Internal and Emergency Medicine (2024) 19:2091–2104
https://doi.org/10.1007/s11739-024-03666-9

IM - REVIEW

# Practical approach to acute pancreatitis: from diagnosis to the management of complications

**Donatella Padula[1] · Aurelio Mauro[2] · Paolo Maggioni[1,3] · Hayato Kurihara[4] · Antonio Di Sabatino[5,6] · Andrea Anderloni[2]**

Received: 13 January 2024 / Accepted: 28 May 2024 / Published online: 8 June 2024


**Abstract**
The purpose of this review is to provide a practical guide for the clinical care of patients with acute pancreatitis (AP) from the management of the early phases of disease to the treatment of local complications. AP is one of the most frequent causes of gastroenterological admission in emergency departments. It is characterized by a dynamic and unpredictable course and in its most severe forms, is associated with organ dysfunction and/or local complications, requiring intensive care with significant morbidity and mortality. Initial therapy includes adequate fluid resuscitation, nutrition, analgesia, and when necessary critical care support. In recent years, the development of minimally invasive tailored treatments for local complications, such as endoscopic drainage, has improved patients' acceptance and outcomes. Despite this, the management of AP remains a challenge for clinicians. The present review was conducted by the authors, who formulated specific questions addressing the most critical and current aspects of the clinical course of AP with the aim of providing key messages.

**Keywords** Acute pancreatitis · Practical guide · Pancreas · ERCP · Walled-off necrosis · Procalcitonin · Intensive-care unit

## Introduction

Acute pancreatitis (AP) is an inflammatory condition caused by the autodigestion of the pancreatic tissue.

With an increasing incidence throughout the years, it is the most common gastrointestinal disease that requires hospitalization [1]. It has a global incidence of 13–40 per 100,000 population-years, burdened by a mortality rate of 1–5% [2].

Patients generally report upper or diffuse abdominal pain (80–95%), that is usually from moderate to severe radiating to the back and exacerbated by eating.

Typically, the first assessment is done in the Emergency Department (ER) and should focus on medical history, with particular attention reserved to the presence of risk factors of AP.

Most patients experience mild acute inflammatory disease that is self-limiting. However, one-fifth of patients develop severe AP with organ failure or local complications requiring admission to Intensive Care Unit (ICU) due to increases in the mortality rate of up to 20–40% [3, 4].

The management of AP has undergone important changes in recent years with the introduction of mini-invasive diagnostic and therapeutic tools, step-up tailored approaches [5], the creation of multidisciplinary dedicated teams, and the improvement of invasive monitoring and supportive care therapies.

Despite these developments, AP remains a challenge for clinicians due to its clinically unpredictable course and its accompanying local and systemic complications. Although

✉ Aurelio Mauro
a.mauro@smatteo.pv.it

1 Emergency Department and Medicine, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, via F Sforza 35, Milan, Italy

2 Gastroenterology and Digestive Endoscopy Unit, Fondazione I.R.C.C.S. Policlinico San Matteo, Viale Camillo Golgi, 19, Pavia, Italy

3 Scuola di Specializzazione in Medicina di Emergenza-Urgenza, Università Degli Studi Di Milano, Milan, Italy

4 Emergency Surgery Unit, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, via F. Sforza 35, Milan, Italy

5 Department of Internal Medicine and Medical Therapeutics, University of Pavia, Pavia, Italy

6 First Department of Internal Medicine, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

AP is a benign disease, mortality and morbidity rates remain high. Moreover, the management of AP is still an "anybody and nobody's land", requiring different clinical specialists who must interact, confer, and work collaboratively, using healthcare resources appropriately.

This review has been conducted with the formulation of 14 specific questions by the authors on the most critical and hot topic of the clinical course of AP to provide clear and practical key messages. It sums up the most recent literature at this point on this disease.

## Question 1: How to identify a patient with acute pancreatitis?

According to the revised Atlanta classification, the diagnosis of AP requires that two out of the three following criteria are met: (1) abdominal pain suggestive of pancreatitis as described above, (2) serum pancreatic enzymes greater than 3 times the normal upper limit of normal, and (3) findings consistent with pancreatitis on cross-sectional abdominal imaging (in adults: contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI)). Generally, the first two criteria well identify a patient with AP and imaging is not required.

Common laboratory panel in clinical practice includes lipase and amylase. In particular, the former has shown, for levels greater than three times the normal limit, a very high sensitivity and specificity for pancreatitis [6]. Other diseases, such as renal injuries, bowel diseases, or diabetic ketoacidosis, can present a high level of lipases but generally with lower values than AP [7]. Amylase is secreted by many tissues, so it is less sensitive and specific than lipase [6], especially for alcohol and hypertriglyceridemia-related pancreatitis. Because of these characteristics many authors, including the American Board of Internal Medicine's Choosing Wisely initiative, recommend a lipase-only policy for the evaluation of suspected acute pancreatitis [8].

CT scan has shown its utility in the process of a differential diagnosis, to rule out other intra-abdominal conditions that could mimic AP symptoms (e.g., gastric/duodenal ulcer perforation, aortic dissection, mesenteric ischemia). However, CT scan is not sensitive for diagnosis of early pancreatitis [9] and it is useful 72–96 h after the onset of symptoms to estimate the presence of local complications [10]. MRI is recommended in patients with allergy to iodinated contrast, renal impairment, pregnant patients, but it is less sensitive than CT for detecting gas in fluid collection [11].

### Key messages

- Clinical features and increase of lypase are sufficient for diagnosis of acute pancreatitis.
- Contrast-enhanced CT may be useful 72–96 h from the onset of AP to detect peripancreatic necrosis and vascular complications

## Question 2: Should the etiology of acute pancreatitis be determined in the Emergency Department?

Current literature suggests that an early identification of the causes of AP in the ER is crucial because some treatments depend on the etiology of the disease. Therefore, a rapid etiological framework influences the management of the patient and the department of destination [12].

The most frequent causes of AP in high-income country are gallstones (45%) and alcohol abuse (20%). Less common causes are hypertriglyceridemia, medications, post endoscopic retrograde cholangiopancreatography (ERCP), hypercalcemia, malignancy, infections, genetics, and autoimmune diseases.

Etiological assessment should focus on a detailed medical history with particular attention reserved for the presence of risk factors of AP, including the presence of gallstones, alcohol abuse (defined as more than 5 years of alcohol consumption of >50 g/days) [13], obesity, smoking, hyperlipidemia, and drugs that can induce the disease [14].

Routine laboratory panel can help identifying underlying etiology. Electrolytes can evidence hypercalcemia. Elevated direct bilirubin and/or alkaline phosphatase levels may indicate a duct obstruction, serum triglyceride level can be considered the cause of AP if the result is >1000 mg/dl [15, 16] but its dosage is not always available in ER setting.

Based on its accessibility, speed, radiation free and low cost, abdominal ultrasound (US) represent the first imaging method to approach a patient with suspicious biliary AP [12, 13]. Nevertheless, US has some limitations related to patients' physical characteristics (i.e., abdominal obesity) or to intestinal air interposition [17] that could limit its sensitivity (25–60%) for choledocholithiasis located in the distal common bile duct (CBD) [18] or for small stones. In case of suspicious microlithiasis or gallstones in the CBD not detected at transabdominal US, endoscopic ultrasound (EUS) or magnetic cholangiopancreatography (MRCP) should be performed to confirm the diagnosis to select AP patient requiring therapeutic ERCP [19].

If it is not possible to identify an etiology in the early phase, the patient should be addressed for secondary exams, especially in case of recurrent episodes, such as IgG4 levels for autoimmunity, MRCP for morphologic abnormalities, genetic counseling and/or testing should be considered [20].

### Key messages

- Early identification of etiology of acute pancreatitis is essential to guide adequate management and allocate resources.
- It is suggested to perform abdominal ultrasound at admission to evaluate the biliary tract.

## Question 3: To hydrate or to hyper-hydrate?

Adequate fluid resuscitation is a cornerstone of initial management of AP of any severity, as it contrasts third-spacing volume loss, and maintains or restores intravascular volume for better tissue perfusion to prevent pancreatic and systemic microcirculatory impairment [21].

It is recommended to start as soon as possible the fluid resuscitation while the patient is still in the ER [22].

