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Practical Guidelines for Acute Pancreatitis

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Italian Association for the Study of the Pancreas

Key Words
Disease management · Diagnosis · Diagnostic imaging · Pancreatic necrosis · Pancreatitis · Prognosis · Therapeutics

Abstract
Introduction: The following is a summary of the official guidelines of the Italian Association for the Study of the Pancreas regarding the medical, endoscopic and surgical management of acute pancreatitis. ***Statements:*** Clinical features together with elevation of the plasma concentrations of pancreatic enzymes are the cornerstones of diagnosis (recommendation A). Contrast-enhanced computed tomography (CT) provides good evidence for the presence of pancreatitis (recommendation C) and it should be carried out 48–72 h after the onset of symptoms in patients with predicted severe pancreatitis. Severity assessment is essential for the selection of the proper initial treatment in the management of acute pancreatitis (recommendation A) and should be done using the APACHE II score, serum C-reactive protein and CT assessment (recommendation C). The etiology of acute pancreatitis should be able to be determined in at least 80% of cases (recommendation B). An adequate volume of intravenous fluid should be administered promptly to correct the volume deficit and maintain basal fluid requirements (recommendation A); analgesia is crucial for the correct treatment of the disease (recommendation A). Enteral feeding is indicated in severe necrotizing pancreatitis and it is better than total parenteral nutrition (recommendation A). The use of prophylactic broad-spectrum antibiotics reduces infection rates in CT-proven necrotizing pancreatitis (recommendation A). Infected pancreatic necrosis in patients with clinical signs and symptoms of sepsis is an indication for intervention, including surgery and radiological drainage (recommendation B). ***Conclusions:*** The participants agreed to revise the guidelines every 3 years in order to re-evaluate each question on the management of acute pancreatitis patients according to the most recent literature.

Introduction

In 1999, the Italian Association for the Study of the Pancreas (AISP) released a position statement on the management of acute pancreatitis [1]. The management of acute pancreatitis has changed in recent years. This has especially been due to the large availability of computed tomography (CT), improved intensive care facilities, knowledge of the central role of pancreatic infection, and refinements in surgical and other interventional techniques; thus, the AISP released a revised version of the

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position statement on acute pancreatitis in 2008 [2]. At the end of this paper, the authors pointed out that the contents of the position paper were not to be taken as a standard of care and that the AISP would release appropriate guidelines in the near future. Thus, the present guidelines of the AISP address the role of the management of acute pancreatitis including indications, timing and techniques of treatment. Developing and updating state-of-the-art clinical practice requires substantial time and resources. A large number of organizations produce guidelines on similar topics; furthermore, several studies have reported that the quality of published guidelines is highly variable [3]. In order to avoid unnecessary duplication and to use resources more efficiently, it has been suggested that adapting the existing guidelines could be more cost-efficient. For this reason, the Scientific Committee of the AISP has decided to use the existing guidelines on the management of acute pancreatitis and adapt them to the needs of the Italian population, using the ADAPTE method, a structured and stepwise approach for the adaptation of guidelines in order to produce updated and appropriate guidelines for the Italian population [4]. In fact, the ADAPTE method defines guideline adaptation as being a systematic approach in considering the use and/or modification of guidelines produced in a particular cultural and organizational setting for application in a different setting. The overall objective of adaptation is to take advantage of existing guidelines in order to enhance the efficient production and use of high-quality adapted guidelines. The adaptation process has been designed to ensure that the resulting and final recommendations address specific health questions relevant to the context of use and that they are suited to the needs, priorities, legislation, policies, and resources in the targeted setting, without undermining their validity. This explicit approach is intended to be useful to users such as local healthcare authorities and organizations, guideline development organizations and international healthcare organizations. The ADAPTE process consists of three main phases (set-up phase, adaptation phase, finalization phase), each with a set of modules. The organizing committee of the AISP guidelines on acute pancreatitis determined the project scope, organization and subcommittees (working group and multidisciplinary panel members), terms of reference and development of an adaptation plan.

The aim of this paper is to report how the AISP group reviewed the existing guidelines on the management of acute pancreatitis and how they proceeded with a specific adaptation for use in a different setting, using the ADAPTE process in order to release the AISP guidelines for the management of acute pancreatitis in Italy. The point of view of the members on some specific topics is also reported but this does not constitute a recommendation.

Methods

The AISP Working Group

The working group of the AISP guidelines on acute pancreatitis is reported in the Appendix.

Data Sources

We searched PubMed for all papers published from 1966 to 2007 using the term 'acute pancreatitis' with the following limits 'humans, practice guideline'. In addition, we searched the Cochrane Library and other databases (ScienceDirect, Scopus, Web of Science) for publications on these topics.

