Study Protocol V.2.2 February 16th, 2021.

coMpliAnce with evideNce-based cliniCal guidelines in the managemenT of acute biliaRy pancreAtitis (MANCTRA-1).

ClinicalTrials.Gov ID Number: NCT04747990

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Italian Society of Endoscopic Surgery and new technologies (SICE)
American College of Surgeons (ACS) Italy Chapter
Association of Italian Surgeons in Europe (ACIE)
Italian Surgical Research Group (ItSurg)
"Mario Negri" Institute for Pharmacological Research, Milan, Italy.

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co**M**pli**A**nce with evide**N**ce-based clini**C**al guidelines in the managemen**T** of acute bilia**R**y pancre**A**titis (**MANCTRA-1**).

Background

Acute pancreatitis (AP) is an inflammatory disease of the pancreas, most commonly caused by gallstones or excessive alcohol use. It represents a management challenge and a significant healthcare burden. The incidence of AP ranges globally from 5 to 30 cases per 100.000 inhabitants/year, and there is evidence that the incidence has been rising in recent years. The overall case-fatality rate for AP is roughly 5%, and it is expectedly higher for more severe stages of the disease [1, 2]. In most cases (80%), the outcome of AP is rapidly favorable [3]. However, acute necrotizing pancreatitis (ANP) may develop in up to 20% of cases and is associated with significant rates of early organ failure (38%), needing some surgical/endoscopic intervention (38%), and death (15%) [4].

In the United States, AP is a leading cause of inpatient care among gastrointestinal conditions: more than 270.000 patients are hospitalized for AP annually, at an aggregate cost of over 2.5 billion dollars per year [5]. In Europe, the UK incidence of AP is estimated as 15-42 cases per 100.000/year and is rising by 2.7% each year [6].

Several scientific societies published their clinical practice guidelines making recommendations on the management of AP [7] (Table_1-4). These guidelines' main topics are the diagnosis, antibiotic treatment, management in the intensive care unit, surgical and operative management, and open abdomen management.

Audits about biliary AP have been performed in Italy, Germany, France, and England, with quite disappointing results [8-11]. Indeed, in these audits, the treatment of biliary AP differed substantially from the recommendations. For example, less than 15% of the responders stated that they strictly followed all recommendations included in the guidelines in Germany, and 25.8% of patients did not receive definitive treatment for biliary AP within one year in the UK [12].

A recent study from Singapore aiming to review the clinical management of patients with AP in an HPB referral center in the light of assessing the compliance to the 2013 International Association of Pancreatology (IAP)/American Pancreatic Association (APA) and the 2015 Japanese guidelines found that only 50% of patients received Ringer lactate for initial fluid resuscitation, 38.7% received antibiotics as prophylaxis, 21.4% of patients with severe AP had early enteral nutrition, and only 21.4% patients with biliary AP had index admission cholecystectomy despite the recommendations [13]. In

another recent study by a Canadian group, only 25% of patients with gallstones AP underwent a cholecystectomy on the same admission. Furthermore, only one-quarter of patients in whom an index admission cholecystectomy was not possible underwent ERCP with sphincterotomy, and only one-third of patients with gallstones AP and an imaging-confirmed obstructed common bile duct had an ERCP and sphincterotomy [14]. Slow implementation of the recommendation on early cholecystectomy has also been reported in a Danish survey seeking compliance with the recommendations of the national reference program for the treatment of patients with gallstone disease [15], and a similar lack of compliance with guidelines was found in Italy, mainly regarding indications for endoscopic and surgical management [16].

Conversely, a recent study from Sweden has shown that the recurrence rate and associated costs can be reduced by improved compliance to current AP guidelines. The authors found that 80% of patients with biliary AP underwent definitive treatment during their first attack (68% cholecystectomy, 17% ERCP and sphincterotomy, 15% both interventions) [17].

Moreover, significant overall differences between the practice of HPB specialists and non-specialists in gallstone AP have been reported, especially regarding severity assessment, indication and timing of requesting CT scan, nutritional support, and in common bile duct assessment before cholecystectomy [18].

These findings support the view that publication alone of nationally or internationally developed and approved guidelines is insufficient to modify the practice of non-specialists and raises the question of how best to spread guideline recommendations. Previous reports, including the one from France in 2012, have shown that major changes in biliary AP patients management were noticed since the French guidelines publication. In particular, after the publication of the mentioned guidelines, lipase levels were measured for establishing AP diagnosis by 99% (vs. 83% pre-guidelines), and a CT scan was performed at 48h by 69% (vs. 29% pre-guidelines) to evaluate AP severity. Antibiotic prophylaxis and enteral nutrition were proposed by 20% (vs. 57% pre-guidelines) and 58% (vs. 25% pre-guidelines) for necrotizing AP [19].

Management of pancreatic necrosis

Infection of pancreatic necrosis is the predominant driver of sustained morbidity and late mortality in patients with severe AP. The subset of patients with ANP may face a complicated and prolonged

clinical course, with an associated mortality of up to 30% if an infection develops in the necrotic collection [20, 21]. Optimal management of patients with pancreatic necrosis requires a multidisciplinary approach, and specific guidelines for this specific subgroup of patients have been recently released (Table_5). Although antibiotic prophylaxis may prevent or reduce necrosis colonization, the results of RCTs evaluating this approach and meta-analyses do not support prophylaxis [22]. Consequently, internationally applicable recommendations are that intravenous antibiotic prophylaxis is not recommended to prevent infectious complications in AP. However, several global overviews assessing reports from across the world of the use of antibiotics in prophylaxis in AP have shown a spread diffusion of such behavior [23].

COVID-19 and management of AP

In 2020, the spread of the virus Covid-19 had represented a pandemic, which also profoundly impacted the surgical community [24, 25]. The constant increase in the number of patients requiring treatment has represented a massive challenge for many involved countries' healthcare systems and could be their breaking point. In an emergency situation, resources must be concentrated and used rationally to handle the pandemic and continue handling the pre-existing diseases. In this context, most surgical departments were forced to re-schedule their activity, giving priority to urgent/emergent surgical cases and non-deferrable oncological cases. There are many ways the outbreak of the Covid-19 pandemic could have influenced daily clinical practice for patients with biliary AP, leading to a failure to adhere to the recommendations coming from the guidelines, especially those regarding the early and definitive treatment with cholecystectomy or ERCP and sphincterotomy. First of all, the recommendation to postpone all non-urgent endoscopic procedures during the peak of the pandemic. Second, the recommendation to conservatively treat inflammatory conditions such as acute cholecystitis and acute appendicitis wherever possible.

