPI – proton pump inhibitor
SGT – single transluminal gateway technique
SGTMD – single transluminal gateway transcystic multiple drainage
SIRS – systemic inflammatory response syndrome
USG – ultrasonography
VARD – video-assisted retroperitoneal debridement
WOPN – walled-off pancreatic necrosis

INTRODUCTION Acute pancreatitis (AP) is an inflammatory disease of the pancreas characterized by progressive involvement of both the peripancreatic tissues and distant organs.[1-8] Pathogenetically, premature activation of pancreatic proenzymes induces gland damage via autodigestion, triggering an inflammatory response, thereby resulting in AP.[8-10]

AP is the most common pancreatic and acute gastroenterological condition. It requires hospitalization, and is a major clinical challenge for physicians across specialties.[6-9,11] The incidence of AP-related intensive care unit (ICU) admissions has been steadily rising globally, with a consequent increase in hospitalization and treatment costs.[8,12-15] An analysis of Polish epidemiological studies, few in number as compared with other countries, indicates that Poland has the highest AP incidence in the world (64.4–99.96/100 000/year vs 33.74/100 000/year worldwide).[12-19]

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Currently, the diagnostic and treatment approaches for AP follow the 2012 revised Atlanta classification, an international and interdisciplinary consensus that additionally standardizes AP-related definitions.[1-3] Accordingly, for a diagnosis of AP, 2 of the 3 following criteria must be met: characteristic epigastric pain radiating to the back, serum enzymatic activity levels at least thrice the upper limit of normal, and imaging findings characteristic of AP.[1-3] Based on severity, AP is classified into 3 categories: mild, moderate, and severe, depending on the presence of new-onset organ failure (determined using a modified Marshall scale) and the duration of organ failure during the disease course.[1-3] Based on the disease severity, as assessed via radiological imaging studies, most commonly multiphasic abdominal contrast-enhanced computed tomography (CECT), AP can be categorized as interstitial edematous or necrotizing pancreatitis.

The clinical course of AP is difficult to predict. Interstitial edematous pancreatitis is associated with a mild-to-moderate clinical course, while necrotizing pancreatitis usually has a severe clinical course.[1-3] The incidence of complications and sequelae of AP, as well as its mortality, vary according to the disease severity. In mild AP, the mortality is approximately 1%. In severe AP, the mortality ranges from 10% (for sterile necrotic collections) to 80% in infected necrotic collections with features of multiple organ failure consequent to septic shock,[6,8,9,11,15,17,20-28] highlighting that AP has a high risk of mortality.

Fundamentally, the management of AP, especially in the early phase (defined as the first week after the disease onset), involves conservative treatment: moderate intravenous fluid resuscitation, analgesics, and nutritional therapy.[1-3,7-9,28-35] Most AP episodes are characterized by mild clinical presentation and are usually self-limiting, with symptoms improving after conservative treatment within the first 48 hours of hospitalization.[1-3,7-9,28-35] Moderate and severe forms of AP are less frequent (occurring in approximately 15%–20% of cases), albeit being associated with significantly more complications and higher mortality rates.[1-3,6-9,11,15,17,20-35]

Diagnostic and therapeutic strategies for patients with AP have undergone significant changes over the last 3 decades. Despite the copious literature on this topic, some aspects related to AP treatment remain debatable and require systematization. Most patients with moderate-to-severe AP require a multidisciplinary approach, namely, cooperation between an anesthesiologist, surgeon, gastroenterologist, and radiologist, which increases the patient's likelihood of recovery. Consequently, they need to be admitted specialized centers facilitating multidisciplinary interspecialist cooperation.

Notwithstanding the development of modern treatment techniques, the implementation of new technologies in daily clinical practice must be reviewed and standardized. The contentious aspects pertaining to the treatment for patients with local complications of AP need systematization. Accordingly, these guidelines aimed to establish standards and provide evidence-based recommendations for endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections.

METHODS The guideline formulation process was developed by Professor Mateusz Jagielski, the first author and chairman of the expert panel.

Preparation of the guidelines involved a thorough analysis of the literature on the treatment of pancreatic and peripancreatic fluid collections related to AP. The summary was prepared following a comprehensive review of all studies published as of December 31, 2024. The main objective was to compile a current body of knowledge and establish a diagnostic and therapeutic regimen for postinflammatory pancreatic and peripancreatic fluid collections, with special emphasis on endoscopic techniques.

The Delphi method was adopted for the evaluation of evidence and recommendation strength. It is a group decision-making technique in which a consensus is reached based on the knowledge, experience, and opinions of field experts. A structured approach is used to reach consensus based on the results of a series of surveys among the experts.

The recommendations were based on a review of the literature indexed in the PubMed, Medline, and Cochrane Library databases (from inception to December 31, 2024), mainly focusing on systematic reviews, clinical recommendations from recognized scientific societies, and monographs. The strength (level) of scientific evidence was assessed based on the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) criteria.[36,37]

Recommendation formulation process The recommendations were formulated in a directive form and evaluated using the Delphi method.[38,39] A summary of the most important recommendations is presented in **TABLE 1**, while a list of all 54 recommendations is provided in **TABLE 2**. The recommendations were reviewed by an expert panel using the following acceptance scale: 1) 3 points, strong acceptance; 2) 2 points, acceptance with some reservations; 3) 1 point, acceptance with serious reservations; and 4) 0 points, rejection.

The recommendations with an average acceptance rate greater than 2 points were considered "strong," those with a score of 1–2 were considered "weak," while those with an average acceptance rate below 1 were rejected. Thus, the strength of a recommendation was based on the degree of expert consensus regarding the strength of the evidence (**TABLE 3**). A "strong" recommendation meant that the patient would benefit from the indicated treatment, and that the recommendation should be followed whenever possible. A "weak" recommendation meant that the patient may benefit from the indicated treatment, and the recommendation should

TABLE 1 Main recommendations

1. Treatment (both conservative and, in the case of no improvement, interventional) of postinflammatory pancreatic and peripancreatic fluid collections is indicated only in patients with collection-related clinical symptoms.
2. Interventional treatment of symptomatic postinflammatory pancreatic and peripancreatic fluid collections should be deferred until collection encapsulation, and in the collections due to necrotizing AP, until collection content liquefaction, which usually occurs 4 weeks after the disease onset.
3. For early symptomatic fluid collections developing during the first 4 weeks of pancreatitis, the recommended management is watchful waiting, possibly with conservative treatment.
4. For symptomatic postinflammatory pancreatic and peripancreatic fluid collections demonstrating no clinical improvement following conservative treatment, interventional treatment should be initiated using minimally-invasive techniques that facilitate access to the fluid collections via a transmural, transpapillary, extraperitoneal, or transperitoneal route. Surgery remains the treatment of choice only if minimally-invasive methods prove ineffective.
5. Regardless of the access route to the collection, the cornerstone of treatment of postinflammatory pancreatic and peripancreatic fluid collections is the establishment of an effective drainage system.
6. The mainstay of endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections is EUS-guided transmural drainage.
7. For WOPN collections, stepping up of the endoscopic treatment via endoscopic necrosectomy may be required.
8. In patients with postinflammatory pancreatic and peripancreatic fluid collections presenting with no clinical improvement, an additional access route to the collection using other interventional treatment techniques may be necessary in addition to endoscopic treatment intensification.
9. Endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections can be terminated after treatment success is acknowledged, at which time, the transmural/transpapillary stents can be removed, and the transmural/transpapillary endoscopic drainage can be completed.
10. Most complications of postinflammatory pancreatic and peripancreatic fluid collection endotherapy can be successfully treated using conservative or endoscopic means. However, in some cases, especially in hemorrhagic complications, interventional radiology or vascular surgery techniques, or conventional surgical treatment may be necessary, depending on the experience of the treating center.
11. If treatment of postinflammatory pancreatic and peripancreatic fluid collections fails despite intensified interventional treatment using minimally-invasive techniques, surgical treatment remains the treatment of choice.
12. For recurrent postinflammatory pancreatic and peripancreatic fluid collections, endoscopic treatment may be repeated postendotherapy.

Abbreviations: AP, acute pancreatitis; EUS, endoscopic ultrasound; WOPN, walled-off pancreatic necrosis

TABLE 2 A summary of all recommendations (continued on the next page)

Postinflammatory pancreatic and peripancreatic fluid collections
1. Postinflammatory pancreatic and peripancreatic fluid collections comprise 4 types, each differing by the type of pancreatitis and the time elapsed since the onset of pancreatitis symptoms: i) APFC; ii) ANC; iii) PP; iv) WOPN. Any of the aforementioned collections can be either sterile or infected.
2. Fluid collections that develop during the first 4 weeks of interstitial edematous pancreatitis are termed APFCs; collections persisting >4 weeks after pancreatitis onset are termed PPs.
3. Fluid collections that develop during the first 4 weeks of necrotizing pancreatitis are termed ANCs; collections persisting >4 weeks after pancreatitis onset are termed WOPN.
Asymptomatic pancreatic and peripancreatic fluid collections
4. For asymptomatic postinflammatory pancreatic and peripancreatic fluid collections, outpatient follow-up involving clinical evaluation with regular abdominal imaging (multiphasic CECT or MRI) should be performed at 3, 6, 12, and 24 months postdischarge or when clinical signs of collections are observed.
5. If asymptomatic collection persists beyond 24 months, interventional treatment should be considered, with the decision-making process including a detailed discussion with the patient regarding the benefits and risks of the procedure.
Indications for the treatment of postinflammatory pancreatic and peripancreatic fluid collections
6. Treatment (both conservative and, in the case of no improvement, interventional) of postinflammatory pancreatic and peripancreatic fluid collections is indicated only in patients with collection-related clinical symptoms.
7. An exception to the aforementioned recommendation is when the asymptomatic postinflammatory pancreatic and peripancreatic fluid collections compress large visceral (especially venous) vessels, which is associated with a high risk of thrombosis, development of collateral circulation, and secondary bleeding. In such cases, patients are eligible for treatment despite the absence of collection-related clinical symptoms.
8. Interventional treatment of symptomatic postinflammatory pancreatic and peripancreatic fluid collections should be deferred until collection encapsulation, and in the collections due to necrotizing AP, until collection content liquefaction, which usually occurs 4 weeks after the onset of the disease.
Early postinflammatory pancreatic and peripancreatic fluid collections
9. Early postinflammatory pancreatic and peripancreatic fluid collections (ANCs and APFCs) usually require no treatment owing to a lack of clinical symptoms and spontaneous regression of most of these lesions.
10. For early symptomatic fluid collections developing during the first 4 weeks of pancreatitis, the recommended management is watchful waiting, possibly with conservative treatment.
11. For early postinflammatory pancreatic and peripancreatic fluid collections, interventional treatment, beginning with minimally-invasive techniques, should be considered if conservative treatment fails.
12. For early postinflammatory pancreatic and peripancreatic fluid collections, endoscopic techniques may be used as a minimally-invasive modality after the patient qualifies for interventional treatment, and if conservative treatment has failed.

TABLE 2 A summary of all recommendations (continued from the previous page)

Interventional treatment of postinflammatory pancreatic and peripancreatic fluid collections
13. For symptomatic postinflammatory pancreatic and peripancreatic fluid collections demonstrating no clinical improvement following conservative treatment, interventional treatment should be initiated using minimally-invasive techniques that facilitate access to the fluid collections via a transmural, transpapillary, extraperitoneal, or transperitoneal route. Surgery remains the treatment of choice only if minimally-invasive methods prove ineffective.
14. The choice of the minimally-invasive treatment approach, and thus the route of access to postinflammatory pancreatic and peripancreatic fluid collections, should primarily depend on the experience of the treating center.
15. Regardless of the access route to the collection, the cornerstone of treatment of postinflammatory pancreatic and peripancreatic fluid collections is the establishment of an effective drainage system.
16. Within a period of 14 days before the interventional treatment of postinflammatory pancreatic and peripancreatic fluid collections, abdominal organ imaging (multiphasic CECT or CE-MRI) should be performed to assess the size and location of the collection and its relation to the adjacent organs.
Endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections
17. Endoscopic treatment, a minimally-invasive technique for the management of fluid collections, facilitates access to the collection via a transmural (via the gastric or duodenal wall) or transpapillary (via the minor or major duodenal papilla) route.
18. Both the transmural and transpapillary endoscopic drainage can be either passive (drainage via stents) or active (drainage via a nasocystic drain–based flushing system).
Transmural endoscopic drainage
19. The mainstay of endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections is EUS-guided transmural drainage.
20. Endoscopic transmural drainage can be established via the gastric (endoscopic cystogastrostomy) or duodenal (endoscopic cystoduodenostomy) wall.
21. The use of EUS during the transmural access to postinflammatory pancreatic and peripancreatic fluid collections facilitates visualization of the collection and the surrounding structures and increases the safety of the procedure by reducing hemorrhagic complications.
22. Transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections is feasible if the distance between the collection and gastrointestinal tract walls observed on EUS does not exceed 20 mm (or 40 mm for expert reference centers).
23. During EUS-guided endoscopic transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections the following tools are used: i) a needle and guidewire or a cystotome needle knife to puncture the collection; ii) a cystotome, dilator, or high-pressure balloon to dilate the established puncture. The selection of the appropriate combination of the aforementioned tools depends on the preferences, experience, and skills of the operating surgeon. An electrocautery-enhanced LAMS deployment kit is an alternative to the aforementioned tools.
24. During endoscopic transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections, a sample of the collection contents should be obtained for cytological, microbiological (culture of the collection contents), and biochemical (amylase activity, carcinoembryonic antigen concentration, and glucose concentration) tests.
25. Following transmural access establishment, plastic double-pigtail stents with a diameter of at least 7-Fr or fully coated self-expandable stents (BFMS/LAMS) with a minimum diameter of 15 mm can be introduced into the postinflammatory pancreatic or peripancreatic fluid collections via the transmural fistula between the gastrointestinal tract and collection lumina.
26. Self-expandable metal stents with a diameter of at least 15 mm facilitate the outflow of contents from the collection lumen during transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections by maintaining a large diameter of the fistula throughout the drainage period. In addition, the silicone membrane coating of the self-expandable metal stents prevents anastomotic leakage and spillage of the collection contents beyond the fistula.
27. Plastic double-pigtail stents are commonly used in transmural drainage of postinflammatory pancreatic and peripancreatic collections owing to their low cost and easy removal, even after a long drainage period. However, self-expandable metal stents ensure more efficient drainage and are associated with a decreased incidence of stent obstruction due to the large diameter of the connection being maintained throughout the drainage period. In addition, fewer endoscopic instruments are required for the insertion of a transmural metal stent, reducing the duration of the procedure.
28. Self-expandable transmural metal stents should not be left in place for >4–6 weeks, as longer periods are associated with a higher incidence of complications, especially hemorrhagic complications. If complete regression of the collection has not been achieved after 4–6 weeks and transmural drainage remains required, the self-expandable metal stent should be replaced with another self-expandable transmural stent or a plastic double--pigtail stent.
29. Plastic double-pigtail stents can solely be used for passive transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections for well-liquefied collections, especially in sterile PPs.
30. For WOPN collections, as well as for infected PPs and sterile PPs >10 cm in diameter, passive transmural drainage is insufficient and active transmural drainage via a nasocystic drain inserted through the transmural fistula into the collection lumen is necessary for active flushing of the lumen in the postoperative period.
31. For WOPN lesions and multiocular PPs, multiplexing the transmural access by establishing several transluminal gateways may be required.
32. For WOPN collections, stepping up of the endoscopic treatment via endoscopic necrosectomy may be required.
33. Direct endoscopic necrosectomy involves inserting an endoscope through a transmural endoscopic fistula into the necrotic collection lumen under carbon dioxide insufflation and removing the necrotic tissue under endoscopic imaging guidance using various types of endoscopic instruments.
34. Self-expandable transmural metal stents are indicated in poorly liquefied necrotic collections where the next step of treatment may involve endoscopic necrosectomy, since these stents facilitate safe insertion of the endoscope into the collection lumen and the performance of endoscopic necrosectomy.
Transpapillary endoscopic drainage
35. Passive transpapillary drainage involving insertion of a stent through the major duodenal papilla into the main pancreatic duct as the only route of access to the collection, is recommended only for PPs communicating with the main pancreatic duct, provided that the cyst size does not exceed 50 mm in diameter.

TABLE 2 A summary of all recommendations (continued from the previous page)

36. For PPs communicating with the main pancreatic duct and exceeding 50 mm in diameter, active transpapillary pancreatic drainage can be used, which involves inserting a nasocystic drain through the major duodenal papilla into the main pancreatic duct in such a manner that the distal end of the nasocystic drain is introduced through the site of pancreatic duct injury into the cyst lumen.
37. When using transpapillary drainage to treat PPs, the establishment of additional transmural access to the PP is not warranted, as the combination of transpapillary and transmural drainage worsens the results of endoscopic treatment and prolongs the drainage time. This is in contrast to necrotic collections, where the combination of transmural and transpapillary drainage improves the results of endoscopic treatment.
38. For WOPN collections, single transpapillary access (active or passive) as the only route of access to the collection is usually insufficient, and endoscopic transmural access is required.
39. Passive transpapillary drainage is often necessary during transpapillary drainage of WOPN collections, as most patients with WOPN present with damage to the main pancreatic duct, and passive transpapillary drainage is an effective method of treating such damage by facilitating physiological drainage of pancreatic juice into the duodenum.
Perioperative management
40. If the patient's clinical condition permits it, and in the absence of other contraindications, oral feeding during endoscopic treatment of fluid collections should be initiated within the first 24 hours postprocedure. If oral feeding is not possible, enteral nutrition is preferred, and parenteral nutrition is indicated only in the cases of intolerance or contraindication to enteral nutrition.
41. Intravenous antibiotic prophylaxis should be administered during drainage of postinflammatory pancreatic and peripancreatic fluid collections.
42. Routine use of proton pump inhibitors during endoscopic drainage of postinflammatory pancreatic and peripancreatic fluid collections is not recommended, unless indicated for other clinical reasons.
43. In patients with postinflammatory pancreatic and peripancreatic fluid collections presenting with no clinical improvement, an additional collection access route using other interventional treatment techniques may be necessary in addition to intensified endoscopic treatment.
44. During endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections, follow-up abdominal imaging examinations with the assessment of treatment efficacy based on the collection size should be performed every 1–4 weeks, depending on the patient's clinical condition, or immediately if new clinical signs or complications of treatment are observed.
45. Abdominal CT is the recommended imaging modality to confirm complete regression of postinflammatory pancreatic and peripancreatic fluid collections.
46. For transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections, the treatment success is acknowledged upon: 1) resolution of clinical symptoms associated with the collection, and 2) complete regression of the collection (<40 mm) on imaging.
47. For postinflammatory pancreatic and peripancreatic fluid collections resulting from necrotizing AP, completion of endoscopic transpapillary drainage should depend on the success of treatment, defined as complete regression of the collection and resolution of clinical symptoms, and on the morphology of the main pancreatic duct, as determined during ERCP or MRCP.
48. With transpapillary drainage as the only access route to the collection, treatment success is acknowledged upon: 1) resolution of the clinical symptoms associated with the collection; 2) complete regression of the collection (<30 mm) on imaging; and 3) closure of the site of damage to the main pancreatic duct, visualized as an absence of contrast leakage outside the pancreatic duct on fluoroscopic imaging during follow-up ERCP.
49. Endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections can be terminated after treatment success is acknowledged, at which time, the transmural/transpapillary stents can be removed, and the transmural/transpapillary endoscopic drainage be completed.
50. For pancreatic fragmentation, or DPDS, permanent transpapillary drainage using plastic double-pigtail stents may be required even after successful treatment of postinflammatory pancreatic and peripancreatic fluid collections.
51. Most complications of postinflammatory pancreatic and peripancreatic fluid collection endotherapy can be successfully treated using conservative or endoscopic means. However, in some cases, especially in hemorrhagic complications, interventional radiology or vascular surgery techniques, or conventional surgical treatment may be necessary, depending on the experience of the treating center.
52. If treatment of postinflammatory pancreatic and peripancreatic fluid collections fails despite intensified interventional treatment using minimally-invasive techniques, surgery remains the treatment of choice.
Post-treatment management
53. Following successful completion of endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections, all patients should be followed in an outpatient setting for at least 2 years, with follow-up abdominal imaging performed at 3, 6, 12, and 24 months post-treatment, or whenever collection recurrence is suspected.
54. For recurrent postinflammatory pancreatic and peripancreatic fluid collections, endoscopic treatment may be repeated postendotherapy.

Abbreviations: ANC, acute necrotic collection; APFC, acute peripancreatic fluid collection; BFMS, biflanged metal stent; CECT, contrast-enhanced computed tomography; CE-MRI, contrast-enhanced magnetic resonance imaging; CT, computed tomography; DPDS, disconnected pancreatic duct syndrome; ERCP, endoscopic retrograde cholangiopancreatography; LAMS, lumen-apposing metal stent; MRCP, magnetic resonance cholangiopancreatography; PP, pancreatic pseudocyst; others, see **TABLE 1**

be considered when making a therapeutic decision. All annotations from the experts were included in the text. After the highest possible strength had been determined for all recommendations and no further suggestions for revisions were offered, the Delphi process was considered complete.[38,39]

The recommendations provided herein have a broad scope and require a case-by-case analysis and adaptation to specific clinical settings.

The recommendations shall be updated every 5 years unless significant changes in the endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections are

TABLE 3 The Grading of Recommendations Assessment, Development and Evaluation (GRADE) criteria for the assessment of the quality (strength) of evidence[36,37]

Quality of evidence	Description
High	One or more high-quality, well-conducted randomized controlled trials that yield consistent and directly applicable conclusions are available. This means that further research is very unlikely to change the estimate of effect.
Moderate	Evidence is derived from randomized controlled trials with important limitations, eg, study bias, significant loss to follow-up, unexplained heterogeneity, indirect evidence derived from similar (but not identical) study populations, and studies with a very small number of patients or observed events (end points). In addition, evidence is available as derived from well--designed, controlled nonrandomized trials, well-designed cohort trials, or case-control trials as well as multiple interventional or noninterventional case series. This means that further research is likely to have an important impact on the estimate of effect and may change the estimate.
Low	Evidence is derived from observational studies, typically of poor quality due to a risk of errors. This means that further research is very likely to have an important impact on the estimate of effect and is likely to change the estimate.
Very low	The evidence is contradictory, of poor quality, or unavailable, and therefore the risk-benefit ratio cannot be established. This means that any estimate of effect is very uncertain or even unavailable or does not allow for any conclusions to be drawn.

introduced, supported by strong scientific evidence, necessitating an immediate update of the guidelines.

RECOMMENDATIONS Postinflammatory pancreatic and peripancreatic fluid collections RECOMMENDATION 1 Postinflammatory pancreatic and peripancreatic fluid collections comprise 4 types, each differing by the type of pancreatitis and the time elapsed since the onset of pancreatitis symptoms: 1) acute peripancreatic fluid collection (APFC); 2) acute necrotic collection (ANC); 3) pancreatic pseudocyst (PP); and 4) walled-off pancreatic necrosis (WOPN).

Any of the aforementioned collections can be either sterile or infected[1-6,11] (*evidence level, low; recommendation, strong [average of votes, 2.96]*).

RECOMMENDATION 2 Fluid collections that develop during the first 4 weeks of interstitial edematous pancreatitis are termed APFCs; collections persisting longer than 4 weeks after pancreatitis onset are termed PPs[1-6,11,20-22,40-43] (*evidence level, low; recommendation, strong [average of votes, 2.91]*).

RECOMMENDATION 3 Fluid collections that develop during the first 4 weeks of necrotizing pancreatitis are termed ANCs; collections persisting longer than 4 weeks after pancreatitis onset are termed WOPN[1-6,11,20,21,23-26,44-47] (*evidence level, low; recommendation: strong [average of votes, 2.93]*).

Moderate-to-severe AP is associated with a high risk of developing local and systemic complications (eg, organ failure), which significantly increase mortality. Pancreatic and peripancreatic fluid collections are major local complications of AP. However, the disease severity is not defined by the mere presence of fluid collections.

According to the 2012 revised Atlanta classification, pancreatic and peripancreatic fluid collections can be classified into 4 types, depending on the type of pancreatitis: APFC, PP, ANC, and WOPN. Any of these pancreatic fluid collections may be sterile or infected. Regardless of the type, early encapsulation of fluid lesions is associated with a lower risk of persistent organ failure.

APFCs often develop in the early phase (<4 weeks) of interstitial edematous AP, evolving into PP thereafter. APFCs are confined within interfascial spaces and have no wall; they occur in 22%–38% of patients. Approximately 60% of APFCs spontaneously regress in the first 4 weeks of the disease. Conversely, PPs are APFCs that persist beyond 4 weeks, observed in approximately 21% of patients (**FIGURE 1A** and **1B**). A PP is a walled fluid collection, usually located peripancreatically (**FIGURE 2A** and **2B**) or, less commonly, intrapancreatically. A pseudocyst has no solid elements (tissue debris) intraluminally, with clear, serous fluid, and has a high pancreatic enzyme activity. PPs occur in 3%–10% of patients in the late phase of interstitial edematous AP, and are more common in the patients with chronic pancreatitis (CP) consequent to acute flare-ups in the disease course.

Necrotizing AP is diagnosed based on the structural changes observed on abdominal imaging. It is characterized by pancreatic and/or peripancreatic tissue necrosis. Mixed-type necrosis (pancreatic and peripancreatic) is the most common (75%–80%), as compared with the less common peripheral (peripancreatic, 20%) or central necrosis (intrapancreatic, 5%). ANCs are fluid collections observed during the first 4 weeks of necrotizing AP, while WOPN refers to fluid collections that persist beyond 4 weeks after pancreatitis onset (**FIGURE 3A–3D**). ANC (**FIGURE 4A** and **4B**) is an ill-bordered lesion containing large quantities of necrotic tissue in its lumen, and occurring in 93%–100% since the patients with necrotic AP within the first 4 weeks of the disease onset. Approximately 50% of ANCs regress spontaneously, while the remaining evolve into WOPNs.

The term "organized pancreatic necrosis" was first proposed in 1996, while its synonym, WOPN, was introduced in 2005. WOPN (**FIGURE 5A** and **5B**) is a fluid collection that persists beyond 4 weeks since the necrotic AP onset. It has a well-defined border and contains liquefied necrotic tissue debris. The quantity of intraluminal debris depends on the degree of necrotic liquefaction (**FIGURE 6**), which, in turn, depends on the time elapsed since the disease onset. WOPN is observed in 23%–59% of the patients with necrotizing pancreatitis.

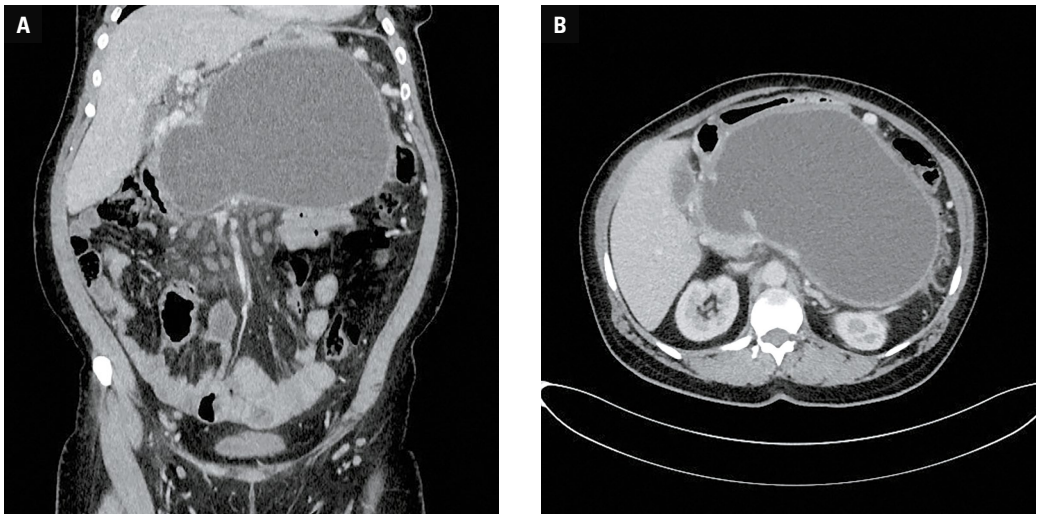


FIGURE 1 **A**, **B** – an extensive pancreatic pseudocyst involving the entire pancreatic field visualized on multiphasic contrast-enhanced abdominal computed tomography

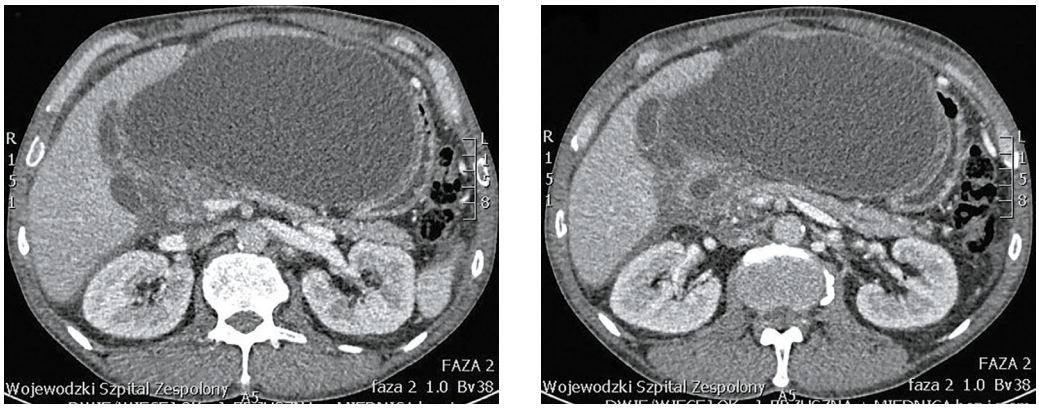


FIGURE 2 **A**, **B** – a pancreatic pseudocyst in the peripancreatic location compressing the gastric wall visualized on multiphasic contrast-enhanced abdominal computed tomography

Asymptomatic pancreatic and peripancreatic fluid collections RECOMMENDATION 4 For asymptomatic postinflammatory pancreatic and peripancreatic fluid collections, outpatient follow-up involving clinical evaluation with regular abdominal imaging (multiphasic CECT or magnetic resonance imaging [MRI]) should be performed at 3, 6, 12, and 24 months postdischarge, or when clinical signs of collections are observed[20-22,40,41,46,48-50] (*evidence level, very low; recommendation, strong [average of votes, 2.82]*).

RECOMMENDATION 5 If asymptomatic collection persists beyond 24 months, interventional treatment should be considered, with the decision-making process including a detailed discussion with the patient regarding the benefits and risks of the procedure[20-22,40,41,46,48-50] (*evidence level, very low; recommendation, strong [average of votes, 2.63]*).

No treatment is required for asymptomatic fluid collections; watchful waiting is recommended. The proposed schedule of outpatient imaging assessment (repeated at 3, 6, 12, and 24 months posthospitalization) is based on the few available studies reporting the occurrence of new clinical symptoms and complications of the hitherto asymptomatic fluid collections, or their regression (**FIGURE 7A–7C**), early in the follow-up period, usually during the first year, and especially during the first 6 months. Assessment of the collection size on abdominal imaging in the early stages of the follow-up period (first 6 months postdischarge), when examinations are performed every 3 months, is crucial. The imaging findings should always be compared with those obtained at the previous assessments. Clinical evaluation of the patient should complement the imaging assessment during the follow-up period.

If collection-related clinical signs appear during the follow-up, immediate abdominal imaging with possible qualification for treatment of pancreatitis complications is necessary, regardless of the aforementioned schedule of follow-up assessments.

The new clinical signs and complications that may appear during the follow-up period most frequently include infection of the collection's contents and compression of the adjacent structures and organs, usually due to expansion of the collection (**FIGURE 8A–8C**).

Importantly, asymptomatic fluid collections do not require treatment regardless of their size; however, it should be noted that large fluid collections (>20 cm) are rarely asymptomatic.

If the fluid collection persists on subsequent abdominal imaging examinations beyond the 2-year follow-up and the patient remains asymptomatic, further follow-up should be ceased. Any further management and intervention-related decisions should be predicated on the benefits and risks of the interventional procedure and comprehensively discussed with the patient, and follow a personalized approach. In exceptional cases, gradual reduction of the collection's size is observed on consecutive abdominal imaging scans, although the collection persists.

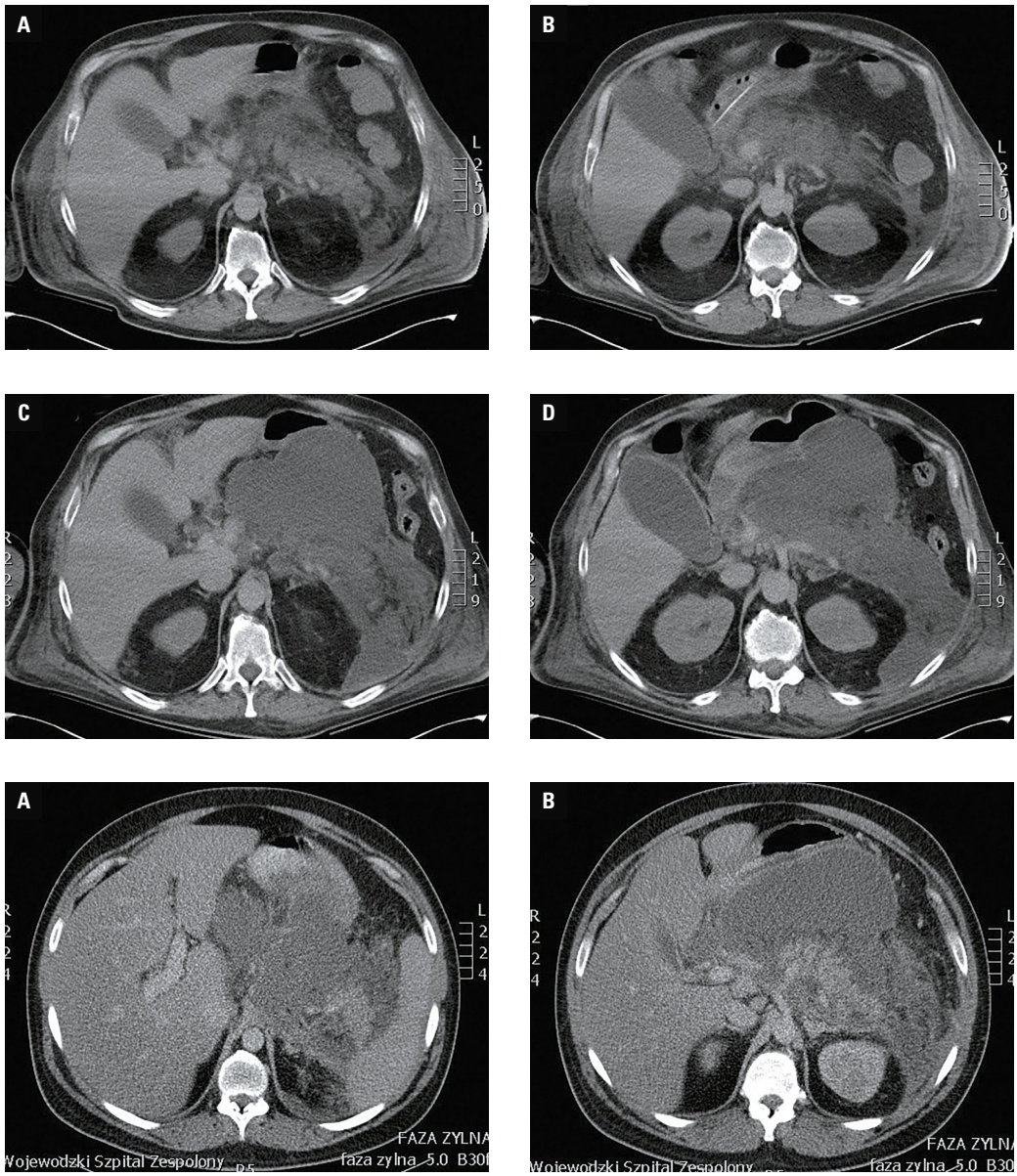


FIGURE 3 Abdominal computed tomography images acquired without contrast enhancement due to chronic renal failure in a patient with necrotizing acute pancreatitis (AP) on day 4 of AP, visible necrosis of the pancreas and peripancreatic tissues (**A**, **B**), with subsequent lesion evolution into acute necrotic collections with indirect signs of infection (luminal gas bubbles) visible on day 17 of AP (**C**, **D**)

FIGURE 4 **A**, **B** – multiphasic contrast--enhanced abdominal computed tomography images acquired 17 days after the onset of necrotizing acute pancreatitis; acute necrotic collections visible within the pancreatic field

In such cases, repeat imaging is recommended 1 year after the end of the 2-year follow-up period.

Indications for the treatment of postinflammatory pancreatic and peripancreatic fluid collections RECOMMENDATION 6 Treatment (both conservative and, in the case of no improvement, interventional) of postinflammatory pancreatic and peripancreatic fluid collections is indicated only in patients with collection-related clinical symptoms[27,29-34,40,51-78] (*evidence level, moderate; recommendation, strong [average of votes, 2.51]*).

RECOMMENDATION 7 An exception to the aforementioned recommendation is when the asymptomatic postinflammatory pancreatic and peripancreatic fluid collections compress large visceral (especially venous) vessels, which is associated with a high risk of thrombosis, development of collateral circulation, and secondary bleeding. In such cases, patients are eligible for treatment despite the absence of collection-related clinical symptoms[1,2,79-86] (*evidence level, very low; recommendation, strong [average of votes, 2.78]*).

Patients with asymptomatic fluid collections do not require interventional treatment, regardless of the size of the collection.

The primary indication for treatment initiation is the presence of collection-related clinical symptoms, which can be divided into 2 groups: 1) symptoms related to infection of the collection, and 2) symptoms related to the collection exerting pressure on the adjacent organs (mass effect).

The first group of clinical symptoms (**FIGURE 9**) is the most common indication for the initiation of interventional treatment. Typically, fluid collections become infected via translocation of intestinal microbiota. The most common pathogens are *Escherichia coli*, *Klebsiella pneumoniae*, *Enterococcus faecalis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Streptococcus* spp. Postinfection, the clinical presentation ranges from fever and chills to septic shock. In patients with infected pancreatic and peripancreatic fluid collections, the clinical presentation depends on the infection severity.