Procedure for Guideline Adaptation

The group had two face-to-face meetings in order to define the methodology of the adaptation of the existing guidelines and had monthly contacts by e-mail or telephone to discuss the steps of the adaptation method chosen (ADAPTE process) [4] (set-up phase).

In the adaptation phase, the group decided to follow the methodology reported below: (a) definition of clinical questions; (b) search for source guidelines; (c) assessment of the guidelines; (d) selection of the recommendations to create an adapted guideline for each clinical question, and (e) adaptation of the guideline format.

For the assessment of the selected guidelines (task c), the working group rated the global quality of the guidelines by using the AGREE (Appraisal of Guidelines, Research and Evaluation in Europe [5]) instrument and tools 11 (Sample Currency Survey of Guideline Developers), 12 (Sample Recommendation Matrices), 14 (Scientific Validity of Guidelines – Consistency between Evidence, Its Interpretation, and Recommendations) and 15 (Evaluation Sheet – Acceptability/Applicability). ADAPTE tool 11 was used to identify any gray areas which needed to be updated or to remove outdated guidelines; ADAPTE tool 12 was used to compare the content and evidence levels of the recommendations of individual guidelines; ADAPTE tool 14 was used to evaluate the consistency between the evidence, its interpretation and its transformation into recommendations, and ADAPTE tool 15 was used to decide whether the recommendations, graded according to the criteria listed in table 1, could be implemented in different contexts.

For the selection of the recommendations (task d), in order to define the final recommendations for each question, ADAPTE tool 17 (Reporting on Results of Update Process) was utilized to reject or accept the whole guideline and all of its recommendations, to accept the evidence summary of the guidelines, and to accept and modify specific recommendations.

When recommendations concerning the same topic were present in two or more guidelines, we combined these recommendations into one which explicitly advises the clinicians or patients as to the preferred course of action [6, 7].

Table 1. Grading of the recommendations used in the present guidelines. The strength of each recommendation depends on the category of the evidence supporting it and is graded according to the following system

Code	Quality of evidence	Definition	Explanation
A	High	Further research is very unlikely to change our confidence in the estimate of effect	It requires at least one randomized controlled trial of overall good quality and consistency addressing the specific recommendation as part of the body of literature
B	Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	It requires the availability of clinical studies without randomization on the topic of recommendation
C	Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	It requires evidence from expert committee reports or opinions, or the clinical experience of respected authorities, in the absence of directly applicable clinical studies of good quality

For the finalization phase of the ADAPTE process, the guidelines were revised by independent expert reviewers and, on October 16th, 2009, a consensus conference held in Milan during the 33rd National Congress of the AISP discussed and approved the final draft of these guidelines.

Ethics

Resources for meeting costs, project management and administrative support were covered by the AISP; the panel members accepted no honoraria. The guideline working group included physicians normally involved in the management of patients with acute pancreatitis. None of the panel members declared a conflict of interest.

Results

Literature Search

We included 21 publications which fulfilled the inclusion criteria and addressed the clinical questions of this analysis [1, 8–27]. Each of these publications was independently and thoroughly reviewed by the panel of experts.

Guideline Inclusion

The participants of the AISP working group selected nine [12, 15, 16, 18–23] of the 21 guidelines, basing their judgment on the ADAPTE procedure [4].

Nine appraisers of the working group evaluated the guidelines selected by means of the AGREE instrument [5]. AGREE assesses both the quality of the reporting and the quality of some aspects of the selected recommendations. It provides an evaluation of the predicted validity of a guideline, that is the likelihood that it will achieve its intended outcome. It does not assess the impact of a guideline on patient outcomes. AGREE consists of 23 key items organized into six standardized domain scores (0–100); each domain is intended to capture a separate dimension of guideline quality [5]. Homogeneity of the six domains among the nine selected guidelines was tested by one-way ANOVA and the guidelines were grouped into homogeneous subsets within each domain by means of the Duncan post-hoc test. The mean ± SD values of the six domains obtained by the nine appraisers for each selected guideline are shown in table 2. The guidelines included in the subset with the highest score are reported in bold. These subsets represent the clusters of guidelines within each domain which showed the highest agreement among the nine appraisers. The 'scope and purpose' domain showed the overall highest score among the nine guidelines while low agreement was found for the 'stakeholder involvement', 'applicability' and 'editorial independence' domains. The guidelines utilized for the purpose of this paper showed complete homogeneity for the 'scope and purpose' domain only, while the 'applicability' and 'editorial independence' domains reached high scores only for the UK guidelines [15]. All nine guidelines had at least one domain in the subsets with the highest scores; in particular, the UK guidelines had all six domains while the European Society for Parenteral and Enteral Nutrition (ESPEN) guidelines [16] had only two domains in these