Many trials have sought to identify the optimal rate of fluid therapy to administer in order to guarantee tissue perfusion, avoiding fluid overload. Inappropriate early fluid resuscitation in the first hours of hospitalization resulting in hemoconcentration, leads to organ failure, local and systemic complications, and increases patient mortality [22–24]. For these reasons, in recent years the approach has been to give large volume of fluids, but recent literature has demonstrated that aggressive hydration is associated with worse outcomes [21, 25]. Several randomized controlled trials (RCT) and reviews have confirmed that hyper hydration should not been utilized in clinical practice. Moderate resuscitation (i.e., 5–10 ml/kg bolus in case of hypovolemia, followed by 1.5 ml/kg/h) has been demonstrated to be superior in terms of reducing complications due to fluid overload with no significant differences compared to aggressive resuscitation (i.e., 20 ml/kg bolus, followed by 3 ml/kg/h) in terms of the clinical outcomes [26, 27]. Initial fluid management should be guided by the hemodynamic status of the patient and their characteristics (age, weight, cardiac, or renal diseases [28, 29]), as well as by close monitoring of vital signs. Intravenous fluid therapy should be titrated until perfusion targets are met: mean arterial pressure between 65 and 85 mmHg, urinary output >0.5 ml/kg/h and heart rate <120/min; hematocrit should be between 35 and 45% [12, 30]. It has been demonstrated that patients who do not respond within the first 12 h of fluid therapy might not benefit from large fluid administration [13]. To be noted that more rare causes of AP such as hypertriglyceridemia or IgG4-related disease need specific therapies and, therefore, fluid management should be less aggressive.

The fluid of choice for rehydration should be isotonic crystalloid, such as Lactate Ringer's solution (LR), because of its demonstrated anti-inflammatory effect and reduced risk of developing systemic inflammatory response syndrome (SIRS) within 24 h compared with normal saline [28]. The only contraindication to LR is for AP caused by hypercalcemia (due to its content of 3 mEq/l of calcium); saline solution should be preferred in this case.

### Key messages

- A moderate resuscitation strategy is preferable to an aggressive strategy with respect to both efficacy and safety outcomes.
- Lactated Ringer's solution is recommended over saline solution for fluid resuscitation.

## Question 4: How can a deteriorating patient be identified?

The revised Atlanta classification system (2012) [29] distinguishes two morphologic subtypes of AP: interstitial edematous pancreatitis and necrotizing pancreatitis, while severity is measured by the presence and duration of organ failure [based on the modified Marshall scoring system, listed in Table 1, that considers respiratory, kidney, and cardiovascular systems [31] and the presence of local

**Table 1** Modified Marshall scoring system for organ dysfunction [2, 14, 31]

| Organ system | Score | | | | |
|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 |
| Respiratory (PaO2/FiO2) | >400 | 301–400 | 201–300 | 101–200 | ≤101 |
| Renal (serum creatinine, micromole/l)[a] | ≤134 | 134–169 | 170–310 | 311–439 | >439 |
| Cardiovascular (systolic blood pressure, mmHg)[b] | >90 | <90 fluid responsive | <90 not fluid responsive | <90, pH < 7.3 | <90, pH < 7.2 |

A score of ≥2 in any system defines the presence of organ failure

[a]The score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥134 micromole/l or ≥1.4 mg/dl

[b]Off inotropic support

complications (i.e., pancreatic or peripancreatic fluid collections or portal vein thrombosis)].

Patients without local complications or organ failure have mild pancreatitis. The presence of transient organ failure (<48 h) and/or local complications are consistent with moderately severe pancreatitis, and patients with persistent organ failure beyond 48 h with or without local complications have severe pancreatitis [14]. The interstitial edematous type is usually associated with mild severity, whereas necrotizing pancreatitis generally presents as moderately severe or severe disease. Mild pancreatitis is the most common form of AP. It is generally treated conservatively, and patients are usually discharged within a few days, while the other two subtypes of disease often take time and medical resources to be resolved and generally patients require intensive care unit admission.

The definition of severity in AP is pivotal to determine patient management, to assess the appropriate level of care (ICU vs. non-ICU) and for patient prognosis [32]. The mortality rate in AP is higher in the early phase of the disease, and the presence of persistent multi-organ failure is the key determining factor [33].

Given the variable and unpredictable clinical course of AP and the high mortality rate in severe AP, several risk scoring systems have been developed to predict outcomes and to adequately address the disease with appropriate measures [34, 35]. However, most of them need a time frame of at least 24 h and several parameters are not easily available on admission. Moreover, there is no clear evidence that scoring systems are superior to the clinical expertise of the physician [36]. Regardless of the type of system used, it is essential to stratify the risk of AP to allocate resources, counsel the patient and guide clinical management.

To assess the AP patient's worsening condition, it is essential to consider, on admission and during all the hospitalization, the intrinsic risk characteristics of the patient (i.e., age, comorbidity, and body mass index—BMI [30, 37]).

Literature on adults shows that the elevation of lipase and amylase do not predict the severity of AP, Moreover data regarding monitoring of serum concentration of these enzymes during the course of the hospitalization are limited; however, the majority of articles suggest that this practice has poor clinical value [38], as the levels of amylase and lipase do not correlate with the severity, course, and outcome of AP. Also, repeating this exam has no indication regarding the role of diagnosing complications of acute pancreatitis, as imaging studies have a higher sensitivity [37]. Low serum albumin on admission has proven to be independently associated with persistent organ failure in severe AP [39].

### Key messages

- The presence of persistent multi-organ failure is the key determining factor for prognosis.
- Scoring systems are not superior to clinical assessment for evaluation of mortality and prognosis. Because of the unpredictable course of the disease, a frequent reassessment of the clinical condition is recommended.

## Question 5: To act or not to act, that is the question

### Pain management

Pain management is an essential aspect in the management of a patient with AP, and an effective analgesia should be reached in every patient; it has been long demonstrated that the employment of adequate analgesia does not increase the risk of diagnosis error or the risk of error in decision-making regarding treatment [38].

Non-steroidal anti-inflammatory drugs (NSAIDs) and opioids are the most frequently prescribed analgesic for pain in AP. Based on their better safety profile and comparable efficacy, NSAIDs may be preferred as first-line analgesia in patients with mild AP, keeping opioids as a reserve treatment in the case of refractory pain [40]. A recent study evidenced that compared to diclofenac, buprenorphine appears to be more effective and equally safe for pain management in AP patients [41]. It is possible to use a multimodal analgesic strategy in order to reach a pain control [20, 32]. In severe intractable pain thoracic epidural analgesia has proven to be effective [40].

### Antimicrobics

Recent guidelines have recommended against the routine use of prophylactic antibiotics in AP patients [13, 42] because it does not reduce the risk of secondary infections, organ failure, and hospital length of stay. On the other hand an uncontrolled use of antibiotics increases the spread of multidrug resistance (MDR) [43, 44]. Antibiotics should be reserved to patients with concomitant acute cholangitis (biliary sepsis), and in patients with concomitant extra pancreatic infection (present in up to 20% of cases) or patients with demonstrated intestinal bacterial translocation due to hypoperfusion.

In patients with acute necrotizing pancreatitis, approximately one third will develop infected necrosis, especially in the late clinical course (about 10 days following admission) [45].

Pathogens responsible for pancreatic infection are mainly Gram-negative bacteria; however, Gram-positive bacteria, anaerobes, and fungi can also be present. Piperacillin/

tazobactam is indicated as the first-line antibiotic therapy where infection is suspected. Quinolone, metronidazole, and carbapenems have shown a good tissue penetration; however, due to the high rate of resistance among bacteria worldwide, their administration should be reserved for patients allergic to beta lactam antibiotics [44]. Fungal infection is a severe complication of AP associated with a high rate of mortality, however, systemic antifungal prophylaxis is not recommended due to the lack of evidence [46].

### Proton pump inhibitors (PPI)

PPI are commonly used in the clinical practice, although their use is controversial [42]. A recent systematic review showed that their administration does not reduce 7-day mortality, length of hospital stay, and acute respiratory distress syndrome, but rather it was found to be associated with an increased risk of bleeding [47]. Considering the lack of supportive literature, we do not recommend the routine administration of PPI in AP.

