

Evidence-based clinical practice guidelines for acute pancreatitis: proposals

TOSHIHIKO MAYUMI^{1,*}, HIDEKI URA^{2,*}, SHINJYU ARATA^{3,*}, NOBUYA KITAMURA^{4,*}, IKUO KIRIYAMA^{5,*}, KAZUHIKO SHIBUYA^{6,*}, MIHO SEKIMOTO^{7,*}, NAOKI NAGO^{8,*}, MASAHIKO HIROTA^{9,*}, MASAHIKO YOSHIDA^{10,*}, YASUO ITO^{11,*}, KOICHI HIRATA^{12,*}, and TADAHIRO TAKADA^{10,**}

¹ Department of Emergency Medicine and Intensive Care, Nagoya University School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya, Aichi 466-8560, Japan

² Department of Traumatology and Critical Care Medicine, Sapporo Medical University School of Medicine, Sapporo, Japan

³ Critical Care Emergency Center, Yokohama City University School of Medicine, Yokohama, Japan

⁴ Department of Emergency and Critical Care Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan

⁵ Department of Gastroenterology, Ogaki Municipal Hospital, Ogaki, Japan

⁶ Division of Gastroenterological Surgery, Tohoku University Graduate School of Medicine, Sendai, Japan

⁷ Department of General Medicine, Kyoto University School of Medicine, Kyoto, Japan

⁸ Tsukude National Health Insurance Clinic, Minami-Shitara, Japan

⁹ Second Department of Surgery, Kumamoto University Medical School, Kumamoto, Japan

¹⁰ Department of Surgery, Teikyo University School of Medicine, Tokyo, Japan

¹¹ Department of Pediatric Surgery, Kyorin University School of Medicine, Mitaka, Tokyo, Japan

¹² First Department of Surgery, Sapporo Medical University School of Medicine, Sapporo, Japan

Abstract

Background/Purpose. To provide a framework for clinicians to manage acute pancreatitis, evidence-based guidelines have been developed by the Japanese Society of Abdominal Emergency Medicine.

Methods. Evidence was collected by a systematic search of MEDLINE and Japana Centra Revuo Medicina. A total of 1348 papers were reviewed and levels of evidence were assessed. Practical recommendations were also graded.

Results. The present guidelines consist of introductions, a summary of recommendations, practice algorithms, definitions, epidemiology, diagnosis, severity assessment, and therapy. The main points of recommendation in these guidelines are: (1) measuring lipase for the diagnosis of acute pancreatitis (recommendation grade [RG], A). (2) The Severity of acute pancreatitis should be assessed using a scoring system, such as that of the Japanese Ministry of Health and Welfare or Acute Physiology and Chronic Health Evaluation (APACHE) II (RG, A). (3) Enhanced computed tomography (CT) should be used for assessment of degree of pancreatic necrosis and inflammation (RG, B). (4) Prophylactic antibiotic administration should be used for severe pancreatitis (RG, A), but not for mild to moderate pancreatitis (RG, D).

(5) Gabexate mesilate should be used for severe pancreatitis (RG, B). (6) Enteral feeding should be used for all pancreatitis (RG, B). (7) Continuous hemodiafiltration and continuous arterial infusion of proteinase inhibitor and antibiotics may be of benefit (RG, C). (8) Fine-needle aspiration should be done for the diagnosis of infectious pancreatic necrosis, and if positive, necrosectomy is indicated (RG, A).

Conclusions. These guidelines provide useful information for physicians to manage this troublesome disease.