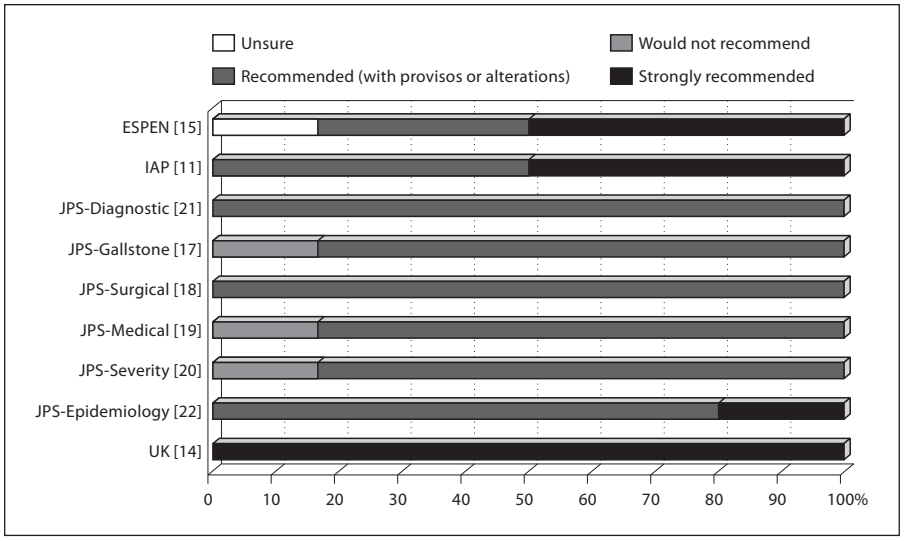

Fig. 1. Overall assessment of the selected guidelines according to the AGREE instrument (the judgment of six appraisers was available).

Table 2. Domain scores of the AGREE instrument: data are reported as mean ± SD

	Scope and purpose	Stakeholder involvement	Rigor of development	Clarity and presentation	Applicability	Editorial independence
ESPEN	**56.5 ± 20.3**	12.5 ± 10.4	30.6 ± 19.3	**48.6 ± 7.5**	15.7 ± 12.1	5.6 ± 12.7
IAP	**63.9 ± 13.8**	**26.4 ± 14.9**	**54.0 ± 15.5**	**49.3 ± 5.8**	23.1 ± 16.0	4.2 ± 8.8
JPS-Diagnostic	**62.0 ± 15.1**	**30.6 ± 16.7**	**34.5 ± 19.4**	**51.4 ± 9.3**	17.6 ± 17.4	8.3 ± 10.8
JPS-Gallstone	**61.1 ± 15.6**	**27.1 ± 10.4**	**40.5 ± 19.1**	40.3 ± 10.4	13.0 ± 13.9	5.6 ± 9.1
JPS-Surgical	**64.8 ± 14.9**	**28.5 ± 10.4**	**40.1 ± 18.7**	**47.9 ± 8.3**	14.8 ± 16.6	5.6 ± 9.1
JPS-Medical	**60.2 ± 15.5**	**27.1 ± 10.4**	**36.5 ± 18.0**	38.2 ± 10.1	12.0 ± 13.2	5.6 ± 9.1
JPS-Severity	**61.1 ± 20.0**	**27.1 ± 11.3**	**38.1 ± 16.5**	41.7 ± 8.8	13.0 ± 15.7	5.6 ± 9.1
JPS-Epidemiology	**61.5 ± 20.4**	**31.3 ± 14.6**	**40.6 ± 20.7**	29.7 ± 17.0	15.5 ± 14.8	6.3 ± 9.4
UK	**64.8 ± 16.0**	**27.8 ± 12.9**	**52.4 ± 22.4**	**56.9 ± 12.7**	**40.7 ± 12.8**	**41.7 ± 30.0**
Overall	61.8 ± 16.3	26.4 ± 13.0	40.8 ± 19.4	45.1 ± 12.4	18.5 ± 16.5	9.8 ± 17.3

Homogeneity subsets within each domain were evaluated by means of the Duncan post-hoc one-way analysis of variance. The values of the guidelines included in the subset with the highest score are shown in bold. These subsets represent the clusters of guidelines within each domain which showed the highest agreement among the nine appraisers.

subsets. Regarding the overall assessment of the quality of the nine guidelines, the appraisers judged all the guidelines as 'strongly recommended' or 'recommended with provisos or alterations' in a range which extended from 83 to 100% (fig. 1).

According to these findings, all nine guidelines met the criteria for answering specific clinical questions.

Questions and Answers

Question 1: Are clinical symptoms and signs useful in diagnosing acute pancreatitis?