### Antithrombotic prophylaxis

In acute pancreatitis, two main vascular complication must be considered: splanchnic thrombosis (with a reported incidence around 14.1%) [48] and hemorrhagic pancreatitis/peripancreatic bleeding (a rarer complication, with an incidence rate that varies from 1 to 23%) [49]. The choice of starting a chemoprophylaxis for VTE has been debated, considering that the molecular mechanism of coagulation disorders of severe acute pancreatitis and the choice of the anticoagulant drugs, the timing, and the amount is yet to be clarified [50]. Recent literature, however, suggests that a antithrombotic prophylaxis in the course of acute pancreatitis is not correlated to an increase risk of bleeding, while the beneficial effect in preventing thrombotic complications (not limited to splanchnic thrombosis) may suggest for introducing this therapy [51].

- Probiotics have been shown to have no benefits in preventing infections in AP. The multicenter randomized PROPATRIA trial has demonstrated a higher mortality rate in patients who have received enteral probiotics, therefore their use is not routinely recommended [52].
- A few studies have investigated the role of human serum albumin infusion in AP. A large retrospective cohort study in an ICU setting has found that the use of albumin does not reduce in-hospital mortality but instead is associated with longer hospital stay [53].
- Somatostatin and its analogs have been used as secretory agents and anti-inflammatory peptides that decrease pancreatic secretion. Recent literature has shown that their administration increases the mortality rate and complications and as a result, most global guidelines do not recommend their routine use [54].
- Placement of urinary catheter should be reserved to patient with severe acute pancreatitis that need an accurate fluid balance record. Urinary catheter should also be considered in severe cases of AP that need invasive monitoring of intra-abdominal pressure.

### Key messages

Non-steroidal anti-inflammatory drugs and opioids are considered the most appropriate analgesic for pain in AP.

- Prophylactic antibiotic as well as antifungal prophylaxis is not routinely recommended for patients with AP.
- Routine administration of proton pump inhibitors (PPI), probiotics, human albumin, and somatostatin its analogs are not recommended in AP. Antithrombotic prophylaxis can be evaluated.

## Question 6: Is procalcitonin useful for the monitoring of infection during the clinical course of AP?

The diagnosis of pancreatic infection during AP is always a clinical dilemma. Usually, patients with necrotizing pancreatitis are at higher risk of developing infection of necrotic areas. However, cross-sectional imaging does not always detect early signs of infection [55]. Moreover, radiological monitoring cannot be performed routinely, and non-invasive monitoring of infection is required. It is known that, during AP, biochemical markers of infections such as CRP or leucocytosis are not useful for the detection of signs of infection because they are altered by the systemic inflammatory response syndrome [55]. In patients with severe AP, PCT demonstrated a high sensitivity and specificity (93% and 88% respectively, with a cut-off of 3.5 ng/ml) compared to CRP, to detect infected necrosis diagnosed with FNA or during intraoperative findings [56]. Assessment of PCT is usually performed more frequently during the first days of AP (every 2–3 days) to early detect signs of infection when the systemic inflammatory response is still high. To date, international guidelines do not specify a recommended PCT cut-off level to indicate the appearance of infection. However, a recent RCT demonstrated that the administration of antibiotics in AP when PCT was above the 1 ng/ml was effective to reduce the use of antibiotics when compared to standard treatment not guided by PCT [57]. However, no studies have demonstrated the utility of PCT monitoring to improve patient outcomes.

### Key message

- Procalcitonin assessment every 48–76 h in the context of a systemic inflammatory response syndrome or in patients at risk to develop severe AP is useful to guide antibiotic treatment.

## Question 7: Is there an ideal department of choice for the management of AP? When should patients be admitted to the ICU?

The choice of where to allocate a patient with AP, determining the appropriate level of care (intensive vs. non intensive care unit) is a key consideration and must consider the clinical status of the patient and hospital resources. Continuous clinical reassessment is crucial, with the monitoring of vital signs, fluid resuscitation response, and searching for organ dysfunction.

The ICU is indicated if there is no adequate response to fluid resuscitation, in particular, if organ failure (respiratory, cardiovascular, renal) is persistent despite adequate hydration. Moreover, the persistence of hemoconcentration (i.e., hematocrit > 50% and hemoglobin [Hb] > 16) despite fluid replacement should indicate the need for a monitored care unit. In this setting, ICU guarantee advanced monitoring (e.g., intra-abdominal pressure monitoring).

Table 2 lists the criteria established by the Society of Critical Care Medicine (SCCM) which state that a patient should be admitted to an intensive care setting [58].

Because of the higher mortality rate, patients with BMI greater than 30 should be monitored and early transferred to a monitored care unit [27].

If patient conditions allow for hospitalization in a non-ICU setting, literature demonstrated the importance of admission in a Gastroenterological unit or, if it is not available, to have a single nominated clinical expert team to manage these patients [20]. It is important to train relevant healthcare professionals to conduct frequent and careful clinical reassessment of vital signs, non-invasive hemodynamic monitoring and to search for complications and organ dysfunction.

**Table 2** Society of Critical Care Medicine criteria to admit a patient to ICU [58]

| |
|---|
| Pulse <40 or >150 beats/min |
| Systolic arterial pressure <80 mmHg or mean arterial pressure <60 mmHgor diastolic arterial pressure >120 mmHg |
| Respiratory rate >35 breaths/min |
| Serum sodium <110 mmol/l or >170 mmol/l |
| Serum potassium <2.0 mmol/l or >7.0 mmol/l |
| PaO2 <50 mmHg |
| pH <7.1 or >7.7 |
| Serum glucose >800 mg/Dl |
| Serum calcium >15 mg/Dl |
| Anuria |
| Coma |

### Key messages

- Intensive Care Unit is indicated if there is no adequate response to fluid resuscitation. It is suggested the presence of dedicated specialistic physicians in the hospital to manage the most complex cases of AP.

## Question 8: Which is the suggested feeding route and optimal timing to begin refeeding in patients with acute pancreatitis?

Several RCTs performed on patients with mild to moderate AP have shown that early oral refeeding, defined as refeeding when patients begins to feel hungry and/or bowel sounds reappear independently to pancreatic enzyme normalization or resolution of pain, is tolerated, safe, and may reduce hospitalization time [59]. Previously, it was recommended to start refeeding with a soft diet [60]. However, more recently, four RCTs have shown that the early introduction of low-fat solid diet (within 24 h of admission) is tolerated and may also accelerate patient recovery [61].

When patients do not tolerate oral nutrition, an artificial feeding route is required. Currently, it is accepted that enteral nutrition (EN) is superior to parenteral nutrition in reducing complication rates, mortality, and organ failure [62]. There is widespread acceptance that EN should be started within 24–72 h following the onset of symptoms [60], whereas contrasting results have been reported about the benefit of a very early refeeding with EN (within 24 h) [63, 64]. Considering the route of administration of EN no studies have demonstrated the superiority of naso-jejunal tube (NJT) over nasogastric tube in improving patient outcomes [65, 66].

### Key messages

- Early (within 24 h after presentation) oral refeeding with a low-fat solid diet is recommended for patients who tolerate an oral diet.
- For patients who are intolerant to an oral diet early enteral feeding (within 24–72 h) via nasogastric tube should always be preferred over parenteral nutrition.

## Question 9: When should ERCP be performed for acute biliary pancreatitis?

The persistence of pancreatic duct obstruction related to the presence of stones in the CBD was thought to worsen the severity of AP [66]. This physio-pathological rationale has led to questions about the efficacy of early ERCP (within 24 h) on AP outcomes. However, different studies showed that early ERCP did not improve patient outcomes compared to delayed ERCP. Indeed, all the most recent guidelines suggest that urgent ERCP is not indicated in acute biliary pancreatitis [12, 13, 42]. Recent RCTs (APEC and APEC-2 trial) performed on patients with predicted severe acute biliary pancreatitis has confirmed that a conservative approach (on-demand ERCP if case of cholangitis and/or persistence of cholestasis and/or retained CBD stone when the patient recovered from pancreatitis) was not inferior to an ERCP performed within 24 h following admission also when early EUS was performed to confirm the diagnosis of CBD stones [67, 68].

It should be emphasized that before commencing ERCP, it is important to have a definitive diagnosis of biliary obstruction especially in patients with low-moderate risk of choledocholithiasis such as those with cholestatic blood indexes in a reduction trend without dilation of the CBD. EUS is the most sensitive diagnostic tool to explore the extrahepatic biliary tract, and one study suggested that EUS could avoid a significant number of unneeded ERCP [69].