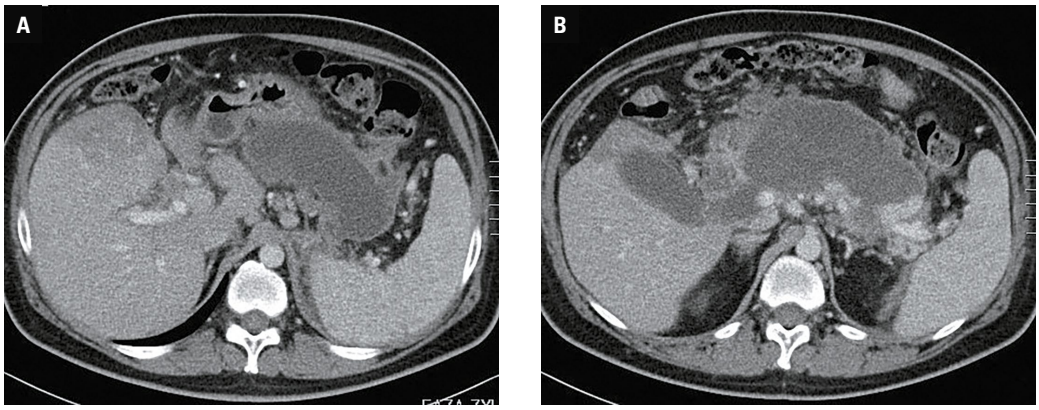


FIGURE 5 **A**, **B** – multiphasic contrast-enhanced abdominal computed tomography visualizing walled-off pancreatic necrosis in necrotizing acute pancreatitis (week 5)

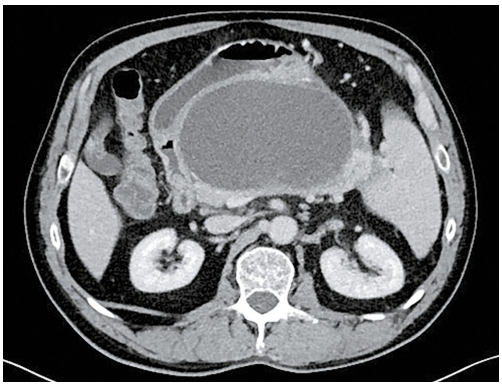


FIGURE 6 Multiphasic contrast-enhanced abdominal computed tomography images acquired 12 weeks after the onset of necrotizing acute pancreatitis. A well-liquefied walled-off pancreatic necrosis is observed in the pancreatic field.

When assessing pancreatic and peripancreatic fluid collections due to necrotizing AP, indirect or direct evidence of the infection of the necrotic areas should be considered to help facilitate the initiation of intravenous antibiotic therapy. Direct evidence of the infection includes a positive culture of necrotic contents collected via fine-needle aspiration biopsy from the lumen of the collection. This procedure is currently not routinely recommended owing to technical difficulties and the potential for causing secondary infection of the necrotic foci.

Indirect evidence of the infection includes the presence of extraluminal gas bubbles observed on multiphasic CT imaging of the abdomen and pelvis after excluding gastrointestinal tract perforation (**FIGURE 10**), or the appearance of new, relatively persistent symptoms of systemic inflammatory response syndrome (SIRS) after at least 7 days since the AP onset. Similarly, both direct and indirect evidence of infection can be used to determine further therapeutic management of other fluid collections that are not a consequence of necrotizing AP.

The antibiotic treatment of infected necrotic collections may include monotherapy with imipenem, meropenem, or piperacillin with tazobactam, or dual therapy comprising metronidazole in combination with either of the following: ceftriaxone, cefotaxime, ceftazidime, or ciprofloxacin. If an infected necrotic collection develops in a patient previously treated with an antibiotic or hospitalized in an ICU for an extended period of time, a broader-spectrum antibiotic should be chosen, with the optional addition of vancomycin. Such an antibiotic selection regimen also applies to the patients with infected fluid collections not due to necrotizing AP. Notably, intravenous antibiotic therapy should precede interventional treatment, as it permits intervention postponement or even avoidance of interventional treatment in some patients.

The second group of symptoms results from the mass effect. Clinical presentation in biliary tract compression is dominated by features of cholestatic jaundice (**FIGURE 11A–11C**). Compression of the gastrointestinal tract can, in turn, lead to subileus or ileus (**FIGURE 12A** and **12B**), wherein the clinical presentation depends mainly on the intra-abdominal location of the collection and the location of the compression-induced narrowing or obstruction of the gastrointestinal lumen.

However, it should be noted that it is not always possible to clearly determine whether the clinical symptoms are collection-related. In differential diagnosis, it is important to distinguish collection-related pain from an ongoing pancreatic inflammation–related pain, as this may affect further management. If the pain is not collection-related, interventional treatment is not justified, as regression of the collection post-treatment would not lead to symptom resolution.

Asymptomatic fluid collections impinging on large visceral, particularly venous, vessels, which are associated with a high risk of thrombosis and are also classified as mass effect–related symptoms, comprise a separate group of indications for interventional treatment. The splenic vein is the most common, and the portal or superior mesenteric veins are less common locations of thrombosis in pancreatitis, especially CP. The incidence of thrombosis correlates with the severity of pancreatitis and the presence of fluid collections. Splenic vein thrombosis results in prehepatic left-sided portal hypertension, a clinical condition in which blood pressure in the prehepatic segment of the portal circulation is elevated due to an increased resistance to portal blood flow, leading to the development of esophageal and/or gastric fundus varices, and potentially contributing to secondary upper gastrointestinal bleeding. Therefore, patients presenting with postinflammatory pancreatic and peripancreatic fluid collections that compress large visceral vessels (**FIGURE 13A** and **13B**) are eligible for interventional treatment despite the absence of

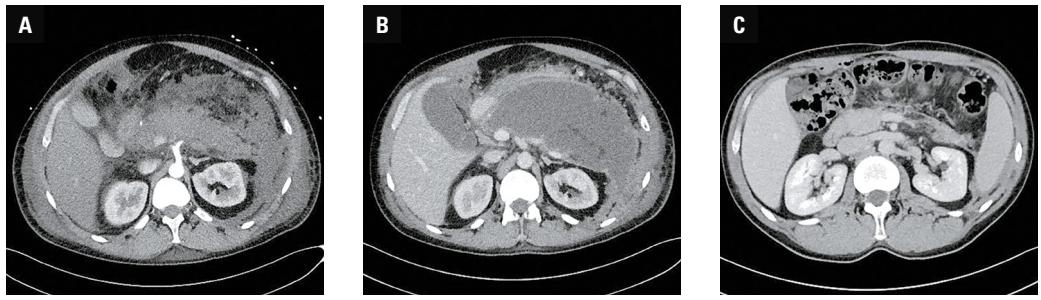


FIGURE 7 **A**–**C** – multiphasic contrast-enhanced abdominal computed tomography (CT) images acquired 8 days after the onset of necrotizing acute pancreatitis presenting with necrotic lesions in the pancreatic field and peripancreatic tissues (**A**). Imaging performed after 3 months shows an asymptomatic walled-off pancreatic necrosis sized 135 mm × 120 mm (**B**), which subsequently regressed spontaneously, as confirmed on multiphasic contrast-enhanced abdominal CT images acquired at 12-month follow-up (**C**).

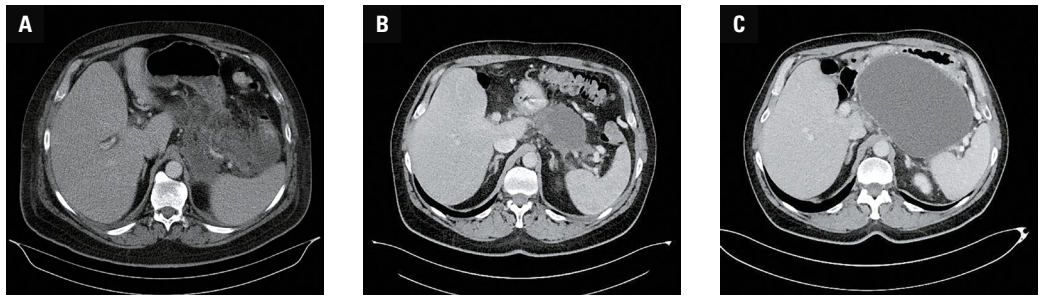


FIGURE 8 **A**–**C** – multiphasic contrast-enhanced abdominal computed tomography (CT) images acquired 12 days after the onset of necrotizing acute pancreatitis with visible necrotic lesions in the pancreas and peripancreatic tissues (**A**). Follow-up imaging performed after 3 months showed an asymptomatic walled-off pancreatic necrosis sized 65 mm × 53 mm (**B**). Because of symptoms of significant gastrointestinal obstruction, the patient underwent multiphasic contrast-enhanced abdominal CT scans 5 months into the follow-up period, which revealed progression of the collection size to 150 mm × 125 mm (**C**).

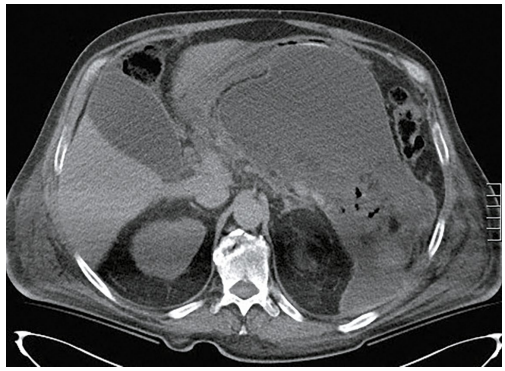


FIGURE 9
A multiphasic contrast--enhanced abdominal computed tomography scan showing an extensive walled-off pancreatic necrotic lesion with gas bubbles visible in the collection lumen, projecting into the pancreatic tail (indirect evidence of infection)

collection-related clinical symptoms. Of note, splanchnic vein thrombosis, a most common vascular complication of pancreatitis, is considered a late local complication according to the 2012 revised Atlanta classification, along with other late local complications, such as colonic necrosis or gastroparesis.

Other rare collection-related vascular complications include arterial complications, such as pseudoaneurysms (**FIGURE 14A–14F**), which are more common in the patients with CP-related PPs. The treatment of choice for hemodynamically stable patients with a pseudoaneurysm and symptomatic fluid collection is endovascular pseudoaneurysm embolization with subsequent collection drainage. Hemodynamic instability in the patients with a pseudoaneurysm and fluid collection is an indication for urgent intervention, for instance, conventional angiography of the visceral arteries with the assessment of the bleeding site and transarterial embolization, or surgical intervention, usually laparotomy to repair the bleeding vessel, and external collection drainage.

Notably, in some patients, a large visceral vessel, commonly the splenic artery, courses through the lumen of the fluid collection (**FIGURE 15A–15D**). It should be noted that if such patients present with collection-related clinical symptoms and are eligible for interventional treatment, they are at a high risk of bleeding from the vessel (**FIGURE 16A–16D**) during collection drainage. Therefore, such cases should be discussed in a multidisciplinary consultation, and the recommended decision regarding closure of the vessel using transarterial embolization should be considered on a case-by-case basis.

RECOMMENDATION 8 Interventional treatment of symptomatic postinflammatory pancreatic and peripancreatic fluid collections should be deferred until collection encapsulation, and in the collections due to necrotizing AP, until collection content liquefaction, which usually occurs 4 weeks after

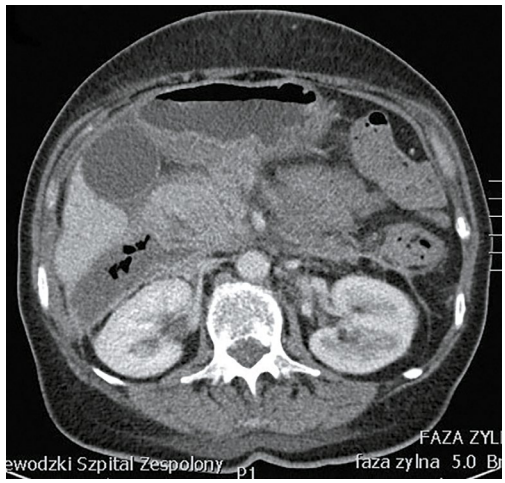


FIGURE 10 Walled-off pancreatic necrosis bulging into the right prerenal region, with gas bubbles (indirect evidence of infection) visible on contrast-enhanced computed tomography

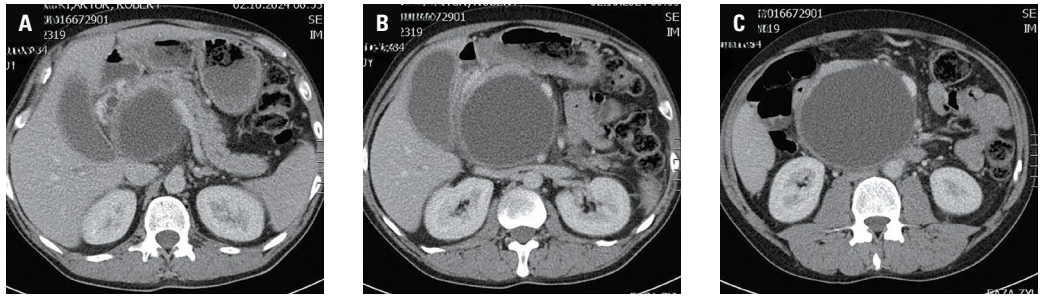


FIGURE 11 **A–C** – multiphasic contrast-enhanced abdominal computed tomography images acquired in a patient with cholestatic jaundice due to a postinflammatory pancreatic pseudocyst compressing the extrahepatic bile ducts

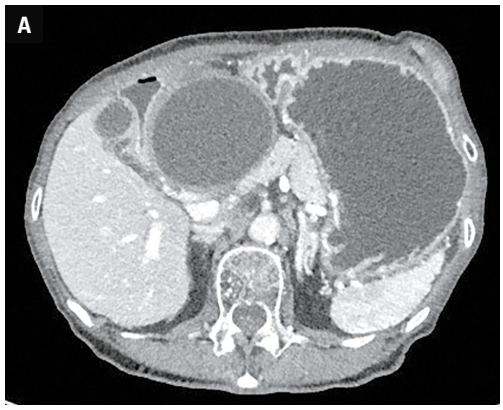
the disease onset[25,26,29-34,51-56,78,87-107] (*evidence level, low; recommendation, strong [average of votes, 2.65]*).

Four to six weeks since the onset of pancreatitis, while debatable, is considered an optimal time for intervention in the cases of postinflammatory pancreatic and peripancreatic fluid collections. In clinical practice, interventional treatment must be deferred for a long as possible.

Available literature indicates that interventional treatment should be deferred until at least 4 weeks after the pancreatitis onset. This is because the fluid collections occurring during the first 4 weeks of AP, that is, ANCs in necrotizing AP and APFCs in interstitial edematous AP, are fluid spaces with ill-defined borders, frequently lacking a wall and delimited by interfascial compartments. Early intervention for postinflammatory PFCs worsens the outcomes and prolongs the treatment time, and is associated with a higher number of complications, including fatal outcomes. However, in medical emergencies, such as gastrointestinal perforation, acute intestinal ischemia, intra-abdominal hemorrhage, or abdominal compartment syndrome (ACS), early surgical intervention is the treatment of choice.

With pancreatitis progression, the collections mature and undergo gradual encapsulation, becoming walled-off collections. The longer the collection persists (ie, the more time passes since the onset of the disease), the better its the degree of organization (ie, wall formation), and, in necrotic collections, the better the degree of liquefaction of the necrotic content. Lower quantities of solid necrotic tissue in the lumen of a necrotic AP-related fluid collection are associated with better results of drainage. The better the encapsulation of the collection and liquefaction of its contents, the better the results of interventional treatment, as evidenced by the results of endotherapy of PP, as compared with those of WOPN, indicating a close relationship with the content type. Regarding PPs containing serous fluid without any solid elements, collecting the content is much easier than in the case of dense necrotic contents containing necrotic tissues, as observed in WOPN. Postponing the intervention until at least 4 weeks postonset improves the intervention's results owing to the better containment and encapsulation of the collections and the improved liquefaction of necrotic contents in necrotic AP. Deferring the intervention, if the patient's clinical condition allows it, improves treatment outcomes and reduces the risk of complications, including those with fatal outcomes. The best results of interventional treatment are obtained when early postinflammatory pancreatic and peripancreatic fluid collections, or ANCs, evolve into WOPN, and APFCs into PPs.

Early postinflammatory pancreatic and peripancreatic fluid collections RECOMMENDATION 9 Early postinflammatory pancreatic and peripancreatic fluid collections (ANCs and APFCs) usually require no treatment owing to a lack of clinical



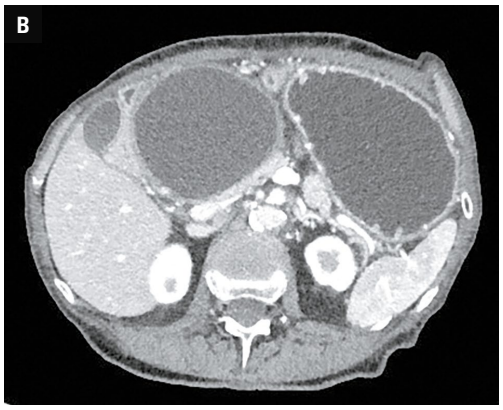
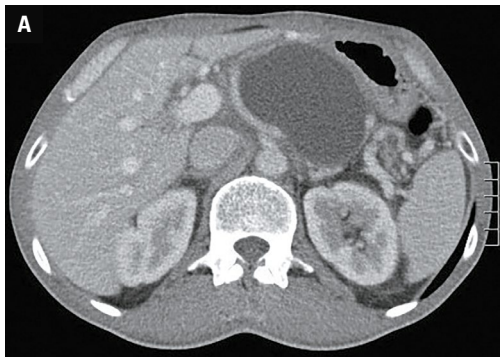


FIGURE 12 **A**, **B** – pancreatic pseudocyst visible on multiphasic contrast-enhanced abdominal computed tomography, causing symptoms of significant obstruction of the gastrointestinal tract while compressing the descending part of the duodenum



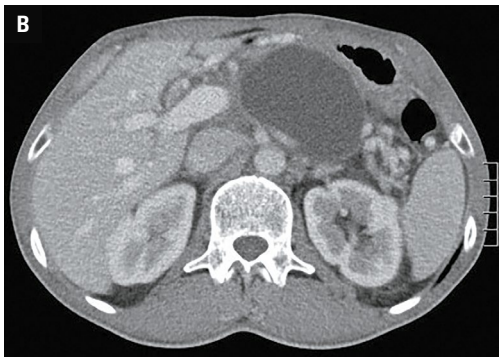


FIGURE 13 **A**, **B** – multiphasic contrast--enhanced abdominal computed tomography images acquired in a patient with an asymptomatic pancreatic pseudocyst compressing the visceral trunk, causing arterial stenosis and exerting a mass effect on the splenic vessels, leading to left portal hypertension with secondary collateral circulation

symptoms and spontaneous regression of most of these lesions[1-3,6,20-22,26,29,30,34,40-42,45,46,51,52,54,78] (*evidence level, very low; recommendation, strong [average of votes, 2.71]*).

RECOMMENDATION 10 For early symptomatic fluid collections developing during the first 4 weeks of pancreatitis, the recommended management is watchful waiting, possibly with conservative treatment[1-3,20-22,24,29,30,32-34,40-43,45-47,51,52,58,78,107-112] (*evidence level, low; recommendation, strong [average of votes, 2.85]*).

Early fluid collections (ANCs and APFCs) occur in the first 4 weeks of the disease, usually in patients hospitalized for pancreatitis. The potential collection-related clinical symptoms, such as abdominal pain, may be masked by ongoing inflammation-related pain, which is characteristic of early-phase disease and listed among the diagnostic components of AP. Most early fluid collections do not trigger any collection-related clinical symptoms, and conservative management, the mainstay of treatment, is usually sufficient, with no additional interventions required. Moreover, most early fluid collections regress spontaneously during the first 4 weeks of pancreatitis. Therefore, the recommended management is watchful waiting, defined as patient observation and possible conservative treatment if hospitalization and AP treatment are required, as no specific conservative treatments aimed at managing either early or late fluid collections are available. In infected fluid collections, intravenous empirical broad-spectrum antibiotics should always be initiated, regardless of the time since the disease onset.

RECOMMENDATION 11 For early postinflammatory pancreatic and peripancreatic fluid collections, interventional treatment, beginning with minimally-invasive techniques, should be considered, if conservative treatment fails[58,64,87-105,110,113-119] (*evidence level, low; recommendation, strong [average of votes, 2.51]*).

RECOMMENDATION 12 For early postinflammatory pancreatic and peripancreatic fluid collections, endoscopic techniques may be used as a minimally-invasive modality after the patient qualifies for interventional treatment, and if conservative treatment has failed[56,58,64,88-105,110,113-120] (*evidence level, low; recommendation, strong [average of votes, 2.76]*).

Most early fluid collections regress spontaneously without a need for intervention during the disease course. Interventions for early fluid collections are associated with poorer treatment outcomes and higher complication rates than the interventions for late fluid collections developing at least 4 weeks after the pancreatitis onset. Nevertheless, indications exist for the initiation of treatment in early fluid collections in some patients. The 2 main indications for interventional treatment include septic shock in infected fluid collections (especially necrotic collections) or ACS due to extensive collections, characterized by intra-abdominal pressure (IAP) greater than 20 mm Hg and newly developed organ failure (at least 1 organ).

A step-up approach applies in the treatment of fluid collections, with subsequent steps of the therapeutic ladder being gradually implemented after the failure of the previous step. Notably, each subsequent step is associated with

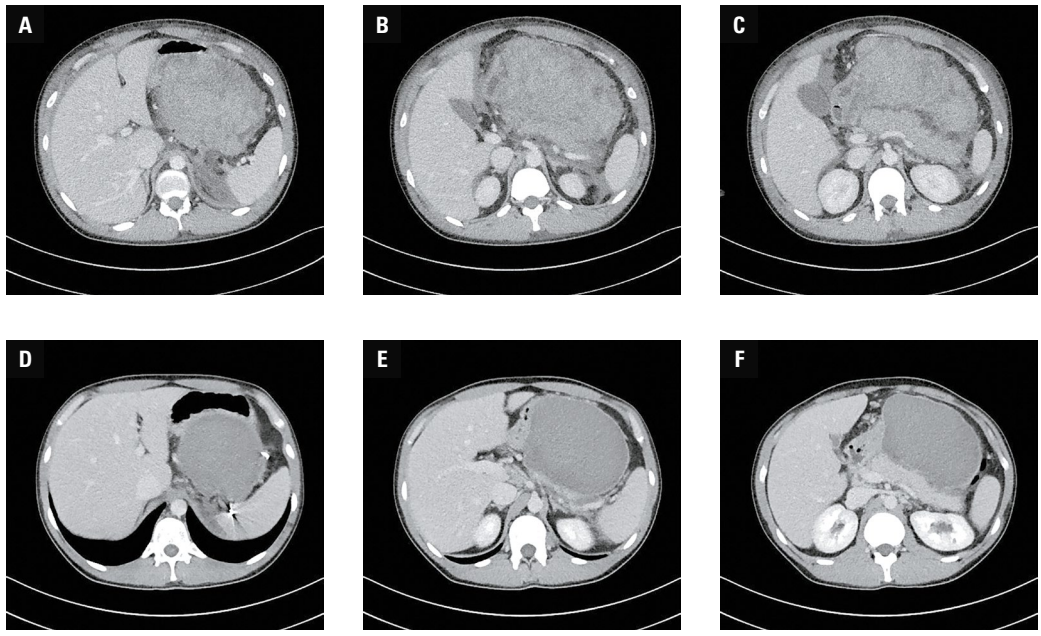


FIGURE 14 Multiphasic contrast-enhanced abdominal computed tomography images acquired in a patient with peripheral peripancreatic necrosis in the course of necrotizing acute pancreatitis complicated by bleeding into the lumen of an acute necrotic collection (ANC) from a splenic artery pseudoaneurysm (**A**–**C**). Following transarterial embolization, conservative treatment was continued, with evolution of the complicated ANC to walled-off pancreatic necrosis (**D**–**F**).

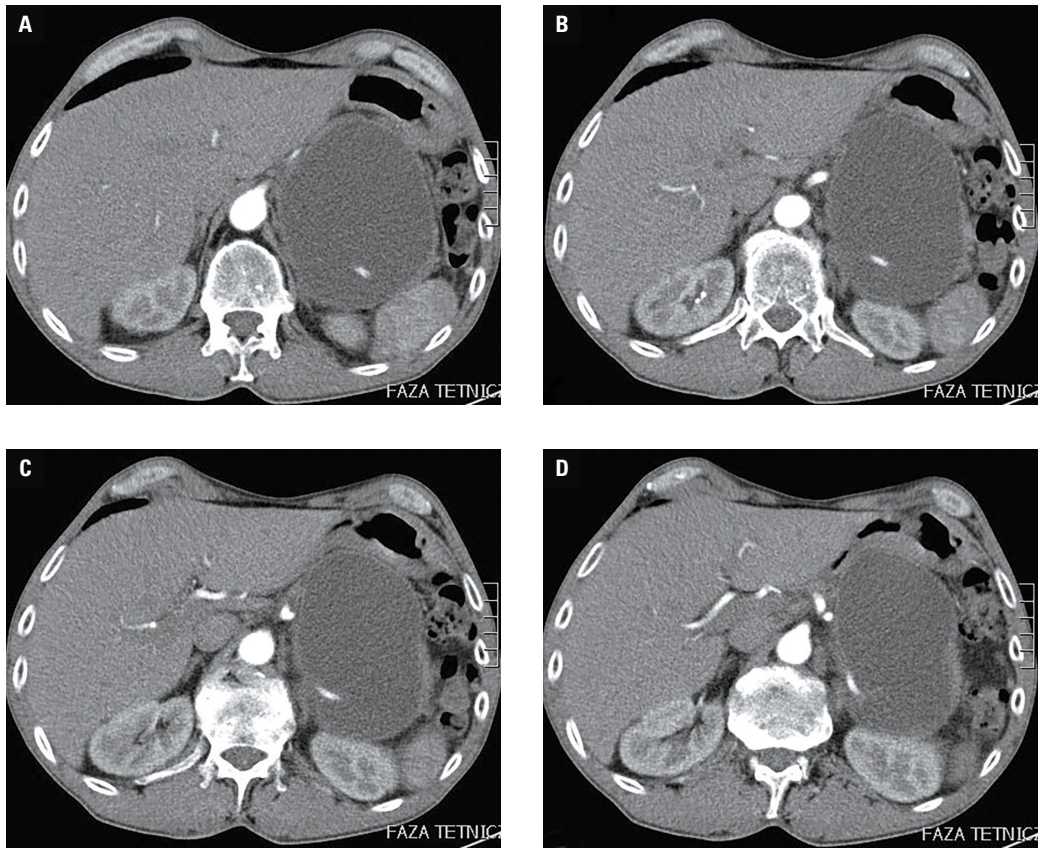


FIGURE 15 **A**–**D** – postinflammatory pseudocyst within the pancreatic body and tail on multiphasic contrast-enhanced abdominal computed tomography, with the splenic artery visible in the cyst lumen

a more aggressive approach. According to the step--up approach, drainage intervention is the first step in the absence of specific conservative treatments for fluid collections. An exception are infected fluid collections, where the treatment can begin with antibiotic therapy (step 0), and the subsequent step can be implemented only if conservative treatment proves ineffective. This involves interventional treatment, such as collection drainage using minimally-invasive techniques (refer to the aforementioned step 1). In necrotizing AP–related fluid collections, the subsequent step (ie, step 2) following drainage failure is minimally-invasive necrosectomy. Frequently, the last step in the step-up approach involves surgical intervention via the conventional access, such as laparotomy.

For early-stage fluid collections, the aim is to defer the intervention until collection

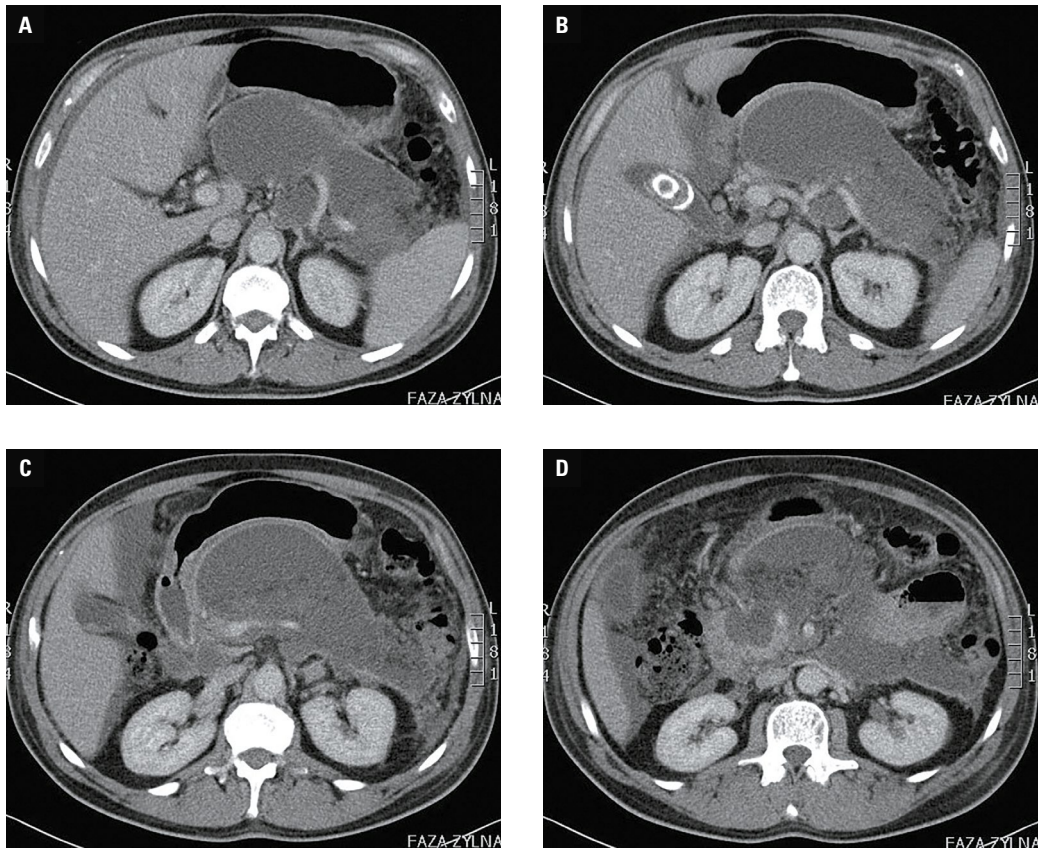


FIGURE 16 A–D – multiphasic contrast--enhanced abdominal computed tomography images acquired in a patient with walled-off pancreatic necrosis, with the visceral trunk and splenic artery visible in the collection lumen

encapsulation, and for necrotic collections, until collection content liquefaction, since the greater the content of solid necrotic tissue in the collection lumen, the worse the results, the longer the treatment time, and the higher the complication rate. However, in some patients, in whom watchful waiting and maximized conservative treatment have proven ineffective, deferring the intervention is not possible, and treatment should be implemented according to the step--up approach. In both aforementioned indications, if intensive conservative treatment is ineffective and the patient develops symptoms of septic shock or ACS, urgent interventional treatment using minimally-invasive techniques is required, usually beginning with percutaneous drainage of the fluid collection. For urgent indications in early fluid collections, endotherapy is an effective drainage modality allowing for the postponement or avoidance of surgery and limiting the use of additional interventional treatments (**FIGURE 17A–17S**). However, it should be noted that the results of endoscopic treatment of early-stage fluid collections are worse (requiring longer endotherapy times and an aggressive approach) than those of endotherapy of late-stage fluid collections, warranting deferral of endoscopic intervention until the collections become limited and encapsulated in late-stage AP.

In early-stage AP, the recommended management involves extensive conservative treatment, possibly supported by intravenous antibiotics, since it allows for intervention postponement and even avoidance of interventional treatment in some patients. However, despite a maximized conservative treatment, some patients require interventional treatment in the first 4 weeks of AP.

Interventional treatment of postinflammatory pancreatic and peripancreatic fluid collections RECOMMENDATION 13 For symptomatic postinflammatory pancreatic and peripancreatic fluid collections demonstrating no clinical improvement following conservative treatment, interventional treatment should be initiated using minimally-invasive techniques that facilitate access to the fluid collections via a transmural, transpapillary, extraperitoneal, or transperitoneal route. Surgery remains the treatment of choice only if minimally-invasive methods prove ineffective[29-34,51-59,64-67,74,77,78,107,113-117,120-186] (*evidence level, moderate; recommendation, strong [average of votes, 2.82]*).

Symptomatic fluid collections are an indication for treatment. Initially, the recommended approach is conservative treatment, and interventional treatment using minimally-invasive techniques should be initiated only if the conservative approach fails. The ineffectiveness of minimally--invasive methods is the only indication for conventional open surgical treatment of fluid collections. The management regimen presented herein is representative of the step-up approach that had been initially introduced for the treatment of local complications of necrotizing AP, having since become the standard of care for the treatment of symptomatic fluid collections, regardless of the primary pancreatitis type.

Minimally-invasive techniques for the treatment of fluid collections facilitate access to

the collection via a transmural, transpapillary, extraperitoneal, or transperitoneal route. Access via the transmural route (via the gastrointestinal tract wall) or transpapillary route (via the greater or lesser duodenal papilla) is established using endoluminal or endoscopic techniques to enable internal drainage of fluid collections (discussed in detail in the subsequent sections of this document).

Access via the extraperitoneal and transperitoneal routes can be established using percutaneous drainage techniques. The extraperitoneal route is the preferred access route, with transperitoneal access being preferred only if extraperitoneal access is technically unfeasible. Percutaneous drainage involves the insertion of drains of varying diameters (10–40 Fr; eg, triple-lumen drains) into the lumbar region (via the extraperitoneal access) or the anterior abdominal wall (via the transperitoneal access) under radiographic imaging guidance using ultrasonography (USG) or CT. The distal end of the percutaneous drain is left in the fluid collection's lumen, while the proximal end is placed externally to evacuate the lumen contents, with possible flushing of the lumen with saline solution. In some patients, external (percutaneous) drainage is an effective minimally-invasive treatment of fluid collections, eliminating the need for other interventional treatment techniques. If guided percutaneous drainage is ineffective and the patient requires interventional treatment, percutaneous drainage may facilitate the postponement of interventional treatment until the collection is better contained (eg, early-stage collections) and the patient improves clinically. Pancreatic–percutaneous fistula is a common complication of percutaneous drainage of fluid collections; therefore, endotherapy is the approach of choice whenever external percutaneous drainage or internal endoscopic drainage is feasible.

Minimally-invasive techniques via the extraperitoneal access, commonly used in the treatment of pancreatic necrosis where percutaneous drainage has failed, include the following:

- sinus tract endoscopy (also referred to as minimally-invasive retroperitoneal pancreatic necrosectomy [MIRPN] or minimal-access retroperitoneal pancreatic necrosectomy [MARPN]);
- video-assisted retroperitoneal debridement (VARD).

In the aforementioned techniques, access to the necrotic cavity via the extraperitoneal route is achieved by prior placement of a percutaneous drain under radiographic guidance.

In sinus tract endoscopy, a canal, formed following the insertion of the percutaneous drain, is gradually widened until it reaches a diameter of a 30-Fr catheter; subsequently, a rigid nephroscope or flexible endoscope is inserted into the necrotic lumen and the necrotic contents are flushed and aspirated or removed using appropriate endoscopic instruments. Necrosectomy procedures should be repeated until the necrotic content is completely removed, even at the patient's bedside, without the need for reoperation in an operating room setting. Sinus tract endoscopy can be used as an adjunct to open necrosectomy.

VARD is another technique for minimally-invasive treatment of pancreatic necrosis via the extraperitoneal route. This technique is a hybrid of sinus tract endoscopy and open necrosectomy via the extraperitoneal access. In VARD, an approximately 5-cm incision is made near the percutaneous drain, the end of which is placed in the necrotic collection lumen; subsequently, the fluid content and the necrotic tissue a removed using a suction device and long forceps, respectively. The procedure is performed under the guidance of a camera inserted into the necrotic lumen via a laparoscopy port. Carbon dioxide is administered into the necrotic lumen via an inserted percutaneous drain. Two large-diameter drains are left in place postprocedure to ensure drainage in the postoperative period.

A transperitoneal access to the fluid collections is the least common approach. It is performed using laparoscopy when percutaneous drainage via the extraperitoneal access is ineffective.

If the aforementioned minimally-invasive techniques prove ineffective, conventional surgical interventions remain the treatment of choice according to the step-up approach. Surgical interventions are indicated in the case of acute complications of pancreatitis, such as gastrointestinal tract perforation, acute intestinal ischemia, or intra-abdominal hemorrhage. The type of surgical access and procedure should be guided by both the experience of the treating center and the clinical circumstances.

RECOMMENDATION 14 The choice of the minimally-invasive treatment approach, and thus the route of access to postinflammatory pancreatic and peripancreatic fluid collections, should primarily depend on the experience of the treating center[29,30,32-34,51-59,67,74,77,78,107,113,116-118,120,127-166,171-182,186-189] (*evidence level, very low; recommendation, strong [average of votes, 2.67]*).