The rationale for the study

Despite existing evidence-based practice guidelines for the management of biliary AP, in Europe, clinical compliance with recommendations is lacking. Studies in this field have identified significant discrepancies between evidence-based recommendations and daily clinical practice.

co**M**pli**A**nce with evide**N**ce-based clini**C**al guidelines in the managemen**T** of acute bilia**R**y pancre**A**titis (**MANCTRA-1**).

It is believed by many that clinical guidelines would help to decrease inappropriate variation in practice, that they provide a rational basis for referral, and that they would help to reduce uncertainty in the management of some conditions. Clinical guidelines also provide a basis for continuing medical education and can improve control of healthcare costs. However, the value of national and/or international guidelines is very much dependent on a strategy for their implementation.
Although different guidelines for the management of biliary AP have been published, they have not been adequately investigated, and compliance has generally been unsatisfactory. Deficiencies and lack of standardization of the management of AP worldwide have been reported.
The most commonly reported gaps between clinical practice and AP guidelines include the indications for CT scan, need and timing of artificial nutritional support, indications for antibiotics, and surgical/endoscopic management of biliary AP.
The MANCTRA-1 can identify a number of areas for quality improvement that will require new implementation strategies. We aim to summarize the main areas of sub-optimal care due to the lack of compliance with current guidelines to provide the basis for introducing a number of bundles in AP patients' management to be implemented during the next years.

Aim of the study

Since the clinical compliance with recommendations about AP is poor and the impact of implementing guideline recommendations in biliary AP has not been well studied globally, we launched the MANCTRA-1 study intending to demonstrate areas where there is currently a sub-optimal implementation of current guidelines on biliary AP.
Moreover, we argue that during the Covid-19 pandemic, the tendency to disregard the guidelines recommendations has been more marked than usual, and we will try to find out if AP patients' care during the Covid-19 pandemic resulted in a higher rate of adverse outcomes compared to non-pandemic times due to the lack in the compliance of the guidelines.

Primary objective

- **To evaluate which items of the current AP guidelines, if disregarded, correlate with**

negative clinical outcomes according to the different clinical presentations of the disease

Secondary objectives

- To assess the compliance of surgeons worldwide to the most up-to-date international guidelines on biliary AP
- To evaluate the medical and surgical practice in the management of biliary AP during the non-pandemic (2019) and pandemic Covid-19 periods (2020)
- To investigate outcomes of patients with biliary AP treatment during the two study periods

Primary outcomes

- 30-day mortality: assessed by the number of AP patients with biliary etiology deceased during the non-pandemic period (2019) and the Covid-19 pandemic period (2020)
- 30-day morbidity: assessed by the number of AP patients with biliary etiology who experienced any type of AP-related complication within 30-days from the hospital admission during the non-pandemic period (2019) and the Covid-19 pandemic period (2020)

Secondary outcomes

- Early definitive treatment rate in 2019 vs. 2020: defined as treatment in accordance with the current guidelines (cholecystectomy or ERCP with endoscopic sphincterotomy during the same hospital admission or within 2 weeks of discharge)
- 30-day hospital readmission rate in 2019 vs. 2020: defined as hospital readmission within 30-days from discharge for recurrent biliary AP while awaiting interval cholecystectomy, or due to post-cholecystectomy complications
- Predictive factors of morbidity and mortality in patients with biliary AP

The compliance of surgeons to the most up-to-date international guidelines on biliary AP will be assessed through the analysis of the following attitudes:

- Use of scoring systems for the diagnosis and severity grading of biliary AP

- Use of lipase dosage (for the diagnosis) and CRP (for the severity grading) during the diagnostic workup
- Use of Ultrasound scan, CT scan, MRCP, and endoscopic Ultrasound scan (EUS) in the correct way and timing
- Use of early ERCP and sphincterotomy in case of cholangitis and/or choledocholithiasis
- Use of percutaneous and/or endoscopic drainage in case of infected pseudocyst or necrosis
- Timing of surgical necrosectomy
- Timing of re-laparotomy in case of open abdomen strategies
- Use of prophylactic antibiotics/antifungals
- Use of somatostatin analogs
- Use of early enteral feeding
- Use of early definitive treatment strategies, including cholecystectomy and/or ERCP and sphincterotomy

Study design

The MANCTRA-1 study (co**M**pli**A**nce with evide**N**ce-based clini**C**al guidelines in the managemen**T** of acute bilia**R**y pancre**A**titis) is an international multicenter, retrospective cohort study to assess the outcomes of patients admitted to hospital with a diagnosis of biliary AP and the compliance of surgeons worldwide to the most up-to-dated international guidelines on biliary AP. The study compares data collected in 2019 (pre-pandemic period) with those of 2020 (Covid-19 pandemic period).

Study population

All consecutive adult patients admitted to the participating surgical departments with a clinical and radiological diagnosis of biliary AP (with and without concomitant cholecystitis) between 01/01/2019 and 31/12/2020. Patient data will be retrospectively analyzed and demographic characteristics, comorbidity status, clinical and radiological findings, treatment strategies, 30-day morbidity and mortality will be evaluated.

Inclusion criteria

Patients of both sexes, ≥ 16 years old, admitted to any of the participating surgical departments and/or

internal medicine or gastroenterology departments for biliary AP in 2019 and 2020.

Exclusion criteria

Patients with AP of etiology other than gallstones; Pregnant patients.

Study periods

The pre-pandemic period runs from 01/01/2019 to 31/12/2019. The Covid-19 pandemic period runs from 01/01/2020 to 31/12/2020. Data will be entered in the database from 01/03/2021 to 31/08/2021.

Data collection (see also the "Analyzed Data" - CRF - paragraph below)

All epidemiological, clinical and surgical data will be collected on a CFR that will be completed by accessing to a protected data system. The link for accessing the completion of the CFR will be sent via email to only one contact person (Local Lead) of each participating center.

Sample size

Studies on biliary AP found a mortality rate of approximately 10%. Patients with biliary AP tend to have a higher mortality than patients with alcoholic pancreatitis. However, this rate has been falling over the last 2 decades as improvements in supportive care have been initiated. In patients with severe disease (organ failure), who account for about 20% of presentations, mortality is approximately 30%. This rate has not decreased in the past 10 years.

We estimate that a minimum of 200 patients per group (2019 vs. 2020) would yield a power of 0.80 (1-ß) to establish whether changes in clinical care for patients with biliary AP during the Covid-19 pandemic has impacted on overall mortality using a one-sided significance α level of 0.05 (5%) with power sample size calculator (sealedenvelope.com).