Answer: Clinical features (abdominal pain and vomiting) together with elevation of the plasma concentrations of the pancreatic enzymes are the cornerstones of diagnosis (recommendation A). A correct diagnosis of acute pancreatitis should be made in all patients within 48 h of admission (recommendation C) [15].

Question 2: Which serum pancreatic enzyme should be measured in order to diagnose acute pancreatitis?

Answer: Although amylase is widely available and provides an acceptable level of accuracy in diagnosis, lipase

estimation, where available, is preferred for the diagnosis of acute pancreatitis (recommendation A) [15].

Question 3: What is the optimal examination for diagnosing acute pancreatitis?

Answer: Pancreatic imaging by contrast-enhanced CT provides good evidence for the presence or absence of pancreatitis (recommendation C) [15]. CT should be carried out 48–72 h from the onset of the symptoms in patients with predicted severe pancreatitis because the evidence of necrosis correlates well with the risk of other local and systemic complications [15]; patients with persisting organ failure, signs of sepsis, or deterioration in clinical status 6–10 days after admission will require an additional CT scan (recommendation B) [15].

Question 4: Is ultrasonography (US) effective in diagnosing acute pancreatitis?

Answer: US is often not helpful in diagnosing acute pancreatitis (recommendation C) [15].

Question 5: Is magnetic resonance imaging (MRI) effective in diagnosing acute pancreatitis?

Answer: Even if, in the last few years, this diagnostic modality has received particular attention in clinical practice, there were no recommendations about this topic in the guidelines considered.

Comment: Enhanced MRI is now comparable to contrast-enhanced CT in the early assessment of the severity of acute pancreatitis, and both methods are equally efficient in predicting the local and systemic complications of acute pancreatitis [28]. MRI has a potential advantage over CT in detecting bile duct lithiasis (>3 mm of diameter) and pancreatic hemorrhage [28].

Question 6: Is severity assessment necessary in the management of acute pancreatitis?

Answer: Severity assessment is essential for proper initial treatment in the management of acute pancreatitis (recommendation A) [21].

Question 7: What is the best severity scoring system for assessing the severity of acute pancreatitis?

Answer: Assessment of severity should be done by a scoring system such as Acute Physiology and Chronic Health Evaluation (APACHE) II (recommendation A) [21].

Comment: An APACHE II score >8 is important for determining treatment policy and identifying the need for transfer to a referral unit.

Table 3. CT grading of severity. Modified from the International Association of Pancreatology and based on the paper of Balthazar et al. [29]

a CT grades

	Points
CT grade	
(A) Normal pancreas	0
(B) Edematous pancreatitis	1
(C) B plus mild extrapancreatic changes	2
(D) Severe extrapancreatic changes including one fluid collection	3
(E) Multiple or extensive extrapancreatic collections	4
Necrosis	
None	0
Less than one third	2
Greater than one third or less than one half	4
Greater than one half	6

b CT severity index (CT grade + necrosis score)

	Complications
Severity index	
0–3	8%
4–6	35%
7–10	92%
Deaths	
0–3	3%
4–6	6%
7–10	17%

Question 8: Are blood tests useful for severity assessment of acute pancreatitis?

Answer: Serum C-reactive protein values are useful for severity assessment, but they may not reflect severity within the first 48 h after onset (recommendation A) [21].

Question 9: Is diagnostic imaging useful for severity assessment of acute pancreatitis?

Answer: Contrast-enhanced CT scanning and contrast-enhanced MRI play an important role in severity assessment (recommendation A) [21]. The CT severity index, as proposed by Balthazar et al. [29], should be used (table 3) (recommendation B) [15].

Comment: The panel writing the present guidelines would like to add a note on the possibility of assessing CT severity according to the Mortelè criteria based on multidetector CT scanning [30]. This index differs from the Balthazar severity index by the addition of a simplified evaluation of the presence and number of fluid collec-

Table 4. CT severity index and patient outcomes using a modified CT severity index [modified from 30]

a Modified CT severity index

Prognostic indicator	Points
Pancreatic inflammation	
Normal pancreas	0
Intrinsic pancreatic abnormalities with or without inflammatory changes in peripancreatic fat	2
Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis	4
Pancreatic necrosis	
None	0
≤30%	2
>30%	4
Extrapancreatic complications (one or more of the following: pleural effusion, ascites, vascular complications, parenchymal complications or gastro-intestinal tract involvement)	2

b Patient outcomes

Outcome factors	Mortelè CT severity index		
	mild pancreatitis (0–2 points)	moderate pancreatitis (4–6 points)	severe pancreatitis (8–10 points)
Patients, n	34	22	10
Length of hospital stay, days	3	8	12
Intervention or surgery	1%	1%	50%
Infection	1%	50%	70%
Organ failure	1%	1%	50%