Key words Evidence-based medicine · Acute pancreatitis · Guidelines · Recommendation · Scoring system

Background and purpose of guidelines

There are several clinical guidelines and recommendations for acute pancreatitis.^{1,2} During recent years many diagnostic and therapeutic methods have been developed for the disease. But some of these interventions for acute pancreatitis are used only in Japan, and not in other countries. In this situation, differences in interventions for the disease between institutions are increasing. However, despite these attempts to intervene in the disease, the mortality rate of severe acute pancreatitis is still 20%–30%.^{3,4} Therefore, to assist physicians in clinical decision-making, by describing a range of generally acceptable approaches for the diagnosis and management of acute pancreatitis, and to inform patients and families about these approaches, the Japanese Society of Emergency Abdominal Medicine

Offprint requests to: T. Mayumi

* Working Group for the Practical Guidelines for Acute Pancreatitis of the Japanese Society of Emergency Abdominal Medicine

** President of the Japanese Society of Emergency Abdominal Medicine, Tokyo, Japan

Received: May 6, 2002 / Accepted: May 17, 2002

(JSEAM) has contributed to producing practice guidelines for the disease. The Working Group for the Practical Guidelines for Acute Pancreatitis of the JSEAM systematically reviews the literature and directs evidence-based practical guidelines, with indications of levels of evidence in the literature and grades of recommendations (hereafter, grade) for interventions. The guidelines are supported and funded by the JSEAM.

These guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the physician and patient in light of all of the circumstances presented by that patient.

The guidelines were presented for discussion at the JSEAM meetings in 2001 and 2002, and on the internet homepage. These guidelines will be approved by JSEAM in 2002 and published in the journal of the JSEAM and updated on the JSEAM internet homepage (<http://plaza.umin.ac.jp/~jaem/>). Therefore, in this article, we will describe the process of the formation of the guidelines, the algorithms, and a brief summary of recommendations in the guidelines.

Process of formation of guidelines

MEDLINE (1960–2000) was searched with the MeSH (explode) terms “pancreatitis”, “acute necrotizing pancreatitis”, and “alcoholic pancreatitis” and the key word “pancreatitis”. Over 28000 papers were searched for these terms, limited to human studies and those re-

ported in English or Japanese, and 14821 papers were listed. Japana Centra Revuo Medicina (1991–2000) was also searched, with “pancreatitis” as the key word. In this way, 1475 papers were listed. Thus, a total of 16296 papers were selected, and 1348 papers and reports of the Working Group for Acute Pancreatitis of the Japanese Ministry of Health were reviewed and assessed according to the levels of evidence and grades of recommendations of the Oxford Centre for Evidence-Based Medicine (Table 1).⁵ Practical recommendations were also graded according to suggestions in a previous report (Table 2).⁶

The guidelines were presented on the JSEAM homepage, and opinions were collected via the internet. After each presentation and discussion at the JSEAM meetings in both 2001 and 2002, the Working Group for the Practical Guidelines for Acute Pancreatitis modified these guidelines based on these collected opinions. The guidelines are still under development and will be approved by the JSEAM in 2002. The content and evidence base of the guidelines will be reviewed in 4 years' time.

Summary of the practice guidelines

The guidelines consist of introductions, a summary of recommendations (Table 3), practice algorithms (Figs. 1–6), definitions, epidemiology, diagnosis, severity assessment, and therapy. The main points are easily understood using practice algorithms and the summary of recommendations.