Statistical analysis

The dichotomous variables will be expressed as numbers and percentages, while continuous variables will be expressed as mean and SD, or median and IQR (minimum and maximum values). Student's t test or ANOVA will be used for comparisons of continuous variables between groups. Chi-squared test or Fisher's exact test, as appropriate, will be used for analysis of categorical data. Multilogistic

regression models will be used to investigate clinical attitudes, physical, laboratory, and radiologic variables predictive of morbidity and mortality. A value of $P < 0.05$ will be considered statistically significant.

Ethical aspects

This is an international observational study, it will not attempt to change or modify the clinical practice of the participating physicians. The study will meet and conform to the standards outlined in the Declaration of Helsinki and Good Epidemiological Practices. Every clinical center attending the study is responsible for Ethics Committee approval depending on the local policy for observational and non-interventional studies. All surgeons involved in the patients' recruitment will be included in the research authorship.

Publication policy

The Local Lead and two Collaborators from each center will be listed as Co-authors in the final publications. Data will be published as a pool from all participating surgical units. Data emerged from the MANCTRA-1 study will be published irrespective of findings. Results will be published on ClinicalTrials.Gov and each manuscript that is generated based on the registry will be disseminated to all participating centers before final publication.

Safety issues

None.

Data collection

In each centre, the coordinator will collect and compile data in an online case report system. Data will be recorded contemporaneously on a dedicated, secure server that allows collaborators to enter and store data in a secure system. No patient identifiable data (name, date of birth, address, telephone number, etc.) will be recorded.

Informed consent

co**M**pli**A**nce with evide**N**ce-based clini**C**al guidelines in the managemen**T** of acute bilia**R**y pancre**A**titis (**MANCTRA-1**).

Due to its retrospective design, this observational study will not attempt to change or modify the laboratory or clinical practices of the participating physicians. Consequently, informed consent will not be required.

Data management

Every local investigator is responsible for entering data on an on line case report form for every patient included in the study.

Funding

This research has not received any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Financial and Insurance

Not applicable.

Analyzed Data – CRF -

Section 1 – General Informations

- Country
- Name and Surname of the Local Lead
- Email address of the local lead
- Name and Surname of the Local Collaborator
- Email address of the Local Collaborator

Section 2 – Demographic Characteristics

- Year of hospital admission for acute biliary pancreatitis (2019 Vs. 2020)
- Patient age
- Sex (Female Vs. Male)
- Covid-19 status on admission (Negative/Positive/Untested)

- Previous episodes of biliary pancreatitis (Yes/No)
- Admitting speciality (HPB surgery/General Surgery/Internal Medicine/Gastroenterology)

Section 3 – Comorbidity

- Charlson's comorbidity index
- Body Mass Index - BMI
- Clinical history of diabetes (No diabetes/Diabetes with organ disfunction/Diabetes without organ disfunction)
- Clinical history of chronic pulmonary disease other than Covid-19 pneumonia (Yes/No)
- Clinical history of hypertension (Yes/No)
- Clinical history of atrial fibrillation (Yes/No)
- Clinical history of ischemic hearth disease (Yes/No)
- Clinical history of chronic kidney disease (Yes-under medications/Yes-in permanent renal replacement therapy or in preparation for it/No)
- Clinical history of diseases of the hematopoietic system (Yes/No)
- Patient on immunosuppressive medications on hospital admission (Yes/No)

Section 4 – Clinical Scores

- Glasgow Coma Scale (GCS)
- qSOFA
- WSES (World Society of Emergency Surgery) sepsis score
- BISAP (Bedside Index of Severity in Acute Pancreatitis) score
- ASA score (1-2-3-4-5)
- Glasgow-Imrie score
- Ranson's score
- Apache II score
- Revised Atlanta Classification (Mild acute pancreatitis/Moderately severe acute pancreatitis/Severe acute pancreatitis)
- Organ failure during the hospital stay (None/Cardiovascular/Respiratory/Renal)

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Section 5 – Vital signs on admission

- Temperature
- Systolic blood pressure
- Hearth rate
- Respiratory rate
- Blood oxygen saturation
- ICU admission during the hospital stay (Yes/No)

Section 6 – Laboratory tests on admission

- WBC
- Neutrophils
- Platelets
- INR (International Normalized Ratio)
- C-reactive protein
- Aspartate aminotransferase – AST
- Alanine aminotransferase – ALT
- Total bilirubin
- Conjugated bilirubin
- Gamma-glutamil-transpeptidase – GGT
- Serum amylase
- Serum lipase
- Lactate DeHydrogenase – LDH
- Procalcitonin – PCT
- Lactates

Section 7 – Diagnostic Imaging

- Initial diagnostic imaging (Ultrasound scan on admission/CT scan on admission/CT scan <24h/CT scan 24-48h/CT scan >48h)

- MRCP (MRCP on admission/MRCP <24h/MRCP >24h/No)
- Endoscopic ultrasound scan (Yes <24 hours/Yes >24 hours/No)
- Re-evaluation with CT scan (None/<7 days/7-14 days/15-30 days/>30 days)

Section 8 – Physical examination on admission (Localized abdominal pain/Localized abdominal rigidity/Diffuse abdominal pain/Diffuse abdominal rigidity/No abdominal pain/No abdominal rigidity)

Section 9 – Concomitant findings on admission

- Choledocholithiasis (Yes/Yes with common bile duct obstruction/No)
- Cholangitis (Yes/No)
- ERCP with sphincterotomy (Yes-within 24 hours/Yes within 24-48 hours/Yes within 48-72 hours/No)

Section 10 – 30-day Morbidity

- Gastric outlet obstruction (Yes/No)
- Pseudocyst (Yes/No)
- Infected necrosis (Yes/No)
- Endoscopic drainage of pseudocyst/walled-off necrosis (Yes/No)
- CT-guided fine needle aspiration in case of infected pseudocyst/walled-off necrosis (Yes/No)
- Surgical necrosectomy (Yes-laparoscopic/Yes-open/No)
- Timing of surgical necrosectomy (< 2 weeks from the onset of symptoms/2-4 weeks/>4 weeks)
- Setting of surgical necrosectomy (Upfront/After failure of endoscopic necrosectomy/After failure of endoscopic and percutaneous necrosectomy)
- Cystogastrostomy (Yes-endoscopic/Yes-surgical/No)
- Abdominal compartment syndrome (Yes/No)
- Open abdomen (Yes/No)
- Timing of re-exploration (24-48 hours/48-72 hours/>72 hours)
- Bleeding (Yes/No)
- Bowel ischemia (Yes/No)

co**M**pli**A**nce with evide**N**ce-based clini**C**al guidelines in the managemen**T** of acute bilia**R**y pancre**A**titis (**MANCTRA-1**).