An important clinical discriminating factor is when AP is associated with cholangitis. It has been demonstrated that early ERCP in patients with AP and cholangitis reduces mortality and local complications [68]. At the same time, it should be acknowledged that in patients with AP, it is not always possible to discriminate signs of cholangitis from sign of SIRS secondary to AP processes.

### Key messages

- Endoscopic retrograde cholangiopancreatography (ERCP) in acute pancreatitis is not an urgent procedure and it is suggested to be preceded by a diagnostic test (EUS or MRCP) when the risk of CBD stones is low. Urgent ERCP should be reserved only in case of concomitant cholangitis and timing is chosen according to the severity of cholangitis.

## Question 10: When is cholecystectomy indicated in patients with acute biliary pancreatitis?

Patients who develop choledocholithiasis are always referred to cholecystectomy in order to reduce the risk of further episodes of biliopancreatic events. This indication is valid also in case of biliary AP because it is clearly demonstrated that cholecystectomy reduces the risk of recurrent biliary pancreatitis [10, 21]. However, timing of cholecystectomy has always been an argument of debate especially for surgeons. The common daily practice feeling is that some surgeons prefer to delay the cholecystectomy for the perceived risk of complications related to the presence of inflammation and edema that could distort biliary anatomy. However, all the available guidelines clearly suggest in case of a mild acute biliary pancreatitis, to perform cholecystectomy during the index admission because it is safe and effective in reducing the risk of biliary complications compared to delayed cholecystectomy [70].

The timing of cholecystectomy after an episode of severe acute biliary is still debated and low-quality studies are available in the literature on this topic. However, retrospective studies suggest that the cholecystectomy should be delayed at least after 2 weeks following the episode of AP [71], but not for longer than 8 weeks, to avoid biliary complications [72]. Moreover when AP is complicated by a peripancreatic fluid collection (PFC), it is suggested to delay cholecystectomy when there is a resolution of PFC because cholecystectomy could increase the risk of infection of PFC [73].

### Key messages

- Cholecystectomy should be performed during the index admission of an episode of mild acute pancreatitis and within 8 weeks following severe pancreatitis when PFC are in resolution phase.

## Question 11: What is the best way to treat local complications of AP?

Most patients with AP have a self-limited course. However, up to 10–20% of patients may develop necrosis of the pancreatic glands which, if infected, is associated with increased hospitalization time and mortality [74].

Local complications of AP are historically classified according to the Atlanta criteria that considers the content (necrotic or fluid) and the time of onset (before or after 4 weeks) of the PFC [2]. When considering necrotic collections, it is also important to evaluate the extension

and the percentage of infected necrosis [75]. Recently, a novel classification for the walled-off necrosis (WON) has been proposed in order to stratify patients at higher risk of receiving intervention [76].

Treatment of PFC is recommended in patients who develop symptoms including persistent pain, signs of gastric outlet obstruction, signs of biliary obstruction such as jaundice or in case of WON when necrosis became infected [77].

In case of pancreatic pseudocyst, it is now accepted that the standard of care is endoscopic drainage with endoscopic ultrasound-guided cysto-gastrostomy. Despite surgical and endoscopic drainage having similar technical successes, endoscopic drainage allows for better patient acceptance, reduced hospital stay and costs [78].

The treatment of WON is quite more challenging because it could include not only the drainage of the collection but also the need for necrosectomy. In this situation multidisciplinary evaluation with surgeon, interventional radiologist and endoscopist is useful to decide the need of treatment and the right timing. The goal of the treatment is to control the source of infection and to be as least invasive as possible to reduce complications. Starting from these assumptions, trials have shown that a step-up approach that begins with a minimally invasive drainage (endoscopic or retroperitoneal percutaneous drainage) and followed by minimally invasive necrosectomy in case of non-response, reduced complications, and mortality rate, compared to open or minimal invasive surgery [79, 80]. An endoscopic step-up approach in comparison to percutaneous step-up approach for WON treatment have shown better results in terms of reducing pancreatico-cutaneous fistula, the need of reintervention and patient acceptance, and therefore it is considered by far the first-line approach [5, 81].

A more aggressive approach with endoscopic drainage and upfront necrosectomy could be proposed to patients at higher risk to require necrosectomy (e.g., WON larger than 10 cm or with paracolic extension or with more than 30% of necrosis) [75]. Moreover recent data are becoming available in literature about the utility of upfront endoscopic necrosectomy [82].

### Key messages

- Multidisciplinary evaluation involving surgeon, interventional radiologist and endoscopist is suggested for patients who require drainage of pancreatic fluid collection.

In the case of walled-off necrosis (WON), an endoscopic step-up approach is recommended over a percutaneous step-up approach.

## Question 12: What is the optimal timing for performing minimally invasive treatment on local complications of acute pancreatitis?

Because early treatment of pancreatic pseudocyst has not demonstrated clinical gains, the choice to place a drainage should be guided by patients' symptoms [77].

Patients who develop necrotizing pancreatitis have a more severe and complicated course of the disease. Timing for the treatment of necrotizing pancreatitis is crucial and it has been extensively studied in the literature. Several RCTs demonstrated that in the early phase of the necrotic tissue infection, characterized by a thin non structured encapsulation of the collection, an early endoscopic approach is not superior to conservative treatment [83]. In this early phase, literature recommends the administration of adequate antibiotic therapy and supportive care followed by drainage only after the encapsulation of largely part of the WON. The historical cut-off designed to obtain the adequate encapsulation of the WON and therefore for starting the endoscopic drainage was 4 weeks. However, subsequent studies showed that earlier treatments were also safe and allowed prompt intervention when necessary [84].

### Key messages

- Pancreatic fluid collections should be drained only when signs of compression or infection appear.
- In the case of infected necrosis, antibiotic therapy is the first-line therapy followed by minimally invasive drainage when necrotic collection forms an adequate wall.

## Question 13: Does multidisciplinary collaboration impact on patient outcomes?

In modern healthcare systems, multidisciplinary collaboration (MDC) has been intended to optimize patient care and has become a requirement for the diagnosis and management of various diseases.

One recent study focused on essential professional roles whose involvement is recommended in the early evaluation of patients with severe or predicted severe AP in the ER. These should be: the anesthesiologist, biliopancreatic surgeon, gastroenterologist, radiologist and interventional radiologist, nutritionist, and microbiologist [85]. It has been demonstrated that the involvement of more specialists is not associated with more efficient decision-making and that it only results in prolonged meeting times [86]. Early MDC aims to manage severe AP in a timely and appropriate manner according to standards, and, following ER evaluation, to

refer patients to the most appropriate department for hospital stay. This type of collaboration requires a global hospital organization that is usually present in high-volume centers. Indeed, some studies showed that high-volume hospitals, defined as those that admit a minimum of 118 AP cases per year (either mild or severe), or more than 14 cases of severe AP, report shorter length of hospital stays and lower mortality rates for AP [87].

It is, therefore, essential to specify that not all patients could be managed using MDC in routine clinical practice or in under-staffed hospitals. Selection of the most appropriate patients that could benefit of a MDC is necessary to optimize local resources. These are the patients that develop necrotizing pancreatitis [88], those with recurrent episodes of AP of unclear etiology and those with a suspected underlying malignancy. It has been shown that MDC changed imaging interpretation in 24% of patients with acute or chronic pancreatitis [89] and changed treatment strategy in 21% of patients [90].

### Key messages

- Multidisciplinary evaluation is suggested for patients with local complications of acute pancreatitis or for patients with an unclear etiology and for those with suspected underlying malignancy.

## Question 14: Is clinical follow-up necessary after resolution of acute pancreatitis?

Patients who are recovering after an episode of acute pancreatitis could have long-term sequelae that should be carefully evaluated and prevented after hospital discharge. Patients who experienced an episode of necrotizing AP should be monitored in order to assess the evolution of the PFC and to evaluate the possible emergence of both endocrine and exocrine insufficiency.

Patients who did not undergo drainage of PFC during hospitalization should be monitored in order to evaluate the appearance of symptoms and consequently, the need for drainage [14]. Closer monitoring it is suggested for patients who received endoscopic drainage of WON. A recent study showed that a standardized radiological monitoring protocol improved outcomes and faster WON resolution [91]. If patients received the implantation of a lumen-apposing metal stents (LAMS) for drainage of WON it is important to carefully evaluate the timing for its removal [92, 93].