Minimally-invasive treatment of symptomatic fluid collections involves the 4 following routes of access: transmural, transpapillary, extraperitoneal, and transperitoneal. A center providing care to patients with fluid collections should be capable of using all the aforementioned interventional treatment techniques, both minimally-invasive (endoluminal, imaging-guided percutaneous drainage, and laparoscopic techniques), and conventional surgical techniques, if the minimally-invasive methods prove ineffective. However, despite all the aforementioned interventional techniques being at a center's disposal, there may be a technique in which the center has the most experience (ie, the largest number of interventions using this particular technique), which would translate into better treatment results and the lowest possible number of complications. In practice, this means that if 2 interventional treatment

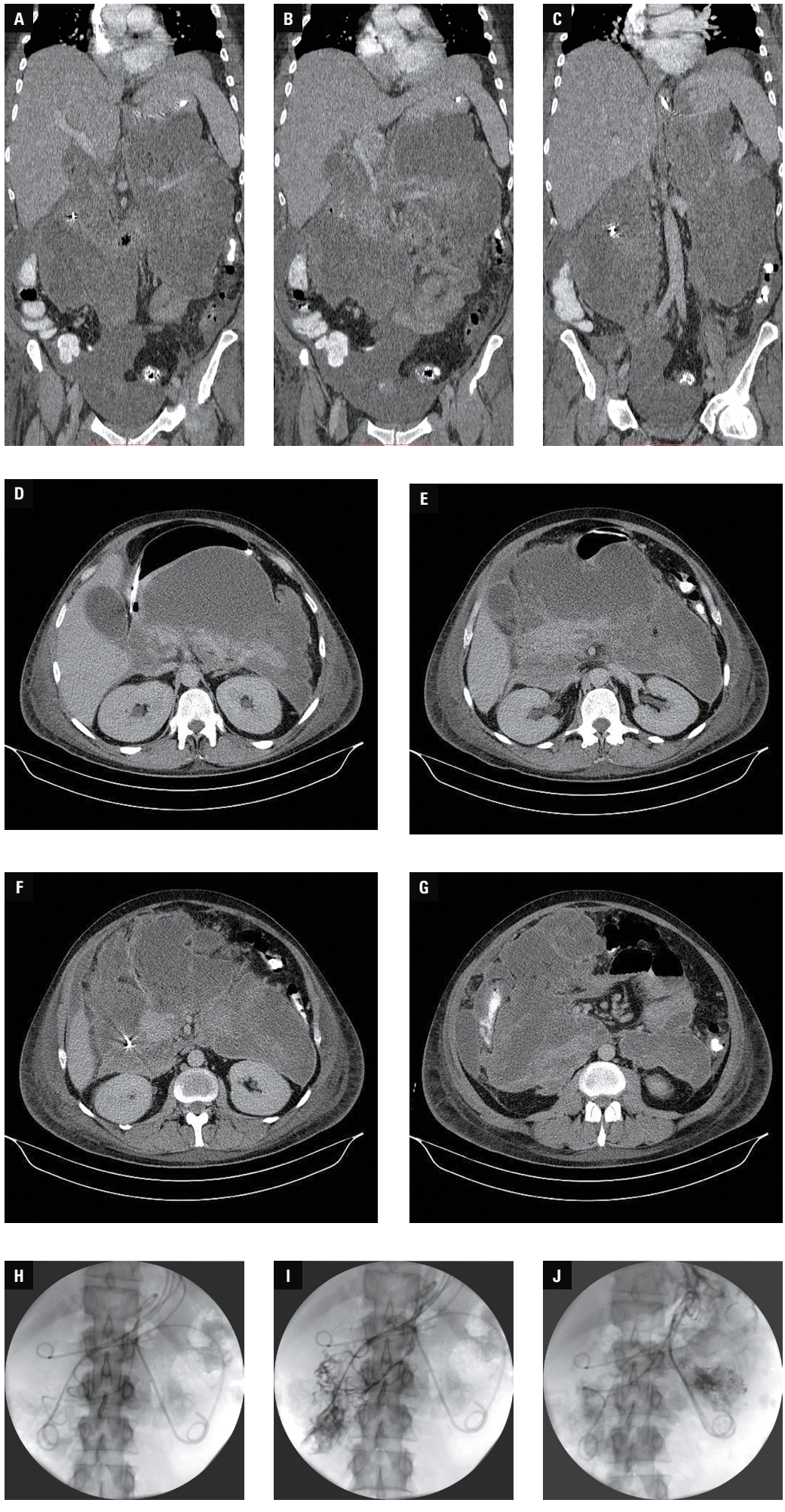
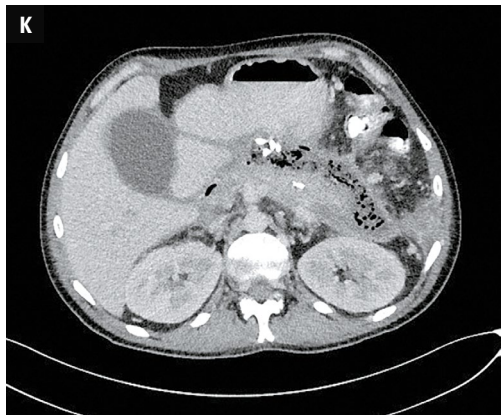
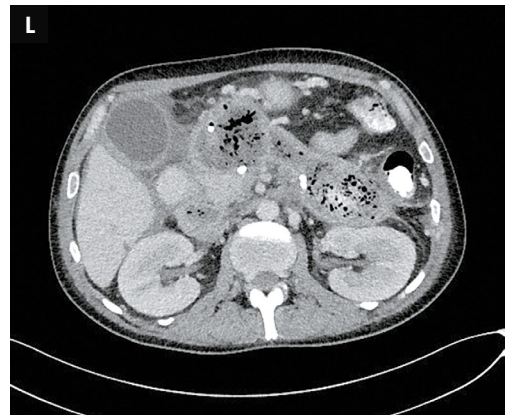
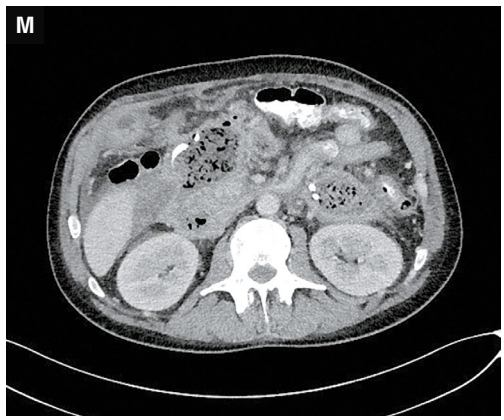
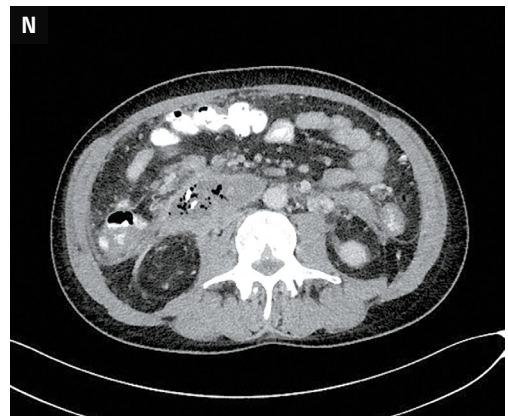


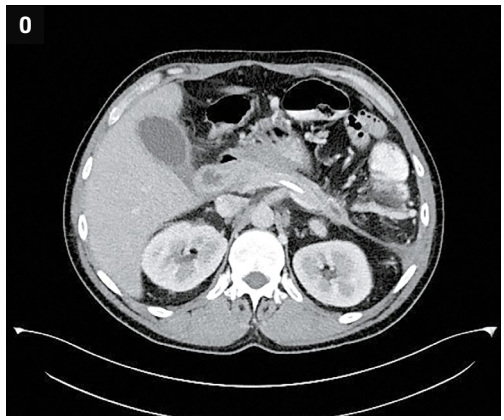
FIGURE 17 Endoscopic treatment of a patient with acute necrotic collections (ANCs) and abdominal compartment syndrome (ACS). A contrast-enhanced multiphasic computed tomography image of the abdomen and pelvis showed extensive ANC (**A**–**G**). The patient was deemed eligible for endoscopic treatment at the early stage of acute pancreatitis (**H**–**J**) owing to the presence of ACS. Complete therapeutic success was achieved, as confirmed by subsequent follow-up imaging studies (**K**–**S**).

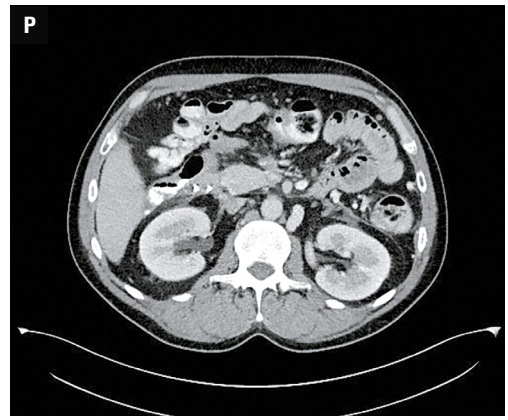


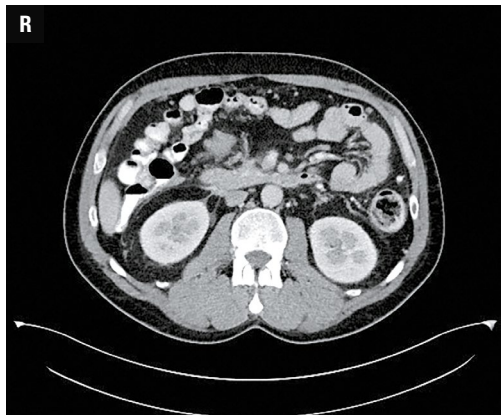


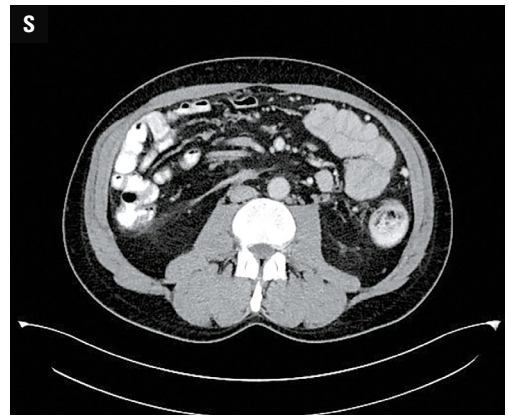












techniques which, according to the literature, have similar efficacy and safety, the choice of a particular method should primarily be guided by the experience of the treatment center. In most patients with symptomatic fluid collections, especially when the collections are large (>10 cm in diameter), the interventional treatment may be pursued via several different modalities.

RECOMMENDATION 15 Regardless of the access route to the collection, the cornerstone of treatment of postinflammatory pancreatic and peripancreatic fluid collections is the establishment of an effective drainage system[23,29,30,32-34,40,51-60,65-67,74,77,78,91-96,113-118,120,124-128,131-135,140,141-156,158-189] (*evidence level, moderate; recommendation, strong [average of votes, 2.96]*).

Interventional treatment of fluid collections involves drainage of the collection contents using an appropriate drainage system. Fundamentally, 2 different drainage system types can be distinguished. The first type, that is, the passive drainage system, involves the free flow of the collection contents via a fistula or a drain inserted into the collection lumen, whereas the second type, the active drainage system, involves the introduction of a solution into the collection lumen via a drain, causing the contents to actively flow out via a fistula or a drain.

The treatment of fluid collections is predicated on establishing an effective drainage system suited to the collection type. An effective drainage system should facilitate drainage of the entire collection lumen. For liquid-only collections, containing no solid elements, passive drainage is usually sufficient. If the collection contains dense contents or tissue elements, or when it is large in size, active drainage should be used to flush the collection through the drain. In such cases, passive drainage might result in treatment failure with secondary superinfection of the collection. This applies mainly to the treatment of necrotizing AP-related fluid collections, where drainage of the liquid-only collection alone may be insufficient owing to the problems caused by the nonliquefied fragments of necrotic tissue.

RECOMMENDATION 16 Within a period of 14 days before the interventional treatment of postinflammatory pancreatic and peripancreatic fluid collections, abdominal organ imaging (multiphasic CECT or MRI with contrast) should be performed to assess the size and location of the collection and its relation to the adjacent organs[1-4,29,30,34,40,44,52,54-58,128,153,160,190-199] (*evidence level, very low; recommendation, strong [average of votes, 2.67]*).

From the operator's (endoscopist's) point of view, an important step in preoperative management of patients with fluid collections involves familiarization with the most recent abdominal CT or MR images; notably, in some patients, the pelvis should also be included in the examination range, especially in the cases where extensive fluid collections extend toward the lower abdomen. Advanced CE imaging of abdominal organs should be recent, that is, performed not earlier than 14 days preprocedure, ensuring that the surgeon can become familiar with the current anatomical conditions that they will encounter during the planned intervention.

Abdominal imaging is used to determine the collection's size and location, as well as its relation to adjacent organs and structures, to ensure that the patient is eligible for a specific type of intervention. Frequently, the imaging presentation is the decisive criterion when ensuring patient eligibility for endotherapy. However, it should be noted that the actual distance of the collection wall from the gastrointestinal wall can only be accurately determined during endoscopy, especially on endosonographic imaging. In addition, up-to-date abdominal imaging assessments provide information regarding the possible and easiest access route to the collection and facilitate procedural preplanning. A crucial part of the presurgical imaging assessment involves determining the degree of the collection's encapsulation with a detailed assessment of the course of the collection's walls. In the case of incomplete encapsulation, which can be observed even 4 weeks after the AP onset, interventional treatment should be deferred until the fluid collections are fully encapsulated, as failure of full encapsulation is a risk factor for failure of interventional treatment, prolonged hospitalization, and persistent organ failure. In addition, the collection's location has a high prognostic value as an indicator of the interventional treatment's effectiveness. Typically, a right-sided fluid collection localization involving the pancreatic head is associated with a significantly worse prognosis than a left-sided localization involving the pancreatic body and tail. Furthermore, the outcomes of interventional treatment are worse if the collection extends beyond the omentum into the pelvis, especially via the paracolic gutters.

When evaluating abdominal imaging scans in patients with fluid collections preoperatively, special attention should be paid to the large visceral vessels coursing in the collection's immediate vicinity or through its lumen, including the collateral circulation vessels in patients with portal hypertension. Free fluid in the peritoneal cavity, if visible on imaging does not disqualify a patient from endoscopic intervention, as therapeutic paracentesis should be performed only for grade II/III ascites before initiating endotherapy via the transmural access.

Eligibility for interventional treatment in patients with fluid collections, similarly to their preoperative evaluation, cannot be based on a dynamic examination, such as an abdominal USG, despite the widespread availability of this modality. In addition, most of the aforementioned elements of interest, assessed preoperatively, are usually not evaluable on abdominal USG. Therefore, the recommended modality for abdominal organ imaging in patients with fluid collections is static image acquisitions for in-depth diagnosis, such as multiphasic CECT or contrast-enhanced MRI (CE-MRI; **FIGURE 18A–18D**). Multiphasic CECT of the abdomen is the recommended modality since it facilitates full evaluation of both the pancreas and the adjacent organs and structures, as well as full preoperative evaluation of the fluid collections. According to the 2012 revised Atlanta

classification, grading of local complications of AP, namely fluid collections, is based on multiphasic CECT abdominal imaging, the recommended modality for preoperative evaluation. However, it should be noted that CT is inferior to MRI in terms of differentiating between pancreatic and peripancreatic fluid collections owing to its lower sensitivity and specificity in confirming tissue debris in the collection's lumen, that is, confirming the diagnosis of necrotizing AP–related fluid collections. However, if pancreatic and/or peripancreatic tissue necrosis has been confirmed on previous CECT images, that is, those acquired in early-phase AP, fluid collections observed on CT in the late phase of AP clearly confirm the diagnosis of necrotic collections (**FIGURE 19A–19C**). Thus, differentiating WOPN from PP on abdominal CT is usually not challenging, if pancreatic necrosis has been observed in early-stage AP.

Widespread availability, achievable reproducibility, and accuracy in predicting pancreatitis severity and treatment outcome are other factors favoring multiphasic abdominal CECT in patients with fluid collections. When this modality is unavailable due to allergy to the contrast agent, noncontrast MRI rather than noncontrast CT is the preferred imaging modality.

Differential diagnosis, particularly differentiation from pancreatic cystic tumors, is a completely separate aspect of the imaging assessments performed in patients with fluid collections. In this regard, MRI is significantly better than CT at differentiating cystic lesions owing to its better visualization of tissue elements in the collection lumen. A pancreatic cyst of unclear etiology, identified on imaging, requires complementary diagnostics, which should be performed in specialized referral centers. Frequently, endoscopic ultrasonography (EUS) is needed to complete the diagnosis of ambiguous pancreatic cysts, with a support of EUS-guided biopsy in determining the exact nature of the cyst.

Endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections RECOMMENDATION 17 Endoscopic treatment, a minimally-invasive technique for the management of fluid collections, facilitates access to the collection via a transmural (via the gastric or duodenal wall) or transpapillary (via the minor or major duodenal papilla) route[23,29,32-34,40,51-60,67,77,78,91-96,106,116-118,128,131,133,134,159-166,171-189,200-206] (*evidence level, low; recommendation, strong [average of votes, 2.93]*).

Endoscopic surgery is a minimally-invasive treatment technique that facilitates the performance of advanced endoluminal procedures via natural body orifices (natural orifice transluminal endoscopic surgery [NOTES]). Endoscopic treatment is a common modality for managing inflammatory diseases of the pancreas. Pancreatic endotherapy for fluid collections can be performed via 2 access routes:

- Transpapillary route: anatomical access (via the major duodenal papilla, or less commonly, the minor duodenal papilla in anatomical pancreas variants) during endoscopic retrograde cholangiopancreatography (ERCP)
- Transmural route: extra-anatomical access (via the gastrointestinal tract wall) under EUS guidance.

The transpapillary route facilitates physiological drainage into the duodenal lumen via an anatomical access involving the pancreatic ducts and structures communicating with the pancreatic ductal system. The limitations of transpapillary drainage include a small diameter of the outflow duct, usually not exceeding several millimeters despite dilatation of the major or minor duodenal papillae, and a small diameter of the transpapillary stent introduced into the pancreatic duct (<10 Fr).

The transmural route, which involves the creation of an extra-anatomical access to the collection lumen, is more invasive than the transpapillary route, with the extra-anatomical access possibly acting as a permanent fistula. If transpapillary access is not feasible, for example, owing to altered anatomical conditions in the gastrointestinal tract, EUS-guided nonanatomical access via a transmural route can be established as an alternative approach.

RECOMMENDATION 18 Both the transmural and transpapillary endoscopic drainage can be either passive (drainage via stents) or active (drainage via a nasocystic drain–based flushing system)[23,29,32-34,40,51,52,54-60,67,77,91-96,106,116-118,-128,131-134,159-166,171-189,200-202,205-210] (*evidence level, low; recommendation, strong [average of votes, 2.85]*).

Endotherapy, an alternative to other minimally-invasive treatment techniques, facilitates drainage via a transmural or transpapillary route by means of passive drainage using a transpapillary or transmural stent, or active endoscopic drainage using a transpapillary or transmural nasocystic drain.

The following drainage techniques can be used via the transpapillary or transmural routes:

- Passive transpapillary drainage with a stent inserted into the lumen of the main pancreatic duct via the major duodenal papilla;
- Active transpapillary drainage with a nasocystic drain inserted into the lumen of the main pancreatic duct via the major duodenal papilla;
- Passive transmural drainage (transgastric/transduodenal) with a stent inserted via a fistula created between the gastrointestinal tract lumen and the fluid collection using endoscopy;
- Active transmural drainage (transgastric/transduodenal) with a nasocystic drain inserted via a transmural fistula created via endoscopy and left in place in the collection lumen.

Transmural endoscopic drainage RECOMMENDATION 19 The mainstay of endoscopic treatment of postinflammatory pancreatic and

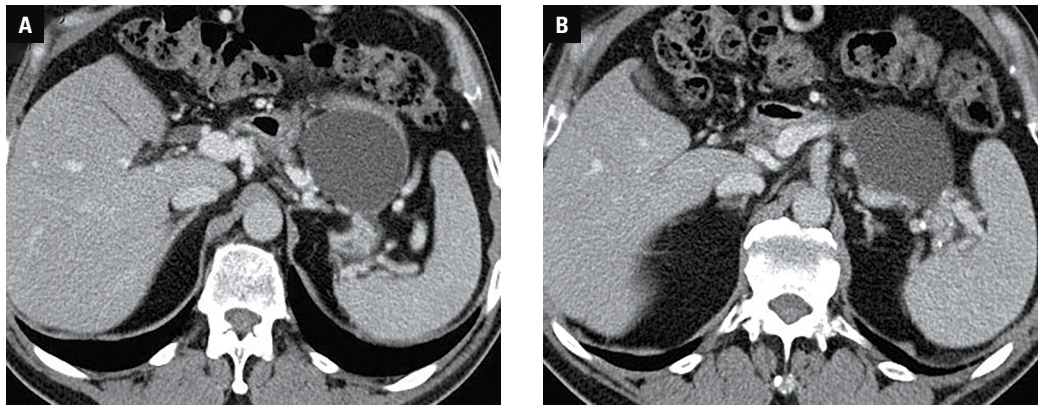


FIGURE 18 Postinflammatory pseudocyst of the pancreatic tail visualized on multiphasic contrast-enhanced abdominal computed tomography (**A**, **B**) and contrast-enhanced abdominal magnetic resonance (**C**, **D**) images

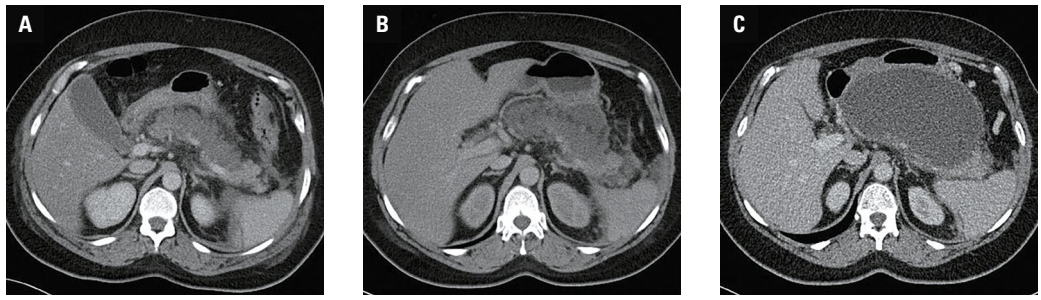


FIGURE 19 Multiphasic contrast-enhanced abdominal computed tomography images acquired in a patient with necrotizing acute pancreatitis (AP). In the early phase of AP, necrosis of the pancreas and peripancreatic tissues was evident (**A**, **B**); it subsequently evolved to a walled-off pancreatic necrotic collection in the late phase of the disease (**C**).

peripancreatic fluid collections is EUS-guided transmural drainage[23,29,30,32-34,40,45,51,52,54-60,67,77,78,91-96,-98,106,114-118,128,131-134,160-167,169-189,193,201,204,208,211-217] (*evidence level, low; recommendation, strong [average of votes, 2.95]*).

RECOMMENDATION 20 Endoscopic transmural drainage can be established via the gastric (endoscopic cystogastrostomy) or duodenal (endoscopic cystoduodenostomy) wall[23,29,30,32-34,40,45,51,52,54-60,67,77,78,91-96,98,106,114-118,128,131-134,160-167,169-189,193,201,204,208,211-221] (*evidence level, low; recommendation, strong [average of votes, 2.87]*).

Endoscopic transmural drainage of fluid collections involves complete removal of the collection contents via a fistula created endoscopically in the gastrointestinal tract wall, between the collection and the upper gastrointestinal tract (the stomach [cystogastrostomy] or duodenum [cystoduodenostomy]) lumina. Transmural drainage of fluid collections can be categorized into 2 types, depending on the method of fistula creation during the endoscopic procedure:

- Conventional drainage, in which an endoscopy-guided fistula is created at the peak of the bulge caused by the fluid collection compressing the gastrointestinal wall;
- EUS-guided drainage, in which a fistula is created under EUS guidance, which facilitates real-time imaging of the fluid collection and assessment of the surrounding structures.

EUS-guided drainage is the recommended type of transmural drainage of fluid collections, as it facilitates full visualization of the anatomical conditions during drainage, as opposed to conventional drainage, which relies on endoscopic images providing no overview of the structures beyond the gastrointestinal tract wall.

The transmural route is the recommended route of access to fluid collections, as it facilitates

the establishment of an effective, larger-diameter (as compared with that established via the transpapillary route) drainage system via an extra-anatomical fistula. Although an effective drainage system facilitates complete evacuation of the fluid collection, access establishment does not automatically translate into an effective drainage system. The advantage of endoscopic transmural drainage, as compared with endoscopic transpapillary drainage, is that wide access to the fluid collection is obtained via a large-diameter transmural fistula (up to 20 mm) throughout the drainage period. In addition, the length of the fistula, that is, the distance between the gastrointestinal tract and collection lumina (for transpapillary drainage, it is the distance from the papilla via the pancreatic duct to the site where the duct communicates with the collection lumen via the drainage site) is greater for the transmural than for the transpapillary access, facilitating the drainage of the collection contents and improving treatment results.

RECOMMENDATION 21 The use of EUS during the transmural access to postinflammatory pancreatic and peripancreatic fluid collections facilitates visualization of the collection and the surrounding structures and increases the safety of the procedure by reducing hemorrhagic complications[29,32-34,51,54-56,58,59,67,78,91-96,98,106,115-117,128,131-134,160-166,169-177,180-189,204,208,211-217,222-227] (*evidence level, moderate; recommendation, strong [average of votes, 2.95]*).

During endoscopic surgery for fistula creation, no structures should be located between the gastrointestinal tract and collection walls; this can only be confirmed using EUS. In addition to the visualization of the fluid collections, EUS facilitates real-time visualization of the surrounding structures and organs adjacent to the collection, providing a complete overview of the surgical field. This aids the operator in bypassing structures, including blood vessels, located on the line of a potential fistula, minimizing the risk of damage. Regarding blood vessels, this approach helps reduce hemorrhagic complications. In conventional endoscopic drainage, presence of structures between the upper gastrointestinal tract and the collection walls cannot be excluded while the transmural access to the fluid collection is being established; hence, conventional drainage without EUS guidance is not currently recommended.

The use of EUS-guided transmural drainage of fluid collections expands the indications and possibilities of endotherapy. Conventional, non–EUS-guided endoscopic drainage may be pursued only if the collection is impinging onto the gastrointestinal wall. However, some fluid collections, especially those localized in the pancreatic tail area, do not exert any pressure on the gastric wall because of the anatomical conditions; in such cases, the unavailability of EUS generally precludes the pursuit of transmural drainage.

In addition, EUS facilitates the determination of the content type of the fluid collections, which is important in the differential diagnosis of pancreatic cystic lesions and often determines further therapeutic management.

RECOMMENDATION 22 Transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections is feasible if the distance between the collection and gastrointestinal tract walls observed on EUS does not exceed 20 mm (or 40 mm for expert reference centers)[29,32-34,51,54-56,58,59,67,78,91-96,98,106,115-118,128,131-134,160-166,169-178,180-189,204,208,211-217,222-231] (*evidence level, very low; recommendation, strong [average of votes, 2.62]*).

Typically, the distance between the upper gastrointestinal tract and the collection walls, which should not exceed 20 mm, is the factor that determines the feasibility of transmural endoscopic drainage of fluid collections. Additional imaging assessments performed before the planned intervention help determine the approximate distance between the gastrointestinal tract wall and the collection wall to ensure patient eligibility for a specific intervention. Frequently, the imaging presentation is the decisive criterion for endotherapy eligibility. However, the actual distance between the collection and gastrointestinal tract walls can be strictly determined on EUS only following aspiration of the contents and gas (desufflation) from the gastrointestinal tract, as the distance measured during insufflation may be inaccurate.

In expert centers where at least 100 endoscopic procedures involving transmural drainage of fluid collections are performed annually, that is, centers with the greatest endotherapy experience in treating local complications of AP, transmural drainage can be pursued if the distance between the collection and gastrointestinal tract walls does not exceed 40 mm. Regardless of whether the procedure is performed in an expert center, it should be noted that the smaller the distance between the gastrointestinal tract and collection walls, as visualized on EUS, the better the results of endoscopic treatment and the lower the number of endotherapy complications, especially those related to endoscopic fistula leakages.

Since the pancreas is located in the upper part of the retroperitoneal space, near the stomach and duodenum, the actual distance between the collection and gastrointestinal tract walls usually does not exceed 20 mm; therefore, most fluid collections can be treated via endoscopic transmural drainage.

RECOMMENDATION 23 During EUS-guided endoscopic transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections the following tools are used:

- a needle and guidewire or a cystotome needle knife to puncture the collection;
- a cystotome, dilator, or high-pressure balloon to dilate the established puncture.

The selection of the appropriate combination of the aforementioned tools depends on the preferences, experience, and skills of the operating surgeon.

An electrocautery-enhanced lumen-apposing metal stent (LAMS) deployment kit is an alternative to the aforementioned tools[32,34,55,56,78,91-96,98,106,114-116,118,128,159-167,171,180-186,208,212-215,224-239] (*evidence level, low; recommendation, strong [average of votes, 2.78]*).

Three types of imaging modalities are used during the creation of transmural fistulas to fluid collections: endoscopy, EUS, and fluoroscopy. All endoscopic procedures should be performed under general anesthesia with endotracheal intubation, which reduces the risk of aspiration. Placing the patient in a supine or lateral position does not affect the effectiveness or safety of the procedure and depends on the operator's preference. All endoscopic procedures should be performed under carbon dioxide insufflation.

Regardless of the fluid collection type, the sequence of steps during fistula creation is identical (**FIGURE 20A–20G**). First, after inserting a linear echoendoscope through the esophagus into the stomach and duodenum, the collection has to be located on EUS imaging; of note, the shortest distance between the gastrointestinal tract and collection walls on the image does not always determine the choice of the fistula site. It is technically feasible to create a fistula in the upper part of the collection adjacent to the wall of the gastrointestinal tract; however, it should be noted that such a fistula hinders the free flow of contents from the collection lumen into the gastrointestinal tract lumen, thus worsening the drainage conditions. Hence, creation of a fistula in the lowest possible part of the collection should be attempted, considering the technical difficulties during the procedure (**FIGURE 21A–21C**). An endoscopic fistula established in this manner should ensure gravitational drainage, allowing the contents to be freely evacuated in the postoperative period (**FIGURE 22A–22U**).

After selecting the anastomosis site and determining the content type of the collection on EUS, the collection is punctured, under EUS guidance, through the gastrointestinal wall, using a 19-G needle or a cystotome needle knife (**FIGURE 23**). Subsequently, after withdrawal of the needle stylet, the collection contents are aspirated to enable the determination of the fluid collection type based on the aspirated fluid (clear serous content is characteristic of a PP; thick, brown content with solid elements is characteristic of WOPN). At this stage of the procedure, fluoroscopic imaging can be used in addition to EUS. As the echoendoscope should remain adherent to the gastrointestinal tract wall, endoscopic imaging is not pursued.

Collection contrastation (**FIGURE 24**), which involves a contrast agent being introduced into the collection lumen after transmural puncture has been performed and the collection contents have been aspirated, is not routinely recommended. Collection contrastation should be performed in the case of any clinical doubts regarding appropriate collection puncturing. In addition, it can be pursued only for small-sized collections, as contrasting the entire collection is usually impossible for larger collections owing to the large volume of the contrast agent required.

Following a transmural puncture, a guidewire is introduced into the collection lumen under EUS and fluoroscopic guidance, and looped therein (**FIGURE 25A** and **25B**). In the case of any clinical doubts regarding appropriate collection puncturing, and when the guidewire does not loop in the collection, as sometimes observed in poorly liquefied WOPN lesions, a contrast agent can be administered into the collection lumen. Subsequently, a dilator is inserted along the guidewire to widen the opening of the pancreatogastric or pancreatoduodenal fistula (**FIGURE 26**). Anastomotic dilatation can be performed using a cystotome (6–10 Fr) or mechanical dilator (6–10 Fr), or pneumatically using a high-pressure balloon (8–20 mm). Fluoroscopic and endoscopic imaging is used at this stage of the procedure.

Fistula dilatation is followed by transmural insertion of a self-expanding metal stent and/or plastic stent(s) and/or a nasocystic drain, depending on the drainage type, which is determined by the type and size of the fluid collections (**FIGURE 27A–27D**). Endoscopic and fluoroscopic imaging are the modalities of choice at this stage of the procedure, with EUS being used less frequently.

As an alternative to the aforementioned sequence of endoscopy procedure steps and the list of endoscopic instruments used, an electrocautery-enhanced LAMS deployment kit can be used. Currently, 2 LAMS implantation kits, featuring a special electrocautery tip and a mechanism to release the stent during the procedure, are available on the market (Hot Axios; Boston Scientific, Marlborough, Massachusetts, United States [**FIGURE 28A–28C**] and Hot Spaxus; Taewoong Medical Co., Gimpo, Korea [**FIGURE 29A–29D**]). Although these kits usually do not require the use of other endoscopic instruments during the procedure, their high cost limits their application in daily clinical practice.

RECOMMENDATION 24 During endoscopic transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections, a sample of the collection contents should be obtained for cytological, microbiological (culture of the collection contents), and biochemical (amylase activity, carcinoembryonic antigen [CEA] concentration, and glucose concentration) tests[32,54-56,60,77,91-96,106,116-118,160-167,172-189,193,201,204,208,211-221,224-236,240-248] (*evidence level, low; recommendation, strong [average of votes, 2.87]*).

EUS helps determine the content type of the fluid collections and harvest the material from the collection lumen. EUS-guided aspiration biopsy is a safe and effective method that

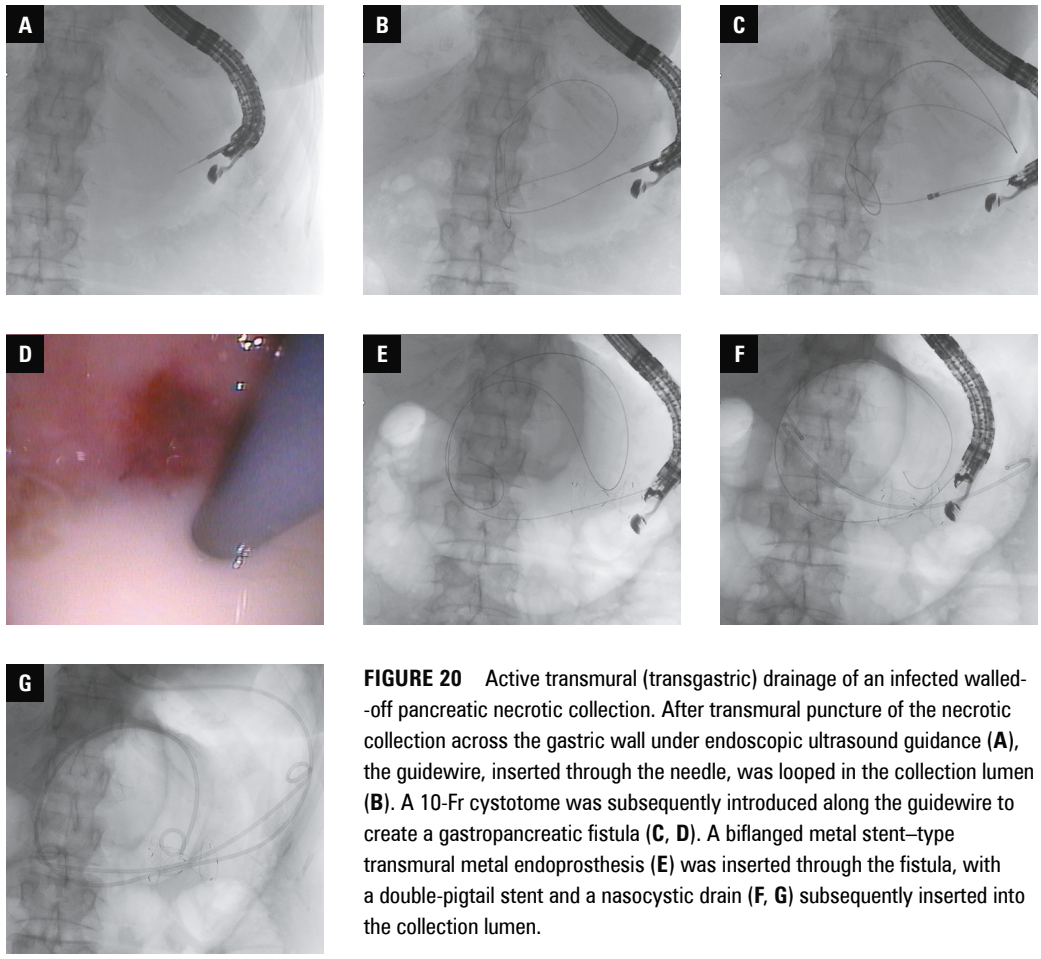


FIGURE 20 Active transmural (transgastric) drainage of an infected walled-off pancreatic necrotic collection. After transmural puncture of the necrotic collection across the gastric wall under endoscopic ultrasound guidance (**A**), the guidewire, inserted through the needle, was looped in the collection lumen (**B**). A 10-Fr cystotome was subsequently introduced along the guidewire to create a gastropancreatic fistula (**C**, **D**). A biflanged metal stent–type transmural metal endoprosthesis (**E**) was inserted through the fistula, with a double-pigtail stent and a nasocystic drain (**F**, **G**) subsequently inserted into the collection lumen.

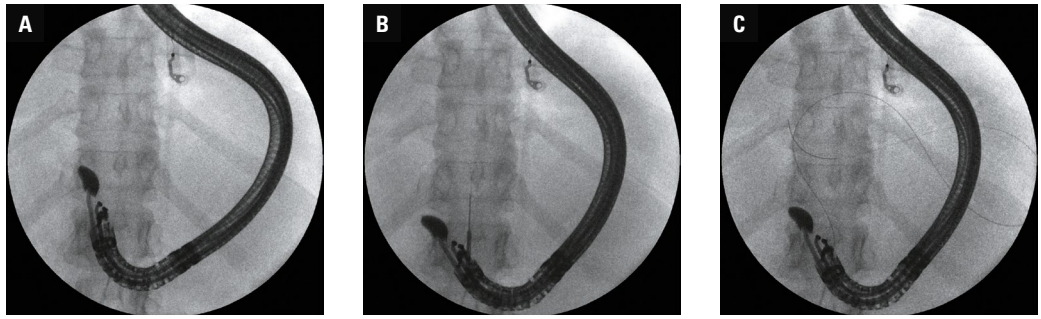


FIGURE 21 **A**–**C** – fluoroscopic images acquired during an endoscopic cystogastrostomy procedure in a patient with a pancreatic pseudocyst visualizing the positioning of the apparatus in the antrum of the stomach to enable the creation of a transmural fistula at the lowest peak of the collection in order to facilitate gravitational drainage

facilitates the differential diagnosis of pancreatic cystic lesions.

In all patients undergoing endoscopic transmural drainage of fluid collections, a sample of the collection contents should be obtained after the collection is punctured for cytological, biochemical, and microbiological testing.

Cytological examination of the sampled fluid facilitates microscopic evaluation of the morphology of the fluid cells to confirm the presence of cells characteristic of postinflammatory lesions while excluding the presence of atypical cells. However, it should be noted that cytological screening of the fluid for cancer cells has a significant rate of false-negative diagnoses. Therefore, a sample of fluid from the collection should be additionally sent for biochemical analysis, in particular for the determination of CEA and glucose levels, which facilitate differentiation of mucinous cystic lesions. High CEA levels (> 200 ng/ml) and low glucose levels are characteristic of mucinous cysts. The characteristic biochemical features of the fluid collections include high amylase and lipase activity (usually higher than that observed in blood), low CEA levels, low protein and albumin contents, as compared with plasma, and an electrolyte profile similar to that of serum. In addition, the culture of the sampled contents facilitates differentiation between sterile and infected fluid collections.