- Bowel fistula (Yes/No)
- Necrotizing cholecystitis (Yes/No)

Section 11 – Medical Therapy

- Antibiotic prophylaxis (Yes/No)
- Antifungal prophylaxis (Yes/No)
- Use of somatostatin analogs (Yes/No)
- Nutritional support on admission (Oral/Enteral via nasogastric feeding tube/Enteral via nasojejunal feeding tube/Total parental nutrition/Nihil per os)

Section 12 – Cholecystectomy (Yes-within 3 days/Yes-within 7 days/Yes-within 14 days/No-delayed cholecystectomy)

Section 13 – 30-day Overall mortality (Yes/No)

Section 14 – Post-cholecystectomy 30-day morbidity and mortality

- Post-cholecystectomy morbidity (Yes/No)
- Post-cholecystectomy mortality (Yes/No)
- 30-day hospital readmission (No/Yes-due to surgical complications/Yes-due to recurrent pancreatitis while awaiting interval cholecystectomy)

co**M**pli**A**nce with evide**N**ce-based clini**C**al guidelines in the managemen**T** of acute bilia**R**y pancre**A**titis (**MANCTRA-1**).

Table_1: Statements and Recommendations from the 2019 WSES guidelines for the management of Acute Pancreatitis patients.

1. Severity grading	! Severe acute pancreatitis is associated with persistent organ failure (cardiovascular, respiratory, and/or renal), and high mortality. Both new classification systems, Revised Atlanta Classification and Determinant-based Classification of Acute Pancreatitis Severity, are similar in establishing the diagnosis and severity of acute pancreatitis (1C). ! Patients who have persistent organ failure with infected necrosis have the highest risk of death (1C). ! Patients with organ failures should be admitted to an intensive care unit whenever possible (1C).
2. Imaging	! On admission, ultrasound (US) should be performed to determine the etiology of acute pancreatitis (biliary) (1C). ! When doubt exists, computed tomography (CT) provides good evidence of the presence or absence of pancreatitis (1C). ! All patients with severe acute pancreatitis need to be assessed with contrast-enhanced computed tomography (CE-CT) or magnetic resonance imaging (MRI). Optimal timing for first the CE-CT assessment is 72–96 h after onset of symptoms (1C). ! Magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasound should be considered to screen for occult common bile duct stones in patients with unknown etiology (1C).
3. Diagnostic laboratory parameters	! The cut-off value of serum amylase and lipase is normally defined to be three times the upper limit. ! C-reactive Protein level ≥ 150 mg/l at third day can be used as a prognostic factor for severe acute pancreatitis (2A). ! Hematocrit > 44% represents an independent risk factor of pancreatic necrosis (1B). ! Urea > 20 mg/dl represents itself as an independent predictor of mortality (2B). ! Procalcitonin is the most sensitive laboratory test for detection of pancreatic infection, and low serum values appear to be strong negative predictors of infected necrosis (2A). ! In the absence of gallstones or significant history of alcohol use, serum triglyceride and calcium levels should be measured. Serum triglyceride levels over 11.3 mmol/l (1000 mg/dl) indicate it as the etiology (2C).
4. Diagnostics in idiopathic pancreatitis	! In idiopathic pancreatitis, biliary etiology should be ruled out with two ultrasound examinations, and if needed MRCP and/or endoscopic ultrasound EUS, to prevent recurrent pancreatitis (2B).

5. Risk scores	! There are no "gold standard" prognostic score for predicting severe acute pancreatitis. Probably the bedside index of severity of acute pancreatitis (BISAP) score is one of the most accurate and applicable in everyday clinical practice because of the simplicity and the capability to predict severity, death, and organ failure as well as the APACHE-II (very complex) and other scores (1B).
6. Follow-up imaging	! In severe acute pancreatitis (computed tomography severity index ≥ 3), a follow-up CECT scan is indicated 7–10 days from the initial CT scan (1C). ! Additional CE-CT scans are recommended only if clinical status deteriorates or fails to show continued improvement, or when invasive intervention is considered (1C).
7. Prophylactic antibiotics	! Recent evidences have shown that prophylactic antibiotics in patients with acute pancreatitis are not associated with a significant decrease in mortality or morbidity. Thus, routine prophylactic antibiotics are no longer recommended for all patients with acute pancreatitis (1A).
8. Infected necrosis and antibiotics	! Antibiotics are always recommended to treat infected severe acute pancreatitis. However the diagnosis is challenging due to the clinical picture that cannot be distinguished from other infectious complications or from the inflammatory status caused by acute pancreatitis (2A). ! Serum measurements of procalcitonin (PCT) may be valuable in predicting the risk of developing infected pancreatic necrosis (1B). ! A CT-guided fine-needle aspiration (FNA) for Gram stain and culture can confirm an infected severe acute pancreatitis and drive antibiotic therapy but is no longer in routine use (1B).
9. Type of antibiotics	! In patients with infected necrosis, antibiotics known to penetrate pancreatic necrosis should be used (1B). ! In patients with infected necrosis, the spectrum of empirical antibiotic regimen should include both aerobic and anaerobic Gram-negative and Gram-positive microorganisms. Routine prophylactic administration of antifungal is not recommended in patients with infected acute pancreatitis, although Candida spp. are common in patients with infected pancreatic necrosis and indicate patients with a higher risk of mortality (1B).
10. Monitoring	! Continuous vital signs monitoring in high dependency care unit is needed if organ dysfunction occurs. Persistent organ dysfunction or organ failure occurrence despite adequate fluid resuscitation is an indication for ICU admission (1C).
11. Fluid resuscitation	! Early fluid resuscitation is indicated to optimize tissue perfusion targets, without waiting for hemodynamic worsening. Fluid

		administration should be guided by frequent reassessment of the hemodynamic status, since fluid overload is known to have detrimental effects. Isotonic crystalloids are the preferred fluid (1B).
12. Pain control	!	No evidence or recommendation about any restriction in pain medication is available. Nonsteroidal anti-inflammatory drugs (NSAID) should be avoided in acute kidney injury (AKI). Epidural analgesia should be an alternative or an agonist with intravenous analgesia, in a multimodal approach. Patient-controlled analgesia (PCA) should be integrated with every described strategy. (1C) Dilaudid is preferred over morphine or fentanyl in the nonintubated patient.
13. Mechanical ventilation	!	Mechanical ventilation must be instituted if oxygen supply, even with high flow nasal oxygen, or continuous positive airway pressure became ineffective in correcting tachypnea and dyspnea. Both non-invasive and invasive techniques can be used, but invasive ventilation is mandatory when bronchial secretions clearance start to be ineffective and/or the patient is tiring of predicted to tire. Lung-protective strategies should be used when invasive ventilation is needed (1C).
14. Increased intra-abdominal pressure	!	Limitation of sedation, fluids, and vasoactive drugs to achieve resuscitative goals at lower normal limits is suggested. Deep sedation and paralysis can be necessary to limit intra-abdominal hypertension if all other nonoperative treatments including percutaneous drainage of intraperitoneal fluid are insufficient, before performing surgical abdominal decompression (1B)
15. Pharmacological treatment	!	No specific pharmacological treatment except for organ support and nutrition should be given (1B).
16. Enteral nutrition	!	Enteral nutrition is recommended to prevent gut failure and infectious complications. Total parenteral nutrition (TPN) should be avoided but partial parenteral nutrition integration should be considered to reach caloric and protein requirements if enteral route is not completely tolerated. Both gastric and jejunal feeding can be delivered safely (1A).
17. Indications for emergent ERCP	! ! ! !	Routine ERCP with acute gallstone pancreatitis is not indicated (grade 1A). ERCP in patients with acute gallstone pancreatitis and cholangitis is indicated (grade 1B). ERCP in acute gallstone pancreatitis with common bile duct obstruction is indicated (grade 2B). ERCP in patients with predicted severe acute gallstone pancreatitis without cholangitis or common bile duct obstruction cannot be