Pancreatic exocrine impairment could develop in up to 35% of patients with AP and in up to 85% of patients to necrotizing AP [14, 94]. It is, therefore, important to explore the presence of steatorrhea and the positivity of pancreatic exocrine insufficiency assays to promptly set up a supplementation therapy and avoid malnutrition.

Pancreatogenic diabetes mellitus (DM) could develop in around 24% of patients with AP [92]. This percentage could increase to 56% if patients have experienced an episode of severe AP [93]. New-onset diabetes usually improves or completely recovers/clears during the follow-up period. However, a proportion of patients (25%) require insulin for 5 years following the episode of AP [92]. Regular glycemic assessment is, therefore, important to avoid diabetes complications or acute decompensation.

AP may also develop in patients with chronic pancreatitis (CP). Usually, these kind of patients have a milder course of the acute disease; however, clinical monitoring is essential in order to confirm the diagnosis of a previously misdiagnosed CP, and to suggests the life-style modifications, especially alcohol and smoke withdrawal, to prevent further episodes of AP and avoid the potential worsening of CP [95].

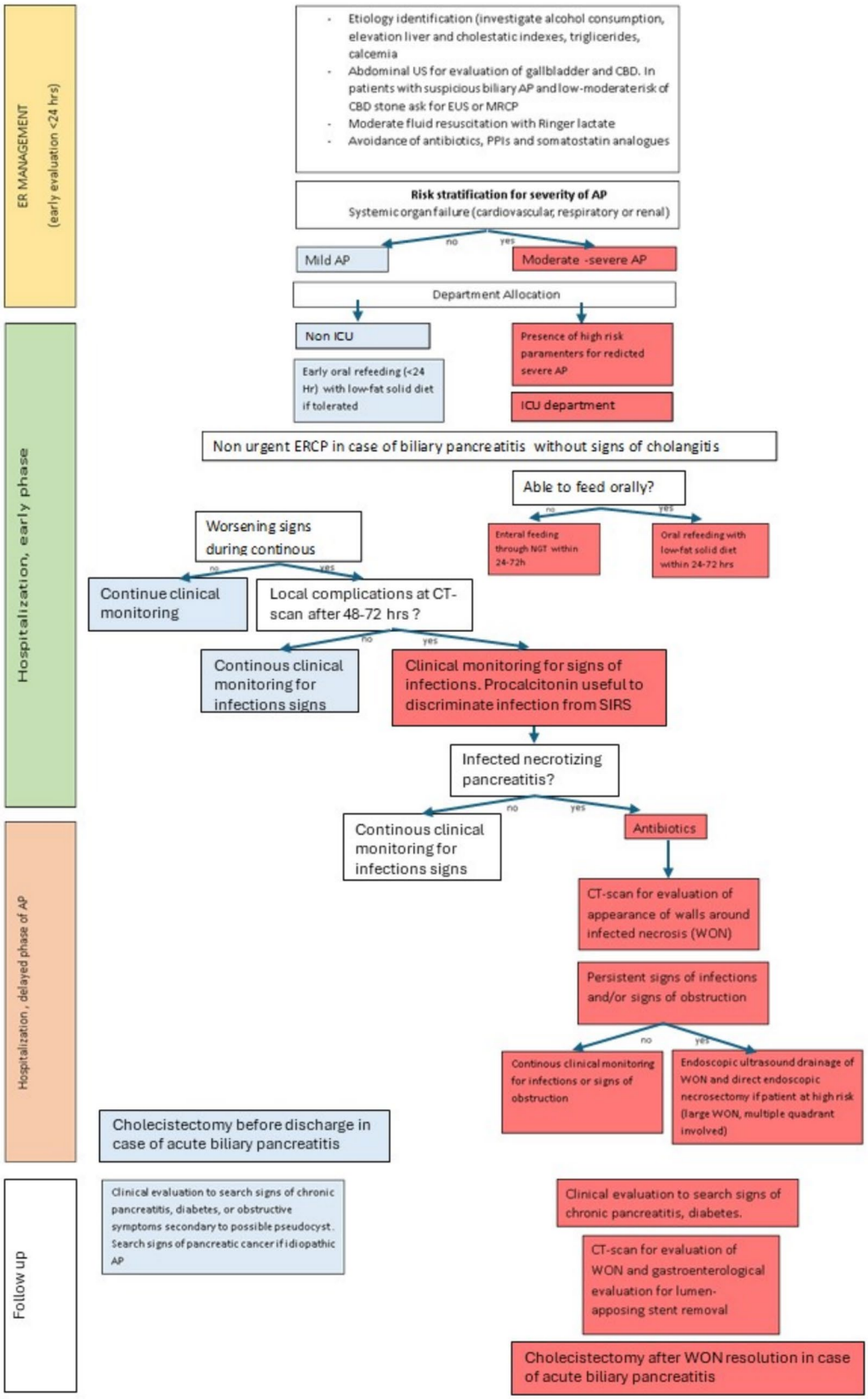
Finally, the correlation between AP and the risk of pancreatic cancer should be noted. A nationwide cohort study performed in Denmark evidenced that patients who experienced an episode of AP showed an increased risk of pancreatic cancer within a 5 year-period [96]. Neoplastic incidence was higher during the first year (OR 23.47) and it progressively reduced during the subsequent years [97]. Idiopathic etiology appeared to be associated with the highest risk of pancreatic cancer (OR 2.52) [96] and, therefore, it is suggested to perform EUS after an episode of AP to early detect also small solid lesions [98].

### Key messages

- Clinical follow-up after an episode of acute pancreatitis is recommended in all patients to correct etiological factors and to search signs of endocrine and exocrine insufficiency. Follow-up is also essential to monitor the evolution of WON.

## Conclusion

Acute pancreatitis is a complex disease with a dynamic and unpredictable course leading, in its most severe forms, to significant morbidity and mortality. Prompt diagnosis, stratification of severity, proper fluid resuscitation and nutrition, prevention, and treatment of complications, are crucial aspects of care. Figure 1 sums up an algorithm for the diagnosis and management of AP. Although in the recent years multidisciplinary dedicated teams, step-up tailored approaches, and the introduction of mini-invasive diagnostic and therapeutic tools have improved outcomes, disease management remains a challenge for clinicians and guidelines are continuously evolving (Fig. 1).


ER MANAGEMENT
(early evaluation <24 hrs)
Etiology identification (investigate alcohol consumption, elevation liver and cholestatic indexes, triglicerides, calcemia
Abdominal US for evaluation of gallbladder and CBD. In patients with suspicious biliary AP and low-moderate risk of CBD stone ask for EUS or MRCP
Moderate fluid resuscitation with Ringer lactate
Avoidance of antibiotics, PPIs and somatostatin analogues
Risk stratification for severity of AP
Systemic organ failure (cardiovascular, respiratory or renal)
no
yes
Mild AP
Moderate -severe AP
Department Allocation
Non ICU
Early oral refeeding (<24 Hr) with low-fat solid diet if tolerated
Presence of high risk paramenters for redicted severe AP
ICU department
Hospitalization, early phase
Non urgent ERCP in case of biliary pancreatitis without signs of cholangitis
Able to feed orally?
no
yes
Enteral feeding through NGT within 24-72h
Oral refeeding with low-fat solid diet within 24-72 hrs
Worsening signs during continous
no
yes
Continue clinical monitoring
Local complications at CT-scan after 48-72 hrs ?
no
yes
Continous clinical monitoring for infections signs
Clinical monitoring for signs of infections. Procalcitonin useful to discriminate infection from SIRS
Infected necrotizing pancreatitis?
no
yes
Continous clinical monitoring for infections signs
Antibiotics
Hospitalization, delayed phase of AP
CT-scan for evaluation of appearance of walls around infected necrosis (WON)
Persistent signs of infections and/or signs of obstruction
no
yes
Continous clinical monitoring for infections or signs of obstruction
Endoscopic ultrasound drainage of WON and direct endoscopic necrosectomy if patient at high risk (large WON, multiple quadrant involved)
Cholecistectomy before discharge in case of acute biliary pancreatitis
Follow up
Clinical evaluation to search signs of chronic pancreatitis, diabetes, or obstructive symptoms secondary to possible pseudocyst. Search signs of pancreatic cancer if idiopathic AP
Clinical evaluation to search signs of chronic pancreatitis, diabetes.
CT-scan for evaluation of WON and gastroenterological evaluation for lumen-apposing stent removal
Cholecistectomy after WON resolution in case of acute biliary pancreatitis

◂**Fig. 1** Practical algorithm for the management of acute pancreatitis (AP). The algorithm is divided in four temporal section: ER management, early and late hospitalization phases and follow-up. The pathway of patients with mild and severe AP are highlighted in light blue and red, respectively (Colour figure online)

This review results in a practical guide for clinicians who have to face patients with acute pancreatitis, providing answers to specific questions and giving useful key messages summarized in Table 3.