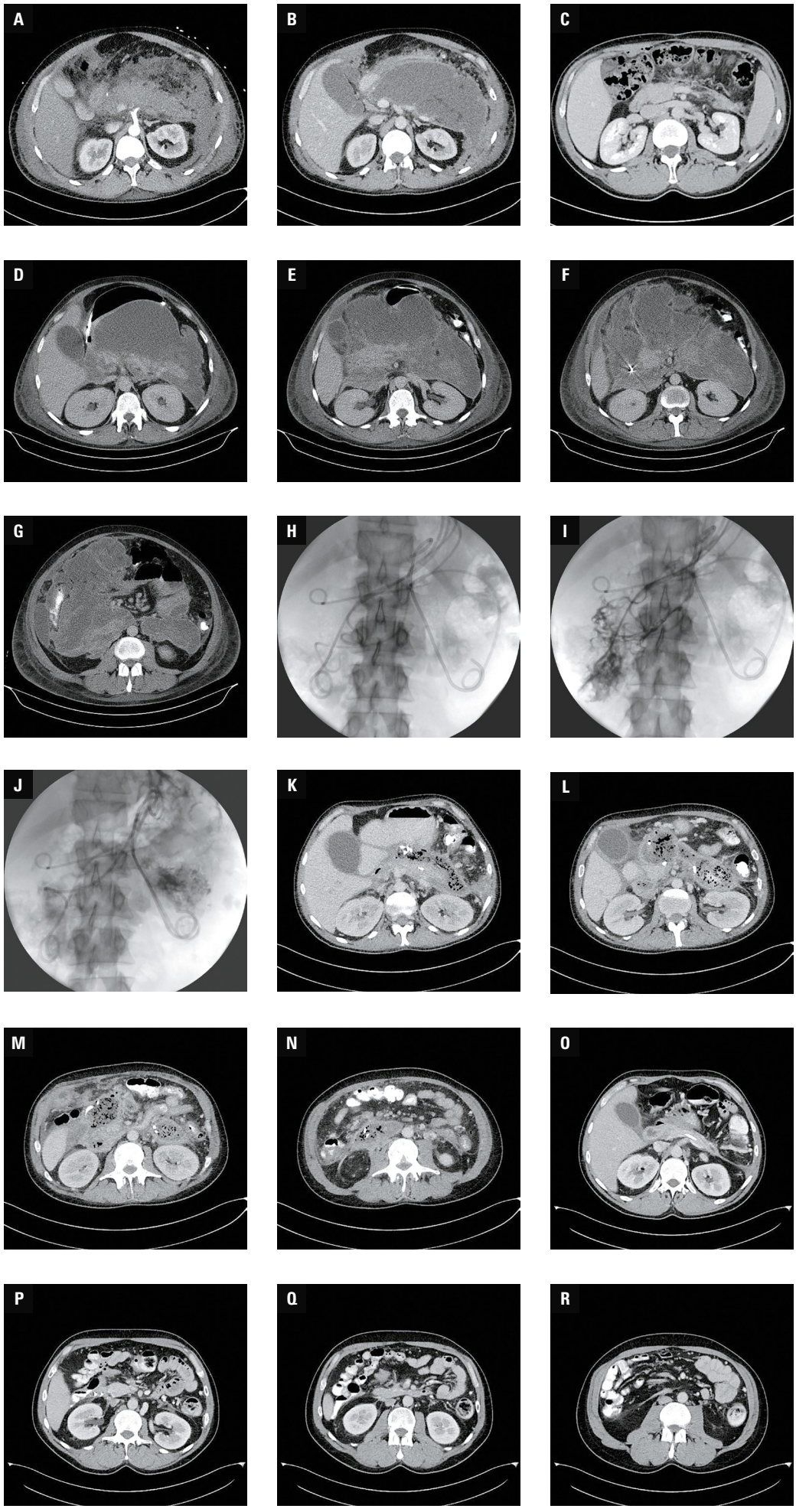
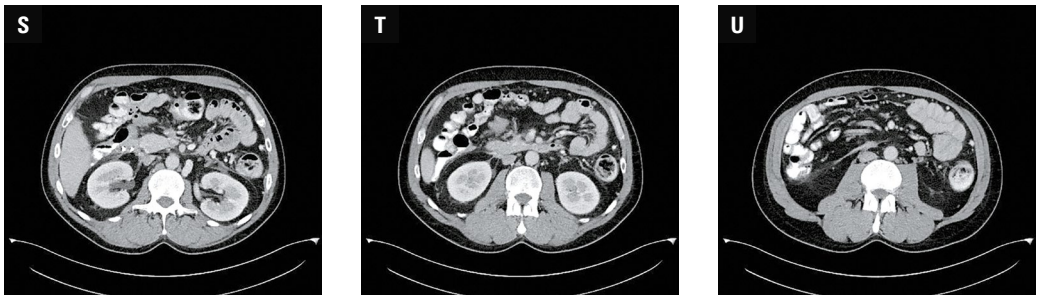


FIGURE 22 Endoscopic cystogastrostomy with active transmural drainage of an infected pancreatic pseudocyst. The cyst was compressing the posterior wall of the stomach (**A**). A transmural puncture using a 19-G needle (**B**–**D**) was performed in the prepyloric part of the stomach under endoscopic ultrasound guidance. The guidewire, inserted through the needle, was looped into the lumen of a large pancreatic pseudocyst (**E**, **F**). A lumen-apposing metal stent (LAMS) prosthesis deployment kit was subsequently inserted along the guidewire to create an endoscopic gastropancreatic fistula at the lowest peak of the collection to facilitate gravitational drainage (**G**–**O**). A 7-Fr, 15-cm double-pigtail plastic stent and a 7-Fr nasocystic drain were inserted through the lumen of the transmural LAMS (**P**–**U**).



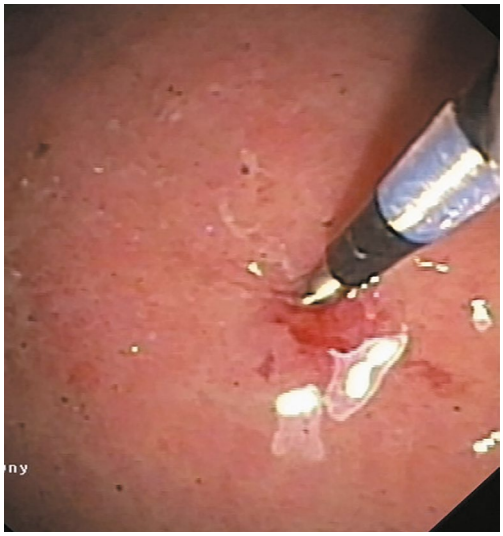


FIGURE 23 Endoscopic cystogastrostomy of a pancreatic pseudocyst; a photograph depicting the first stage of the procedure, ie, puncture of the collection with a cystotome needle knife

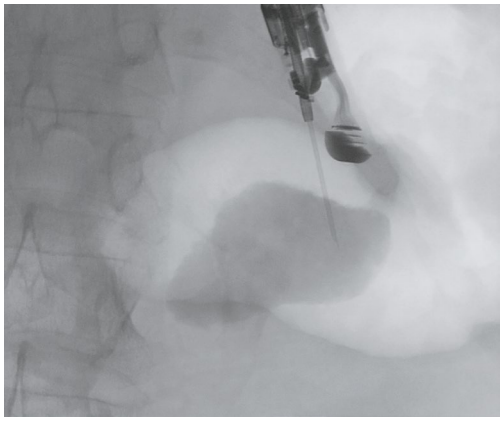


FIGURE 24 Fluoroscopic image acquired following a transmural puncture of an infected central pancreatic necrosis collection, showing the contrast agent administered through the needle filling the collection lumen

Frequently, in poorly liquefied WOPN collections, the collection contents cannot be aspirated following transmural puncture. In such cases, approximately 5–10 ml of sterile saline solution can be injected via a needle into the collection lumen, and a small amount of the diluted collection contents can be sampled for microbiological examination alone, since targeted antibiotic therapy of infected necrotic collections as based on the result of an antibiogram is often crucial for the subsequent disease progression and the effectiveness of endoscopic treatment, especially for poorly liquefied collections developing during necrotizing pancreatitis.

RECOMMENDATION 25 Following transmural access establishment, plastic double-pigtail stents with a diameter of at least 7 Fr or fully coated self-expandable stents (biflanged metal stents [BFMSs] / LAMSs) with a minimum diameter of 15 mm can be introduced into the postinflammatory pancreatic or peripancreatic fluid collections via the transmural fistula between the gastrointestinal tract and collection lumina[23,29,30,32-34,40,51,52,54-60,67,77,78,91-96,98,106,114-118,128,131-134,160-167,169-189,193,201,204,208,211-221,224-239,249-259] (*evidence level, moderate; recommendation, strong [average of votes, 2.84]*).

RECOMMENDATION 26 Self-expandable metal stents with a diameter of at least 15 mm facilitate the outflow of contents from the collection lumen during transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections by maintaining a large diameter of the fistula throughout the drainage period. In addition, the silicone membrane coating of the self-expandable metal stents prevents anastomotic leakage and spillage of the collection contents beyond the fistula[32-34,54-60,78,106,118,128,180,187-189,204,220,221,225,228,230,232-239,249-263] (*evidence level, low; recommendation, strong [average of votes, 2.87]*).

RECOMMENDATION 27 Plastic double-pigtail stents are commonly used in transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections owing to their low cost and easy removal, even after a long drainage period. However, self-expandable metal stents ensure more efficient drainage and are associated with a decreased incidence of stent obstruction due to the large diameter of the connection being maintained throughout the drainage period. In addition, fewer endoscopic instruments are required for the insertion of a transmural metal stent, reducing the duration of the procedure[32-34,40,54-60,67,77,78,106,118,128,143,180-183,187-189,204,207,212-215220,221,225,226,228,230,232-236,249-289] (*evidence level, low; recommendation, strong [average of votes, 2.84]*).

RECOMMENDATION 28 Self-expandable transmural metal stents should not be left in place for more than 4–6 weeks, as longer periods are associated with a higher incidence of complications, especially hemorrhagic complications. If complete regression of the collection has not been achieved after 4–6 weeks and transmural drainage remains required, the self-expandable metal stent should be replaced with another self-expandable transmural stent or a plastic double-pigtail stent[32-34,54-56,106,118,180,187-189,204,220,232-239,249-265,267-285,289-300] (*evidence*

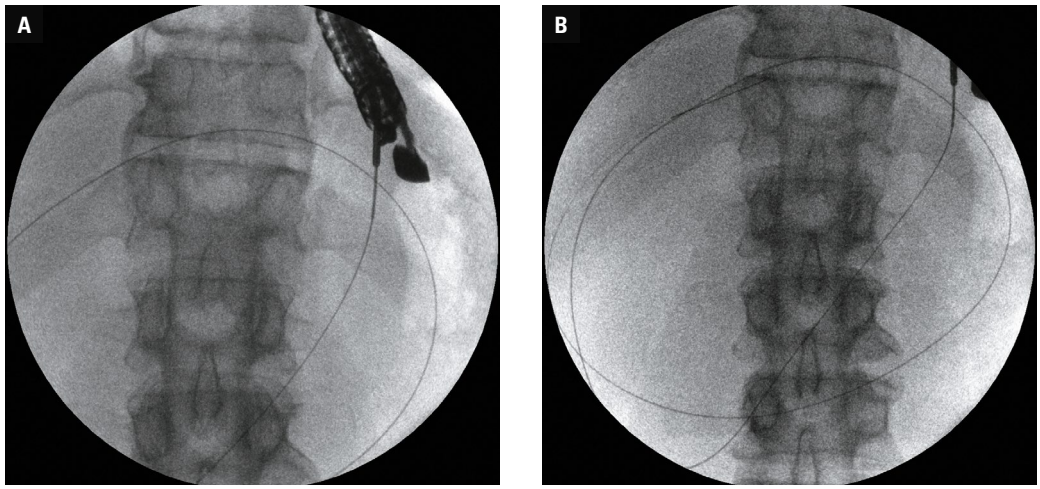


FIGURE 25 **A**, **B** – following a transmural/transgastric puncture, the guidewire inserted through the needle is looped inside into the lumen of the pancreatic pseudocyst under fluoroscopic guidance.

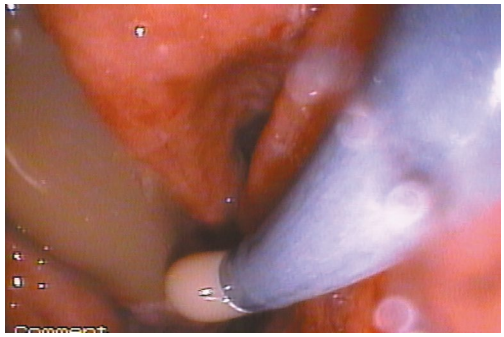


FIGURE 26 Endoscopic presentation after a gastropancreatic fistula has been created using a 10-Fr cystotome in a patient with infected walled-off pancreatic necrosis. Extensive outflow of necrotic contents through the endoscopic fistula is visible.

level, very low; recommendation, strong [average of votes, 2.55]).

During the endoscopic procedure, once the transmural fistula has been established and widened, further therapeutic management is decided upon, which is largely based on the ability to establish an effective drainage system. With the guidewire extending along the fistula into the collection lumen, an appropriate transmural stent is chosen regardless of the type of transmural drainage (passive or active); the transmural stent should be inserted after the a fistula is created endoscopically (**FIGURE 30A–30I**).

There are 2 types of transmural endoprostheses. The first type is a conventional plastic (Teflon) double-pigtail stent, widely used in biliary endotherapy. The "hook" (pigtail) at both ends of the stent reduces the risk of internal (ie, proximal migration into the collection lumen) and external (ie, distal migration into the stomach/duodenum lumen) migration. The second type comprises fully coated self-expandable metal stents (BFMSs and LAMSs) dedicated to draining pancreatic fluid collections. Both of these stent types feature 2 flanges (distal and proximal) that prevent their migration during the ongoing drainage. The main difference between the 2 stent types is that the special design of the flanges in LAMS facilitates the creation of force that closely approximates the walls of the 2 lumina (gastrointestinal tract and the drained collection), which further reduces the risk of LAMS migration, as compared with the BFMS. Although transmural metal stents have been developed as prostheses dedicated to draining fluid collections, they do not completely supplant the conventional plastic double-pigtail stents.

The choice of the appropriate stent type for transmural endoscopic drainage of fluid collections remains debatable. The numerous studies in the available literature comparing the efficacy and safety of drainage with plastic stents vs metal self-expandable stents often report contradictory results, either suggesting no difference in the treatment outcomes depending on the stent used, or suggesting better treatment outcomes with metal stents, albeit with a higher number of complications than that with plastic stents. Nevertheless, available data suggest that in some clinical situations a particular stent type is preferred. Although the choice of the stent type for transmural drainage of fluid collections is difficult, each stent has its own advantages and disadvantages, which should be considered during stent selection.

The general strategy for the selection of a transmural stent is based on the assumption that the larger the diameter of the fistula, the better the drainage conditions, because the wider the fistula, the easier the drainage of liquid contents from the collection lumen into the gastrointestinal tract lumen (**FIGURE 31A–31M**). Hence, for metal self-expandable stents, the diameter of the stent for transmural drainage should be at least 15 mm, whereas for plastic double-pigtail stents, a stent with a diameter of at least 7 Fr is required. Plastic double-pigtail stents with a diameter of 10 Fr provide a larger diameter for transmural drainage; however, they confer a higher risk of complications due to the stiffness of the stent, which may damage the collection wall and surrounding structures, including vascular structures, resulting in mechanical trauma–induced bleeding. If plastic stents are used, several stents should be inserted transmurally (**FIGURE 32A** and **32B**) to facilitate drainage of the collection contents through both the lumina of the stents and between the inserted stents. The insertion of several plastic stents further helps maintain a large diameter of the fistula throughout the drainage period and reduces the risk of anastomotic obstruction,

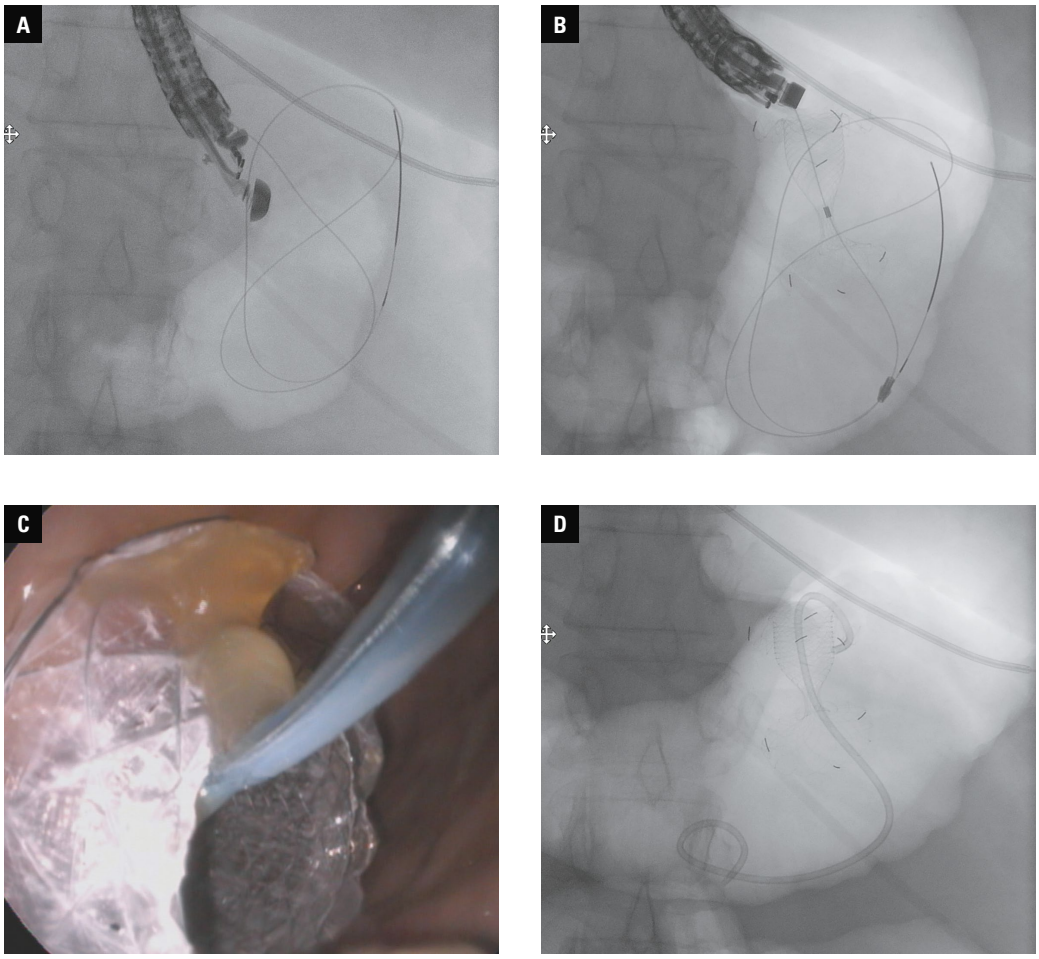


FIGURE 27 Passive endoscopic transmural drainage using a lumen--apposing metal stent (LAMS) in a patient with a 60 mm × 80 mm sterile pancreatic pseudocyst. After performing a transmural/transgastric puncture of the collection under endoscopic ultrasound guidance, the guidewire inserted through the needle was looped inside the collection lumen (**A**). A LAMS prosthesis deployment kit was subsequently inserted along the guidewire to create a transmural endoscopic fistula (cystogastrostomy; **B**, **C**) and achieve the outflow of clear, serous contents. A 7-Fr, 12-cm double--pigtail plastic stent was inserted through the lumen of the metal stent (**D**).

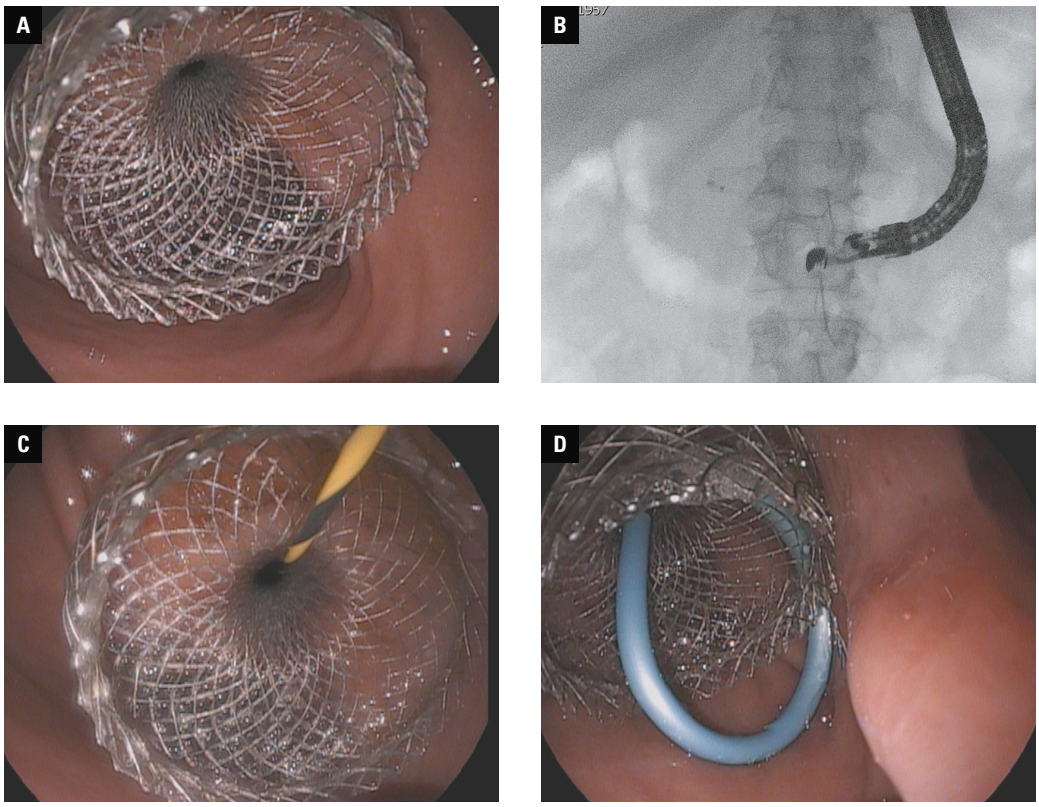


FIGURE 28 **A–D** – endoscopic cystogastrostomy with passive transmural drainage of a 85 mm × 95 mm sterile pancreatic pseudocyst using a Hot Axios electrocautery-enhanced lumen-apposing metal stent deployment kit

which can be encountered with a single plastic transmural stent, where stent obstruction usually results in fistula obstruction. An exception are patients with PPs (up to 10 cm in diameter) during pancreatic fragmentation, or those with disconnected pancreatic duct syndrome (DPDS). In such patients, a transmural endoscopic fistula is usually created using a single plastic stent to provide permanent transmural drainage of both the fluid collection and the disconnected

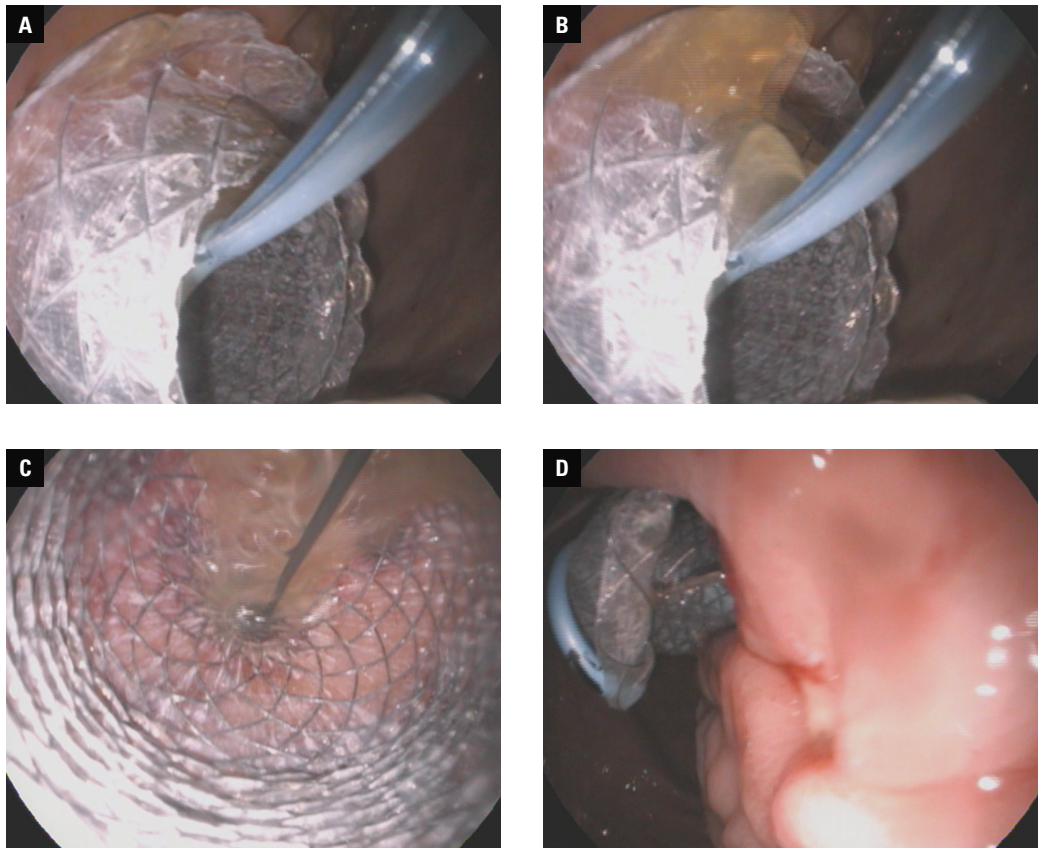


FIGURE 29 A–D – endoscopic cystogastrostomy with passive transmural wall drainage of a 80 mm × 80 mm sterile pancreatic pseudocyst, using a Hot Spaxus electrocautery-enhanced lumen-apposing metal stent deployment kit

pancreatic fragment. Another exception are patients with a residual collection during the ongoing transmural drainage, in whom a single plastic double-pigtail stent is left in place to continue endotherapy upon stent replacement. Overall, in patients with DPDS, PP, and residual fluid collection, the use of a single double-pigtail plastic stent is permissible for transmural drainage.

Self-expandable metal stents (BFMSs/LAMSs) ensure the maintenance of a large diameter of the transmural fistula throughout the drainage procedure; the large diameter (at least 15 mm) of these stents ensures free drainage of the collection contents into the gastrointestinal tract lumen to reduce the duration of transmural endoscopic drainage as well as the total duration of endotherapy of fluid collections. A large-diameter endoscopic fistula, achieved via self-expandable metal stents, translates to better efficiency of drainage and a lower incidence of episodes of stent obstruction and secondary superinfection of collection contents owing to the large diameter of the stent and effective drainage throughout the endotherapy period. Moreover, the full silicone membrane coating of self-expandable metal stents prevents anastomotic leakage and spillage of the collection contents beyond the fistula, which is more common with plastic stents. In addition, owing to the dual-flange design, self-expandable metal stents are less likely to migrate during endotherapy, thus preventing anastomotic leakage.

The length of a self-expandable transmural stent should be at least 20 mm, with longer stents being associated with a lower risk of stent migration during drainage.

During the transmural endoscopic drainage procedure using self-expanding metal stents, fewer endoscopic accessories are usually required, reducing the duration of the procedure. Nevertheless, the procedure performed with plastic double-pigtail stents is less costly; therefore, these stents are commonly used for transmural drainage of fluid collections. In addition, plastic double-pigtail stents are easy to remove, even after a long drainage period. In comparison, self-expandable metal stents, except in selected cases, should not be left in place for more than 4–6 weeks. Longer periods of transmural metal stent retention are associated with an increased incidence of complications, especially hemorrhagic complications. These are more often observed with LAMSs, where the force generated between the flanges of the stent approximating the walls of the 2 cavities creates conditions for granulation tissue overgrowth at the collection healing stage, despite the stent's coating. Granulation tissue in the fistula often results in bleeding into the gastrointestinal tract lumen and can contribute to difficulty in removing the transmural stent (buried stent syndrome; **FIGURE 33A–33C**). In addition, transmural metal stents can cause bleeding consequent to mechanical trauma caused by the distal flange of the transmural stent on the posterior wall of the collection. Insertion of a plastic double-pigtail stent through the transmural metal stent's lumen moves the posterior wall of the collection away from the distal flange of the stent (**FIGURE 34A** and **34B**), which

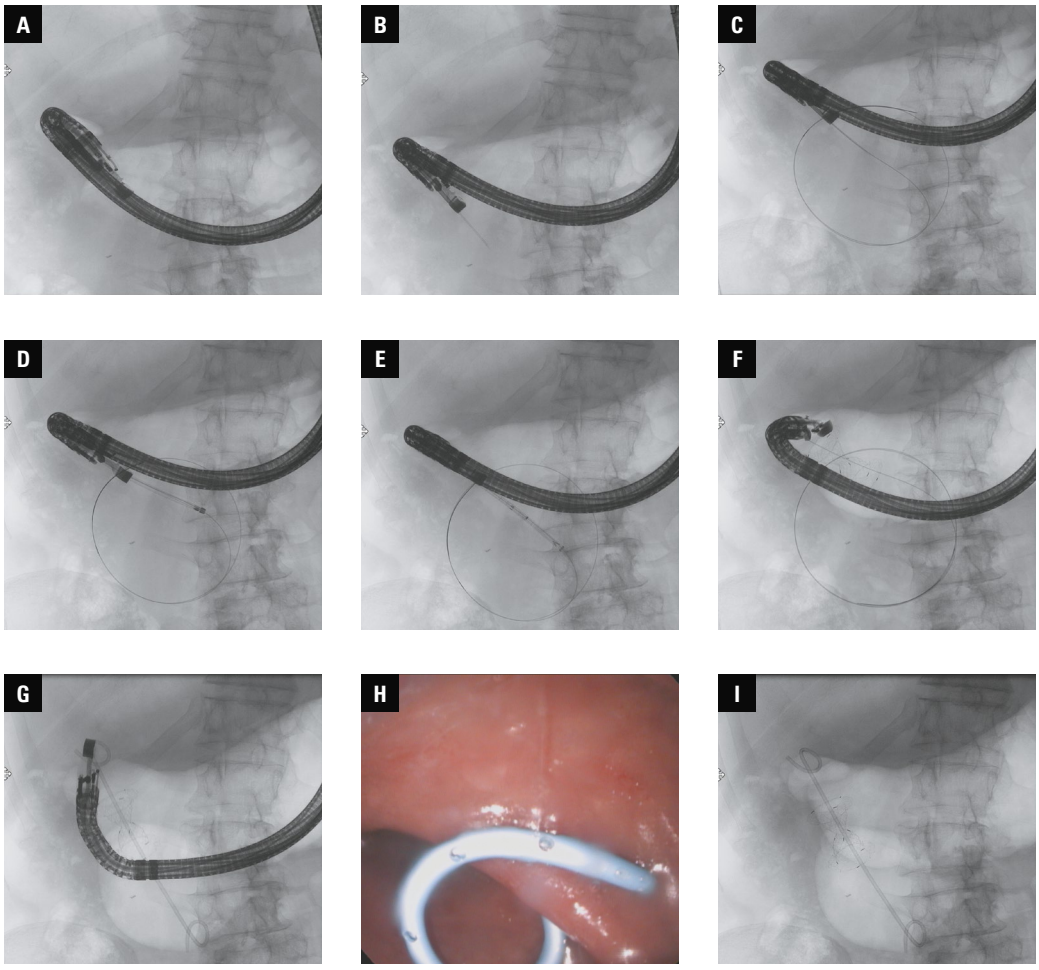


FIGURE 30 Endoscopic cystoduodenostomy of a sterile postinflammatory pseudocyst cyst located in the pancreatic head in a patient with chronic pancreatitis. After transmural/transduodenal puncture of the pancreatic pseudocyst with a 19-G needle (**A**, **B**), a guidewire was inserted through the needle and looped inside the lumen of the cyst (**C**). A 10-Fr cystotome was subsequently used to create an endoscopic pancreatoduodenal fistula (**D**). A biflanged metal stent, 30 mm in length and 16 mm in diameter (**E**, **F**) and a 7-Fr, 12-cm double-pigtail plastic stent were inserted through the anastomotic lumen (**G–I**).

reduces the risk of mechanical trauma. In addition, by pushing away the posterior wall, the plastic double-pigtail stent facilitates uniform evacuation of the collection contents and prevents the wall from prolapsing toward the distal flange, which might cause uneven drainage and retention of contents in the peripheral parts of the collection, leading to superinfection of the collection contents and failure of endoscopic drainage. For extensive fluid collections, the insertion of several plastic double-pigtail stents into the distal parts of the collection facilitates uniform drainage of the entire fluid collection, preventing the collection walls from collapsing and forming superinfected subcompartments requiring separate drainage. Although the large lumen of the transmural metal stent reduces the risk of anastomotic obstruction, such obstruction may occur in poorly liquefied necrotic collections (**FIGURE 35**). In addition, transmural endoscopic stents placed in the distal part of the gastric body or in the prepyloric part of the stomach may result in the stent being obstructed by food content. In such cases, obstruction of the metal stent can be prevented by introducing a plastic double-pigtail stent through the lumen of the transmural metal stent (**FIGURE 36A–36C**), facilitating drainage of the collection contents between the plastic stents even in the cases of obstruction of the transmural stent.

Regarding bleeding from the site of a transmural endoscopic fistula, self-expandable metal stents have an advantage over plastic double-pigtail stents because of their design. The fully-coated transmural stents facilitate bleeding stoppage (tamponade principle) consequent to pressure applied at the fistula site after the stent expansion. A technique to hasten hemostasis, achieved through full expansion of the self-expandable metal stent (usually within 24 hours of stent insertion), is the pneumatic dilatation of the anastomotic lumen using a high-pressure balloon, which further allows the free flow of the collection contents through the fistula into the gastrointestinal tract lumen. Balloon dilatation is not routinely recommended during procedures involving the creation of a transmural fistula and the insertion of a transmural metal stent at the anastomotic site owing to a high risk of migration of the self-expandable transmural stent.

Self-expandable transmural metal stents should not be left in place for more than 4–6 weeks, except where the risk of complications associated with stent removal (anastomotic leakage) is greater than the risk associated with leaving the stent for a longer period. If complete regression of the collection has not been achieved after 4–6 weeks and transmural drainage remains required, the self-expandable metal stent should be replaced with another self-expandable metal stent or a plastic double-pigtail stent (multiple, if required), depending on the volume and type of

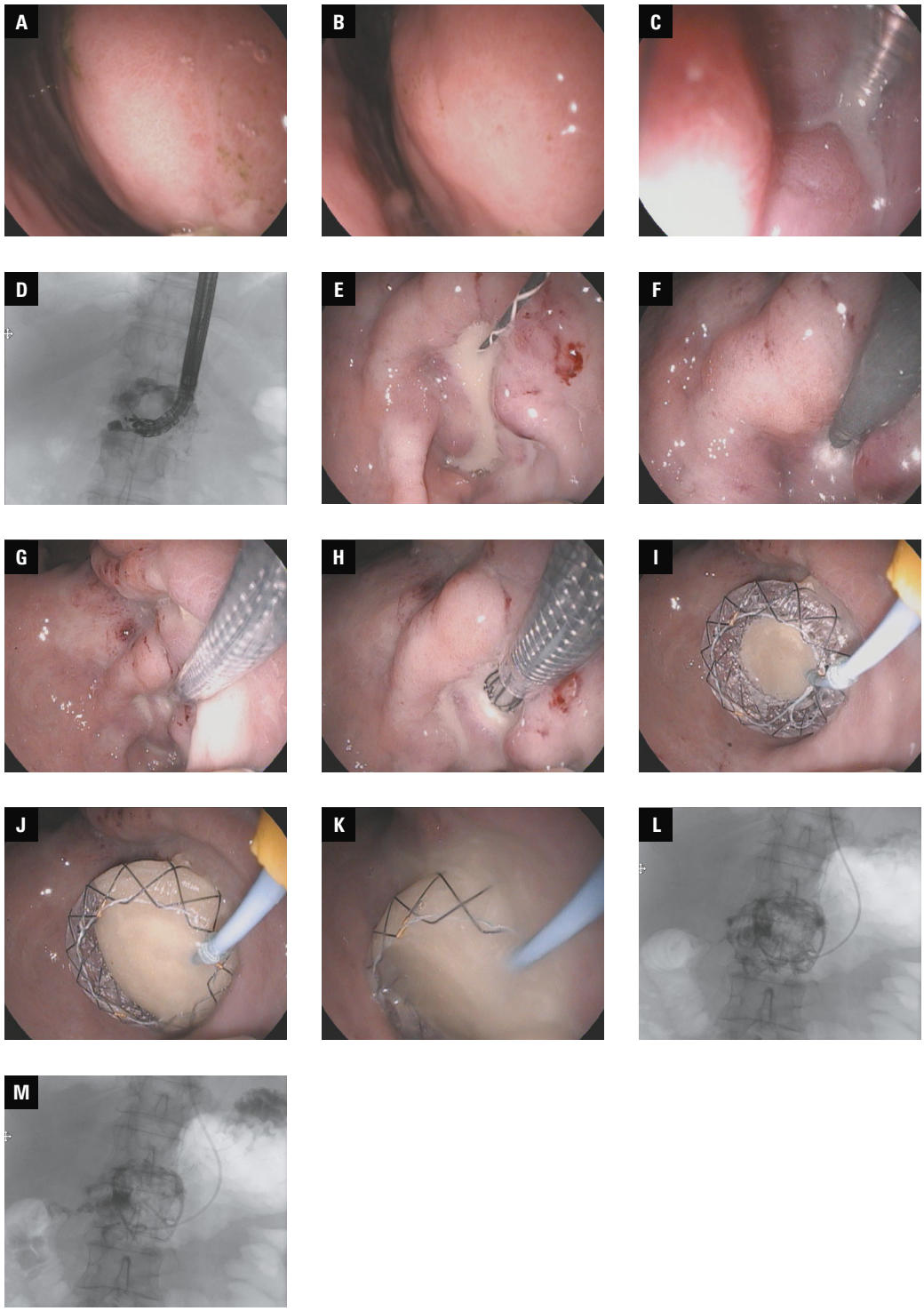


FIGURE 31 Active endoscopic transmural/transgastric drainage of infected walled-off pancreatic necrosis. The necrotic collection was compressing the posterior wall of the stomach (**A**, **B**). A transmural/transgastric puncture of the necrotic collection was performed under endoscopic ultrasound guidance using a 19-G needle (**C**, **D**). Contrast administered through the needle filled the lumen containing irregular necrotic collection, including dense fluid and numerous necrotic tissues (**D**). A transmural guidewire was left in the lumen of the collection (**E**), and a 10-Fr cystotome (**F**) was introduced along the guidewire to create a gastropancreatic fistula. A biflanged metal stent, 30 mm in length and 16 mm in diameter, was inserted through the anastomotic lumen (**G**–**K**), causing visible extensive outflow of the infected necrotic content. A 7-Fr, 12-cm double pigtail plastic stent and 7-Fr nasal drain were inserted through the lumen of the transmural metal stent (**L**). Contrast administered through the nasocystic drain filled the necrotic collection and freely draining through the transmural endoscopic fistula into the gastric lumen (**M**).

the evacuated collection. More frequent replacement of self-expandable metal stents increases the treatment costs, as compared with plastic stents. Thus, better clinical results of endoscopic treatment of fluid collections using transmural metal stents are associated with higher costs and a greater number of endoscopic interventions needed to achieve treatment success.