	recommended at this time (grade 2B).
18. Indications for percutaneous/endoscopic drainage of pancreatic collections	! Clinical deterioration with signs or strong suspicion of infected necrotizing pancreatitis is an indication to perform intervention (percutaneous/endoscopic drainage) *After 4 weeks after the onset of the disease:* – On-going organ failure without sign of infected necrosis – On-going gastric outlet, biliary, or intestinal obstruction due to a large walled off necrotic collection – Disconnected duct syndrome – Symptomatic or growing pseudocyst *After 8 weeks after the onset of the disease:* – On-going pain and/or discomfort (grade 1C)
19. Indications for surgical intervention	! As a continuum in a step-up approach after percutaneous/endoscopic procedure with the same indications – Abdominal compartment syndrome – Acute on-going bleeding when endovascular approach is unsuccessful – Bowel ischaemia or acute necrotizing cholecystitis during acute pancreatitis – Bowel fistula extending into a peripancreatic collection (Grade 1C)
20. Timing of surgery	! Postponing surgical interventions for more than 4 weeks after the onset of the disease results in less mortality (2B).
21. Surgical strategy	! In infected pancreatic necrosis, percutaneous drainage as the first line of treatment (step-up approach) delays the surgical treatment to a more favorable time or even results in complete resolution of infection in 25–60% of patients and it is recommended as the first line of treatment (1A). ! Minimally invasive surgical strategies, such as transgastric endoscopic necrosectomy or videoassisted retroperitoneal debridement (VARD), result in less postoperative new-onset organ failure but require more interventions (1B). ! Considering mortality, there is insufficient evidence to support open surgical, mini-invasive, or endoscopic approach (1B). ! In selected cases with walled-off necrosis and in patients with disconnected pancreatic duct, a single stage surgical transgastric necrosectomy is an option (2C).

	! A multidisciplinary group of experts should individualize surgical treatment taking local expertize into account (2C)
22. Timing of cholecystectomy	! Laparoscopic cholecystectomy during index admission is recommended in mild acute gallstone pancreatitis (1A). ! When ERCP and sphincterotomy are performed during the index admission, the risk for recurrent pancreatitis is diminished, but same admission cholecystectomy is still advised since there is an increased risk for other biliary complications (1B). ! In acute gallstone pancreatitis with peripancreatic fluid collections, cholecystectomy should be deferred until fluid collections resolve or stabilize and acute inflammation ceases (2C).
23. Open abdomen	! In patients with severe acute pancreatitis unresponsive to conservative management of IAH/ ACS, surgical decompression and use of open abdomen are effective in treating the abdominal compartment syndrome (2C). ! We suggest that clinicians should be cautious not to over-resuscitate patients with early SAP and measure intra-abdominal pressure regularly (1C). ! We suggest that the open abdomen (OA) be avoided if other strategies can be used to mitigate or treat severe intra-abdominal hypertension in SAP (1C). ! We recommend not to utilize the OA after necrosectomy for SAP (unless severe IAH mandates OA as a mandatory procedure) (1C). ! We recommend not to debride or undertake early necrosectomy if forced to undertake an early OA due abdominal compartment syndrome or visceral ischemia (1A).
24. Open abdomen management and temporary abdominal closure	! We recommend the use of negative pressure peritoneal therapy for OA management (1B). ! We suggest fascial traction be added to NPWT methods (2B). ! We suggest that further controlled studies be conducted on intra-peritoneal osmotic therapies in SAP (no recommendation)
25. Timing of dressing changes	! Open abdomen re-exploration should be conducted no later than 24–48 h after the index and any subsequent operation, with the duration from the previous operation shortening with increasing degrees of patient non-improvement and hemodynamic instability (1C).
26. Timing for abdominal closure	! Early fascial and/or abdominal definitive closure should be the strategy for management of the open abdomen once any requirements for on-going resuscitation have ceased, the source control has been definitively reached, no concern regarding intestinal viability persist, no further surgical re-exploration is needed, and there are no concerns for abdominal compartment syndrome (1B).

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From: Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, Ball CG, Parry N, Sartelli M, Wolbrink D, van Goor H, Baiocchi G, Ansaloni L, Biffl W, Coccolini F, Di Saverio S, Kluger Y, Moore E, Catena F. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg. 2019 Jun 13;14:27. doi: 10.1186/s13017-019-0247-0. PMID: 31210778; PMCID: PMC6567462.

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Table_2. Statements and Recommendations from the 2005 UK guidelines for the management of Acute Pancreatitis.

1. Diagnosis	! The correct diagnosis of acute pancreatitis should be made in all patients within 48 hours of admission (recommendation grade C). ! The etiology of acute pancreatitis should be determined in at least 80% of cases and no more than 20% should be classified as idiopathic (recommendation grade B). ! Although amylase is widely available and provides acceptable accuracy of diagnosis, where lipase estimation is available it is preferred for the diagnosis of acute pancreatitis (recommendation grade A). ! Where doubt exists, imaging may be used: ultrasonography is often unhelpful and pancreatic imaging by contrast enhanced computed tomography provides good evidence for the presence or absence of pancreatitis (recommendation grade C).
2. Assessment	! The definitions of severity, as proposed in the Atlanta criteria, should be used. However, organ failure present within the first week, which resolves within 48 hours, should not be considered an indicator of a severe attack of acute pancreatitis (recommendation grade B). ! Available prognostic features which predict complications in acute pancreatitis are clinical impression of severity, obesity, or APACHE II>8 in the first 24 hours of admission, and C reactive protein>150 mg/l, Glasgow score 3 or more, or persisting organ failure after 48 hours in hospital (recommendation grade B). ! Patients with persisting organ failure, signs of sepsis, or deterioration in clinical status 6– 10 days after admission will require computed tomography (recommendation grade B).
3. Prevention of complications	! The evidence to enable a recommendation about antibiotic prophylaxis against infection of pancreatic necrosis is conflicting and difficult to interpret. Some trials show benefit, others do not. At present there is no consensus on this issue. ! If antibiotic prophylaxis is used, it should be given for a maximum of 14 days (recommendation grade B). Further studies are needed (recommendation grade C). ! The evidence is not conclusive to support the use of enteral nutrition in all patients with severe acute pancreatitis. However, if nutritional support is required, the enteral route should be used if that can be tolerated (recommendation grade A).