Severity score: mild pancreatitis = 0–2 points; moderate pancreatitis = 4–6 points; severe pancreatitis = 8–10 points.

tions and the extent of pancreatic necrosis, and assessment, with different weighting factors, of the presence of extrapancreatic findings, such as pleural fluid, ascites, extrapancreatic parenchymal abnormalities (infarction, hemorrhage or subcapsular fluid collection), vascular complications (venous thrombosis, arterial hemorrhage or pseudoaneurysm formation) and involvement of the gastrointestinal tract (inflammation, perforation, or intramural fluid collection). The index proposed by Mortelè and the patient outcomes of those using it are reported in table 4. Another suggested possibility for scoring the severity of acute pancreatitis is the use of Extra-Pancreatic Inflammation on Computed Tomography (EPIC) score (table 5) [31].

Question 10: What are the indications for transferring patients with acute pancreatitis to a referral unit?

Answer: Every hospital in which there are acute admissions should have a single nominated clinical team to manage all patients with acute pancreatitis (recommendation C) [15]. Management in, or referral to, high-volume units is necessary for patients with extensive necrotizing pancreatitis or other complications who may require care in the intensive therapy unit or interventional radiological, endoscopic or surgical procedures (recommendation B) [15].

Question 11: How should the etiology of acute pancreatitis be assessed in an emergency situation?

Answer: The etiology of acute pancreatitis in an emergency situation should be assessed by: clinical history (gallstones, alcohol abuse, drugs [23, 32], metabolic and autoimmune disorders, the presence of affected family members, infections and trauma); laboratory tests such as serum liver function tests (serum ALT concentration three times the normal upper limit is the best single predictor of biliary etiology of acute pancreatitis within 48 h from the onset of the disease, but any significant increase

Table 5. The Extra-Pancreatic Inflammation on Computed Tomography (EPIC) score [modified from 31]

Signs of extrapancreatic inflammation	Points
Pleural effusion	
None	0
Unilateral	1
Bilateral	2
Ascites in any of these locations: perisplenic, perihepatic, interloop, pelvis	
None	0
One location	1
More than 1 location	2
Retroperitoneal inflammation	
None	0
Unilateral	1
Bilateral	2
Mesenteric inflammation	
Absent	0
Present	1

Score range: 0–7. Score 0–3: mortality 0%; score 4–7: mortality 67%.

in liver biochemistry may suggest gallstone pancreatitis) [33–35], measurement of serum calcium and serum triglycerides (when available in emergency situations) and external US (recommendation C) [15, 22, 23].

Question 12: What are the criteria for a definitive etiological assessment of acute pancreatitis?

Answer: The etiology of acute pancreatitis should be able to be determined in at least 80% of cases (recommendation B) [15].

When acute pancreatitis has been classified as idiopathic after the emergency assessment, additional investigation is warranted; these examinations need to be performed after recovery from the acute episode (recommendation C) [15, 22]: repeat external US [15], laboratory tests (IgG4 and autoimmune markers [15, 36]), repeat measurement of fasting serum triglycerides and serum calcium [15] and endoscopic US to search for lithiasis or sludge, chronic pancreatitis, neoplasm and anatomical abnormalities such as pancreas divisum, choledochal cysts, pancreatobiliary maljunction, duodenal duplication and paravaterian diverticulum [22, 37–40]. Many infectious agents have been associated with acute pancreatitis [41], but routine antibody titers for assessing a possible infectious etiology are not recommended in clinical practice. In the case of recurrent idiopathic acute pancreatitis, further investigation may be appropriate, such as genetic tests (analysis of mutations in exon 3 of SPINK-1, exon 2–3 of PRSS-1 and available exons of CFTR) [42].

Comment: Unlike the previous guidelines [15], we do not recommend either ERCP, for sampling the bile and evaluating the presence of crystals at microscopy, or sphincter of Oddi manometry. ERCP alone without tissue sampling is not considered in the ASGE endoscopic guidelines [43], and sphincter of Oddi manometry is not performed in European clinical practice because of the risk of severe complications [44]. The exact role of MRCP with secretin stimulation in patients with recurrent idiopathic acute pancreatitis needs to be defined [45].

Question 13: Fluid replacement in the management of acute pancreatitis: when and how?

Answer: An adequate volume of intravenous fluid should be administered promptly in order to correct the volume deficit and maintain basal fluid requirements (recommendation A) [20].

Comment: Fluid needs should be reassessed at frequent intervals, and the rate of infusion may need to be adjusted in patients with cardiac, renal or liver disease because they are at risk for developing volume overload.