**Table 3** Key messages for AP management

| Key messages |
|---|
| Clinical features and increase of lypase are sufficient for diagnosis of acute pancreatitis (AP) |
| Contrast-enhanced CT may be useful 72–96 h from the onset of AP to detect peripancreatic necrosis and vascular complications |
| Early identification of etiology of acute pancreatitis is essential to guide adequate management, and allocate resources |
| It is suggested to perform abdominal ultrasound at admission to evaluate the biliary tract |
| A moderate resuscitation strategy is preferable to an aggressive strategy with respect to both efficacy and safety outcomes |
| Lactated Ringer's solution is recommended over saline solution for fluid resuscitation |
| The presence of persistent multi-organ failure is the key determining factor for prognosis |
| Scoring systems are not superior to clinical assessment for evaluation of mortality and prognosis Because of the unpredictable course of the disease, a frequent reassessment of the clinical condition is recommended |
| Non-steroidal anti-inflammatory drugs and opioids are considered the most appropriate analgesic for pain in AP |
| Prophylactic antibiotic as well as antifungal prophylaxis is not routinely recommended for patients with AP |
| Routine administration of proton pump inhibitors (PPI), probiotics, human albumin, and somatostatin its analogs are not recommended in AP. Antithrombotic prophylaxis can be evaluated |
| Procalcitonin assessment every 48–76 h in the context of a systemic inflammatory response syndrome or in patients at risk to develop severe AP, is useful to guide antibiotic treatment |
| Intensive Care Unit is indicated if there is no adequate response to fluid resuscitation. It is suggested the presence of dedicated specialistic physicians in the Hospital in order to manage the most complex cases of AP |
| Early (within 24 h after presentation) oral refeeding with a low-fat solid diet is recommended for patients who tolerate an oral diet |
| For patients who are intolerant to an oral diet early enteral feeding (within 24–72 h) via nasogastric tube should always be preferred over parenteral nutrition |
| Endoscopic retrograde cholangiopancreatography (ERCP) in acute pancreatitis is not an urgent procedure and it is suggested to be preceded by a diagnostic test (EUS or MRCP) when the risk of CBD stones is low. Urgent ERCP should be reserved only in case of concomitant cholangitis and timing is chosen according to the severity of cholangitis |
| Cholecystectomy should be performed during the index admission of an episode of mild acute pancreatitis and within 8 weeks following resolution of severe pancreatitis |
| Multidisciplinary evaluation involving surgeon, interventional radiologist, and endoscopist is suggested for patients who require drainage of pancreatic fluid collection |
| In the case of walled-off necrosis (WON), an endoscopic step-up approach is recommended over a percutaneous step-up approach |
| Pancreatic fluid collections should be drained only when signs of compression or infection appear |
| In the case of infected necrosis, antibiotic therapy is the first-line therapy followed by minimally invasive drainage when necrotic collection forms an adequate wall |
| Multidisciplinary evaluation is suggested for patients with local complications of acute pancreatitis or for patients with an unclear etiology and for those with suspected underlying malignancy |
| Clinical follow-up after an episode of acute pancreatitis is recommended in all patients to correct etiological factors and to search signs of endocrine and exocrine insufficiency. Follow-up is also essential to monitor the evolution of WON |

**Data Availability** Not Applicable.

**Human and animals rights statement** Not Applicable.

**Informed consent** Not Applicable.

**Ethical approval** Not Applicable.

## References


1. Iannuzzi JP, King JA, Leong JH, Quan J, Windsor JW, Tanyingoh D et al (2022) Global incidence of acute pancreatitis is increasing over time: a systematic review and meta-analysis. Gastroenterology 162(1):122–134
2. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG et al (2013) Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut 62(1):102–111
3. Schepers NJ, Bakker OJ, Besselink MG, Ahmed Ali U, Bollen TL, Gooszen HG et al (2019) Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis. Gut 68(6):1044–1051
4. Lankisch PG, Apte M, Banks PA (2015) Acute pancreatitis. Lancet 386(9988):85–96
5. van Brunschot S, van Grinsven J, van Santvoort HC, Bakker OJ, Besselink MG, Boermeester MA et al (2018) Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet 391(10115):51–58
6. Gumaste VV, Roditis N, Mehta D, Dave PB (1993) Serum lipase levels in nonpancreatic abdominal pain versus acute pancreatitis. Am J Gastroenterol 88(12):2051–2055
7. Yadav D, Nair S, Norkus EP, Pitchumoni CS (2000) Nonspecific hyperamylasemia and hyperlipasemia in diabetic ketoacidosis: incidence and correlation with biochemical abnormalities. Am J Gastroenterol 95(11):3123–3128
8. Alter D, Koch DD (2021) A review of acute pancreatitis. JAMA 325(23):2402
9. Arvanitakis M, Delhaye M, De Maertelaere V, Bali M, Winant C, Coppens E et al (2004) Computed tomography and magnetic resonance imaging in the assessment of acute pancreatitis. Gastroenterology 126(3):715–723
10. Raghuwanshi S, Gupta R, Vyas MM, Sharma R (2016) CT Evaluation of acute pancreatitis and its prognostic correlation with CT severity index. J Clin Diagn Res JCDR 10(6):TC06-11.
11. McPherson SJ, O'Reilly DA, Sinclair MT, Smith N (2017) The use of imaging in acute pancreatitis in United Kingdom hospitals: findings from a national quality of care study. Br J Radiol 90(1080):20170224
12. Working Group IAP/APA Acute Pancreatitis Guidelines (2013) IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology 13(4 Suppl 2):1–15
13. Tenner S, Baillie J, DeWitt J, Vege SS (2013) American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol 108(9):1400–1415
14. Mederos MA, Reber HA, Girgis MD (2021) Acute pancreatitis: a review. JAMA 325(4):382–390
15. Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA et al (2020) Acute pancreatitis. Lancet 396(10252):726–734
16. Garg R, Rustagi T (2018) Management of hypertriglyceridemia induced acute pancreatitis. Biomed Res Int 2018:4721357
17. Türkvatan A, Erden A, Türkoğlu MA, Seçil M, Yener Ö (2015) Imaging of acute pancreatitis and its complications. Part 1: acute pancreatitis. Diagn Interv Imaging 96(2):151–160
18. Cucher D, Kulvatunyou N, Green DJ, Jie T, Ong ES (2014) Gallstone pancreatitis: a review. Surg Clin North Am 94(2):257–280
19. Somani P, Sunkara T, Sharma M (2017) Role of endoscopic ultrasound in idiopathic pancreatitis. World J Gastroenterol 23(38):6952–6961
20. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW et al (2019) 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg 14:27
21. Yaowmaneerat T, Sirinawasatien A (2023) Update on the strategy for intravenous fluid treatment in acute pancreatitis. World J Gastrointest Pharmacol Ther 14(3):22–32
22. Johnson CD, Abu-Hilal M (2004) Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. Gut 53(9):1340–1344
23. Brown A, Orav J, Banks PA (2000) Hemoconcentration is an early marker for organ failure and necrotizing pancreatitis. Pancreas 20(4):367–372
24. UK Working Party on Acute Pancreatitis (2005) UK guidelines for the management of acute pancreatitis. Gut 54(Suppl 3):iii1–iii9
25. Messmer AS, Zingg C, Müller M, Gerber JL, Schefold JC, Pfortmueller CA (2020) Fluid overload and mortality in adult critical care patients-a systematic review and meta-analysis of observational studies. Crit Care Med 48(12):1862–1870
26. Jaber S, Garnier M, Asehnoune K, Bounes F, Buscail L, Chevaux JB et al (2022) Guidelines for the management of patients with severe acute pancreatitis, 2021. Anaesth Crit Care Pain Med 41(3):101060
27. Walkowska J, Zielinska N, Tubbs RS, Podgórski M, Dłubek-Ruxer J, Olewnik Ł (2022) Diagnosis and treatment of acute pancreatitis. Diagnostics 12(8):1–35
28. Iqbal U, Anwar H, Scribani M (2018) Ringer's lactate versus normal saline in acute pancreatitis: a systematic review and meta-analysis. J Dig Dis 19(6):335–341
29. Machicado JD, Yadav D (2017) Epidemiology of recurrent acute and chronic pancreatitis: similarities and differences. Dig Dis Sci 62(7):1683–1691
30. van den Berg FF, Boermeester MA (2023) Update on the management of acute pancreatitis. Curr Opin Crit Care 29(2):145–151
31. Marshall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ (1995) Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. Crit Care Med 23(10):1638–1652
32. Greenberg JA, Hsu J, Bawazeer M, Marshall J, Friedrich JO, Nathens A et al (2016) Clinical practice guideline: management of acute pancreatitis. Can J Surg 59(2):128–140
33. Mole DJ, Olabi B, Robinson V, Garden OJ, Parks RW (2009) Incidence of individual organ dysfunction in fatal acute pancreatitis: analysis of 1024 death records. HPB 11(2):166–170
34. Lee DW, Cho CM (2022) Predicting severity of acute pancreatitis. Medicina 58(6):787
35. Kiat TTJ, Gunasekaran SK, Junnarkar SP, Low JK, Woon W, Shelat VG (2018) Are traditional scoring systems for severity stratification of acute pancreatitis sufficient? Ann Hepatobiliary Pancreat Surg 22(2):105–115
36. Capurso G, Ponz de Leon Pisani R, Lauri G, Archibugi L, Hegyi P, Papachristou GI et al (2023) Clinical usefulness of scoring systems to predict severe acute pancreatitis: a systematic review and meta-analysis with pre and post-test probability assessment. United European Gastroenterol J 11(9):825–836
37. Magier SJ, Muniraj T, Merchant N (2023) Serial serum lipase testing after the initial diagnostic workup for inpatients with