	! The nasogastric route for feeding can be used as it appears to be effective in 80% of cases (recommendation grade B).
4. Treatment of gallstones	! Urgent therapeutic endoscopic retrograde cholangiopancreatography (ERCP) should be performed in patients with acute pancreatitis of suspected or proven gallstone etiology who satisfy the criteria for predicted or actual severe pancreatitis, or when there is cholangitis, jaundice, or a dilated common bile duct. The procedure is best carried out within the first 72 hours after the onset of pain. All patients undergoing early ERCP for severe gallstone pancreatitis require endoscopic sphincterotomy whether or not stones are found in the bile duct (recommendation grades B and C). ! Patients with signs of cholangitis require endoscopic sphincterotomy or duct drainage by stenting to ensure relief of biliary obstruction (recommendation grade A). ! All patients with biliary pancreatitis should undergo definitive management of gallstones during the same hospital admission, unless a clear plan has been made for definitive treatment within the next two weeks (recommendation grade C).
5. Management of necrosis	! All patients with severe acute pancreatitis should be managed in a high dependency unit or intensive therapy unit with full monitoring and systems support (recommendation grade B). ! All patients with persistent symptoms and greater than 30% pancreatic necrosis, and those with smaller areas of necrosis and clinical suspicion of sepsis, should undergo image guided fine needle aspiration to obtain material for culture 7–14 days after the onset of pancreatitis (recommendation grade B). ! Patients with infected necrosis will require intervention to completely debride all cavities containing necrotic material (recommendation grade B). ! The choice of surgical technique for necrosectomy, and subsequent postoperative management, depends on individual features and locally available expertise (recommendation grade B).
6. Provision of services	! Every hospital that receives acute admissions should have a single nominated clinical team to manage all patients with acute pancreatitis (recommendation grade C). ! Management in, or referral to, a specialist unit is necessary for patients with extensive necrotising pancreatitis or with other complications who may require intensive therapy unit care, or interventional radiological,

	endoscopic, or surgical procedures (recommendation grade B).

From: Working Party of the British Society of Gastroenterology; Association of Surgeons of Great Britain and Ireland; Pancreatic Society of Great Britain and Ireland; Association of Upper GI Surgeons of Great Britain and Ireland. UK guidelines for the management of acute pancreatitis. Gut. 2005 May;54 Suppl 3(Suppl 3):iii1-9. doi: 10.1136/gut.2004.057026. PMID: 15831893; PMCID: PMC1867800.

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Table_3. Statements and Recommendations from the 2018 American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis.

1.	! Recommendation 1A. In patients with AP, the AGA suggests using goal-directed therapy for fluid management. Conditional recommendation, very low quality evidence. Comment: The AGA makes no recommendation whether normal saline or Ringer's lactate is used. ! Recommendation 1B. In patients with AP, the AGA suggests against the use of hydroxyethyl starch (HES) fluids. Conditional recommendation, very low quality evidence.
2.	! Recommendation 2. In patients with predicted severe AP and necrotizing pancreatitis, the AGA suggests against the use of prophylactic antibiotics. Conditional recommendation, low quality evidence.
3.	! Recommendation 3. In patients with acute biliary pancreatitis and no cholangitis, the AGA suggests against the routine use of urgent ERCP. Conditional recommendation, low quality evidence.
4.	! Recommendation 4. In patients with AP, the AGA recommends early (within 24 hours) oral feeding as tolerated rather than keeping the patient nil per os. Strong recommendation; moderate quality evidence.
5.	! Recommendation 5. In patients with AP and inability to feed orally, the AGA recommends enteral rather than parenteral nutrition. Strong recommendation, moderate quality evidence.
6.	! Recommendation 6. In patients with predicted severe or necrotizing pancreatitis requiring enteral tube feeding, the AGA suggests either nasogastric or nasoenteral route. Conditional recommendation, low quality evidence.
7.	! Recommendation 7. In patients with acute biliary pancreatitis, the AGA recommends cholecystectomy during the initial admission rather than after discharge. Strong recommendation, moderate quality evidence.

From: Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN; American Gastroenterological Association Institute Clinical Guidelines Committee. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. Gastroenterology. 2018 Mar;154(4):1096-1101. doi: 10.1053/j.gastro.2018.01.032. Epub 2018 Feb 3. PMID: 29409760.

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Table_4. Statements and Recommendations from the 2015 Japanese guidelines for the management of acute pancreatitis.

1. Diagnosis	! The measurement of serum lipase is recommended for the diagnosis of acute pancreatitis. However, when the measurement of lipase is difficult, serum amylase (pancreatic amylase) should be measured. (1B) ! 2 Urinary trypsinogen-2 dipstick may be useful for minimally invasive method and rapid diagnosis of acute pancreatitis. However, this is not commercially available in Japan and therefore it cannot be recommended at this time. (ungraded B)
2. Diagnostic imaging	! When acute pancreatitis is suspected, ultrasonography is recommended. (1C) ! CT is recommended for the diagnosis of acute pancreatitis. (1C) ! MRI is more useful than CT in diagnosing bile duct stones causing pancreatitis and hemorrhagic necrotizing pancreatitis. (2C) ! Contrast-enhanced CT is useful for the diagnosis of active hemorrhage and thrombosis associated with pancreatitis. (1C)
3. Etiology	! During etiological diagnosis, the diagnosis of gallstone-induced acute pancreatitis should be determined as the most important and urgent issue, as this greatly affects the treatment, such as whether endoscopic papillary treatment should be performed or not. (1A)
4. Severity assessment	! In principle, it is recommended that a severity assessment be made immediately after diagnosis and repeated over time (especially within 48 h of the diagnosis). (1C) ! It is recommended that a scoring system is used for severity assessments. (1B) ! Contrast-enhanced CT is recommended for identifying poorly contrasted areas of acute pancreatitis and is also useful in the diagnosis of complications. However, the possibility of exacerbating pancreatitis and renal function and allergic reactions associated with the contrast must be considered. (2B)
5. Transfer indication	! Severe cases should be treated immediately at a facility capable of providing treatment for severe acute pancreatitis. Where such treatment is difficult at the facility, it is strongly recommended that the consideration be given to the immediate transfer of the patient. Even where the case is mild in the early stages, severity assessments should be carried out repeatedly over time, and when the criteria are met, transfer should be considered. (1C)
6. Fluid therapy	! An extracellular solution (Ringer's Lactate solution, etc.) is recommended as the initial infusion solution for acute pancreatitis. (1C) ! For patients in shock or with dehydration in the early phases of acute pancreatitis, short-time rapid fluid resuscitation (150–600mL/h depending