Question 14: Should pain be treated in acute pancreatitis?

Answer: Acute pancreatitis is accompanied by persistent severe abdominal pain. Analgesia is crucial (recommendation A) [20].

Comment: The pain associated with acute pancreatitis may cause anxiety in patients and adversely affect their clinical course; this may include respiratory distress which should be relieved shortly after it develops. The non-narcotic analgesic buprenorphine has an effect superior to procaine and, unlike procaine, it does not exacerbate the pathology of acute pancreatitis by including the contraction of the sphincter of Oddi. Buprenorphine has an analgesic effect similar to that of pethidine [20].

Question 15: Is nasogastric suction necessary? Are H_2 blockers or proton pump inhibitors necessary?

Answer: Nasogastric suction through a nasogastric tube is unnecessary in patients with acute pancreatitis unless the disease is associated with paralytic ileus and/or frequent vomiting (recommendation B) [20]. H_2 blockers are also unnecessary unless a stress ulcer develops (recommendation C) [20].

Comment: No indications for proton pump inhibitor use are present in the guidelines evaluated.

Question 16: Is the continuous intravenous administration of protease inhibitors useful in treating severe acute pancreatitis?

Answer: Continuous intravenous infusion of an elevated dose of protease inhibitor reduces the incidence of complications in the early phase of severe acute pancreatitis (recommendation B) [20].

Comment: Although the efficacy of protease inhibitors in severe acute pancreatitis is still a matter of controversy, their use is recommended only by Japanese authors [20, 46] and the medical community should be aware of this.

Question 17: What is the best nutritional support in severe acute pancreatitis?

Answer: Enteral nutrition starting in the early phase of severe acute pancreatitis is superior to total parenteral nutrition unless paralytic ileus is present (recommendation A) [20]. Tube feeding is possible in the majority of patients but may need to be supplemented by the parenteral route (recommendation A) [16]. Continuous tube feeding with peptide-based formulae is possible in the majority of patients; the jejunal route is recommended if gastric feeding is not tolerated (recommendation C) [16]. In severe acute pancreatitis, it is also possible to combine total parenteral nutrition and enteral nutrition when adequate caloric support cannot be obtained by the enteral route alone (recommendation C) [16].

Question 18: Is prophylactic antibiotic administration necessary for the prevention of infections in severe acute pancreatitis? What is the antibiotic of choice for the prophylaxis of infected pancreatic necrosis?

Answer: The use of prophylactic broad-spectrum antibiotics reduces infection rates in CT-proven necrotizing pancreatitis but may not improve survival (recommendation A) [12]. However, broad-spectrum antibiotics with good tissue penetration are necessary to prevent infection in severe acute pancreatitis (recommendation A) [20].

Comment: The panel of experts writing the present guidelines suggests the use of the carbapemenic family as recommended by Villatoro et al. [47] at a dosage of 1,500 mg/day for at least 14 days. We should also point out that, in a recent meta-analysis [48], the authors concluded that antibiotic prophylaxis is not protective in severe acute pancreatitis. However, we should call attention to the fact that there are several limitations of the studies considered in this meta-analysis inherent in the primary study design, such as inclusion criteria, duration and dosage of antibiotics, assessment of the severity of disease, nutritional support, and resuscitative measures, the relatively small number of patients in each individual study and different outcome measurements. In addition, the inclusion of non-blinded studies in this meta-analysis limits the findings because many patients should have received surgical intervention when investigators realized that they were not receiving antibiotics [49].

Question 19: What is the timing for refeeding in mild acute pancreatitis?

Answer: In mild acute pancreatitis, enteral nutrition is unnecessary if the patient can consume normal food after 5–7 days; oral food intake should be tried as soon as possible (recommendation B) [16].

Comment: This recommendation should be taken with caution because the guideline reporting it [16] had a low score in the 'rigor of development' domain when using the AGREE instrument (table 2).

Question 20: What is the optimal diet for refeeding in mild acute pancreatitis?

Answer: Oral refeeding with a diet rich in carbohydrates and protein and low in fat (<30% of total energy intake) is recommended (recommendation C) [16].

Comment: This recommendation should be taken with caution because the guideline reporting it [16] had a low score in the 'rigor of development' domain when using the AGREE instrument (table 2). However, some authors have suggested that patients can eat light food only when the pancreatic gland has returned to normal at imaging [50]. Other authors have suggested that initiating oral nutrition after mild acute pancreatitis with a low-fat solid diet is safe and provides more calories than a clear liquid diet, but did not result in a shorter length of hospitalization [51, 52]. Thus, our recommendation is to initiate refeeding with a low-fat solid diet when pain disappears; in fact, in mild acute pancreatitis, immediate oral feeding is feasible and safe and may accelerate recovery without adverse gastrointestinal events [53]. It is also necessary to determine the exocrine pancreatic function in patients who have experienced an acute episode of pancreatitis in order to cure possible maldigestion; for example, in patients with alcoholic pancreatitis, enzyme supplementation is necessary during refeeding if the elastase-1 fecal determination is clearly abnormal [54].