acute pancreatitis: What is the evidence? Cleve Clin J Med 90(6):341–343
38. Manterola C, Vial M, Javier M, Astudillo P (2011) Analgesia in patients with acute abdominal pain. Cochrane Database Syst Rev. https://doi.org/10.1002/14651858.CD005660.pub3
39. Li S, Zhang Y, Li M, Xie C, Wu H (2017) Serum albumin, a good indicator of persistent organ failure in acute pancreatitis. BMC Gastroenterol 17(1):59
40. Cai W, Liu F, Wen Y, Han C, Prasad M, Xia Q et al (2021) Pain management in acute pancreatitis: a systematic review and meta-analysis of randomised controlled trials. Front Med 8:782151
41. Saini M, Samanta J, Kumar A, Choudhury A, Dhar J, Jafra A et al (2024) Buprenorphine versus diclofenac for pain relief in acute pancreatitis: a double-blinded randomized-controlled trial. Clin Gastroenterol Hepatol 22(3):532-541.e8
42. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN, Crockett S et al (2018) American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. Gastroenterology 154(4):1096–1101
43. Kuo DC, Rider AC, Estrada P, Kim D, Pillow MT (2015) Acute pancreatitis: What's the score? J Emerg Med 48(6):762–770
44. Severino A, Varca S, Airola C, Mezza T, Gasbarrini A, Franceschi F et al (2023) Antibiotic utilization in acute pancreatitis: a narrative review. Antibiotics 12(7):1–12
45. Jiang K, Huang W, Yang XN, Xia Q (2012) Present and future of prophylactic antibiotics for severe acute pancreatitis. World J Gastroenterol 18(3):279–284
46. Schwender BJ, Gordon SR, Gardner TB (2015) Risk factors for the development of intra-abdominal fungal infections in acute pancreatitis. Pancreas 44(5):805–807
47. Horváth IL, Bunduc S, Hankó B, Kleiner D, Demcsák A, Szabó B et al (2023) No evidence for the benefit of PPIs in the treatment of acute pancreatitis: a systematic review and meta-analysis. Sci Rep 13(1):1–10
48. Butler JR, Eckert GJ, Zyromski NJ, Leonardi MJ, Lillemoe KD, Howard TJ (2011) Natural history of pancreatitis-induced splenic vein thrombosis: a systematic review and meta-analysis of its incidence and rate of gastrointestinal bleeding. HPB 13(12):839–845
49. Gupta V, Krishna P, Kochhar R, Yadav TD, Bargav V, Bhalla A et al (2020) Hemorrhage complicating the course of severe acute pancreatitis. Ann Hepatobiliary Pancreat Surg 24(3):292–300
50. Gui M, Zhao B, Huang J, Chen E, Qu H, Mao E (2023) Pathogenesis and therapy of coagulation disorders in severe acute pancreatitis. J Inflamm Res 16:57–67
51. Vadlamudi RS, Matli VVK, Thoguluva Chandrasekar V, Kalakonda A, Rawlins SR (2021) Chemoprophylaxis to prevent deep venous thrombosis in patients hospitalized for pancreatitis: beneficial or harmful? Cureus 13(11):1–9
52. Besselink MG, van Santvoort HC, Buskens E, Boermeester MA, van Goor H, Timmerman HM et al (2008) Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial. Lancet 371(9613):651–659
53. Ma Y, Yan T, Xu F, Ding J, Yang B, Ma Q et al (2022) Infusion of human albumin on acute pancreatitis therapy: new tricks for old dog? Front Pharmacol 13:842108
54. Moggia E, Koti R, Belgaumkar AP, Fazio F, Pereira SP, Davidson BR et al (2017) Pharmacological interventions for acute pancreatitis. Cochrane Database Syst Rev 4(4):CD011384
55. van Santvoort HC, Bollen TL, Besselink MG, Banks PA, Boermeester MA, van Eijck CH et al (2008) Describing peripancreatic collections in severe acute pancreatitis using morphologic terms: an international interobserver agreement study. Pancreatology 8(6):593–599
56. Rau BM, Kemppainen EA, Gumbs AA, Büchler MW, Wegscheider K, Bassi C et al (2007) Early assessment of pancreatic infections and overall prognosis in severe acute pancreatitis by procalcitonin (PCT): a prospective international multicenter study. Ann Surg 245(5):745–754
57. Siriwardena AK, Jegatheeswaran S, Mason JM (2022) A procalcitonin-based algorithm to guide antibiotic use in patients with acute pancreatitis (PROCAP): a single-centre, patient-blinded, randomised controlled trial. Lancet Gastroenterol Hepatol 7(10):913–921
58. (1999) Guidelines for intensive care unit admission, discharge, and triage. Task Force of the American College of Critical Care Medicine, Society of Critical Care Medicine. Crit Care Med 27(3):633–638
59. Ramírez-Maldonado E, López Gordo S, Pueyo EM, Sánchez-García A, Mayol S, González S et al (2021) Immediate oral refeeding in patients with mild and moderate acute pancreatitis: a multicenter, randomized controlled trial (PADI trial). Ann Surg 274(2):255–263
60. Arvanitakis M, Ockenga J, Bezmarevic M, Gianotti L, Krznarić Ž, Lobo DN et al (2020) ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. Clin Nutr 39(3):612–631
61. Meyers C, Rigassio Radler D, Zelig RS (2023) Impact of solid food provision within 24 h of hospital admission on clinical outcomes for adult patients with acute pancreatitis: a literature review. Nutr Clin Pract 38(5):976–986
62. Al-Omran M, Albalawi ZH, Tashkandi MF, Al-Ansary LA (2010) Enteral versus parenteral nutrition for acute pancreatitis. Cochrane Database Syst Rev 2010(1):CD002837
63. Bakker OJ, van Brunschot S, van Santvoort HC, Besselink MG, Bollen TL, Boermeester MA et al (2014) Early versus on-demand nasoenteric tube feeding in acute pancreatitis. N Engl J Med 371(21):1983–1993
64. Nakashima I, Horibe M, Sanui M, Sasaki M, Sawano H, Goto T et al (2021) Impact of enteral nutrition within 24 h versus between 24 and 48 h in patients with severe acute pancreatitis: a multicenter retrospective study. Pancreas 50(3):371–377
65. Nally DM, Kelly EG, Clarke M, Ridgway P (2014) Nasogastric nutrition is efficacious in severe acute pancreatitis: a systematic review and meta-analysis. Br J Nutr 112(11):1769–1778
66. Acosta JM, Rubio Galli OM, Rossi R, Chinellato AV, Pellegrini CA (1997) Effect of duration of ampullary gallstone obstruction on severity of lesions of acute pancreatitis. J Am Coll Surg 184(5):499–505
67. Schepers NJ, Hallensleben NDL, Besselink MG, Anten MGF, Bollen TL, da Costa DW et al (2020) Urgent endoscopic retrograde cholangiopancreatography with sphincterotomy versus conservative treatment in predicted severe acute gallstone pancreatitis (APEC): a multicentre randomised controlled trial. Lancet 396(10245):167–176
68. Tse F, Yuan Y (2012) Early routine endoscopic retrograde cholangiopancreatography strategy versus early conservative management strategy in acute gallstone pancreatitis. Cochrane Database Syst Rev 5:CD009779
69. De Lisi S, Leandro G, Buscarini E (2011) Endoscopic ultrasonography versus endoscopic retrograde cholangiopancreatography in acute biliary pancreatitis: a systematic review. Eur J Gastroenterol Hepatol 23(5):367–374
70. van Baal MC, Besselink MG, Bakker OJ, van Santvoort HC, Schaapherder AF, Nieuwenhuijs VB et al (2012) Timing of cholecystectomy after mild biliary pancreatitis: a systematic review. Ann Surg 255(5):860–866
71. Di Martino M, Ielpo B, Pata F, Pellino G, Di Saverio S, Catena F et al (2023) Timing of cholecystectomy after moderate and severe acute biliary pancreatitis. JAMA Surg 158(10):e233660
72. Hallensleben ND, Timmerhuis HC, Hollemans RA, Pocornie S, van Grinsven J, van Brunschot S et al (2022) Optimal timing