In summary, for extensive fluid collections, transmural metal stents improve drainage outcomes owing to the wider diameter of the endoscopic fistula, which facilitates the free flow of the collection contents into the gastrointestinal tract lumen. Self-expandable transmural metal stents can be used for endoscopic drainage of PPs, and especially for WOPN, where their benefits are greater than those of endotherapy for PPs.

RECOMMENDATION 29 Plastic double-pigtail stents can solely be used for passive transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections for well-liquefied collections, especially in sterile PPs[5,34,40,54-59,67,77,-181-183,187,212-215,221,225,226,230,250-254,258,263-266] (*evidence level, low; recommendation, strong [average of votes, 2.84]*).

Passive transmural endoscopic drainage (transgastric or transduodenal) involves the establishment of a transmural endoscopic fistula between the upper gastrointestinal tract and collection

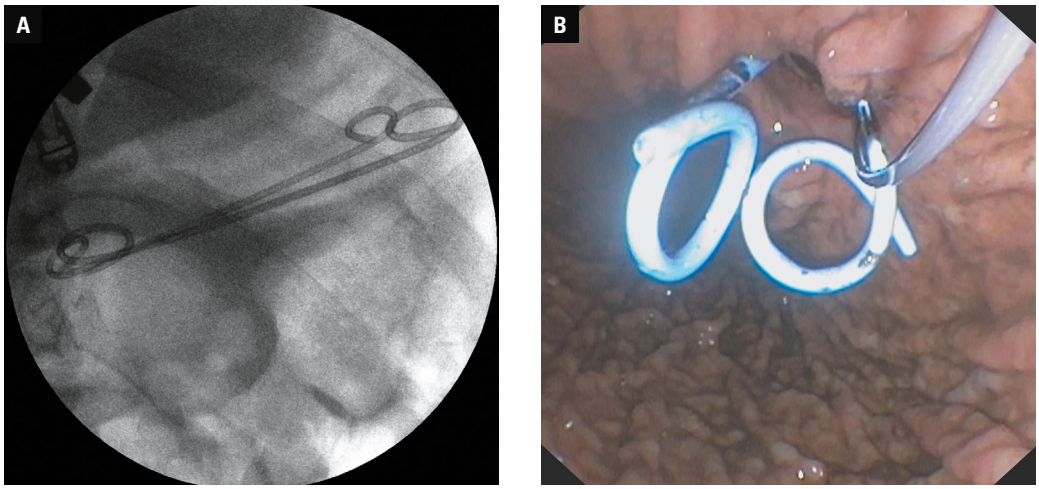


FIGURE 32 **A**, **B** – passive transmural/transgastric drainage of a 70 mm × 80 mm sterile pancreatic pseudocyst, using a 7-Fr, 12-cm double-pigtail plastic stent

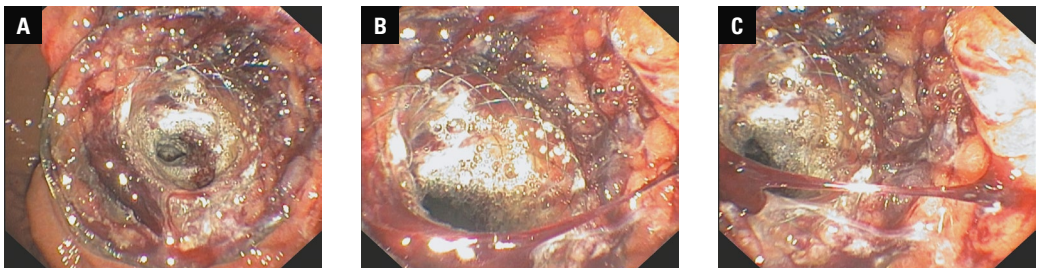


FIGURE 33 **A**–**C** – buried stent syndrome: endoscopic image of a lumen-apposing metal stent demonstrating granulation tissue hyperplasia with spontaneous bleeding from the granulation tissue on day 36 of transmural endoscopic drainage of walled-off pancreatic necrosis

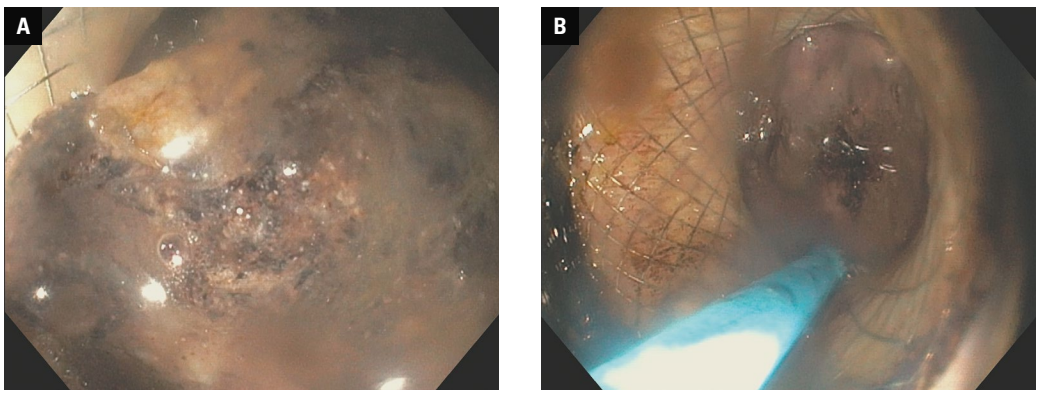


FIGURE 34 **A** – Transmural lumen-apposing metal stent with the collapse of the posterior wall of the walled-off pancreatic necrotic collection resulting in obstruction of the endoscopic fistula; **B** – A double-pigtail plastic stent was inserted through the lumen of the transmural metal stent to push the posterior wall of the collection away from the distal flange of the transmural stent, ensuring patency of the endoscopic fistula.

lumina, followed by the insertion of a stent or stents through the fistula to ensure free drainage of the collection contents into the gastrointestinal tract lumen, that is, from a high-pressure to a low-pressure compartment. Passive transmural drainage can be achieved via metal self-expandable stents (BFMSs/LAMSs) and/or plastic double-pigtail stents.

Passive transmural drainage is an effective method for endoscopic treatment of sterile PPs that contain clear, serous fluid without solid debris, provided that the diameter of the cyst does not exceed 10 cm. For sterile PPs, passive transmural drainage can be achieved via plastic double-pigtail stents alone (**FIGURE 37A–37E**), without the need for self-expandable stents, as the clear, serous contents will drain freely into the gastrointestinal tract through the lumina of plastic stents as well as between the plastic stents without a risk of tissue elements obstructing the fistula. This is in contrast to fluid collections containing dense debris, such as infected PPs and fluid collections in necrotizing AP, where passive transmural drainage using plastic double-pigtail stents is often insufficient, and self-expandable metal stents and active drainage methods via a nasocystic drain are required. Similarly, active transmural drainage via plastic double-pigtail stents and a nasocystic drain should be used for large sterile PPs with a diameter greater than 10 cm, where passive drainage may be insufficient.

Notably, for sterile PPs up to 10 cm in diameter, passive transmural drainage using self-expandable metal stents can also be pursued (**FIGURE 38A–38G**). Similarly, metal transmural stents can be used for larger PPs when active transmural drainage is necessary.

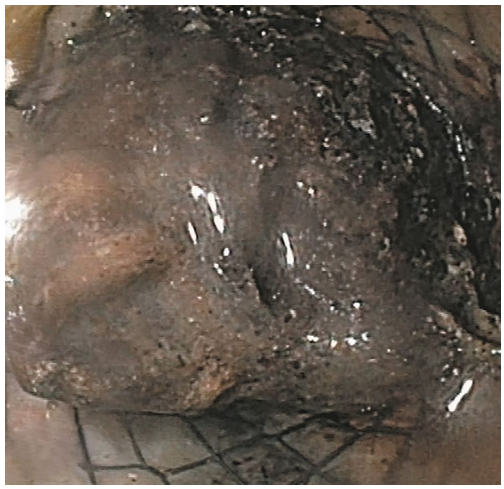


FIGURE 35
A transmural biflanged metal stent obstructed by a fragment of necrotic tissue visualized on endoscopic imaging

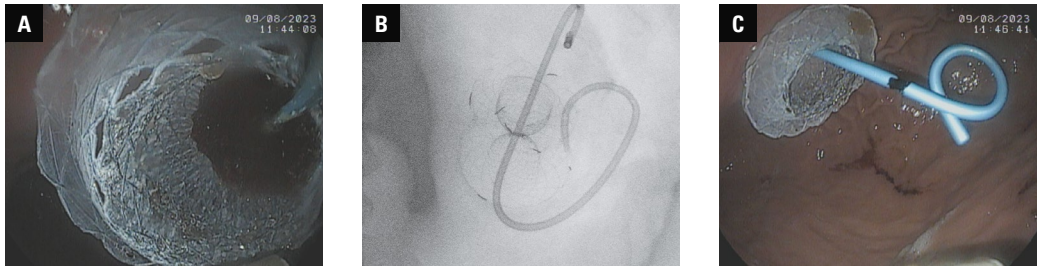


FIGURE 36 **A–C** – endoscopic cystogastrostomy of a sterile pancreatic pseudocyst with passive transmural/transgastric drainage. A transmural lumen-apposing metal stent and a plastic 7-Fr 9-cm double-pigtail stent were introduced through the fistula.

RECOMMENDATION 30 For WOPN collections, as well as for infected PPs and sterile PPs greater than 10 cm in diameter, passive transmural drainage is insufficient and active transmural drainage via a nasocystic drain inserted through the transmural fistula into the collection lumen is necessary for active flushing of the lumen in the postoperative period[34,55,56,159-164,166,169,207-210,217,227-231,301-309] (*evidence level, low; recommendation, strong [average of votes, 2.55]*).

Active transmural endoscopic drainage involves creating a transmural fistula between the upper gastrointestinal tract and collection lumina, and inserting a stent or stents (metal self-expandable stents [BFMSs/LAMSs] and/or plastic double-pigtail stents) through the fistula along with a nasocystic drain, the distal end of which is left in the collection lumen and the proximal end is extracted through the nose to facilitate active flushing of the collection lumen in the postoperative period. The optimum size of the nasocystic drain is 7 Fr, similar to the plastic double-pigtail stents. Such a size is large enough to facilitate free insertion of the drain through the fistula during the procedure and free drainage of the collection in the postoperative period via flushing of the collection cavity while remaining flexible (similarly to drains >7 Fr) to prevent stiffness-induced mechanical trauma to the collection wall and surrounding structures.

Indications for active transmural drainage of fluid collections include sterile PPs greater than 10 cm in diameter and, regardless of their size, infected PPs (**FIGURE 39A–39K**) and WOPN collections (**FIGURE 40A–40F**). In addition, active transmural drainage should be pursued if the passive transmural drainage proves ineffective. For necrotic collections, several nasocystic drains (**FIGURE 41A** and **41B**), inserted through a transmural fistula, may be necessary, with their distal ends located in different parts of the collection.

Flushing of the fluid collection through a nasocystic drain with 0.9% sodium chloride (saline) solution should be performed in the post-operative period in an intermittent rather than continuous manner. The standard drain flushing schedule includes administering 200 ml of saline every 4–6 hours, usually without aspiration. Solution volume greater than 200 ml is usually not needed, while smaller amounts are required for small collections, usually approximately 5 cm in diameter. Aspiration of the contents via the drain is necessary when the drainage system is not effective enough to allow the contents to flow freely from the collection into the gastrointestinal tract lumen under flushing through the nasocystic drain. For poorly liquefied necrotic collections and infected collections, more frequent flushing may be necessary, for example, up to every 2 hours. However, it should be noted that the volume of the flushing solution, the interval between flushings, and the duration of active drainage depend on the clinical situation. In the absence of contraindications, in stable patients who are able

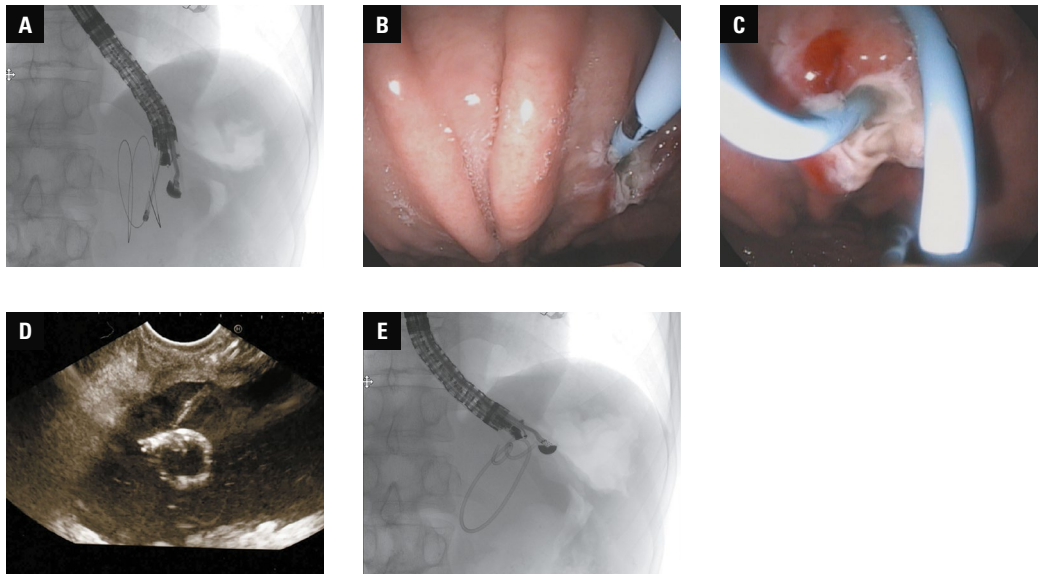


FIGURE 37 Passive endoscopic transmural/transgastric drainage (cystogastrostomy) in a patient with a postinflammatory pancreatic pseudocyst and pancreatic fragmentation (disconnected pancreatic duct syndrome). A transgastric puncture was performed, and an approximately 50-mm pseudocyst was localized in the pancreas on endoscopic ultrasound imaging, followed by guidewire insertion. A 10-Fr cystotome was inserted along the guidewire to create a transmural endoscopic fistula (**A**). A 7-Fr, 9-cm double-pigtail stent was inserted through the fistula for permanent transmural drainage (**B**–**E**).

to flush the collection independently through the nasocystic drain in the postoperative period, flushing can be continued on an outpatient basis postdischarge, with the recommendation of periodic follow-ups to be determined on an individual basis.

When creating the transmural endoscopic fistula, the goal should be to maximize aspiration of the collection contents, usually after a stent is inserted through the fistula. Such aspiration usually reduces the collection drainage time and is particularly important for draining infected fluid collections.

Solutions other than saline are not recommended for flushing the nasocystic drain. Flushing the nasocystic drain with a hydrogen peroxide solution, other antimicrobial agents, or antibiotics is contraindicated owing to an increased risk of complications, especially hemorrhagic complications. Similarly, negative pressure endoscopic drainage (Endo-VAC) is not recommended during endotherapy of fluid collections.

The timing of termination of active transmural drainage, that is, the removal of the nasocystic drain, depends on the clinical setting and is strictly personalized; therefore, it is difficult to define unambiguous criteria indicating the need to remove the nasocystic drain. Often, the decision is based on the patient's clinical condition (clinical improvement with resolution of collection-related complaints) and partial regression of the collection observed on abdominal imaging scans. Completion of active transmural drainage involves the removal of the nasocystic drain, with the transmural stents being left in place to ensure passive transmural drainage of the collection during further endotherapy.

RECOMMENDATION 31 For WOPN lesions and multiocular PPs, multiplexing the transmural access by establishing several transluminal gateways may be required[32-34,55-56,78,118,128,180,228,231,232,310-316] (*evidence level, very low; recommendation, strong [average of votes, 2.67]*).

The mainstay of endoscopic treatment of fluid collections is transmural drainage, which involves the creation of a transmural endoscopic fistula between the upper gastrointestinal tract and collection lumina. Usually, a single transmural luminal access that is established via the single transluminal gateway technique (SGT) is sufficient to completely drain the collection through a single endoscopic fistula (**FIGURE 42**).

The single transluminal gateway transcystic multiple drainage (SGTMD) technique, a modification of the SGT of endoscopic drainage, involves accessing extensive fluid collections, especially necrotic collections, from a single transluminal access site, with distal ends of plastic double-pigtail stents, inserted through a transmural metal stent, left in place in remote parts of the collection located away from the transmural fistula. When establishing multiplexed access through a single transmural fistula, especially in the cases of necrotic collections, several nasocystic drains may need to be inserted through the transmural endoscopic fistula, with their distal ends being placed in different parts of the collection. The indication for the use of the SGTMD technique is the failure of endoscopic drainage via the SGT in patients with extensive

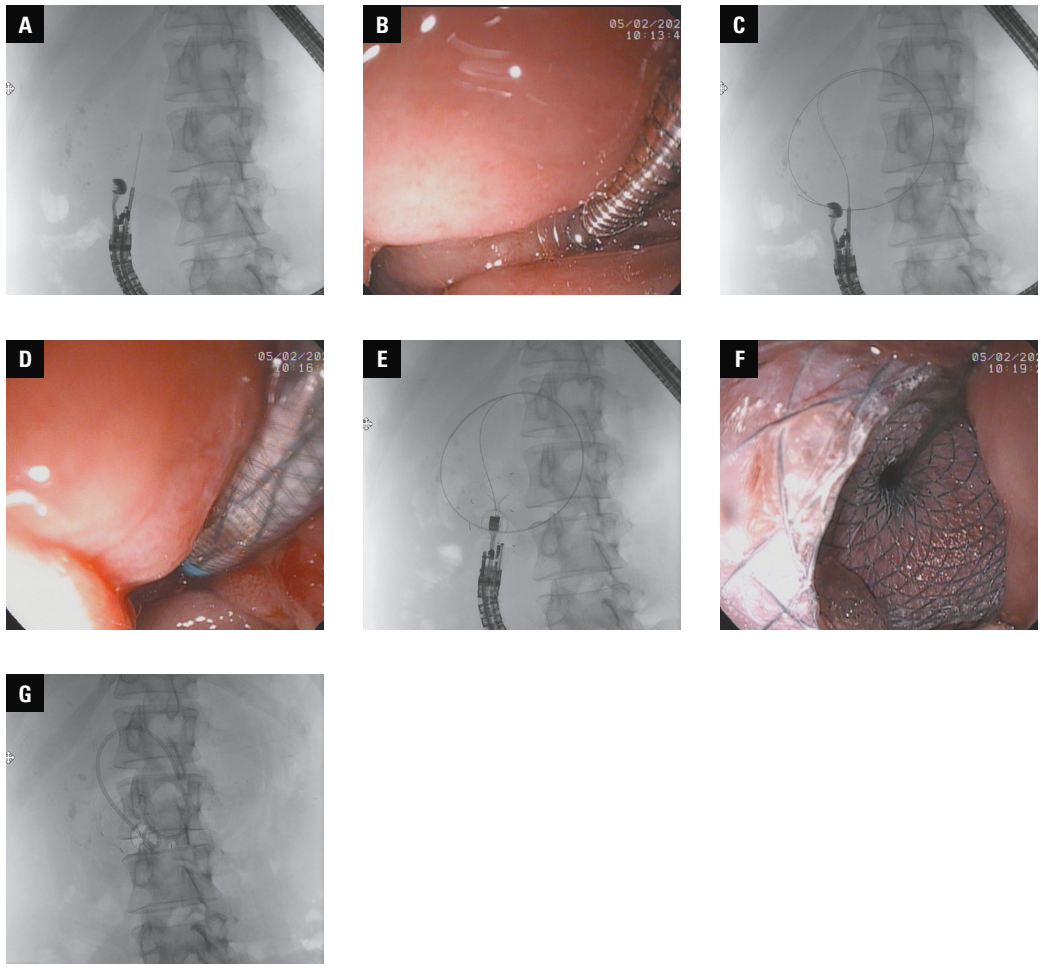


FIGURE 38 Endoscopic cystoduodenostomy with passive transmural/transduodenal drainage of an 80-mm sterile pancreatic pseudocyst in the pancreatic head in a patient with chronic pancreatitis. Fluoroscopy showed multiple calcifications in the pancreatic field (**A**, **C**, **E**, **G**). Following transmural/transduodenal puncture of the pancreatic pseudocyst using a 19-G needle (**A**, **B**), the inserted guidewire was looped into the lumen of the collection (**C**). An electrocautery-enhanced lumen-apposing metal stent (LAMS) deployment kit was subsequently inserted along the guidewire (**D**) to create an endoscopic pancreatoduodenal fistula for the insertion of a LAMS-type stent (**E**, **F**). A 7-Fr, 12-cm double-pigtail plastic stent was inserted through the lumen of the metal stent (**G**).

collections of poorly liquefied WOPN, provided that the compartments and subcompartments of the collection are interconnected.

If the SGT or SGTMD technique fails, multiple transluminal gateway techniques (MTGTs) are indicated, which involve the creation of more than 1 transmural fistula. Usually, a dual transmural fistula (**FIGURE 43A–43D**), established during sequential endoscopic procedures rather than as part of a single procedure, is sufficient to achieve the goal. The use of MTGTs in patients with WOPN, especially those with extensive collections (>10 cm), improves drainage conditions and increases the effectiveness of endotherapy. In addition, MTGTs are indicated in the case of multilocular fluid collections with no communication between the collection's compartments or subcompartments (**FIGURE 44A–44C**), as they ensure free flow of contents from each of the collection's compartments through a separate transmural fistula into the gastrointestinal tract lumen.

RECOMMENDATION 32 For WOPN collections, stepping up of the endoscopic treatment via endoscopic necrosectomy may be required[32-34,45,52,54-56,60,67,74,78,91-96,98-101,106,110,114-118,125,130-135,161-180,189,218,221,228-231,270-272,274,279-281,286,291,301,306,308,316-327] (*evidence level, moderate; recommendation, strong [average of votes, 2.93]*).

RECOMMENDATION 33 Direct endoscopic necrosectomy involves inserting an endoscope through a transmural endoscopic fistula into the necrotic collection lumen under carbon dioxide insufflation and removing the necrotic tissue under endoscopic imaging guidance using various types of endoscopic instruments[32-34,45,52,54-56,60,67,74,78,91-96,98-101,106,110,114-118,125,130-135,161-180,188,218,221,228-231,270-272,274,279-281,286,291,301,306,316-336] (*evidence level, moderate; recommendation, strong [average of votes, 2.91]*).

RECOMMENDATION 34 Self-expandable transmural metal stents are indicated in poorly liquefied necrotic collections where the next step of treatment

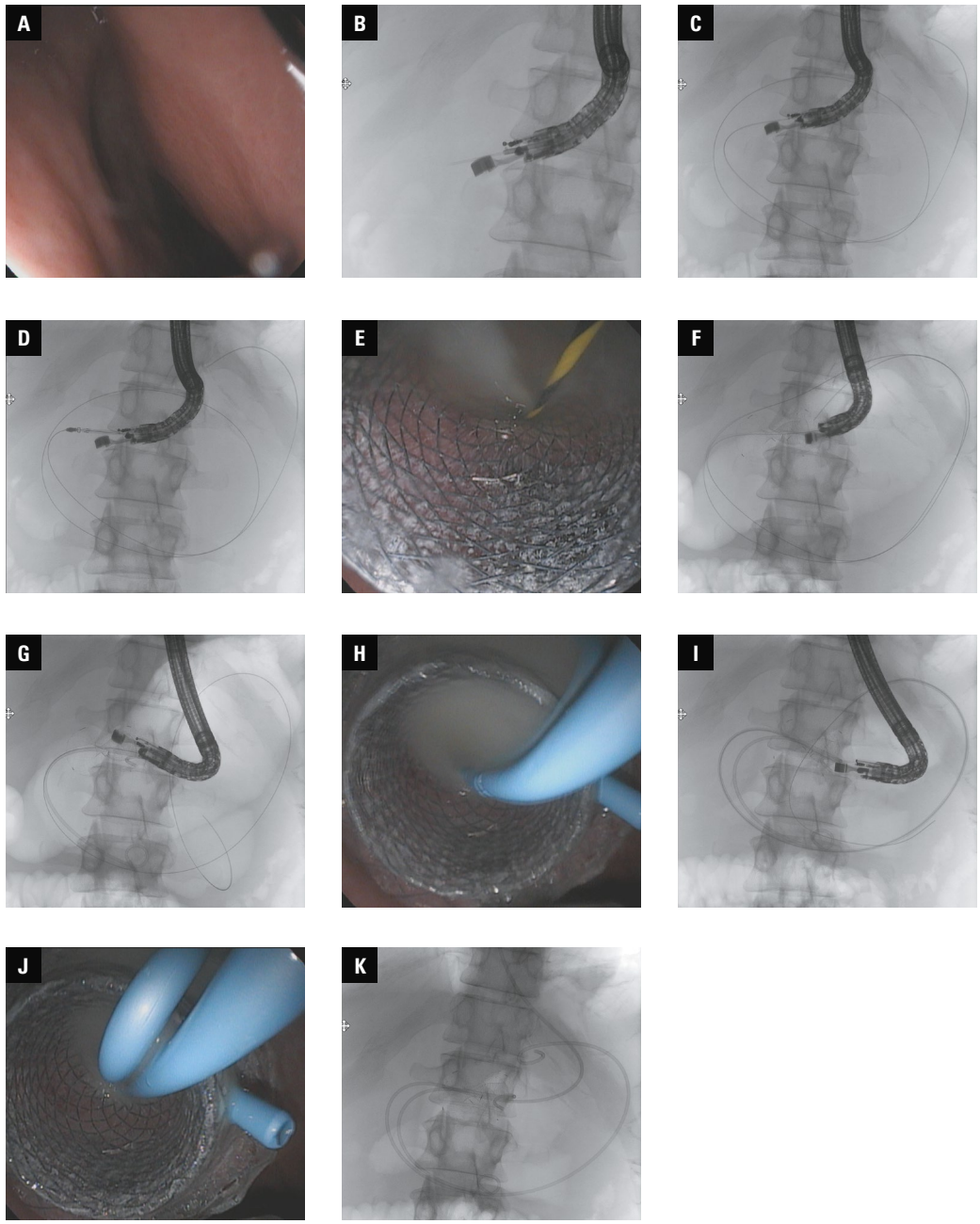


FIGURE 39 Active endoscopic transmural/transgastric drainage of an infected postinflammatory pancreatic pseudocyst. The endoscopic image shows the cyst heavily compressing the posterior wall of the stomach (**A**). Transgastric puncture of the collection was performed in the peak region of the compression under endoscopic ultrasound guidance using a 19-G needle (**B**). A guidewire was inserted through the needle and looped inside the lumen of the cyst (**C**). An endoscopic gastropancreatic fistula was created over the guidewire, followed by lumen-apposing metal stent (LAMS) deployment (**D**), with the outflow of infected contents from the collection lumen being documented on endoscopic imaging (**E**). A guidewire was inserted through the lumen of the transmural metal stent, followed by a 7-Fr, 12-cm double-pigtail stent (**F**). A nasocystic drain (**G**–**K**) was inserted through the LAMS lumen along the plastic stent for active drainage in the postoperative period.

may involve endoscopic necrosectomy, since these stents facilitate safe insertion of the endoscope into the collection lumen and the performance of endoscopic necrosectomy[32-34,54-56,78,106,114-118,128,-161-180,188,228,230,237-239,317-319,327] (*evidence level, very low; recommendation, strong [average of votes, 2.87]*).

The commonly recommended and accepted treatment strategy for local complications of necrotizing AP involves a step-up approach, including endoscopic techniques via the transmural route (endoscopic step-up approach) or surgical techniques via the percutaneous route (surgical step--up approach). According to this strategy, the necrotic collection should be progressively multiplied using minimally-invasive techniques, with open abdominal necrosectomy remaining the treatment of choice only if the aforementioned approach fails. The step-up approach, involving minimally-invasive techniques for

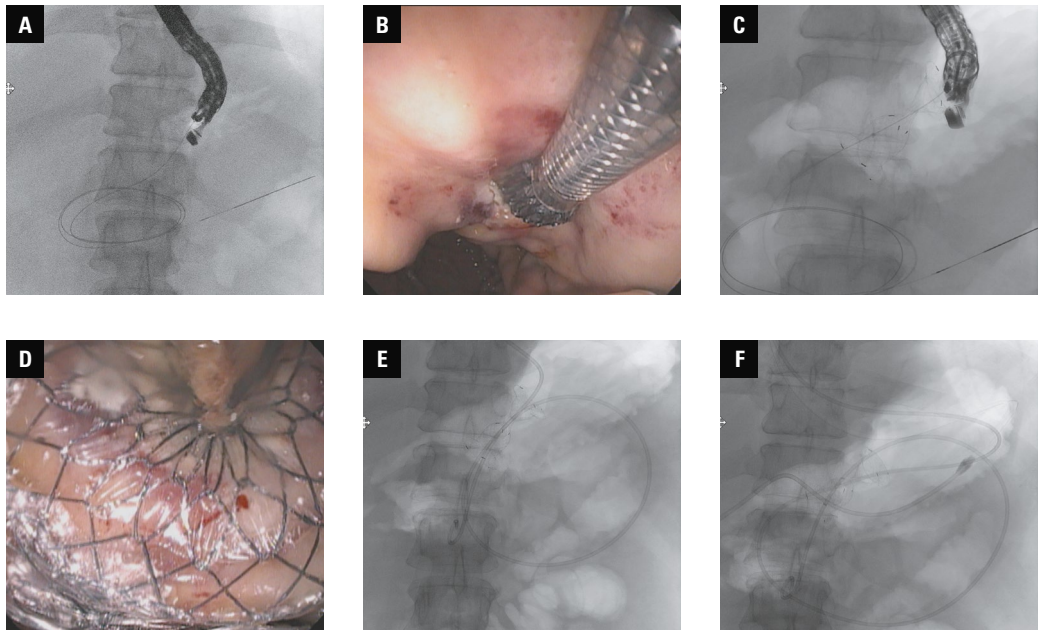


FIGURE 40 Active transmural/transgastric endoscopic drainage of a walled-off pancreatic necrotic collection. After transgastric puncture of the necrotic collection under endoscopic ultrasound guidance, a guidewire inserted through the needle was looped inside the collection lumen (**A**). Following the creation of a gastropancreatic fistula, a transmural biflanged metal stent, 30 mm in length and 16 mm in diameter, was inserted through the anastomotic lumen (**B**, **C**), with the outflow of necrotic contents and necrotic tissue fragments visualized on endoscopic imaging (**D**). A 7-Fr nasocystic drain was inserted through the lumen of the stent and looped inside the collection lumen (**E**, **F**). Fluoroscopy showed a feeding probe (**G**) inserted into the lumen of the jejunum after the endoscopic procedure.

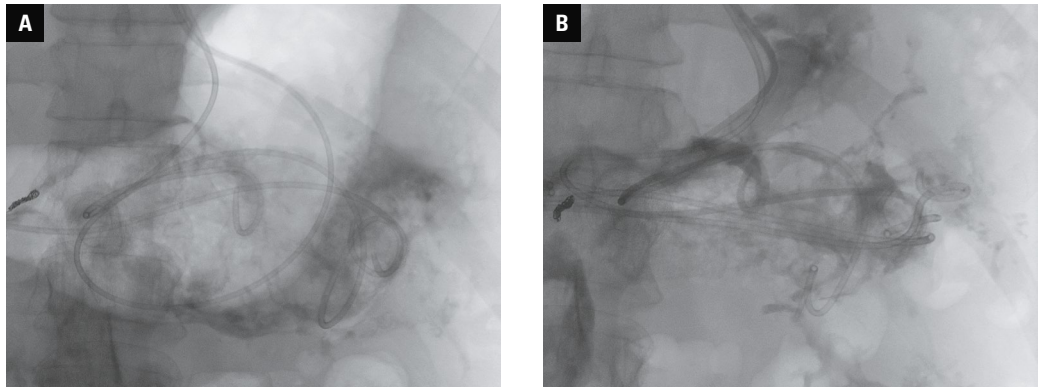


FIGURE 41 **A**, **B** – active transmural/transgastric drainage of a walled-off pancreatic necrotic (WOPN) lesion using 2 nasocystic drains inserted through the lumen of a transmural metal stent into the collection lumen. The contrast administered through the drains filled the WOPN lesion and freely drained into the gastric lumen. Vascular coils inserted into a branch of the common hepatic artery due to bleeding into the collection lumen are visible on the fluoroscopic image.

patients with pancreatic necrosis, improves patient outcomes and reduces complications, as compared with traditional management based on open necrosectomy procedures.

According to the endoscopic step-up approach strategy, in the case of failure of active endoscopic drainage of WOPN collections, further interventional treatment should involve endoscopic necrosectomy with mechanical removal of the necrotic tissue fragments in the collection lumen using various types of endoscopic tools (**FIGURE 45A–45F**). All endoscopic procedures should be performed under carbon dioxide insufflation. Direct endoscopic necrosectomy involves inserting an endoscope through a transmural endoscopic fistula into the necrotic collection lumen under carbon dioxide insufflation, removing the necrotic tissue using endoscopic instruments under direct endoscopic imaging guidance, and flushing the collection cavity with saline with simultaneous aspiration of the contents. Blunt removal of the necrotic tissues using a Dormia basket or an extraction balloon is preferred, since, unlike the sharp removal of necrotic tissue using forceps or coagulation, it facilitates selective removal of well-defined necrotic tissue fragments, partially liquefied and separated during active transmural drainage, reducing the risk of damage to other structures, including vascular structures, and thereby reducing the risk of bleeding (**FIGURE 46**).

Direct endoscopic necrosectomy has no specific indications. Endoscopic necrosectomy procedures should be performed in the patients with WOPN lesions who experience no clinical improvement under active endoscopic drainage. The endoscopic necrosectomy procedure should involve removal of the necrotic tissue in a continuous manner via the transmural fistula into the gastrointestinal tract lumen. In the patients with poorly liquefied

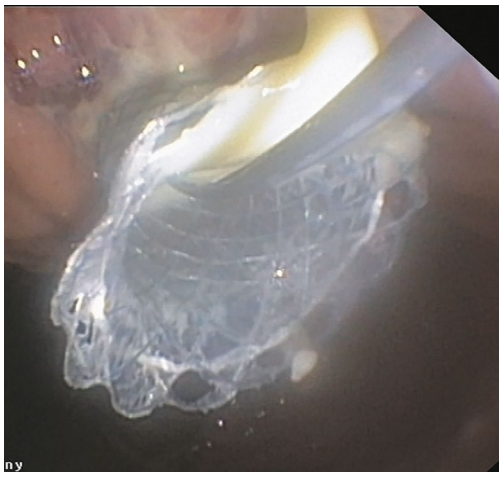


FIGURE 42 Endoscopic single transluminal gateway image showing an intense outflow of purulent contents from an infected pancreatic pseudocyst through a self-expanding transmural biflanged metal stent

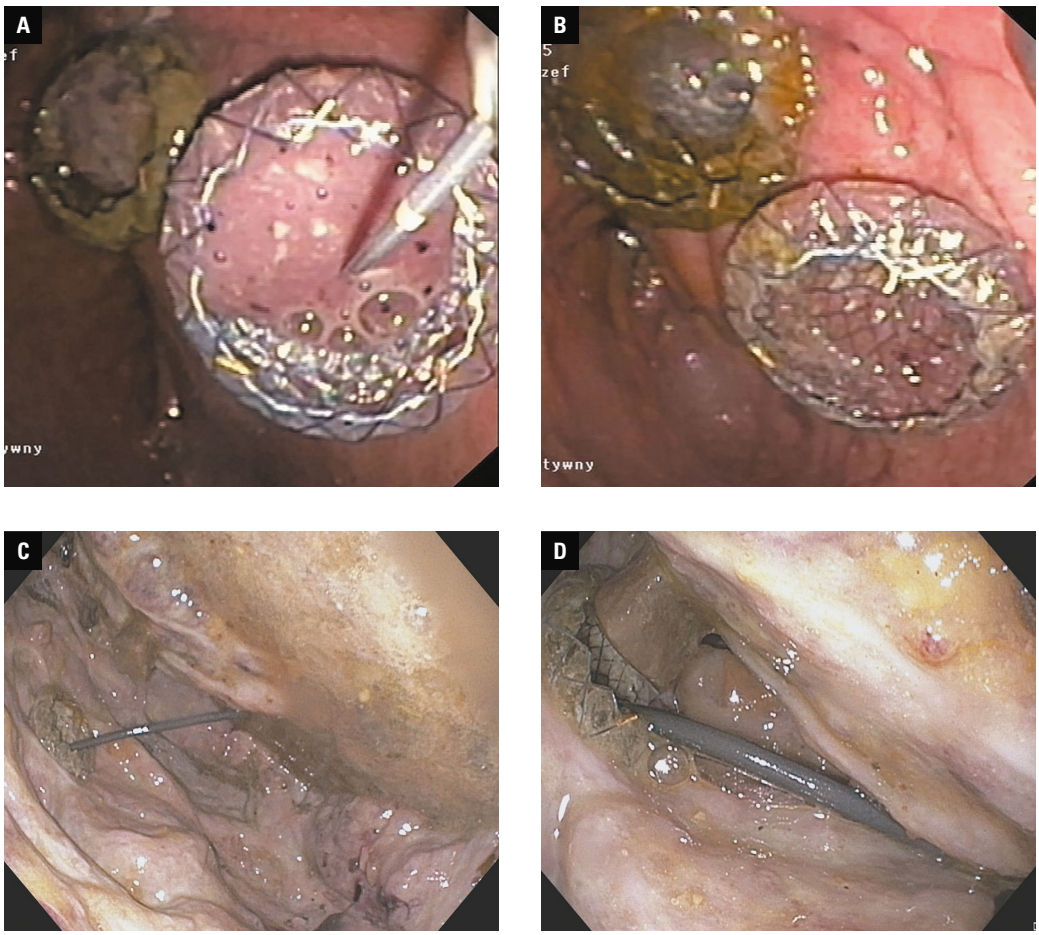


FIGURE 43 Multiple transluminal gateway access using biflanged metal stents. Two transmural endoscopic fistulas are visible on the endoscopic image on the side of the gastric lumen (**A**, **B**). Following the insertion of the endoscope through the lower transmural fistula, an endoscopic image of the lumen of a walled-off pancreatic necrotic lesion, with the endoscope positioned in inversion, showed the upper transseptal fistula visible from the collection lumen (**C**, **D**).

infected necrosis of the pancreas and peripancreatic tissues, necrosectomy procedures should usually be performed every 2–3 days. The number of endoscopic necrosectomy procedures performed during transmural drainage depends on the patient's clinical condition and is strictly personalized (**FIGURE 47A–47I**).