Question 21: Is an emergency endoscopic approach beneficial for the treatment of jaundice and/or cholangitis in patients with acute pancreatitis?

Answer: An emergency endoscopic approach is beneficial in patients with acute pancreatitis in whom bile duct

obstruction is suspected or where there is evidence of cholangitis (recommendation A) [18].

Comment: The role of early ERCP in patients with severe acute biliary pancreatitis is still controversial [55, 56]; we believe that an emergency endoscopic sphincterotomy is beneficial in patients with severe acute pancreatitis due to gallstones, especially in the case of associated cholangitis. To have effective results, a specialized medical institution is required with experienced specialists and a special unit whose staff is capable of carrying out emergency ERCP/ES examinations and dealing with bleeding and other complications.

Question 22: When should laparoscopic cholecystectomy be undertaken in patients with gallstone pancreatitis?

Answer: Laparoscopic cholecystectomy should be considered after recovery from an attack of gallstone pancreatitis and, like an open cholecystectomy, should be performed during the same hospital stay (choledochotomy and common bile duct clearance should be performed as required) (recommendation B) [18]. Laparoscopic cholecystectomy in mild gallstone-associated acute pancreatitis should be performed as soon as the patient has recovered and during the same hospital admission (recommendation B) [12]. In severe gallstone-associated acute pancreatitis, cholecystectomy should be delayed until there is sufficient resolution of the inflammatory response and clinical recovery (recommendation B) [12].

Question 23: What is the indication for surgical intervention in necrotizing pancreatitis?

Answer: Infected pancreatic necrosis in patients with clinical signs and symptoms of sepsis is an indication for intervention including surgery and radiological drainage (recommendation B) [12].

Question 24: Which procedure will best result in a definitive diagnosis of infected pancreatic necrosis?

Answer: Fine needle aspiration with a culture of the tissue obtained should be performed to differentiate between sterile and infected pancreatic necrosis in patients with sepsis (recommendation B) [12].

Question 25: How should sterile pancreatic necrosis be managed?

Answer: Patients with sterile pancreatic necrosis should be managed conservatively and undergo intervention only in selected cases, such as those patients with multiorgan failure who do not improve despite maximal therapy in the intensive care unit (recommendation B) [12].

Question 26: What is the optimal timing for surgical intervention?

Answer: Surgery earlier than 14 days after onset of the disease is not recommended in patients with necrotizing pancreatitis unless there are specific indications, such as multiorgan failure, which do not improve despite maximal therapy, and in those who develop abdominal compartment syndrome (recommendation B) [12].

Question 27: What is the optimal surgical procedure for infected pancreatic necrosis?

Answer: Necrosectomy is recommended as the optimal surgical procedure for infected pancreatic necrosis (recommendation A) [19].

Question 28: How should a pancreatic abscess be managed?

Answer: Surgical or percutaneous drainage should be performed for a pancreatic abscess (recommendation C) [19]. If the clinical findings of a pancreatic abscess are not improved by percutaneous drainage, surgical drainage should be performed immediately (recommendation B) [19].

Question 29: What is the indication for percutaneous intervention in necrotizing pancreatitis?

Answer: Even if, in the last few years, this therapeutic modality has received particular attention in clinical practice, there were no recommendations about this topic in the guidelines considered.

Comment: The panel writing these guidelines suggests that the presence of well-demarcated necrosis could be treated using percutaneous drainage; in selected cases, this approach can be combined with a minimally invasive surgical approach (videoscopic assisted retroperitoneal debridement) [57]. In any case, the clinical condition of the patient should be taken into account when deciding on the therapeutic approach.

Question 30: What are the indications for drainage treatment in pancreatic pseudocysts?

Answer: Pancreatic pseudocysts which give rise to symptoms and complications or in which the diameter increases require drainage treatment (recommendation B) [19].

Question 31: What is the indication for surgical intervention in pancreatic pseudocysts?

Answer: Hemorrhagic pseudocysts or pseudocysts which do not tend to improve in response to percutaneous or endoscopic drainage should be managed surgically (recommendation C) [19].

Question 32: What is the indication for endoscopic intervention in pancreatic pseudocysts?

Answer: This indication was not present in the guidelines evaluated even if there are many suggestions for the treatment of pseudocysts using an interventional non-surgical approach.