	on the presence of shock and the dehydration level) is recommended. However, this should be carried out with great care in order to avoid excessive fluid infusion. For patients without dehydration, they should be monitored closely with an appropriate amount of fluid infusion (130–150mL/h). Particularly for patients with comorbidities such as cardiac or renal failure, the circulating blood volume should be careful evaluated to determine the rate of fluid infusion. (1C) ! If a mean arterial pressure of 65mmHg or more and a urine output of 0.5mL/kg per h or more has been secured in patients with acute pancreatitis, rapid fluid infusion should be discontinued and a reduction of the rate of fluid infusion is suggested. The volume of infusion should be adjusted to maintain these levels. (2C)
7. Nasogastric tube	! No remedial effect of nasogastric tube insertion has been observed for mild acute pancreatitis. Therefore, the routine use of nasogastric suction tubes is not required. (1A)
8. Pain control	! Pain associated with acute pancreatitis is severe and persistent, raising the need of sufficient pain control. (1A)
9. Antibiotics prophylaxis	! The prophylactic administration of antibiotics is not necessary in mild acute pancreatitis, since the incidence and mortality rates of infectious complications from mild acute pancreatitis are low. (1A) ! The prophylactic administration of antibiotics in severe acute pancreatitis and necrotizing pancreatitis may improve the prognosis, if carried out in the early phases of pancreatitis (within 72 h of onset). (2B) ! No remedial effect of the prophylactic administration of antifungal agents for acute pancreatitis has been observed. Therefore, routine administration is not recommended. (1C)
10. Protease inhibitor	! The effectiveness of intravenous administration of protease inhibitor (gabexate mesilate) for improving the life prognosis and the rate of complications of acute pancreatitis has not been clearly proven. Further consideration of the efficacy of continuous high-dose intravenous administration for severe cases is required. (ungraded B)
11. Nutritional support	! Intravenous hyperalimentation is not recommended for mild cases. (1B) ! Total parenteral nutrition (not performed with oral or enteral nutrition) should be avoided if possible. (1B) ! In severe cases, it is more significant as a measure to prevent infection rather than as a route of nutrition support. It can be applied and implemented for severe cases which do not have accompanying intestinal complications. (1A) ! If initiated in the early phase, enteral nutrition can reduce the incidence of complications and can contribute to an increased rate of survival. Therefore, it is desirable that it be started within at least 48 h of admission. (2A)

	! In principle, it is recommended that enteral feeding tubes be inserted into the jejunum through the Treitz ligament. However, if a feeding tube cannot be inserted into the jejunum, nutrients can be infused into the duodenum or stomach instead. (2B) ! The initiation of oral administration should be determined using indicators such as the subsidence of abdominal pain and the serum pancreatic enzyme (especially serum lipase) level, etc. (2B)
12. Intensive care	! No life-saving effect has been observed from peritoneal lavage for acute pancreatitis, and therefore it is not recommended. (2B) ! For severe cases where circulation dynamics are not stable with anuria even after sufficient initial fluid infusion or cases with abdominal compartment syndrome (ACS), CHF/CHDF should be introduced. (1C) ! The efficacy of CHF/CHDF in cases of severe acute pancreatitis not mentioned above is uncertain. Therefore, routine use is not recommended. (2C) ! Continuous Regional Arterial Infusion therapy is reported to be effective in reducing pancreatic infection and mortality rates for severe acute pancreatitis and acute necrotizing pancreatitis, but its efficacy has not been confirmed. (ungraded B)
13. Management of biliary pancreatitis	! Early ERCP/ES should be performed in gallstone-induced acute pancreatitis when complications of cholangitis or prolonged passage disorder of the biliary tract are suspected. (1A) ! To prevent the recurrence of gallstone-induced acute pancreatitis, cholecystectomy is recommended for cases where such surgery is possible. (1B) ! A cholecystectomy should be performed as soon as gallstone-induced acute pancreatitis has been resolved. (1B)
14. Management of abdominal compartment syndrome	! The sequential measurement of IAP is recommended for cases with excessive fluid infusion, high severity, renal and respiratory complications, and fluid accumulation in multiple areas as observed by CT, since the onset of ACS increases the mortality rate in such cases. (2C) ! When there is persistent or recurrent IAPЯ12mmHg, conservative treatment (gastrointestinal decompression, intra-abdominal decompression, improvement of abdominal wall compliance, appropriate fluid infusion and circulation management) should be initiated. The goal should be to manage for IAPЮ15mmHg. Surgical decompression should be considered only when internal treatment is not effective for patients with IAP>20mmHg and where the additional complication of organ failure is of concern. (2D)
15. Interventions for the local complications	! In principle, conservative treatment should first be performed for necrotizing pancreatitis. The best indication for intervention is applied to cases of infected pancreatic necrosis with suspected or confirmed infection

	accompanying an aggravated general condition. (1C) ! Infected pancreatic necrosis should be suspected when clinical symptoms and blood test findings deteriorate. Routine use of FNA is not required for diagnosis, and clinical signs and CT should be used for a comprehensive determination. If an aggravated general condition is observed, percutaneous drainage or endoscopic drainage should be given for diagnosis and treatment. (1C) ! If possible, therapeutic intervention for infected pancreatic necrosis should be performed after 4 weeks of onset, when the necrosis has been sufficiently walled off, or in other words, during WON period. (2C) ! During therapeutic intervention for infected pancreatic necrosis, percutaneous (retroperitoneal) drainage or endoscopic transluminal drainage should be first given, and if no improvement is achieved, necrosectomy should then be performed. Necrosectomy by endoscopic or retroperitoneal approach is recommended. (2B)
16. Post-ERCP pancreatitis	! Prophylactic temporary pancreatic stent placement is useful as an effective endoscopic procedure for the prevention of post-ERCP pancreatitis. This should only be performed in the high-risk groups for post-ERCP pancreatitis given the risks and cost. (2A) ! The guidewire method is very likely to reduce the incidence of post-ERCP pancreatitis. (2A) ! For the prevention of post-ERCP pancreatitis, the intrarectal administration of NSAIDs should be carried out for all cases undergoing ERCP with no contraindications. (2A) (Other drugs should not be used as routine preventive measures, since their efficacy has been refuted or is uncertain.)
17. Clinical indicators (pancreatic bundles)	! A high rate of implementation of the pancreatitis bundles may contribute to improving prognosis of patients with severe acute pancreatitis. (1C)

From: Yokoe M, Takada T, Mayumi T, Yoshida M, Isaji S, Wada K, Itoi T, Sata N, Gabata T, Igarashi H, Kataoka K, Hirota M, Kadoya M, Kitamura N, Kimura Y, Kiriyama S, Shirai K, Hattori T, Takeda K, Takeyama Y, Hirota M, Sekimoto M, Shikata S, Arata S, Hirata K. Japanese guidelines for the management of acute pancreatitis: Japanese Guidelines 2015. J Hepatobiliary Pancreat Sci. 2015 Jun;22(6):405-32. doi: 10.1002/jhbp.259. Epub 2015 May 13. PMID: 25973947.