Notably, initial endoscopic necrosectomy procedures frequently involve establishing access via the transmural fistula to the more distal parts of the collection, amid the necrotic masses. It is possible to insert the endoscope into the necrotic collection lumen and perform mechanical removal of the necrotic tissue only after such access is gained, usually via an extraction balloon. In addition, the necrotic collection should be repeatedly flushed during each endoscopic necrosectomy procedure through the working channel of the endoscope, and the contents should be aspirated from the collection lumen by suction.

Owing to their ability to maintain a wide lumen of the transmural fistula and their fully-coated design that prevents the contents from leaking beyond the fistula, self-expandable transmural metal stents (**FIGURE 48A** and **48B**) facilitate safe insertion of the endoscope into the collection cavity to perform endoscopic necrosectomy. Therefore, self-expandable transmural metal stents are indicated in poorly liquefied necrotic collections,

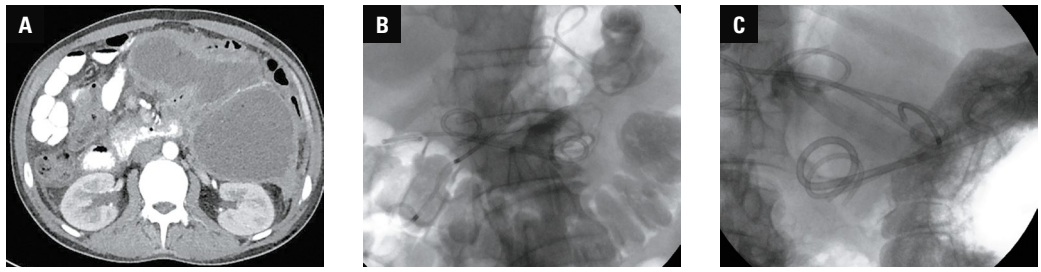


FIGURE 44 Multiple transluminal gateway technique (MTGT) access using paramural double-pigtail plastic stents. A 2-compartment pancreatic pseudocyst without communication between the collection compartments is visible on multiphasic computed tomography of the abdomen and pelvis with contrast enhancement (**A**). The patient underwent passive MTGT access, involving plastic 7-Fr double-pigtail stent insertion through each endoscopic transmural/transgastric fistula (**B**, **C**).

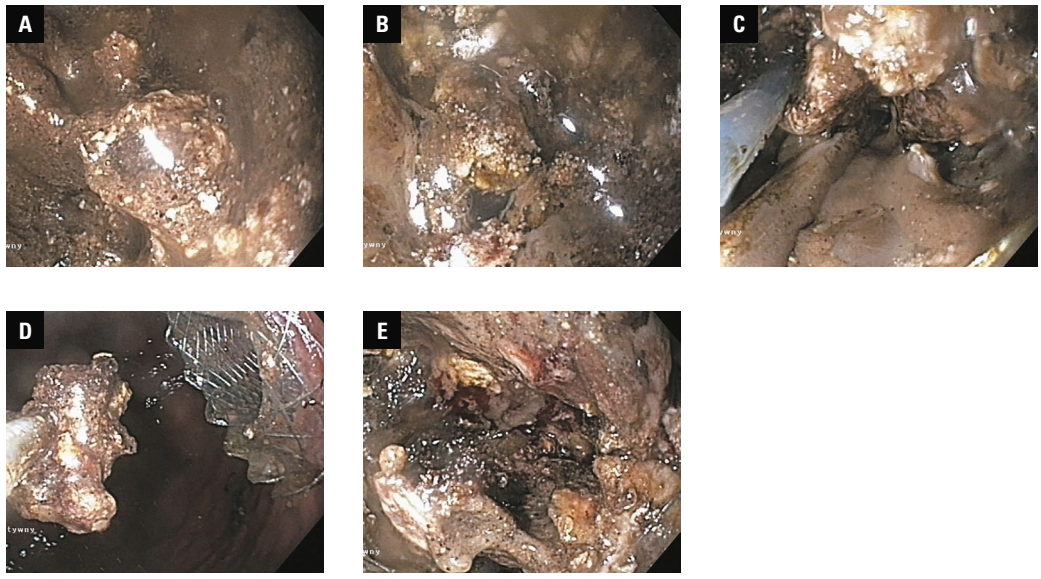


FIGURE 45 Direct endoscopic necrosectomy in a patient with infected walled-off pancreatic necrosis. A large amount of necrotic tissue was visualized in the necrotic collection lumen during endoscope insertion through the transmural/transgastric access (**A**, **B**). The necrotic tissues were removed into the gastric lumen using a Dormia basket (**C**, **D**) to gain gradual access to further parts of the necrotic collection (**E**).

where the next step of the endoscopic step-up approach may involve endoscopic necrosectomy.

During sequential direct endoscopic necrosectomy procedures, access is gained to deeper parts of the collection. The walls of the healing fluid collection are susceptible to bleeding from the granulation tissue (**FIGURE 49A–49C**), which is a frequent source of bleeding during direct endoscopic necrosectomy procedures. In such cases, hemostasis can be effectively achieved using hemostatic powder; in addition, patients may require blood and blood product transfusions. Conservative treatment combined with endoscopic techniques is usually sufficient for the management of bleeding from the collection wall granulation tissues during endoscopic necrosectomy.

The use of direct endoscopic necrosectomy is a step-up treatment and a more aggressive approach to treating pancreatic necrosis. However, despite being associated with better clinical outcomes, it carries a greater risk of complications. It should be noted that not every patient with WOPN requires necrosectomy, even in the presence of a large amount of necrotic debris in the collection lumen, as assessed before endotherapy. Active endoscopic drainage, leading to liquefaction of the necrotic tissue, is often an effective method of treatment, eliminating the need for endoscopic necrosectomy.

Transpapillary endoscopic drainage RECOMMENDATION 35 Passive transpapillary drainage involving insertion of a stent through the major duodenal papilla into the main pancreatic duct as the only route of access to the collection, is recommended only for PPs communicating with the main pancreatic duct, provided that the cyst does not exceed 50 mm in diameter[57,59,67,133,200,202,209,337-353] (evidence level, low; recommendation, strong [average of votes, 2.56]).

RECOMMENDATION 36 For PPs communicating with the main pancreatic duct and exceeding 50 mm in diameter, active transpapillary

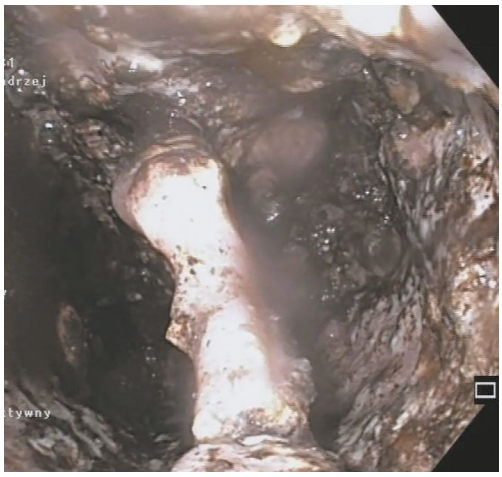


FIGURE 46 Direct endoscopic necrosectomy in a patient with infected walled-off pancreatic necrosis. The endoscopic image shows the splenic artery coursing through the lumen of the necrotic collection.

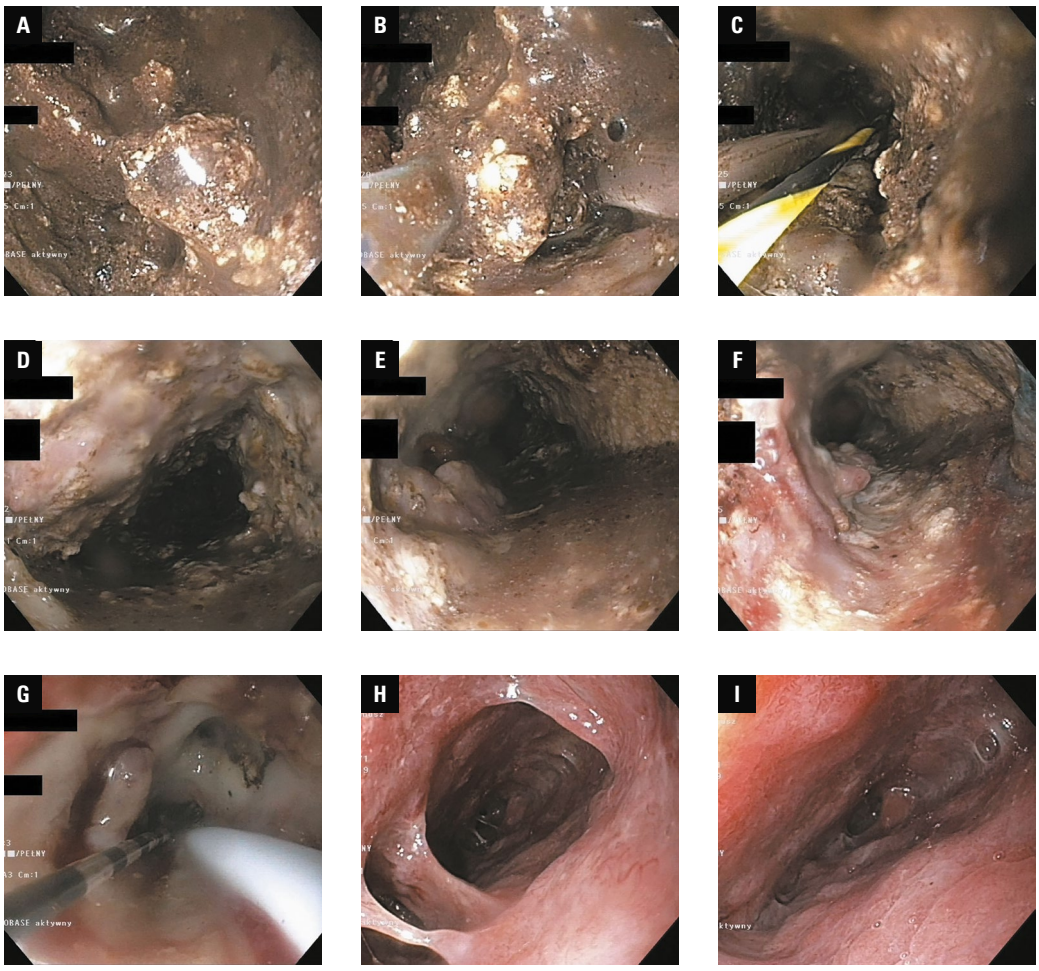


FIGURE 47 Direct endoscopic necrosectomy. Endoscopic images of the lumen of the necrotic collection obtained during subsequent endoscopic necrosectomy procedures. Initially, only fragments of necrotic tissue were visible in the lumen of the collection (**A**). As access to further parts of the collection was gradually gained during subsequent endoscopic procedures (**B**, **C**), the walls of the collection covered with granulation tissue in the healing stage and the lumen of the collection became visible (**D**–**G**). Fully granulated and healed walls of the necrotic collection were visualized during the final endoscopic procedure (**H**–**I**).

pancreatic drainage can be used, which involves inserting a nasocystic drain through the major duodenal papilla into the main pancreatic duct in such a manner that the distal end of the nasocystic drain is introduced through the site of pancreatic duct injury into the cyst lumen[57,59,67,201-203,209,339,345,347-349,351-356] (*evidence level, very low; recommendation, strong [average of votes, 2.4]*).

In addition to transmural pancreatic drainage, which is the preferred method of fluid collection drainage via an extra-anatomical route, transpapillary drainage is another available option. It ensures anatomical access through the major or minor duodenal papillae to the main pancreatic duct and structures communicating with the pancreatic duct, providing physiological drainage into the duodenal lumen. Similarly to transmural drainage, transpapillary drainage may be accomplished using either stents alone, identical to those used in transmural drainage (passive transpapillary drainage), or a nasocystic drain with / without a pancreatic plastic stent (active transpapillary drainage). Passive transpapillary drainage facilitates free flow of the collection contents through the stent and along the stent inserted into the main pancreatic duct, while active drainage ensures an active flow of the contents from the main pancreatic duct via flushing of the nasocystic drain.

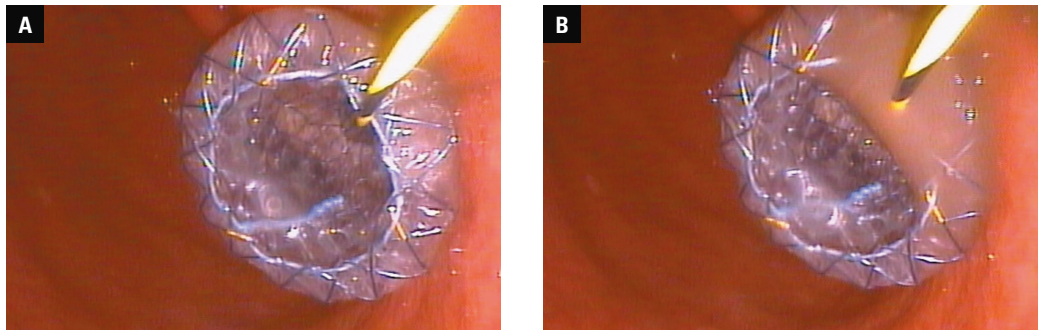


FIGURE 48 **A**, **B** – a self-expanding transmural biflanged metal stent inserted through a gastropancreatic fistula in a patient with an infected pancreatic pseudocyst

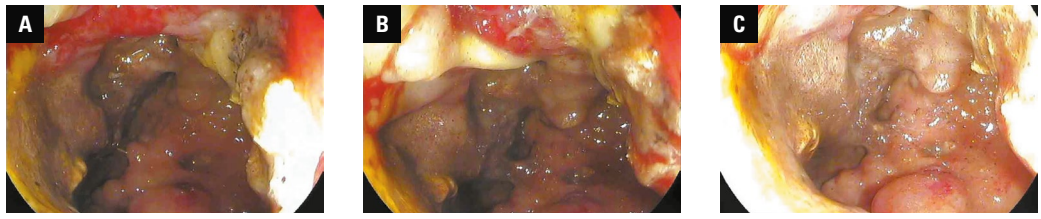


FIGURE 49 **A**–**C** – endoscopic image showing granulation tissue in the lumen of a walled-off pancreatic necrotic collection at the healing stage

Transpapillary drainage is an effective method for the treatment of PPs if transmural access is not feasible and the fluid collection communicates with the main pancreatic duct (**FIGURE 50A–50D**). A prerequisite for the use of transpapillary drainage during the treatment of fluid collections is damage to the main pancreatic duct facilitating communication between the main pancreatic duct and the collection lumen. Disruption of the main pancreatic duct is visualized by leakage of contrast into the peripancreatic region during ERCP.

Disruption of the main pancreatic duct can be divided into 2 types:

- Partial pancreatic duct disruption (**FIGURE 51**): contrast leaking outside the duct with contrastation of the distal part of the main pancreatic duct;
- Complete pancreatic duct disruption (**FIGURE 52**): contrast leaking outside the duct without contrastation of the distal part of the main pancreatic duct.

The type of disruption determines further treatment of patients with fluid collections, since an appropriate drainage system can be created depending on the lesion type. An effective drainage system should facilitate the evacuation of the entire collection.

Passive transpapillary drainage involves inserting a pancreatic stent of the largest possible diameter (at least 7 Fr) into the main pancreatic duct after prior sphincterotomy and possible dilatation of the main pancreatic duct by mechanical or pneumatic means. In the patients with partial disruption of the main pancreatic duct, the distal end of the pancreatic stent, inserted during passive transpapillary drainage, should be placed behind the site of the pancreatic duct to bridge the disruption site. Conversely, in the patients with complete disruption of the main pancreatic duct, the distal end of the pancreatic stent, inserted during passive transpapillary drainage, should be placed in the collection lumen.

Active transpapillary drainage involves inserting a nasocystic drain through the greater duodenal papilla into the main pancreatic duct, so that the distal end of the nasocystic drain, inserted through the site of the pancreatic duct disruption, is placed in the collection lumen (**FIGURE 53A–53D**). Thus, in the case of partial damage to the main pancreatic duct, active transpapillary drainage is not warranted, since it is usually technically impossible to insert a nasocystic drain to the main pancreatic duct through a partial disruption site. Active transpapillary drainage should be used only in the patients with complete disruption of the main pancreatic duct, with the distal end of the drain inserted into the collection lumen through the disruption site. In the postoperative period, the collection should be flushed through the nasocystic drain with saline in a volume that strictly depends on the size of the collection, every 6 hours. Aspiration of the contents through the nasocystic drain is usually required.

For PPs communicating with the main pancreatic duct, transpapillary drainage can be used as the only route of access to the collection, especially for sterile PPs located proximally to the duodenum, that is, in the pancreatic head or body. This is because of the short length of the pancreatic duct section between the duodenal papilla and the duct-to-collection leakage site, which, during transpapillary drainage, provides a route for collection content drainage into the duodenal lumen, ensuring effective drainage. For PPs located in the pancreatic tail, transpapillary drainage is usually effective and does not contribute to an increased risk of collection infection.

Passive transpapillary drainage as the only route of access to the collection is recommended in sterile PPs communicating with the main

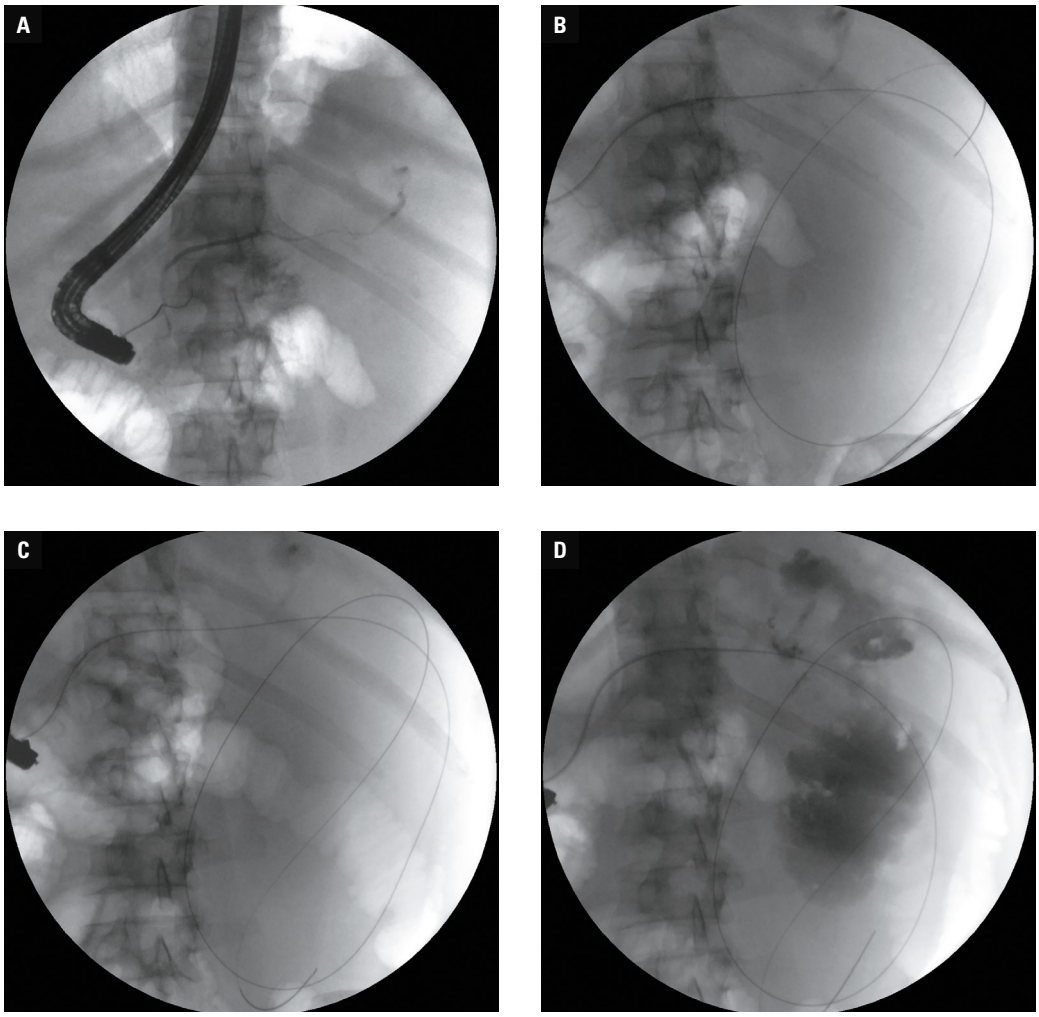


FIGURE 50 Endoscopic retrograde pancreatography. Contrast leaking through the site of damage to the main pancreatic duct (**A**) within the pancreatic tail into the pseudo--pancreatic cyst is visible on a fluoroscopic image. A guidewire inserted through the lesion site was looped inside the lumen of an extensive pancreatic pseudocyst >20 cm in size (**B**–**D**).

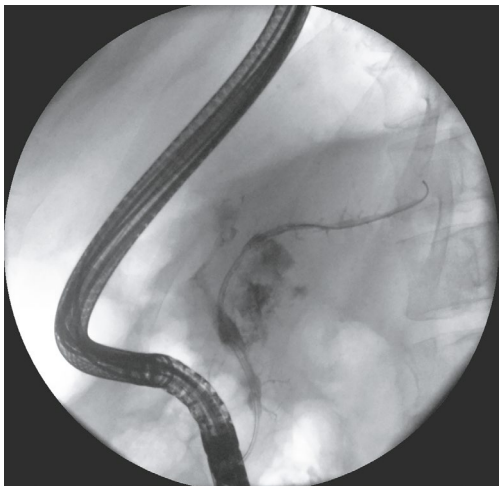


FIGURE 51 Endoscopic retrograde pancreatography in a patient with walled-off pancreatic necrosis. Fluoroscopy showed contrast leakage from the main pancreatic duct into the peripancreatic region, through partial damage to the pancreatic body.

pancreatic duct, if the cyst does not exceed 50 mm in diameter (**FIGURE 54A–54F**). If the diameter exceeds 50 mm, active transpapillary drainage should be used.

The effectiveness of transpapillary drainage for treating sterile PPs may be due to the fact that the clear serous contents of a PP easily drain through the stent into the duodenal lumen, and the diameter of the main pancreatic duct usually does not affect the drainage conditions. Better results of transpapillary drainage are observed in the patients with sterile PPs than those with infected PPs, where the thick purulent contents worsen drainage conditions. However, an infected PP does not preclude the use of active transpapillary drainage.

Notably, good results of transpapillary drainage of PPs are obtained in patients with CP-related PPs. Such patients usually present with a large diameter of the dilated main pancreatic duct, which facilitates drainage of the cyst contents into the gastrointestinal tract lumen.

RECOMMENDATION 37 When using transpapillary drainage to treat PPs, the establishment of additional transmural access to the PP is not warranted, as the combination of transpapillary and transmural drainage worsens the results of endoscopic treatment and prolongs the drainage time. This is in contrast to necrotic collections, where the combination of transmural and transpapillary drainage improves the results of endoscopic treatment[57,59,67,120,133,199,200,202,205,206,209,289,337-366] (*evidence level, very low; recommendation, strong [average of votes, 2.44]*).

Both interstitial edematous and necrotizing AP can result in damage to the main pancreatic duct. Most individuals with fluid collections present with such disruption; hence, it should be suspected in every patient with fluid collections, even though interventional treatment may not be required in all cases. The indications for endoscopic treatment of main pancreatic duct injuries are

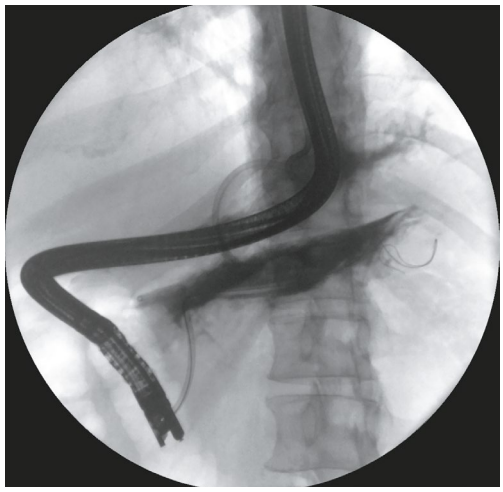


FIGURE 52 Endoscopic retrograde pancreatography in a patient with walled-off pancreatic necrosis (WOPN). The fluoroscopic image showed contrast leakage from the main pancreatic duct through a complete disruption in the pancreatic neck area. The administered contrast spilled into the lumen of the WOPN subjected to transmural drainage.

closely related to the fluid collection type. The use of passive transpapillary drainage, that is, placement of a stent within the main pancreatic duct in patients undergoing transpapillary drainage of fluid collections, depends on the fluid collection type. In patients with WOPN, the use of passive transpapillary drainage improves endoscopic outcomes (**FIGURE 55A–55G**). Conversely, in individuals undergoing transpapillary drainage of PPs, the use of passive transpapillary drainage negatively affects the short- and long-term results of endotherapy and prolongs the duration of endoscopic treatment.

Generally, in the case of PPs, the collection develops as a consequence of damage to the main pancreatic duct, that is, pancreatic juice feeds into the PP through the main pancreatic duct disruption site. For symptomatic PPs communicating with the main pancreatic duct, the preferred method of endoscopic drainage (ie, transmural drainage) should be performed first, with transpapillary drainage being reserved only for the cases in which transmural drainage is technically impossible. If the PP communicates with the main pancreatic duct through the duct disruption site, the aim of transpapillary drainage is to drain the PP and close the site of the duct injury (which is a direct cause of the PP) by reversing the pressure gradient. Thus, the integrity of the main pancreatic duct need not be assessed nor should additional transpapillary drainage be used while performing transpapillary drainage of a PP. ERCP with endoscopic sphincterotomy and passive transpapillary drainage should only be performed to treat persistent damage to the main pancreatic duct in the case of PPs recurring after transpapillary drainage; the recurrent cyst can be treated either via the previous transpapillary drainage site or via an additional, newly established transpapillary drainage site.

In the patients with fluid collections who are diagnosed with a concomitant pancreatic fistula or an abnormal connection between the pancreatic ducts and another epithelium-lined surface, resulting in pancreatic juice leaking outside the pancreatic ducts, the endoscopic treatment is completely different. Internal pancreatic fistulas, or the pathological connections between the pancreatic ducts to other organs, spaces, or structures, are common in pancreatitis. Predominant among the postinflammatory pancreatic fistulas are pancreato-peritoneal fistulas, resulting in pancreatic ascites, and pancreato-pleural fistulas, resulting in pleural fluid collections. Postinflammatory internal pancreatic fistulas are most common in patients with CP, and for those with concomitant fluid collections, a diagnosis of PP is common. Endoscopic treatment of patients with fluid collections and comorbid pancreatic fistulas should commence with endotherapy of the fluid collection. The mainstay of endoscopic treatment of pancreatic fistulas following pancreatitis is endotherapy of the fluid collections. Endoscopic drainage of the fluid collection leads to the closure of the pancreatic fistula on the principle of the pressure gradient being reversed in the fistula. Only if the pancreatic fistula persists despite the regression of the endoscopically drained fluid collection should endoscopic treatment of the fistula be initiated, most frequently, endoscopic sphincterotomy and stenting of the main pancreatic duct (passive transpapillary drainage) to ensure physiological drainage of the pancreatic juice into the duodenum.

RECOMMENDATION 38 For WOPN collections, single transpapillary access (active or passive) as the only route of access to the collection is usually insufficient, and endoscopic transmural access is required[23,32-34,45,51,52,55,56,60,67,78,98,106,114-116,118,128,131-134,143,159-167,171,182,205,218,224,227-229,231,256,268,269,271,272,274,285,286,296,306-311,316,317,320-324,326,328-331,333] (*evidence level, very low; recommendation, strong [average of votes, 2.76]*).

The main limitation of transpapillary drainage is the small diameter of the duct used as the outflow route, which usually does not exceed a diameter of several millimeters, even after dilatation of the major or minor duodenal papilla, and the small diameter of the transpapillary stent introduced into the pancreatic duct (not exceeding 10 Fr). In collections filled with dense contents, such as WOPN lesions, transpapillary drainage (active or passive) as the only route to access the collection is ineffective. Transpapillary drainage alone is often sufficient for fluid collections filled with serous contents, such as sterile PPs.

For WOPN collections, the use of endoscopic transpapillary drainage without concomitant transmural drainage results in collection contents drainage via the transpapillary route, while the necrotic elements remain in the collection lumen and may become superinfected during transpapillary drainage. Thus, additional use of transmural drainage following transpapillary drainage of pancreatic necrosis collections is usually technically difficult and associated with poorer endotherapy outcomes. The establishment of transpapillary drainage before the establishment of transmural drainage in patients with symptomatic WOPN is contraindicated.

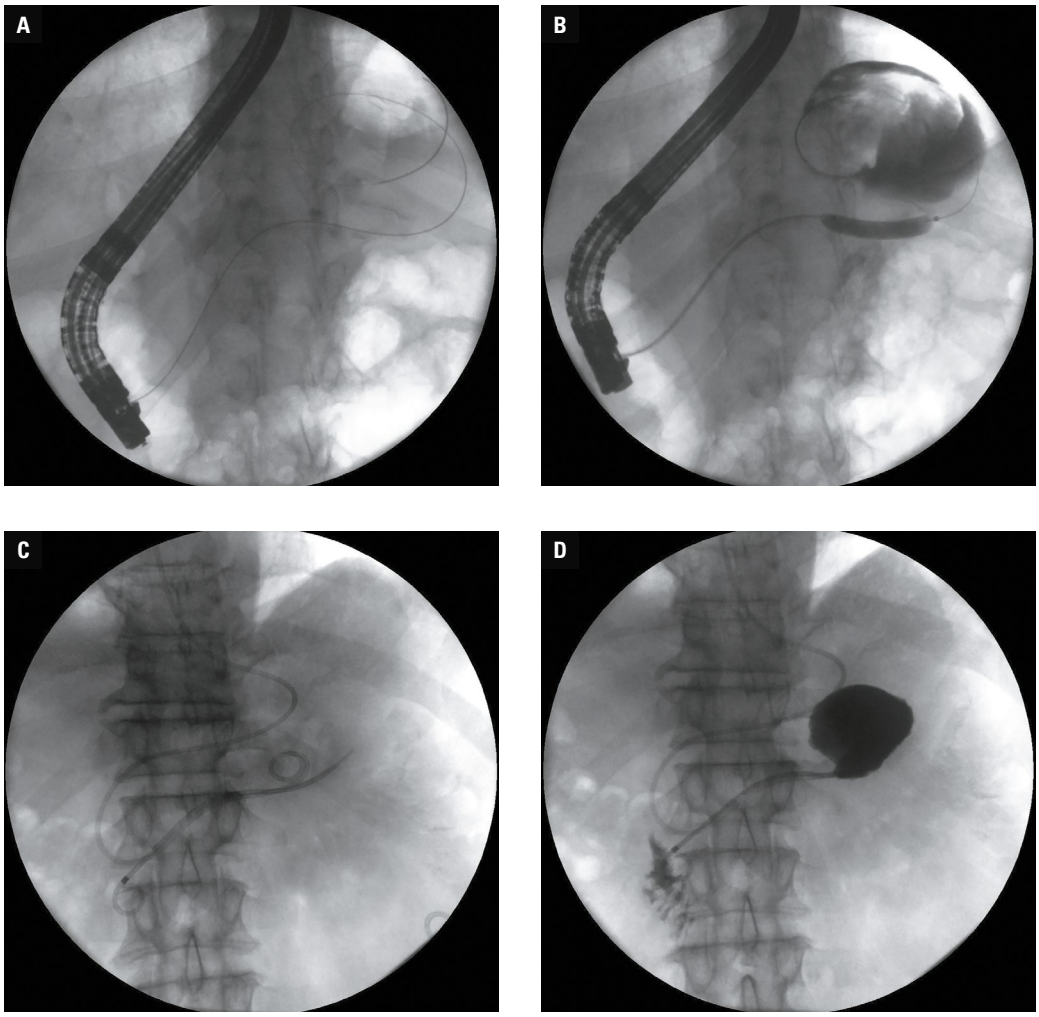


FIGURE 53 Active transpapillary drainage of a pseudocyst of the pancreatic tail. During endoscopic retrograde pancreatography, a transpapillary guidewire inserted into the main pancreatic duct through the site of the duct injury in the tail of the pancreas was looped inside the lumen of a 65-mm pancreatic pseudocyst (**A**). Following dilatation of the main pancreatic duct using a high--pressure balloon (**B**), a 7-Fr pancreatic stent and a 7-Fr nasocystic drain were inserted transpapillarily, the distal ends of both passing across the disruption site and left inside the collection lumen (**C**). The contrast agent, administered after the procedure via the nasocystic drain, filled the pancreatic pseudocyst and freely drained through the papilla into the duodenal lumen (**D**).

RECOMMENDATION 39 Passive transpapillary drainage is often necessary during transpapillary drainage of WOPN collections, as most patients with WOPN present with damage to the main pancreatic duct, and passive transpapillary drainage is an effective method of treating such damage by facilitating physiological drainage of pancreatic juice into the duodenum[67,120,199,205,206,289,337-344,354,355,357-364] (*evidence level, very low; recommendation, strong [average of votes, 2.22]*).

Most patients with WOPN present with damage to the main pancreatic duct. Partial disruption of the main pancreatic duct is more common than complete disruption of the duct in necrotizing AP. In patients with WOPN, endotherapy is more effective when treating partial rather than complete duct disruptions. Despite the inferior results of endoscopic treatment, main pancreatic duct stents should additionally be used in the patients with complete duct disruption.

Stenting of the main pancreatic duct is a key element of endoscopic treatment of WOPN in patients with damage to the main pancreatic duct in necrotizing AP (**FIGURE 56A–56C**). Passive transpapillary drainage, which involves stenting of the pancreatic duct, is an effective method of treating the disruption of the main pancreatic duct, improving the long-term endoscopic results in patients with WOPN and reducing the number of recurrent pancreatic collections. Therefore, ERCP, with the assessment the main pancreatic duct integrity, should be performed in all patients with WOPN during endoscopic transpapillary drainage. If damage to the main pancreatic duct is detected, ERCP facilitates physiological drainage of pancreatic juice into the duodenum via endoscopic sphincterotomy of the major duodenal papilla, with a stent being placed in the main pancreatic duct (passive transpapillary drainage).

In the case of partial disruption of the main pancreatic duct, the distal end of the pancreatic stent should be located behind the duct disruption site for the best treatment outcomes. In the patients with complete disruption of the main pancreatic duct, the distal end of the pancreatic stent, inserted via the transpapillary access, must be positioned near the injury site to ensure optimal drainage. For passive transpapillary drainage, the optimum diameter of the pancreatic stent in patients undergoing transpapillary drainage of WOPN collections is 7 Fr. The first replacement of the pancreatic stent should take place after 6 months, with subsequent replacements occurring every 12 months until the ductal damage site is closed on a follow-up ERCP, which should always be performed after the pancreatic stent is removed during the same endoscopic procedure. If the diameter of the main pancreatic duct does not permit the placement of a 7-Fr pancreatic

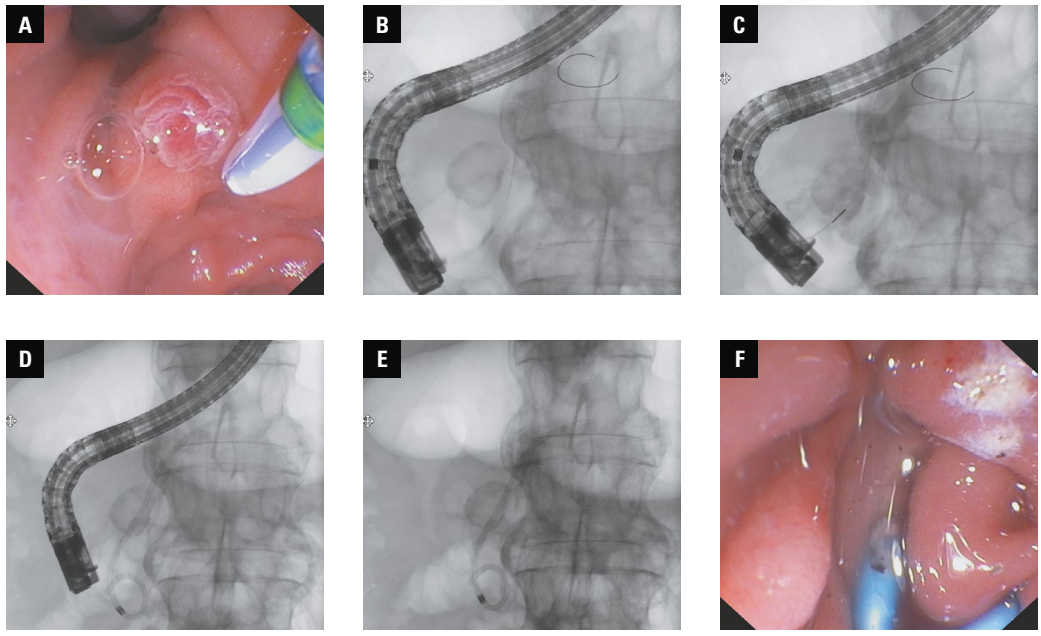


FIGURE 54 Passive endoscopic drainage of a pseudocyst located in the pancreatic head in a patient with chronic pancreatitis. Endoscopic retrograde pancreatography revealed spontaneous discharge of turbid contents from the main pancreatic duct through the native major duodenal papilla (**A**). Following transpapillary catheterization of the main pancreatic duct along a guidewire, the administered contrast agent filled the dilated main pancreatic duct, leaking into a 40-mm pseudocyst within the pancreatic head through the site of partial ductal disruption in the pancreatic neck area (**B**, **C**). Following endoscopic sphincterotomy, a 7-Fr, 9-cm pancreatic stent was inserted transpapillarily into the main pancreatic duct to splint the site of the duct injury (**D**–**F**).

stent despite previous dilatation of the duct using mechanical dilators, a 5-Fr stent should be left in place for up to 3 months, with possible replacement with a larger-diameter stent as part of the subsequent endoscopic procedure.