Comment: The endoscopic approach can be performed in the case of favorable anatomical contiguity of the wall with the adjacent viscera (stomach, duodenum) and a minimum diameter of 5–6 cm. The authors of the present guidelines suggest that EUS-guided drainage may be safer than conventional endoscopic drainage [58].

Conclusions

The participants agreed to revise the guidelines every 3 years in order to re-evaluate each question on the management of acute pancreatitis patients according to the most recent literature.

Appendix

Working Group of the AISP on Acute Pancreatitis

Group	Member	Specialization	Address	City	Role
Governing of the guidelines	Raffaele Pezzilli	Internal medicine	Pancreas Unit, Department of Digestive Diseases and Internal Medicine, Sant'Orsola-Malpighi Hospital	Bologna	Question formulation
	Alessandro Zerbi	Surgery	Pancreas Unit, Department of Surgery, Scientific Institute Humanitas	Rozzano (Milan)	Question formulation
	Gianfranco Delle Fave	Gastroenterology	Digestive and Liver Disease Unit, 2nd School of Medicine, University La Sapienza	Rome	AISP deputy
	Valerio Di Carlo	Surgery	Pancreas Unit, Department of Surgery, Vita-Salute University, San Raffaele Hospital	Milan	AISP deputy
Methodology and monitoring	Maria Pia Fantini	Public health	Department of Medicine and Public Health, University of Bologna	Bologna	Coordinator
	Laura Dall'Olio	Public health	Department of Medicine and Public Health, University of Bologna	Bologna	Monitor
	Giuliana Fabbri	Public health	Department of Medicine and Public Health, University of Bologna	Bologna	Monitor
	Antonio M. Morselli-Labate	Biomedical technologies	Department of Clinical Medicine, University of Bologna	Bologna	Statistical analysis
Diagnostic and severity assessment	Claudio Bassi	Surgery	Department of Surgery, University of Verona, GB Rossi Hospital	Verona	Coordinator
	Lucia Calculli	Radiology	Cardiothoracic Radiology, Sant'Orsola-Malpighi Hospital	Bologna	Panelist
	Laura Castoldi	Surgery	Department of Surgery and Emergency Surgery, Maggiore, Mangiagalli e Regina Elena Hospitals, IRCCS Foundation	Milan	Panelist
	Piergiorgio Rabitti	Internal medicine	Internal Medicine, Cardarelli Hospital	Naples	Panelist
Etiology assessment	Gianpaolo Balzano	Surgery	Pancreas Unit, Department of Surgery, Vita-Salute University, San Raffaele Hospital	Milan	Coordinator
	Ezio Gaia	Gastroenterology	Department of Internal Medicine, S. Luigi Gonzaga Hospital	Orbassano	Panelist
	Massimiliano Mutignani	Gastroenterology	Surgical Digestive Endoscopy, Catholic University of the Holy Heart, A. Gemelli Hospital	Rome	Panelist

Appendix (continued)

Group	Member	Specialization	Address	City	Role
Medical and nutritional treatment	Generoso Uomo	Internal medicine	Internal Medicine, Cardarelli Hospital	Naples	Coordinator
	Luca Brazzi	Anesthesiology	Institute of Anesthesiology and Intensive Care, Maggiore Hospital	Milan	Panelist
	Alessandro D'Alessandro	Gastroenterology	Department of Gastroenterology, San Bortolo Hospital	Vicenza	Panelist
	Luca Frulloni	Gastroenterology	Department of Biomedical and Surgical Sciences, University of Verona	Verona	Panelist
	Paolo Scarpellini	Microbiology	Clinic of Infectious Diseases, Vita-Salute University, San Raffaele Hospital	Milan	Panelist
Endoscopic treatment	Armando Gabbrielli	Gastroenterology	Department of Biomedical and Surgical Sciences, University of Verona	Verona	Coordinator
	Marco Del Chiaro	Surgery	Regional Referral Center for Pancreatic Diseases Treatment, University of Pisa	Pisa	Panelist
	Alberto Mariani	Gastroenterology	Department of Gastroenterology, Vita-Salute University, San Raffaele Hospital	Milan	Panelist
Surgical treatment	Paolo De Rai	Surgery	Department of Surgery and Emergency Surgery, Maggiore, Mangiagalli e Regina Elena Hospitals, IRCCS Foundation	Milan	Coordinator
	Paola Billi	Gastroenterology	Unit of Gastroenterology and Digestive Endoscopy, Maggiore Hospital	Bologna	Panelist
	Riccardo Casadei	Surgery	Department of Surgery, Sant'Orsola-Malpighi Hospital	Bologna	Panelist
	Roberto Nicoletti	Radiology	Department of Radiology, Vita-Salute University, San Raffaele Hospital	Milan	Panelist

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