of cholecystectomy after necrotising biliary pancreatitis. Gut 71(5):974–982
73. Nealon WH, Bawduniak J, Walser EM (2004) Appropriate timing of cholecystectomy in patients who present with moderate to severe gallstone-associated acute pancreatitis with peripancreatic fluid collections. Ann Surg 239(6):741–751
74. Baron TH, DiMaio CJ, Wang AY, Morgan KA (2020) American gastroenterological association clinical practice update: management of pancreatic necrosis. Gastroenterology 158(1):67-75.e1
75. Chandrasekhara V, Elhanafi S, Storm AC, Takahashi N, Lee NJ, Levy MJ et al (2021) Predicting the need for step-up therapy after EUS-guided drainage of pancreatic fluid collections with lumen-apposing metal stents. Clin Gastroenterol Hepatol 19(10):2192–2198
76. Baroud S, Chandrasekhara V, Storm AC, Law RJ, Vargas EJ, Levy MJ et al (2023) Novel classification system for walled-off necrosis: a step toward standardized nomenclature and risk-stratification framework. Gastrointest Endosc 97(2):300–308
77. Bhakta D, de Latour R, Khanna L (2022) Management of pancreatic fluid collections. Transl Gastroenterol Hepatol 7:17
78. Varadarajulu S, Bang JY, Sutton BS, Trevino JM, Christein JD, Wilcox CM (2013) Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. Gastroenterology 145(3):583–90.e1
79. van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH et al (2010) A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med 362(16):1491–1502
80. Hollemans RA, Bakker OJ, Boermeester MA, Bollen TL, Bosscha K, Bruno MJ et al (2019) Superiority of step-up approach vs. open necrosectomy in long-term follow-up of patients with necrotizing pancreatitis. Gastroenterology 156(4):1016–1026
81. Onnekink AM, Boxhoorn L, Timmerhuis HC, Bac ST, Besselink MG, Boermeester MA et al (2022) Endoscopic versus surgical step-up approach for infected necrotizing pancreatitis (ExTENSION): long-term follow-up of a randomized trial. Gastroenterology 163(3):712-722.e14
82. Bang JY, Lakhtakia S, Thakkar S, Buxbaum JL, Waxman I, Sutton B et al (2024) Upfront endoscopic necrosectomy or step-up endoscopic approach for infected necrotising pancreatitis (DESTIN): a single-blinded, multicentre, randomised trial. Lancet Gastroenterol Hepatol 9(1):22–33
83. Van Veldhuisen CL, Sissingh NJ, Boxhoorn L, van Dijk SM, van Grinsven J, Verdonk RC et al (2024) Long-term outcome of immediate versus postponed intervention in patients with infected necrotizing pancreatitis (POINTER): multicenter randomized trial. Ann Surg 279(4):671–678
84. Trikudanathan G, Tawfik P, Amateau SK, Munigala S, Arain M, Attam R et al (2018) Early (<4 weeks) versus standard (≥4 weeks) endoscopically centered step-up interventions for necrotizing pancreatitis. Am J Gastroenterol 113(10):1550–1558
85. Yin J, Chen Z, Niu W, Feng L, Fan B, Zhou L et al (2021) Using a multidisciplinary team for the staged management and optimally minimally invasive treatment of severe acute pancreatitis. Biosci Trends 15(3):180–187
86. Bekkali NLH, Murray S, Winter L, Sehgal V, Webster GJM, Chapman MH et al (2017) The role of multidisciplinary meetings for benign pancreatobiliary diseases: a tertiary centre experience. Frontline Gastroenterol 8(3):210–213
87. Pezzilli R, Zerbi A, Campra D, Capurso G, Golfieri R, Arcidiacono PG et al (2015) Consensus guidelines on severe acute pancreatitis. Dig Liver Dis 47(7):532–543
88. Fotoohi M, Traverso LW (2006) Pancreatic necrosis: paradigm of a multidisciplinary team. Adv Surg 40:107–118
89. Chingkoe CM, Brook A, Moser AJ, Mortele KJ (2018) Subspecialized radiology review at multidisciplinary pancreas conference: impact on patient management. Abdom Radiol 43(10):2783–2789
90. Brauer DG, Strand MS, Sanford DE, Kushnir VM, Lim KH, Mullady DK et al (2017) Utility of a multidisciplinary tumor board in the management of pancreatic and upper gastrointestinal diseases: an observational study. HPB 19(2):133–139
91. Baroud S, Chandrasekhara V, Storm AC, Law RJ, Vargas EJ, Levy MJ et al (2023) A Protocolized management of walled-off necrosis (WON) reduces time to won resolution and improves outcomes. Clin Gastroenterol Hepatol 21(10):2543-2550.e1
92. Zhi M, Zhu X, Lugea A, Waldron RT, Pandol SJ, Li L (2019) Incidence of new onset diabetes mellitus secondary to acute pancreatitis: a systematic review and meta-analysis. Front Physiol 10:637
93. Garip G, Sarandöl E, Kaya E (2013) Effects of disease severity and necrosis on pancreatic dysfunction after acute pancreatitis. World J Gastroenterol 19(44):8065–8070
94. Gupta R, Wig JD, Bhasin DK, Singh P, Suri S, Kang M et al (2009) Severe acute pancreatitis: the life after. J Gastrointest Surg 13(7):1328–1336
95. Sharma D, Mallick B, Samanta J, Gupta V, Sinha SK, Kochhar R (2021) Acute-on-chronic pancreatitis: analysis of clinical profile and outcome. Cureus 13(4):e14242
96. Kirkegård J, Cronin-Fenton D, Heide-Jørgensen U, Mortensen FV (2018) Acute pancreatitis and pancreatic cancer risk: a nationwide matched-cohort study in Denmark. Gastroenterology 154(6):1729–1736
97. Liu J, Wang Y, Yu Y (2020) Meta-analysis reveals an association between acute pancreatitis and the risk of pancreatic cancer. World J Clin Cases 8(19):4416–4430
98. Umans DS, Hoogenboom SA, Sissingh NJ, Lekkerkerker SJ, Verdonk RC, van Hooft JE (2021) Pancreatitis and pancreatic cancer: a case of the chicken or the egg. World J Gastroenterol 27(23):3148–3157