Perioperative management RECOMMENDATION 40 If the patient's clinical condition permits it, and in the absence of other contraindications, oral feeding during endoscopic treatment of fluid collections should be initiated within the first 24 hours postprocedure. If oral feeding is not possible, enteral nutrition is preferred, and parenteral nutrition is indicated only in the cases of intolerance or contraindication to enteral nutrition[29,30,32,33,54-56,193,217,337-375] (*evidence level, moderate; recommendation, strong [average of votes, 2.93]*).

Recent years have witnessed a paradigm shift in the nutritional treatment strategy in patients with AP, which stipulates that oral nutrition should be incorporated as soon as possible, including in patients with local complications of pancreatitis. Early feeding via the gastrointestinal route reduces the risk of infections, septic complications, organ failure, and mortality during the disease course, while simultaneously reducing the duration of hospitalization. A lower risk of developing infections and septic complications is associated with a lower risk of bacterial translocation in patients fed via the gastrointestinal route. If the patient does not tolerate oral nutrition, enteral nutrition through a nasogastric or nasoenteral tube should be undertaken, unless contraindications to enteral nutrition (mainly due to gastrointestinal obstruction) are present. Nutritional supplementation via the parenteral route may be necessary if oral and/or enteral nutrition does not meet the energy demand of patients with pancreatitis and its local complications. Conversely, total parenteral nutrition should be used only when feeding via the gastrointestinal tract is not feasible. Total parenteral nutrition should be terminated as soon as oral or enteral nutrition becomes feasible. The nutritional treatment regimen outlined herein applies to patients with AP, as well as to those with local complications of pancreatitis, namely, fluid collections.

Endoscopic treatment of fluid collections, including endoscopic transpapillary drainage, is not a contraindication to oral nutrition. A strict diet is required in patients with fluid collections on the day of the transpapillary endoscopic fistula creation. Clinical condition permitting, and in the absence of other contraindications to feeding via the gastrointestinal route, patients can receive oral nutrition on the subsequent days. It should be noted that in patients with a transmural endoscopic fistula, food will naturally pass through the gastrointestinal tract, as its diameter is much greater than that of the transmural fistula, which reduces the risk of food content entering the collection lumen through the fistula. With an effective fluid collection drainage system established during endotherapy, the results of endoscopic treatment are not affected by any potential leaking of orally ingested food

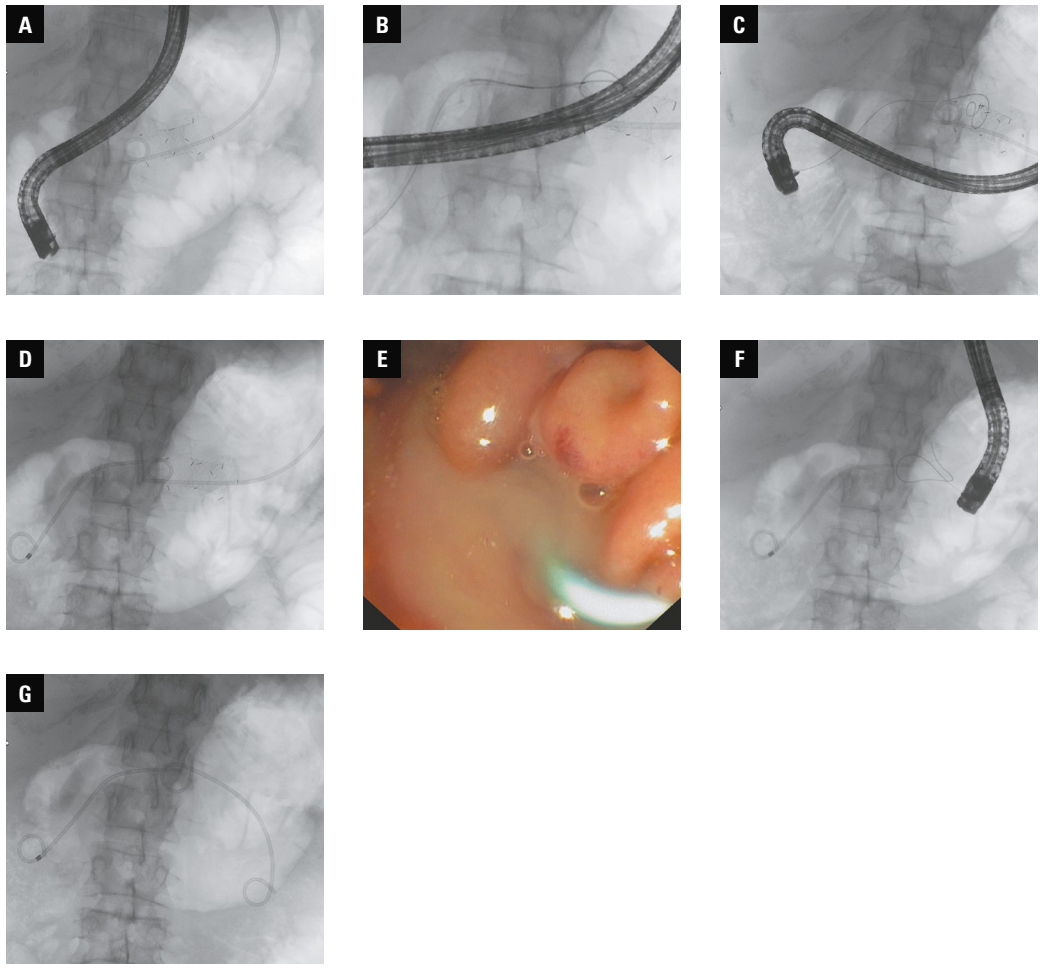


FIGURE 55 Passive transpapillary drainage in a patient with walled-off pancreatic necrosis undergoing transpapillary/transgastric drainage. Endoscopic retrograde pancreatography revealed a complete disruption of the main pancreatic duct within the pancreatic body, with contrast leaking into the area of the transmural stents (**A**–**C**). A 7-Fr, 9-cm pancreatic stent was inserted transpapillarily (**D**, **E**), its distal end passing through the duct disruption site and left in the lumen of the residual necrotic space. Owing to the regression of the necrotic collection (collection diameter of approximately 55 mm), the stents (metal and plastic) were removed in a single procedure, and a 7-Fr, 9-cm double-pigtail stent was inserted through the transmural endoscopic fistula for passive transmural drainage of the residual necrotic space (**F**, **G**).

into the collection lumen, especially during active transmural drainage. Similarly, in patients undergoing transpapillary endoscopic drainage of fluid collections who receive enteral feeding, the distal end of the feeding probe does not need to be located in the gastrointestinal tract distally to the site of the transmural endoscopic fistula.

The assessment of the patient's nutritional status is another important aspect in the context of nutrition during endotherapy of fluid collections. Pancreatitis is associated with metabolic hypercatabolism requiring increased calorific intake, which can lead to malnutrition, and even cachexia, if inadequate nutritional treatment is provided, especially during a prolonged course of the disease. This may result in interventional treatment failure. Therefore, special attention should be paid to the nutritional status of patients with fluid collections before endotherapy initiation; if malnutrition is detected, nutritional treatment should be implemented before the intervention. This is especially important for patients with CP, in whom nutritional disturbances manifesting as cachexia are more common owing to the long-term course of the disease.

RECOMMENDATION 41 Intravenous antibiotic prophylaxis should be administered during drainage of postinflammatory pancreatic and peripancreatic fluid collections[29,30,32-34,54-56,68-77,193,368,376-385] (*evidence level, very low; recommendation, strong [average of votes, 2.89]*).

Antibiotic therapy is an important element of the conservative treatment of AP. The primary indications for antibiotic therapy in patients with AP are the following: 1) extrapancreatic infection, most commonly of the respiratory, urinary, or biliary tract; and 2) infection of the areas of pancreatic/peripancreatic necrosis, including infected fluid collections, most frequently due to translocation of intestinal bacteria. The most common pathogens include *E. coli*, *K. pneumoniae*, *Enterococcus faecalis*, *S. aureus*, *P. aeruginosa*, *Proteus mirabilis*, and

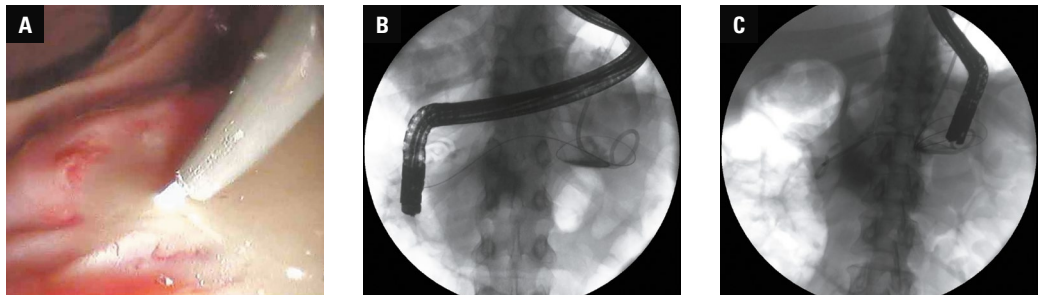


FIGURE 56 Passive transpapillary drainage during endotherapy of walled-off pancreatic necrosis (WOPN). Following the completion of active transmural drainage of the WOPN due to the regression of the collection, the patient was left on passive transmural/transgastric drainage and was deemed eligible for endoscopic retrograde pancreatography. The outflow of necrotic contents through the greater duodenal papilla during the procedure was observed after cannulation of the main pancreatic duct (**A**). The guidewire, inserted through a complete disruption of the pancreatic duct, was looped inside the residual necrotic space subjected to transmural drainage (**B**). A 7-Fr, 9-cm pancreatic stent was inserted transpapillarily, its distal end passing through the duct disruption site and left in the lumen of the residual necrotic space (**C**). The guidewire, inserted transmurally along the transmural stent, was looped inside the residual necrotic space subjected to transmural and transpapillary drainage (**C**).

Streptococcus spp. Antibiotic treatment of infected fluid collections may include monotherapy (imipenem, meropenem, piperacillin with tazobactam) or combination therapy (metronidazole with either ceftriaxone, cefotaxime, ceftazidime, or ciprofloxacin). If an infection occurs in a patient previously treated with an antibiotic or hospitalized in an ICU for an extended period of time, a broader-spectrum antibiotic should be chosen, with vancomycin as an optional addition. In empirical antibiotic therapy, antibiotics should be chosen according to their organ penetration ability. In targeted antibiotic therapy, the antibiotic should be chosen based on the result of the antibiotic sensitivity profile as determined on the basis of the collection culture. The optimum duration of antibiotic therapy in AP remains unknown.

Prophylactic use of antibiotics to prevent the infection of fluid collections is not recommended in patients with AP.

However, it should be noted that the aforementioned recommendations for antibiotic therapy in pancreatitis apply only to the patients receiving conservative treatment, and not to those treated using interventional techniques.

The use of antibiotic prophylaxis in patients undergoing gastrointestinal endoscopy should primarily be determined by assessing the risk of bacteremia associated with endoscopic procedures. Bacterial translocation of endogenous microbiota into the bloodstream (bacteremia) can occur during endoscopy consequent to procedure--related damage to the gastrointestinal wall. In such cases, antibiotic prophylaxis is indicated. Thus, intravenous antibiotic prophylaxis should be used in the individuals undergoing endoscopic transmural drainage of fluid collections, since secondary infection of the collection contents (even sterile ones) may occur after transpapillary puncture of the collection under EUS guidance. The principles of antibiotic prophylaxis during transmural drainage of fluid collections do not differ from those applying to perioperative antibiotic prophylaxis for the biopsies of sterile PPs under EUS guidance.

In the case of sterile fluid collections, no indications exist for antibiotic therapy during transmural drainage. Conversely, in infected fluid collections, antibiotic therapy is the cornerstone of conservative treatment, and is crucial for infection control. Once endoscopic treatment of infected fluid collections is initiated, an effective drainage system, that is, a system capable of draining the entire collection cavity, assumes the infection-control role, and antibiotic treatment is no longer required. In the cases of successful endoscopic drainage of infected fluid collections, antibiotic therapy is not required as the effective drainage system ensures infection control.

RECOMMENDATION 42 Routine use of proton pump inhibitors (PPIs) during endoscopic drainage of postinflammatory pancreatic and peripancreatic fluid collections is not recommended, unless indicated for other clinical reasons[33,54-56,217,368,386-389] (*evidence level, very low; recommendation, strong [average of votes, 2.84]*).

Historically, the use of antisecretory drugs, that is, drugs that inhibit gastric acid secretion, in patients at the early stages of AP was controversial. Currently, the use of drugs that inhibit hydrochloric acid secretion, including PPIs, in such patients is not routinely recommended, unless indicated for other clinical reasons. This also applies to patients with local complications of pancreatitis (ie, fluid collections).

Routine use of antisecretory drugs during endoscopic drainage of fluid collections is not recommended, unless indicated for other reasons. During endoscopic drainage of WOPN collections, gastric juice that enters the collection through the endoscopic fistula can digest the necrotic

tissue, thus contributing to chemical cleansing of the necrotic collection. In addition, the low-pH physiological environment of the stomach can prevent excessive bacterial growth, potentially contributing to effective control of local infection in the collection lumen connected to the gastric lumen via the endoscopic fistula. Thus, by changing the composition of the gastrointestinal microbiome, antisecretory drugs have a significant impact on endotherapy of fluid collections, including the risk of the collection content infection. Therefore, the use of antisecretory drugs is contraindicated unless other strong clinical indications for drugs exist in a particular clinical case. Discontinuing the use of PPIs in patients undergoing transmural drainage of fluid collections reduces the risk of secondary infection of the collection contents, simultaneously reducing the number of endoscopic interventions required to achieve treatment success. However, continuous exposure to low-pH gastric juice can be a risk factor for bleeding from the gastrointestinal tract and the collection lumina.

RECOMMENDATION 43 In patients with postinflammatory pancreatic and peripancreatic fluid collections presenting with no clinical improvement, an additional access route to the collection using other interventional treatment techniques may be necessary in addition to endoscopic treatment intensification[29,32-34,51,54-56,91-96,98,106,-113-120,121-187,193-199,205,206,208,212-215,224,227-232,236,-250,266,268,272,285,288,306,308,309,317,320,334,336,390-394] (*evidence level, low; recommendation, strong [average of votes, 2.91]*).

The step-up strategy is a widely accepted therapeutic approach for the treatment of WOPN, as well as other fluid collections. According to this strategy, access to the fluid collection should be gradually multiplied with the use of minimally-invasive techniques, with traditional surgery remaining the treatment of choice only if the aforementioned approach fails.

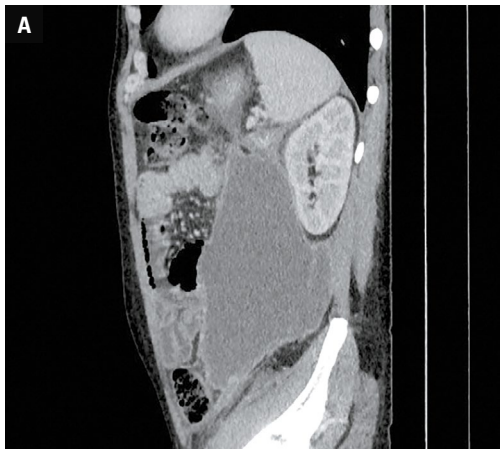
Endoscopic treatment of fluid collections is based on the establishment of an effective drainage system for complete collection evacuation. If endoscopic drainage fails despite the intensification of endotherapy techniques (endoscopic step-up approach), an additional route to access the collection may be pursued, according to the step-up strategy, using other interventional treatments, beginning with minimally-invasive methods. The preferred additional minimally-invasive treatment to be pursued during endotherapy is percutaneous drainage via the extraperitoneal or, less commonly, transperitoneal access. Typically, a contralateral (relative to the endoscopic fistula) incision (counter-incision) of the skin layers with insertion of a percutaneous drain to provide fluid drainage in the postoperative period is sufficient. It should be noted that the need for an additional access route to the collection using other interventional treatment techniques during endotherapy most often applies to the patients with WOPN, in whom endotherapy has worse efficacy than in individuals with PPs.

The need to establish additional access using a different minimally-invasive technique during endotherapy for WOPN, most commonly percutaneous drainage via the extraperitoneal access, usually applies to the patients in whom an extensive necrotic collection penetrates beyond the omentum into the pelvis (**FIGURE 57A** and **57B**), especially along the paracolic gutters. In such patients, an effective drainage system cannot be established using endoscopic techniques alone, and additional percutaneous drainage improves the results of the treatment.

However, it should be noted that interventional treatment via percutaneous drainage of WOPN collections should not be initiated before the scheduled endoscopic drainage, because percutaneous access and the resulting drainage of liquid necrotic content frequently lead to decompression of the collection and the collection wall being pushed away from the gastrointestinal wall, rendering endoscopic drainage technically impossible owing to the excessive distance between the collection and gastrointestinal walls. Percutaneous drainage should be performed only as an additional access route to the collection in the case of endotherapy failure.

In line with the surgical step-up approach, percutaneous drainage is often an alternative to endoscopic drainage, especially in fluid collections located more than 40 mm away from the gastrointestinal tract, which is a contraindication for endoscopic drainage. Interventional treatment should commence with extraperitoneal percutaneous drainage, possibly with surgical necrosectomy via the extraperitoneal access. Percutaneous endoscopic necrosectomy (PEN) is another method of performing extraperitoneal necrosectomy; it involves accessing the necrotic collection via an extraperitoneal route through percutaneous drainage, followed by widening the access and deploying a fully-coated large-diameter self-expandable esophageal stent percutaneously to facilitate percutaneous insertion of the endoscope into the necrotic area to perform endoscopic necrosectomy (**FIGURE 58A–58J**).

RECOMMENDATION 44 During endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections, follow-up abdominal imaging examinations with the assessment of treatment efficacy based on the collection size should be performed every 1–4 weeks, depending on the patient's clinical condition, or immediately if new clinical signs or complications of treatment are observed[29,32-34,51,54-56,91-96,98,106,114-119,-128,143,159-167,171-187,190-199,205,206,208,212-215,224,227-232,-234,250,266,268,272,285,288,306,308,309,317,320,334,336] (*evidence level, very low; recommendation, strong [average of votes, 2.78]*).



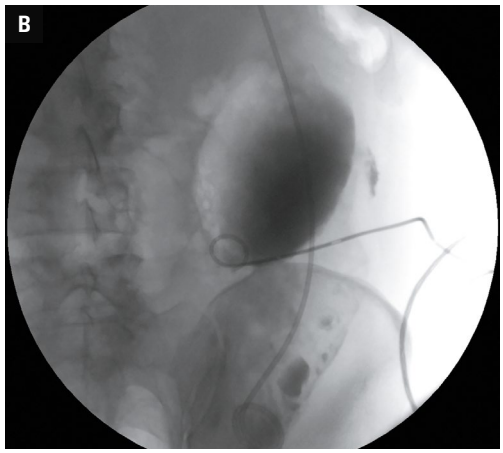


FIGURE 57 **A**, **B** – extensive pancreatic walled-off necrotic collection penetrating beyond the omentum visible on multiphasic contrast-enhanced computed tomography of the abdomen and pelvis (**A**). The patient underwent active endoscopic drainage via the transmural/transgastric access and active percutaneous drainage via the extraperitoneal access in the left lumbar region (**B**).

RECOMMENDATION 45 Abdominal CT is the recommended imaging modality to confirm complete regression of postinflammatory pancreatic and peripancreatic fluid collections[32-34,44,51,54-58,91-96,102,106,114-119,128,160-167,171-186,190-192,194-196,198,205,208,212-215,224,227-232,236,250,266,268,272,285,288,306,308,309,317,320,334-336,338-341,343,344,354,358,360,361,365,390-394] (*evidence level, very low; recommendation, strong [average of votes, 2.8]*).

In addition to clinical evaluation, assessment of treatment efficacy based on abdominal imaging is a crucial part of the management of patients with fluid collections.

The first abdominal imaging assessment during active endoscopic drainage is performed, depending on the clinical condition, after 7 days of drainage, when the patient remains hospitalized. Subsequent imaging assessments during active endoscopic drainage should be repeated, depending on the patient's clinical condition, at intervals of no more than 4 weeks, until active endoscopic drainage is completed. Conventional abdominal USG is the recommended modality to assess the outcomes of endoscopic treatment of fluid collections, provided that the fluid collection had been clearly visible in USG images performed before endotherapy initiation. Otherwise, a more advanced imaging modality (CECT or CE-MRI) should be used to visualize the abdominal organs.

Conversely, in passive endoscopic drainage, the first abdominal imaging assessment should be performed after 4 weeks of drainage, usually before making a decision regarding stent replacement or removal (ie, continuation or termination of endoscopic drainage). In these cases, multiphasic abdominal CECT is the recommended modality to confirm complete regression of fluid collections. Every patient should undergo a static abdominal imaging assessment (multiphasic CECT of the abdomen) at the time of endoscopic treatment completion. Multiphasic CT of the abdomen is the recommended modality, as it facilitates complete evaluation of both the pancreas and the surrounding structures along with adjacent organs, and permits a comparative evaluation of lesions against CT acquisitions performed before the interventional treatment.

It should be noted that the aforementioned regimen of repeat follow-up abdominal imaging scans acquired every 1–4 weeks, with the assessment endoscopic treatment effectivenes, applies to clinically stable patients. If new clinical signs or treatment complications are observed during endoscopic drainage, abdominal imaging should be performed immediately.

There are no clearly defined criteria regarding the size of the collection after a certain drainage period (relative to the initial dimensions of the collection) that would indicate effectiveness of endotherapy. Beyond doubt, partial regression of the collection, defined as a reduction in its dimensions on a follow-up abdominal imaging assessment performed during endotherapy, as compared with the dimensions observed before endoscopic treatment initiation, is sufficient to acknowledge clinical improvement. However, the decision regarding termination of endoscopic treatment is a completely different matter. In this context, the dimension of the collection is the key element defining treatment success and warranting termination of endoscopic treatment.

RECOMMENDATION 46 For transmural drainage of postinflammatory pancreatic and peripancreatic fluid collections, the treatment success is acknowledged upon: 1) resolution of clinical symptoms associated with the collection, and 2) complete regression of the collection (<40 mm) on imaging[33,34,54-56,91-96,98,106,114-119,128,143,159-167,171-187,193-199,205,206,208,212-215,224,227-232,236,250,266,268,272,285,288,306,308,309,317,320,334,336,393,394] (*evidence level, very low; recommendation, strong [average of votes, 2.75]*).

Indications for initiating interventional treatment, including endoscopic treatment, include the presence of collection-related clinical symptoms, regardless of the collection size. Therefore, resolution of clinical symptoms is an important determinant of treatment success and completion. Regression of the collection is the second most important element, which, for transmural drainage, translates to achieving a collection size of less than 40 mm on follow-up imaging. As mentioned, the recommended abdominal imaging modality to confirm complete regression of fluid collections is multiphasic CECT of the abdomen.

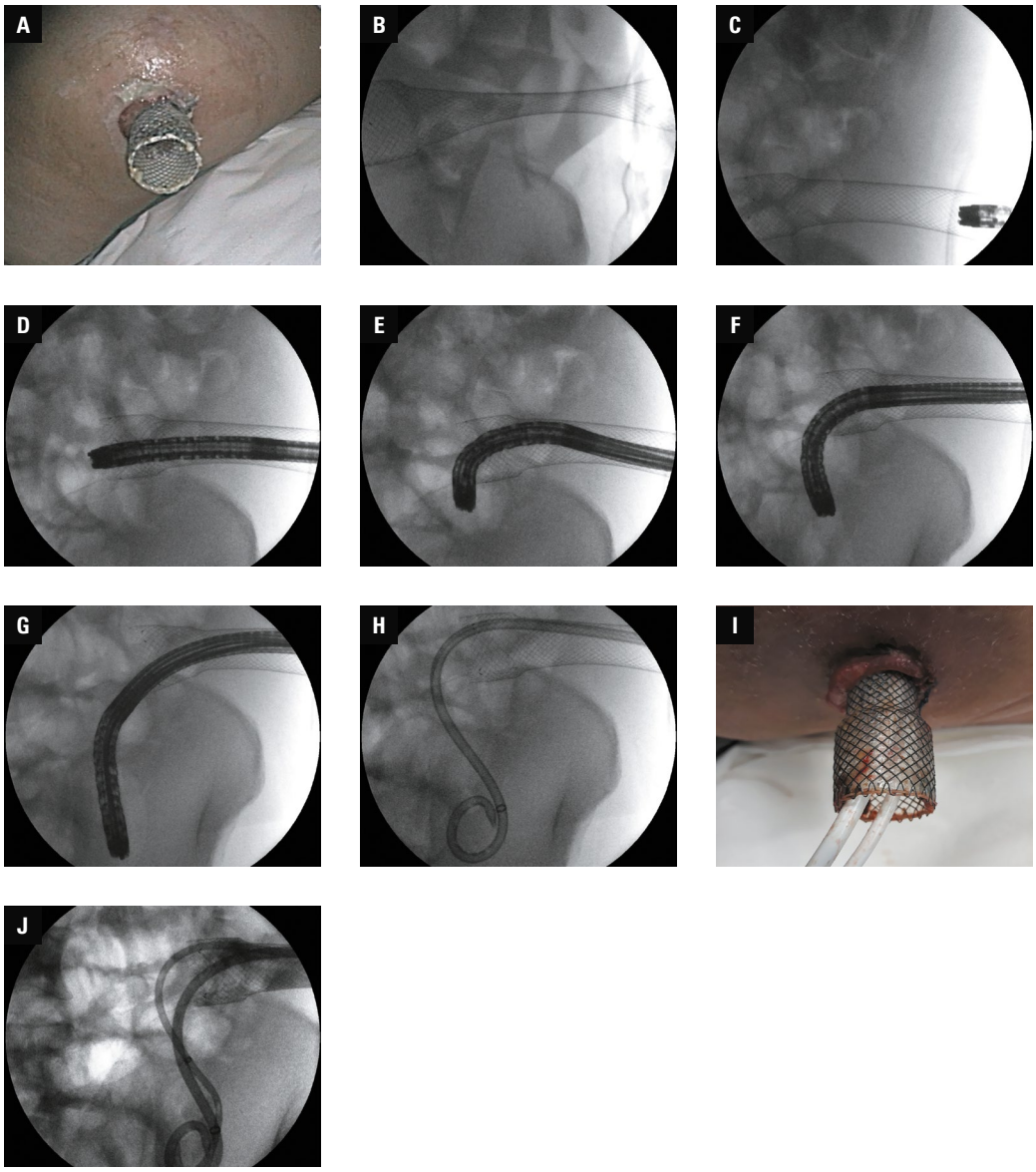


FIGURE 58 Percutaneous endoscopic necrosectomy of infected walled-off pancreatic necrosis. A fully-coated esophageal stent, 22 mm in diameter and 12 cm in length, was inserted percutaneously along a guidewire into the post-percutaneous drain site in the left lumbar region (**A**, **B**). A gastroscope was subsequently inserted percutaneously through the stent lumen to perform percutaneous endoscopic necrosectomy (**C**–**G**). After the endoscopic procedure, 2 drains (**H**–**J**) were inserted through the lumen of the percutaneous stent to flush the collection in the postoperative period, until the next percutaneous endoscopic necrosectomy procedure.

Such a size of the transpapillary drained collection, visible on multiphasic CECT, indicates complete regression of the collection.

Notably, for transmurally drained collections, achieving regression resulting in the collection being invisible on imaging studies is only possible after the transmural drainage is completed, because the residual space within the distal ends of transmural stents will persist on imaging assessments as long as the stents remain in the collection lumen.

The success of endoscopic treatment with transmural drainage involves complete regression of the drained collection as observed on abdominal imaging assessments and resolution of collection-related clinical symptoms. The acknowledgment of treatment success mandates the termination of endotherapy.

RECOMMENDATION 47 For postinflammatory pancreatic and peripancreatic fluid collections resulting from necrotizing AP, completion of endoscopic transpapillary drainage should depend on the success of treatment, defined as complete regression of the collection and resolution of clinical symptoms, and on the morphology of the main pancreatic duct, as determined during ERCP or magnetic resonance cholangiopancreatography (MRCP)[32,33,67,196,197,199,205,206,289,290,337-344,-354,355,357-364,395,396] (*evidence level, very low; recommendation, strong [average of votes, 2.6]*).

In patients with WOPN, endotherapy of any damage to the main pancreatic duct is a key element of endoscopic treatment. Passive transpapillary drainage pursued during transmural drainage improves the long-term results of endoscopic treatment in patients with WOPN, reducing the number of recurrent pancreatic collections. Therefore, in patients with fluid collections, the integrity of the main pancreatic duct (absence of damage to the main pancreatic duct) must be confirmed via ERCP or MRCP to help determine the success of endoscopic treatment, in addition to the resolution of collection-related clinical symptoms and complete regression of the collection following transmural drainage. Typically, a fluoroscopic image, acquired during ERCP performed after the removal of the transpapillary stent during the endoscopic procedure, is sufficient to confirm the integrity of the main pancreatic duct. The image should visualize the absence of contrast leakage beyond the duct.

The success of endoscopic treatment of any damage to the main pancreatic duct is an indicator of the success of endoscopic treatment of WOPN. The lack of such success, defined as persistent leakage outside the pancreatic duct, negatively affects the long-term results of endotherapy, increasing the number of recurrent fluid collections. Therefore, the integrity of the main pancreatic duct should be assessed in patients undergoing passive transmural drainage of the residual necrotic collection after completion of active transmural drainage, before removal of transmural stents, and after successful endoscopic treatment via the transmural access. If no damage is found in the main pancreatic duct, the transmural stents can be removed, and endoscopic treatment can be completed. If damage to the main pancreatic duct is found, endoscopic treatment of the duct damage, such as passive transpapillary drainage, should be applied before completion of transmural drainage. If passive endoscopic drainage was not used in the treatment of the main pancreatic duct damage, the transmural stents should be left in place even if resolution of clinical symptoms and complete regression of the collection have been achieved. The remaining stents drain the site of the duct injury through passive transmural drainage, preventing collection recurrence. If passive transpapillary drainage of the main pancreatic duct lesion is not possible, permanent transmural drainage should be maintained.

RECOMMENDATION 48 With transpapillary drainage as the only access route to the collection, treatment success is acknowledged upon: 1) resolution of the clinical symptoms associated with the collection; 2) complete regression of the collection (<30 mm) on imaging; and 3) closure of the site of damage to the main pancreatic duct, visualized as an absence of contrast leakege outside the pancreatic duct on fluoroscopic imaging during follow-up ERCP[57,59,67,133,200-203,205,206,209,337-345,347-349,351-356,365,366] (*evidence level, very low; recommendation, strong [average of votes, 2.76]*).

For PPs communicating with the main pancreatic duct and treated with transpapillary drainage as the only access route to the collection, the success of treatment is based on the clinical presentation and the result of imaging assessments, including assessment of the main pancreatic duct morphology. The resolution of collection-related clinical symptoms is 1 of the 3 criteria needed to declare the success of endoscopic treatment. The second criterion is complete regression of the transpapillary drainage collection, confirmed via static imaging of the abdominal organs with contrast enhancement. Multiphasic CECT of the abdomen is the recommended modality for evaluating regression of fluid collections because it is a static study that allows for a comparison with previous imaging assessments. For fluid collections drained via the transpapillary route, a diameter of less than 30 mm, achievable with effective transpapillary drainage, is considered to indicate complete regression of the collection, in contrast to transpapillary drainage, where a diameter of less than 40 mm is considered the criterion of complete regression. Closure of the site of damage to the main pancreatic duct is considered the third criterion for treatment success in the case of transpapillary drainage. All 3 criteria must be met for the success of the treatment of transpapillary drainage of PPs to be acknowledged, warranting the completion of endoscopic treatment and removal of the transpapillary stent.

RECOMMENDATION 49 Endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections can be terminated after treatment success is acknowledged, at which time, the transmural / transpapillary stents can be removed, and the transmural / transpapillary endoscopic drainage be completed[32-34,51,54-59,67,91-96,102,106,114-119,128,133,143,160-167,171-186,190-192,194-196,198,200-203,205,206,208,209,212-215,224,227-232,236,250,266,268,272,285,287,288,306,308,309,317,320,334-345,347-349,351-356,360,361,365,366,390-394] (*evidence level, very low; recommendation, strong [average of votes, 2.8]*).

The success of endoscopic treatment of fluid collections is based on the clinical presentation and abdominal imaging findings. In the cases where transpapillary drainage has been used during endotherapy, the integrity of the main pancreatic duct must additionally be assessed as a determinant of treatment success. Determination of the success of endoscopic treatment based on detailed criteria mandates treatment termination and removal of the transmural and, in the cases of transpapillary drainage, transpapillary stents. An exception are patients with DPDS, in whom transpapillary stents are left in place permanently for drainage.

RECOMMENDATION 50 For pancreatic fragmentation, or DPDS, permanent transpapillary drainage using plastic double-pigtail stents may be required

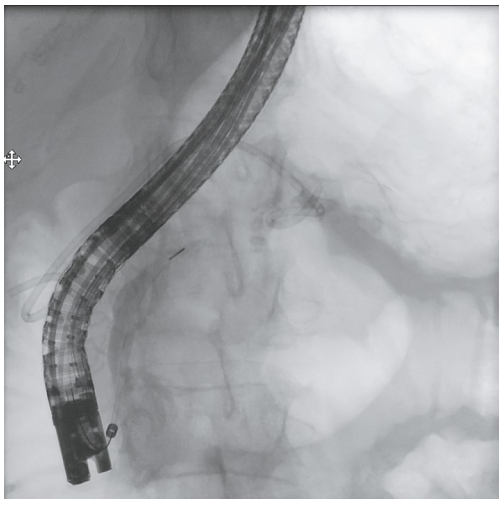


FIGURE 59 Endoscopic retrograde pancreatography in a patient with pancreatic fragmentation (disconnected pancreatic duct syndrome). The fluoroscopic image shows a transpapillarily--contrasted fragment of the pancreatic duct in the head and part of the body of the pancreas. The remaining, disconnected fragment of the body and tail of the pancreas, not filled with the contrast agent, was subjected to transmural/transgastric drainage using a double-pigtail plastic stent.

even after successful treatment of postinflammatory pancreatic and peripancreatic fluid collections[32-34,55,56,67,199,287,289,290,337-344,354,355,357-366,395-412] (*evidence level, very low; recommendation, strong [average of votes, 2.45]*).

Pancreatic fragmentation, or DPDS, is a variant of damage to the main pancreatic duct, which can manifest during ERCP as follows:

- partial disruption of the main pancreatic duct;
- complete disruption of the main pancreatic duct;
- contrastation of the main pancreatic duct without visible leakage of the contrast agent outside the duct.

Regardless of the presentation during ERCP (**FIGURE 59**), presence of a disconnected pancreatic parenchyma fragment distal to the site of the ductal injury visible on imaging is necessary to establish a diagnosis of DPDS. The most common cause of pancreatic fragmentation is central parenchymal necrosis of the pancreas (**FIGURE 60A** and **60B**).

DPDS is difficult to treat, as it often requires permanent drainage of the peripheral pancreatic fragment via a transmural access (**FIGURE 61A–61F**). Transpapillary access (**FIGURE 62A–62C**) is possible only in less common cases involving contrast agent leakeage during ERCP and partial or complete damage to the main pancreatic duct with concomitant pancreatic fragmentation. In most patients with pancreatic fragmentation, a fragment of the contrasted pancreatic duct with no visible streaking can be observed during ERCP. A pancreatic fluid collection develops due to pancreatic juice secretion from the disconnected distal fragment of the pancreas, requiring extra-anatomical transmural drainage. Removal of the transmural stents and termination of the transmural drainage after collection regression achieved in patients with DPDS leads to rapid recurrence of the collection and the need for repeat endoscopic intervention. Hence, in such patients, the plastic stents (usually a single, 7-Fr double-pigtail stent) should be left in place for permanent transmural drainage. Similarly, permanent transmural drainage is recommended for patients with drained WOPN lesions and damage to the main pancreatic duct in whom transpapillary drainage is not feasible. Notably, it is frequently impossible to perform transpapillary drainage in patients with transmurally drained WOPN collections owing to the presence of pancreatic fragmentation.

Surgical resection of the distal (disconnected) portion of the pancreas is another option for interventional treatment in patients with DPDS. However, most such patients are ineligible for surgical treatment owing to persistent inflammatory infiltration, which prevents safe resection of the disconnected fragment of the pancreas.

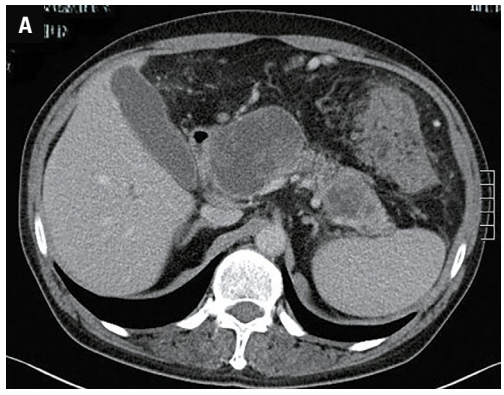
Regarding permanent transmural drainage, the transmural stents are left in place permanently, with no periodic replacements. Considering the high risk of transmural access loss during endoscopic surgery, transmural stents are usually not replaced. This is because even if stent obstruction occurs, pancreatic juice outflow remains possible via the fistula along the stent. During permanent transmural drainage, abdominal imaging follow-up with clinical evaluation of the patient is necessary every 12 months. The first signs of obstruction of the transpapillary endoscopic fistula include increasing abdominal pain, and abdominal imaging initially shows dilatation of the main pancreatic duct, followed by a gradual increase in the size of the transpapillary drainage collection. In such cases, the transmural stent should be replaced, and if transmural access is lost, endoscopic transmural drainage of the fluid collection with the insertion of a plastic transmural double-pigtail stent should be repeated.

RECOMMENDATION 51 Most complications of postinflammatory pancreatic and peripancreatic fluid collection endotherapy can be successfully treated using conservative or endoscopic means. However, in some cases, especially in hemorrhagic complications, interventional radiology or vascular surgery techniques, or conventional surgical treatment may be necessary, depending on the experience of the treating center[32-34,54-58,91-96,102,106,-114-117,128,143,160-167,171-186,205,208,212-215,224,227-232,236,-250,266,268,270-272,274,279-281,285,288,291,306,308,309,316,317,320-326,328-336,338-341,343,344,354,358,360,361,365,390-394,397,413-419] (*evidence level, low; recommendation, strong [average of votes, 2.82]*).

The most common complications of fluid collection endotherapy include bleeding into the upper gastrointestinal tract lumen, gastrointestinal tract perforation, transmural stent migration, and fluid collection perforation.

Bleeding into the upper gastrointestinal tract lumen involves bleeding into the collection lumen or bleeding from the site of a transmural endoscopic fistula (**FIGURE 63A–63C**). Less frequently, the bleeding is caused by gastric or duodenal ulcers. In addition, in transpapillary drainage, bleeding may originate from the greater duodenal papilla following sphincterotomy.