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Table_5: Statement and Recommendations from the AGA guidelines for the management of patients with pancreatic necrosis

BEST PRACTICE ADVICE 1	Pancreatic necrosis is associated with substantial morbidity and mortality and optimal management requires a multidisciplinary approach, including gastroenterologists, surgeons, interventional radiologists, and specialists in critical care medicine, infectious disease, and nutrition. In situations where clinical expertise may be limited, consideration should be given to transferring patients with significant pancreatic necrosis to an appropriate tertiary-care center.
BEST PRACTICE ADVICE 2	Antimicrobial therapy is best indicated for culture-proven infection in pancreatic necrosis or when infection is strongly suspected (ie, gas in the collection, bacteremia, sepsis, or clinical deterioration). Routine use of prophylactic antibiotics to prevent infection of sterile necrosis is not recommended.
BEST PRACTICE ADVICE 3	When infected necrosis is suspected, broad-spectrum intravenous antibiotics with ability to penetrate pancreatic necrosis should be favored (eg, carbapenems, quinolones, and metronidazole). Routine use of antifungal agents is not recommended. Computed tomography–guided fine-needle aspiration for Gram stain and cultures is unnecessary in the majority of cases.
BEST PRACTICE ADVICE 4	In patients with pancreatic necrosis, enteral feeding should be initiated early to decrease the risk of infected necrosis. A trial of oral nutrition is recommended immediately in patients in whom there is absence of nausea and vomiting and no signs of severe ileus or gastrointestinal luminal obstruction. When oral nutrition is not feasible, enteral nutrition by either nasogastric/ duodenal or nasojejunal tube should be initiated as soon as possible. Total parenteral nutrition should be considered only in cases where oral or enteral feeds are not feasible or tolerated.
BEST PRACTICE ADVICE 5	Drainage and/or debridement of pancreatic necrosis is indicated in patients with infected necrosis. Drainage and/or debridement may be required in patients with sterile pancreatic necrosis and persistent unwellness marked by abdominal pain, nausea, vomiting, and nutritional failure or with associated complications, including gastrointestinal luminal obstruction; biliary obstruction; recurrent acute pancreatitis; fistulas; or persistent systemic inflammatory response syndrome.
BEST PRACTICE ADVICE 6	Pancreatic debridement should be avoided in the early, acute period (first 2 weeks), as it has been associated with increased morbidity and mortality. Debridement should be optimally delayed for 4 weeks and performed earlier only when there is an organized collection and a strong indication.
BEST PRACTICE ADVICE 7	Percutaneous drainage and transmural endoscopic drainage are both appropriate first-line, nonsurgical approaches in managing patients with walled-off pancreatic necrosis (WON). Endoscopic therapy through transmural drainage of WON may be preferred, as it avoids the risk of forming a pancreatocutaneous fistula.

BEST PRACTICE ADVICE 8	Percutaneous drainage of pancreatic necrosis should be considered in patients with infected or symptomatic necrotic collections in the early, acute period (<2 weeks), and in those with WON who are too ill to undergo endoscopic or surgical intervention. Percutaneous drainage should be strongly considered as an adjunct to endoscopic drainage for WON with deep extension into the paracolic gutters and pelvis or for salvage therapy after endoscopic or surgical debridement with residual necrosis burden.
BEST PRACTICE ADVICE 9	Self-expanding metal stents in the form of lumen-apposing metal stents appear to be superior to plastic stents for endoscopic transmural drainage of necrosis.
BEST PRACTICE ADVICE 10	The use of direct endoscopic necrosectomy should be reserved for those patients with limited necrosis who do not adequately respond to endoscopic transmural drainage using large-bore, self-expanding metal stents/lumen-apposing metal stents alone or plastic stents combined with irrigation. Direct endoscopic necrosectomy is a therapeutic option in patients with large amounts of infected necrosis, but should be per- formed at referral centers with the necessary endoscopic expertise and interventional radiology and surgical backup.
BEST PRACTICE ADVICE 11	Minimally invasive operative approaches to the debridement of acute necrotizing pancreatitis are preferred to open surgical necrosectomy when possible, given lower morbidity.
BEST PRACTICE ADVICE 12	Multiple minimally invasive surgical techniques are feasible and effective, including videoscopic-assisted retroperitoneal debridement, laparoscopic transgastric debridement, and open transgastric debridement. Selection of approach is best deter- mined by pattern of disease, physiology of the patient, experience and expertise of the multidisciplinary team, and available resources.
BEST PRACTICE ADVICE 13	Open operative debridement maintains a role in the modern management of acute necrotizing pancreatitis in cases not amenable to less invasive endoscopic and/or surgical procedures.
BEST PRACTICE ADVICE 14	For patients with disconnected left pancreatic remnant after acute necrotizing mid-body necrosis, definitive surgical management with distal pancreatectomy should be undertaken in patients with reasonable operative candidacy. Insufficient evidence exists to support the management of the disconnected left pancreatic remnant with long- term transenteric endoscopic stenting.
BEST PRACTICE ADVICE 15	A step-up approach consisting of percutaneous drainage or endoscopic transmural drainage using either plas- tic stents and irrigation or self-expanding metal stents/lumen- apposing metal stents alone, followed by direct endoscopic necrosectomy, and then surgical debridement is reasonable, although approaches may vary based on the available clinical expertise.

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From: Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association Clinical Practice Update: Management of Pancreatic Necrosis. Gastroenterology. 2020 Jan;158(1):67-75.e1. doi: 10.1053/j.gastro.2019.07.064. Epub 2019 Aug 31. PMID: 31479658.

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co**M**pli**A**nce with evide**N**ce-based clini**C**al guidelines in the managemen**T** of acute bilia**R**y pancre**A**titis (**MANCTRA-1**).

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