Undoubtedly, the introduction of intraprocedural EUS assessments during the transmural approach has helped reduce the rates of hemorrhagic



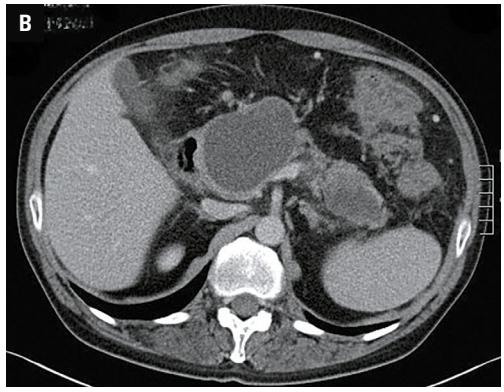


FIGURE 60 A, B – central pancreatic necrosis in the necrotizing phase visualized on multiphasic contrast--enhanced abdominal computed tomography

complications of endotherapy. Accurate visualization of vascular structures on EUS images, or visualization of flows on Doppler imaging, facilitates prevention of blood vessel damage during transmural puncture, and helps avoid close proximity to the vessels coursing around the anastomotic site, contributing to reduced bleeding during both the transmural access and the subsequent transmural drainage. Despite the development of advanced endoscopic imaging techniques, hemorrhagic complications remain the most common complication of endoscopic treatment of fluid collections, frequently due to damage to the blood vessels coursing in close proximity to the fluid collection. Frequently, bleeding is caused by mechanical trauma to the collection wall by the distal flange of the LAMS. A plastic double-pigtail stent inserted through the lumen of the metal transmural stent reduces the risk of damage to the posterior wall of the fluid collection; however, bleeding into the lumen of the collection remains a major clinical problem. If damage to large visceral vessels coursing in the vicinity of the transmurally drained fluid collection is suspected in hemodynamically stable patients, CT angiography should be performed, with possible qualification of the patient for endovascular intervention, mainly transarterial embolization (**FIGURE 64A–64G**). In hemodynamically unstable patients, CT angiography is usually omitted and immediate intervention, such as conventional angiography of the visceral vessels with intraoperative evaluation of the bleeding site and transarterial embolization, or most frequently, urgent laparotomy with repair of the bleeding vessel, is the treatment of choice. The most common source of bleeding is the damaged splenic artery, and less frequently, the gastroduodenal or left gastric artery. In the case of damage to smaller blood vessels coursing across the collection wall or granulation tissue resulting from collection healing (**FIGURE 65**), conservative treatment, such as blood and blood product transfusions with subsequent endoscopic intervention can be used, including an attempt at endoscopic treatment, most frequently via spraying of hemostatic powders into the collection lumen. This is especially applicable to bleeding from the collection's granulation tissue. If conservative and endoscopic treatment fails, endovascular treatment with vascular surgery or interventional radiology techniques (**FIGURE 66A** and **66B**), or surgical intervention remain the treatment of choice.

Bleeding from the transmural endoscopic fistula site (**FIGURES 67** and **68**) can be stopped by inserting a self-expandable metal stent, usually on the principle of tamponade, or mechanical compression (**FIGURE 69A–69C**). If this fails, endoscopic hemostasis methods should be used in combination therapy, similar to that used in nonvariceal upper gastrointestinal bleeding. Failure to achieve hemostasis using endoscopic techniques is an indication for endovascular intervention or surgical treatment.

Gastrointestinal tract perforation is the second most common serious complication of endotherapy of fluid collections. If gastrointestinal perforation with acute abdominal symptoms is diagnosed during peritonitis in a patient undergoing transmural drainage of pancreatic fluid collections, surgical treatment should involve damage control strategy, that is, suturing of the perforation site in the upper gastrointestinal tract with possible removal of the dislocated transpapillary stent and external drainage of the collection, with the external drainage being replaced with internal (endoscopic) drainage in the postoperative period. The posterior wall of the stomach is the most common site of perforation. Gastrointestinal tract perforation during endotherapy does not preclude the use of laparoscopic techniques.

Stent migration is another complication of endotherapy; it can be either distal (into the gastrointestinal tract lumen) or proximal (into the collection lumen). Early stent migration, usually within the first week of endoscopic drainage, is associated with a high risk of gastrointestinal tract perforation, requiring surgical treatment (**FIGURE 70A–70C**). Conversely, late stent migration, after the first week of endotherapy, can usually be treated endoscopically by grasping and removing the transmural stent using various endoscopic tools. This mainly applies to proximal migration, where the endoscope must be inserted into the collection lumen, and the stent is removed under endoscopic imaging guidance. Conversely, distal migration of a transmural stent usually requires no treatment, as the stent is spontaneously passed along the gastrointestinal tract to be excreted (**FIGURE 71A–71C**). An exception is

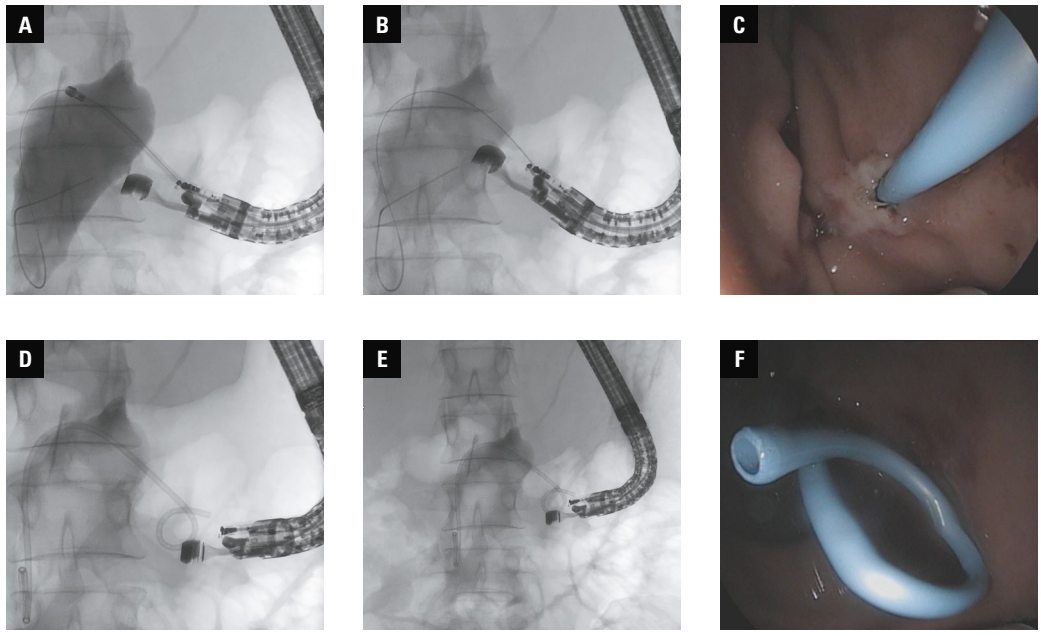


FIGURE 61 Permanent transmural/transgastric endoscopic drainage in a patient with pancreatic fragmentation (disconnected pancreatic duct syndrome) and central pancreatic head necrosis. A gastropancreatic fistula was established endoscopically using a 10-Fr cystotome (**A**, **B**) and a transmural 7-Fr, 9-cm double pigtail plastic stent (**C**–**F**). The fluoroscopic image revealed enhancement of a narrow main pancreatic duct of the disconnected pancreatic fragment (**A**, **B**, **D**, **E**) during the procedure.

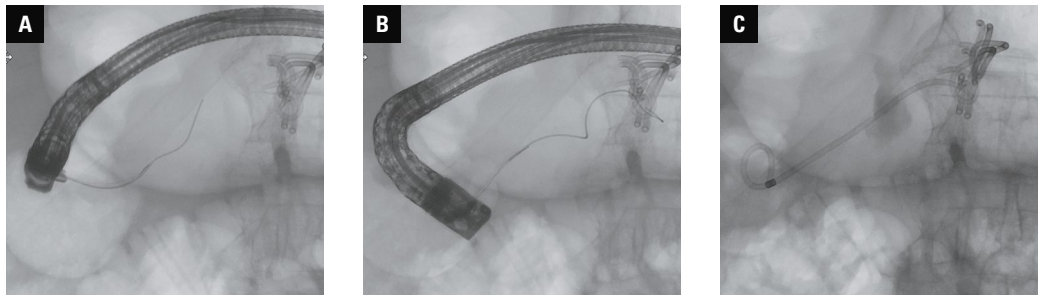


FIGURE 62 Passive transpapillary drainage and passive transmural drainage in a patient with pancreatic fragmentation (disconnected pancreatic duct syndrome). A guidewire, inserted through the major duodenal papilla into the main pancreatic duct (**A**) and further across the duct disruption site, is looped in the area of the transmural stents draining the disconnected part of the duct (**B**). The distal end of the transpapillary stent passing through the lesion site is located in the area of the transmural stents (**C**).

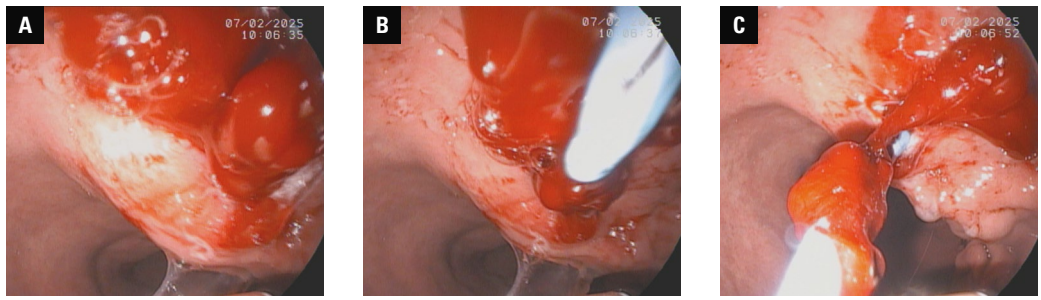


FIGURE 63 **A**–**C** – intraoperative bleeding from a transmural fistula site on the posterior gastric wall in a patient with a pancreatic pseudocyst during endoscopic cystogastrostomy. The bleeding ceased spontaneously during the procedure.

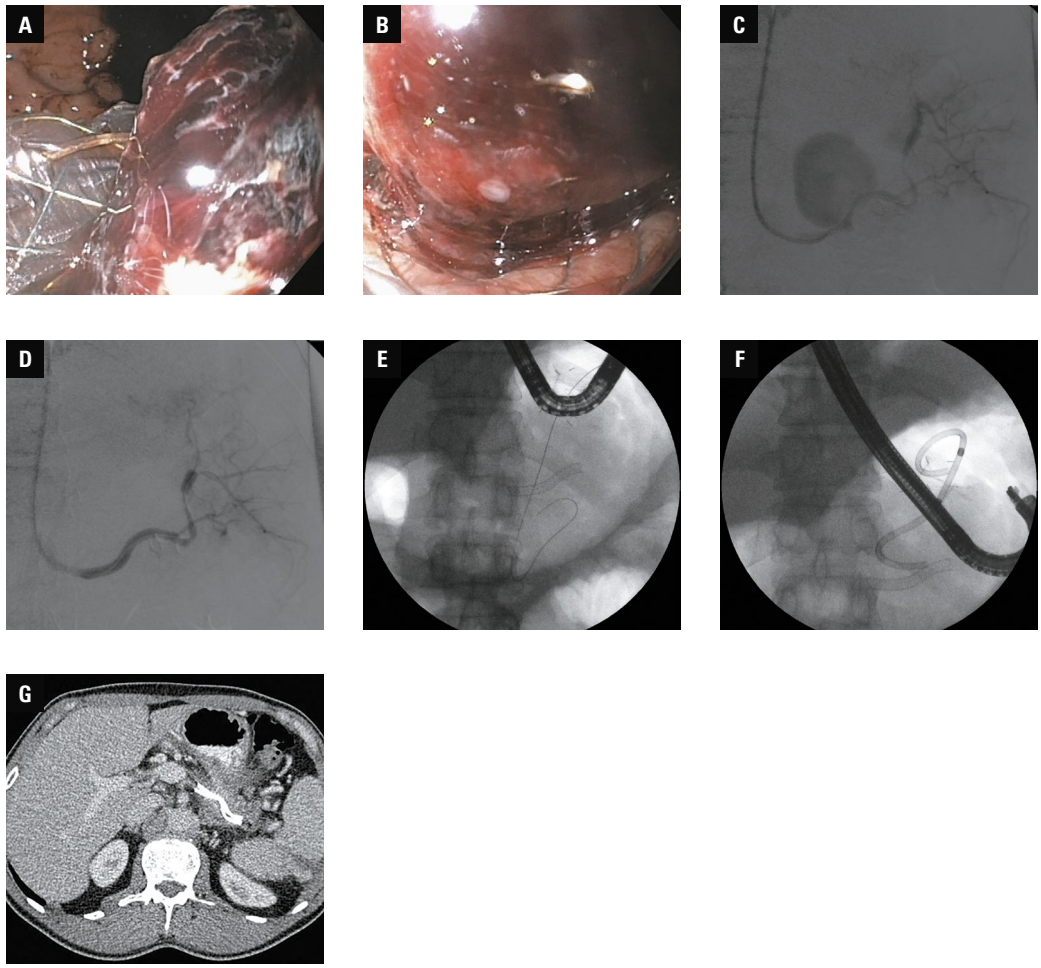


FIGURE 64 Splenic artery bleeding into the lumen of the pancreatic walled-off necrosis collection. Gastroscopy performed owing to the features of massive bleeding into the gastrointestinal tract during endoscopic drainage showed a clot obstructing the stent lumen, with blood flowing from beneath the clot (**A**, **B**). Following computed tomography (CT) angiography, the patient was deemed eligible for endovascular treatment for splenic artery bleeding. Classic angiography revealed active splenic artery bleeding into the collection lumen (**C**), and splenic artery stenting was performed to bypass the site of arterial injury (**D**). After the endovascular procedure, endoscopic treatment was continued (**E**, **F**) to achieve complete regression of the necrotic collection as confirmed on a multiphasic contrast--enhanced abdominal CT scan (**G**).

where the distally migrated transmural stent remains within the upper gastrointestinal tract; in such a case, removal of the dislocated stent can be attempted via endoscopic means during esophagogastroduodenostomy.

For perforation of fluid collections, the therapeutic approach depends on the patient's clinical condition. If perforation of the collection is accompanied by symptoms of diffuse peritonitis, surgery remains the treatment of choice. When performing a laparotomy, external drainage of the fluid collection should be pursued after peritoneal lavage, consistent with the damage control principle. If the perforation is accompanied only by symptoms of local rather than diffuse peritonitis, therapeutic management can commence with conservative treatment, primarily broad-spectrum empirical antibiotic therapy and, possibly, minimally-invasive interventional treatment, such as percutaneous external drainage. If the clinical condition worsens despite conservative or minimally-invasive treatment, surgical treatment is indicated.

Most complications of endotherapy of fluid collection can be successfully treated conservatively or endoscopically. However, in some cases, especially in hemorrhagic complications, surgery may be necessary. A center providing endoscopic treatment of fluid collections should offer a 24-hour surgical on-call service to ensure immediate surgical management of patients.

RECOMMENDATION 52 If treatment of postinflammatory pancreatic and peripancreatic fluid collections fails despite intensified interventional treatment using minimally-invasive techniques, surgery remains the treatment of choice[5,23,31-34,40,45,51,52,54-60,74,77,91-96,98-106,109,110,113-119,121-189,-200-209,212-219,221,227-231,236,266,268,270-272,274,279-281,285,288,291,306,308-317,320-326,328-336,338-341,343,344,354,358,360,361,365,390-394,397,414,415]

(*evidence level, moderate; recommendation, strong [average of votes, 2.76]*).

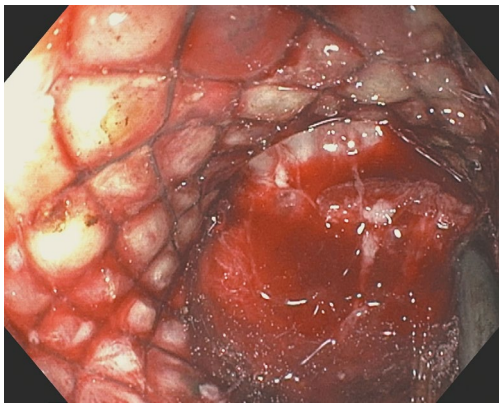


FIGURE 65 Bleeding from the granulation tissue on the posterior wall of the postinflammatory pancreatic and peripancreatic fluid collection subjected to transmural drainage

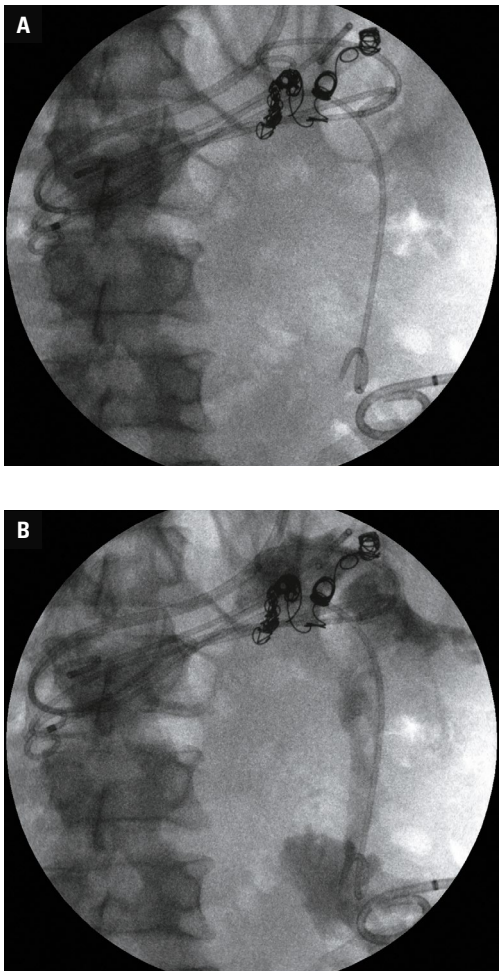


FIGURE 66 Active transmural drainage and percutaneous drainage of walled-off pancreatic necrosis (WOPN). Vascular coils inserted into the lumen of the necrotic collection during transarterial embolization of splenic artery bleeding are visible on the fluoroscopic image (**A**). Contrast administered through the nasocystic drain filled the WOPN collection (**B**).

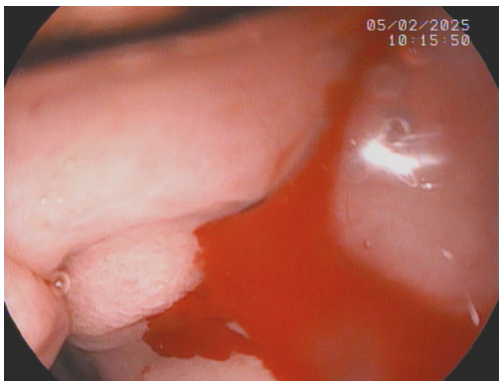


FIGURE 67 Bleeding from the site of transmural puncture using a 19-G needle during endoscopic cystoduodenostomy

Consistent with the step-up strategy, the ineffectiveness of interventional treatment of fluid collections using minimally-invasive techniques despite the intensification of treatment is an indication for conventional, open surgery. The type of surgical access and procedure should be guided by both the experience of the treating center and the clinical circumstances. The need for surgical treatment owing to the ineffectiveness of minimally-invasive techniques, including endoscopic techniques, is more common in patients with WOPN. Early open surgical interventions for the treatment of AP have a high risk of complications and mortality. Conversely, the use of minimally-invasive techniques, even if ultimately ineffective, frequently facilitates the postponement of conventional surgical treatment, which significantly reduces the number of complications of surgical treatment, including fatalities.

In addition, the use of surgical treatment following failure of endoscopic techniques in the treatment of fluid collections often yields better results than conventional surgical treatment without prior endotherapy, as in such a case, no drainage of the retroperitoneal space is required, and the drainage of the peritoneal cavity alone is sufficient during surgery. This is because transmural endoscopic drainage frequently facilitates full regression of the retroperitoneal fluid collections, and the failure of endotherapy is related to fluid collections persisting in the lateral flanks of the abdominal cavity along the paracolic gutters and in the pelvic cavity, where endoscopic drainage, without additional percutaneous drainage, is often insufficient. In such cases, laparotomy with abdominal drainage and evacuation of the collections usually yields satisfactory results. Conversely, if conventional access to the retroperitoneal space is required after endotherapy failure, typical transmural endoscopic drainage facilitates partial liquefaction of the necrotic tissue, thus enabling necrosectomy, and consequently, further reducing the surgery complication rates.

In addition, conventional surgery is indicated during minimally-invasive treatment of fluid collections in complicated pancreatitis, including pancreatitis with gastrointestinal tract perforation, acute intestinal ischemia, or intra-abdominal hemorrhage. In such cases, urgent surgery is performed as per the damage control strategy, regardless of the effectiveness of minimally-invasive techniques in the treatment of fluid collections, which can be resumed thereafter.

Post-treatment management RECOMMENDATION 53 Following successful completion of endoscopic treatment of postinflammatory pancreatic and peripancreatic fluid collections, all patients should be followed in an outpatient setting for at least 2 years, with follow-up abdominal imaging performed at 3, 6, 12, and 24 months post-treatment, or whenever collection recurrence is suspected[33,34,54-58,106,114-119,128,131-134,143,160-167,171-186,190-192,194-196,198,205,207,208,212-215,218,227-231,236,266,268,270-272,274,279-281,285,288,291,306,308-317,320-326,328-336,338-341,343,344,354,358,360,361,365,390-394]

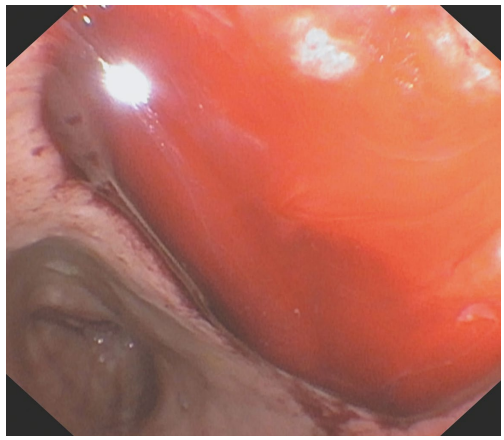


FIGURE 68 Massive arterial hemorrhage during endoscopic cystogastrostomy of walled-off pancreatic necrosis

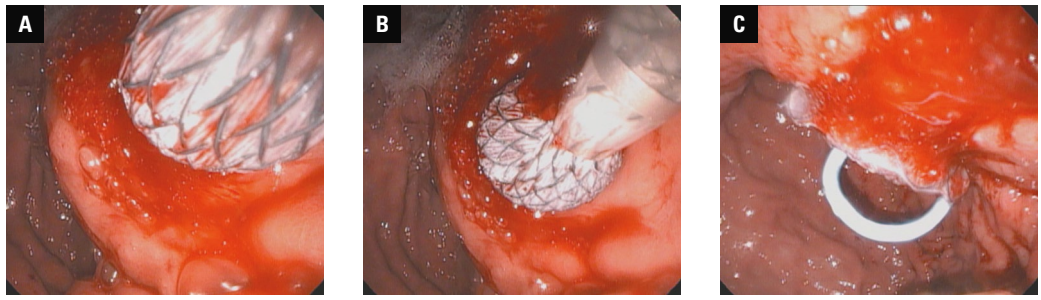


FIGURE 69 **A**–**C** – intraoperative bleeding during endoscopic cystogastrostomy. The bleeding ceased after transmural insertion of a self-expanding lumen-apposing metal stent (tamponade principle)

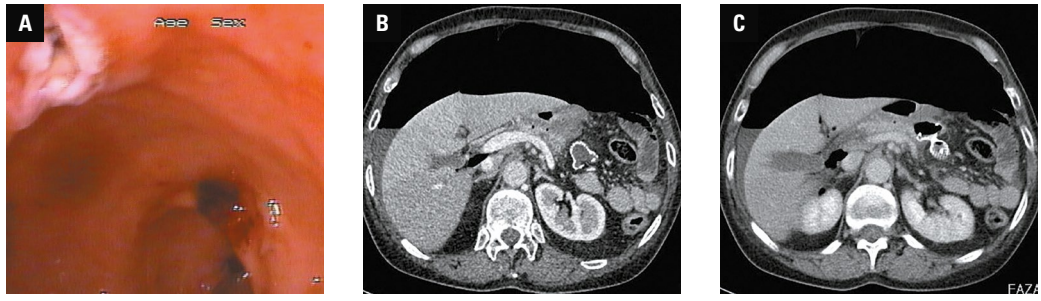


FIGURE 70 **A**–**C** – early proximal migration of a transmural stent. Endoscopic imaging showed a gastro-pancreatic fistula with no transmural stent visible (**A**). A multiphasic contrast-enhanced abdominal computed tomography scan revealed features of gastrointestinal tract perforation with proximal migration of a transmural biflanged metal stent (**B**, **C**).

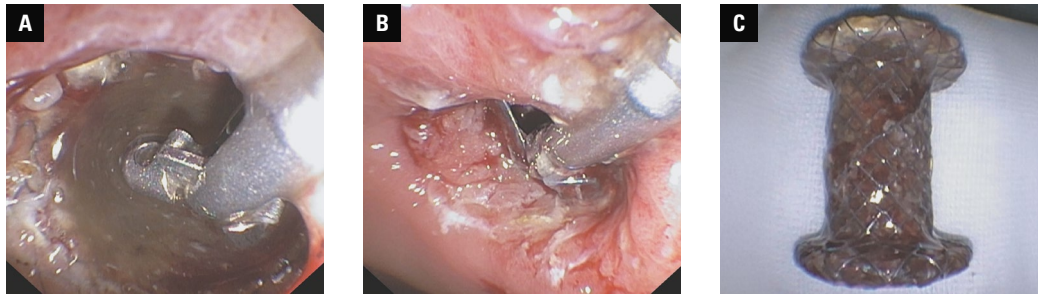


FIGURE 71 Late proximal migration of a transmural stent. A dislocated biflanged metal self-expanding transmural stent (**A**), found during the procedure, was grasped with endoscopy forceps (**B**) and removed (**C**).

[414,415] (*evidence level, very low; recommendation, strong [average of votes, 2.4]*).

Following endoscopic treatment, outpatient medical care, including follow-up visits for clinical evaluation and follow-up imaging, is recommended. The recommended follow-up period postendotherapy is 2 years, as the possible recurrence of fluid collections usually occurs no later than

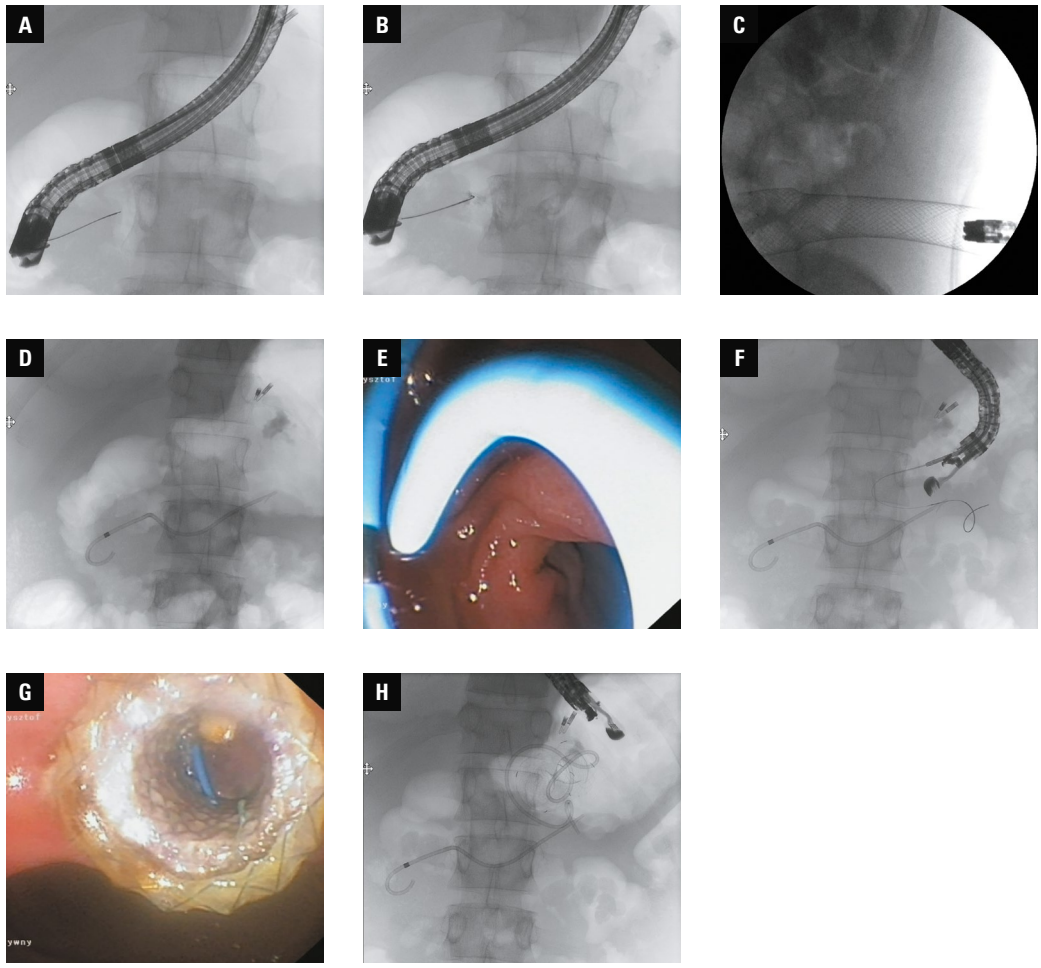


FIGURE 72 Endoscopic treatment of a recurrent pancreatic pseudocyst. Endoscopic retrograde pancreatography showed contrast leakage through a partial ductal defect in the pancreatic body (**A**–**C**). A 7-F, 12-cm pancreatic stent was inserted transpapillarily to splint the lesion site (**D**, **E**); followed by an endoscopic cystogastrostomy with passive transmural drainage (**F**–**H**). A transpapillarily inserted pancreatic stent is visible through the lumen of the self-expanding transmural stent, beneath a pancreatic pseudocyst (**G**).

2 years after therapeutic success, which mandates termination of endotherapy.

The proposed regimen of outpatient follow-up imaging at 3, 6, 12, and 24 months postendotherapy is based on the literature data, which show that recurrent fluid collections typically occur early in the follow-up period, usually during the first year.

Over the 2-year follow-up period following therapeutic success, conventional abdominal USG is the recommended imaging modality, provided that the fluid collection had been clearly visible on USG imaging performed before endotherapy initiation. Else, a more advanced imaging modality (CECT or CE-MRI) should be used to visualize the abdominal organs. In addition, advanced abdominal imaging should be performed at the end of the follow-up period, that is, 2 years postendotherapy.

Clinical evaluation of the patient is the second crucial component of outpatient care following endoscopic treatment. If clinical signs suggesting collection recurrence develop during the follow-up period, immediate imaging assessment of abdominal organs is necessary. Clinical signs indicative of suspected fluid collection recurrence during the follow-up period usually include signs of the collection compressing the neighboring structures and organs, as well as signs of infection of the collection contents. The occurrence of collection-related clinical signs during the follow-up period is an indication for abdominal imaging, regardless of the aforementioned schedule of follow-up imaging examinations.

RECOMMENDATION 54 For recurrent postinflammatory pancreatic and peripancreatic fluid collections, endoscopic treatment may be repeated post endotherapy[32-34,54-60,106,114-117,128,131-134,143,160-167,171-186,-205,208,212-215,218,227-231,236,266,268,270-272,274,279-281,285,287-289,-291,306,308-317,320-326,328-336,338-341,343,344,354,355,357-365,390-402,404,406,410,414,415] (*evidence level, low; recommendation, strong [average of votes, 2.87]*).

If a recurrent fluid collection is diagnosed during the follow-up period, endoscopic drainage should be repeated.

The eligibility criteria for endotherapy of recurrent fluid collections are similar to those for de novo fluid collections. Patients with recurrent fluid collections presenting with no collection-related clinical symptoms do not require

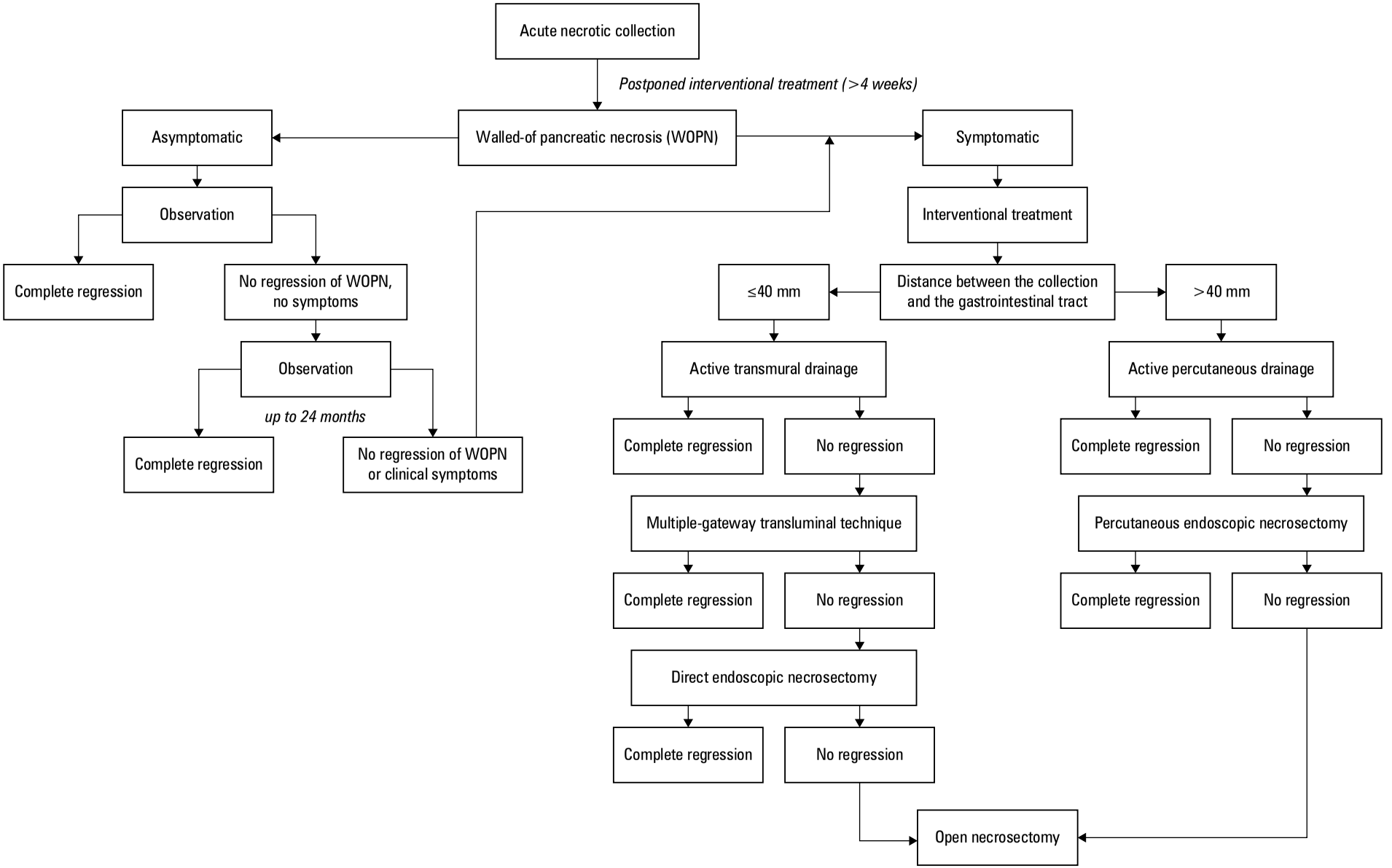


FIGURE 73 Algorithm of therapeutic management of patients with pancreatic/peripancreatic necrosis

interventional treatment regardless of the collection size.

The most common recurrent fluid collections are PPs formed by pancreatic juice leaking through a pancreatic duct injury into the previously drained collection space. The most common cause of recurrent fluid collections following endotherapy include persistent damage to the main pancreatic duct. Hence, when approaching the treatment of recurrent fluid collections, the integrity of the main pancreatic duct should be assessed via passive transpapillary drainage, if ductal damage has been confirmed (**FIGURE 72A–72H**). In addition, a large number of recurrent fluid collections result from pancreatic fragmentation in DPDS without permanent drainage of the peripancreatic (disconnected) fragment that feeds the recurrent fluid collection.

In the diagnostic and therapeutic management of patients with recurrent fluid collections, it is crucial to distinguish a recurrent fluid collection from a newly formed collection during a subsequent episode of pancreatitis. Therefore, it is important to evaluate previous imaging data, which usually facilitate this differentiation. A recurrent fluid collection can lead to recurrent pancreatitis, which, in turn, can result in a new collection being formed during another episode of pancreatitis.

SUMMARY Initiation of interventional treatment of local complications of AP, such as pancreatic and peripancreatic fluid collections, is indicated when collection-related clinical symptoms are observed despite conservative treatment. Interventional treatment of fluid collections should be deferred as long as possible. The optimum time for intervention is approximately 4–6 weeks after the onset of pancreatitis.

Interventional treatment of fluid collections should commence with minimally-invasive techniques according to the step-up strategy. Endoscopic techniques for the treatment of postinflammatory fluid collections are the preferred treatment method when endotherapy is available. The choice of interventional treatment should depend on the experience of the treating center. The basis for the treatment of fluid collections is the establishment of an effective drainage system, which, in the case of endotherapy, may require intensification of endoscopic treatment and the use of additional access routes with other minimally-invasive techniques. Endotherapy provides an alternative to other minimally-invasive techniques for the treatment of fluid collections and enables transmural (ie, through the gastrointestinal tract wall) and transpapillary (ie, through the major or minor duodenal papilla) collection drainage. The mainstay of endoscopic treatment of fluid collections is transmural drainage of the collection under EUS guidance. Necrotizing AP–related fluid collections often require intensive interventional treatment using minimally-invasive techniques, and, in some cases, establishment of other collection access gateways or necrosectomy.

Conventional surgical intervention remains the treatment of choice when minimally-invasive techniques for fluid collections have failed despite the maximization of treatment. A summary of management steps in patients with pancreatic and peripancreatic necrosis is presented in **FIGURE 73**.

ARTICLE INFORMATION

NOTE All figures used in this document are derived from files of the Department of General, Gastroenterological and Oncological Surgery, Collegium Medicum, Nicolaus Copernicus University in Toruń, Poland, from 2018–2025.

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