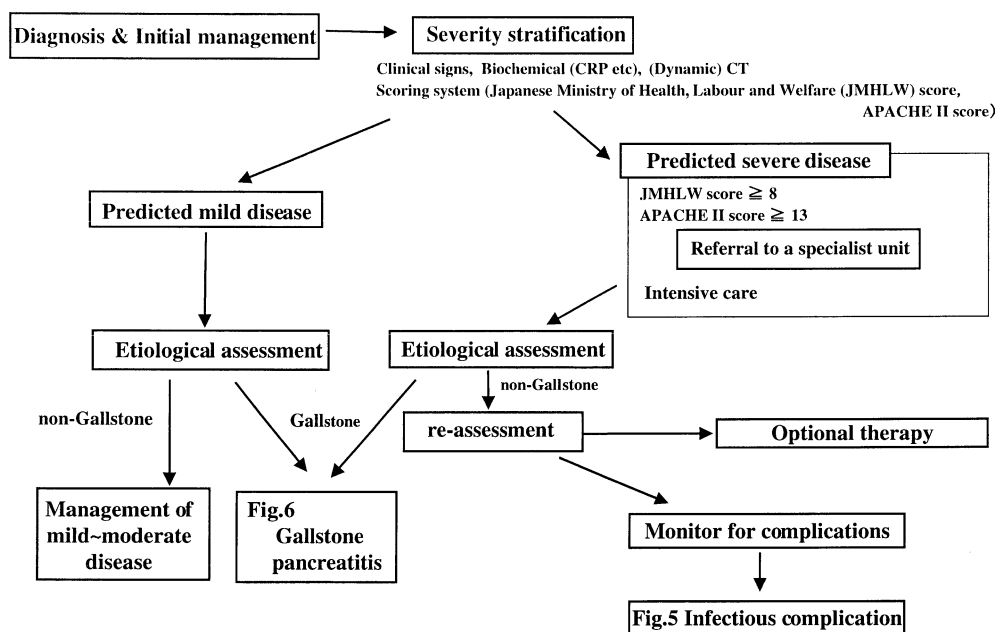


Fig. 1. Summary of management steps in acute pancreatitis. *CRP*, C-reactive protein; *CT*, computed tomography; *APACHE*, Acute Physiology and Chronic Health Evaluation

Table 1. Levels of evidence: 23 November, 1999 (<http://cebmrj2.ox.ac.uk/docs/levels.html>)

Level of evidence	Therapy/prevention, Etiology/harm	Prognosis	Diagnosis	Economic analysis
1a	SR (with homogeneity ^a) of RCTs	SR (with homogeneity ^a) of inception cohort studies; or a CPG validated on a test set	SR (with homogeneity ^b) of level 1 diagnostic studies; or a CPG validated on a test set	SR (with homogeneity ^a) of level 1 economic studies
1b	Individual RCT (with narrow confidence interval ^b)	Individual inception cohort study with ≥80% follow-up	Independent blind comparison of an appropriate spectrum of consecutive patients, all of whom have undergone both the diagnostic test and the reference standard	Analysis comparing all (critically validated) alternative outcomes against appropriate cost measurement, and including a sensitivity analysis incorporating clinically sensible variations in important variables
1c	All or none ^c	All or none case-series ^d	Absolute SpPins and SnNouts ^e	Clearly as good or better ^f , but cheaper Clearly as bad or worse, but more expensive Clearly better or worse at the same cost
2a	SR (with homogeneity ^a) of cohort studies	SR (with homogeneity ^a) of either retrospective cohort studies or untreated control groups in RCTs	SR (with homogeneity ^b) of level ≥2 diagnostic studies	SR (with homogeneity ^a) of level ≥2 economic studies
2b	Individual cohort study (including low-quality RCT; e.g., <80% follow-up) a test set	Retrospective cohort study or follow-up of untreated control patients in an RCT; or CPG not validated in non-consecutive patients, or	Any of: • Independent blind or objective comparison • Study performed in a set of analysis incorporating clinically confined to a narrow spectrum of study individuals (or both), all of whom have undergone both the diagnostic test and the reference standard • A diagnostic CPG not validated in a test set	Analysis comparing a limited number of alternative outcomes against appropriate cost measurement, and including a sensitivity analysis incorporating clinically sensible variations in important variables
2c	“Outcomes” research	“Outcomes” research		
3a	SR (with homogeneity ^a) of case-control studies			
3b	Individual case-control study		Independent blind comparison of an appropriate spectrum, but the reference standard was not applied to all study patients	Analysis without accurate cost measurement, but including a sensitivity analysis incorporating clinically sensible variation in important variables

Table 1. Continued

Level of evidence	Therapy/prevention, Etiology/harm	Prognosis	Diagnosis	Economic analysis
4	Case-series (and poor quality cohort and case-control studies ^g)	Case-series (and poor quality prognostic cohort studies ^h)	Any of: <ul style="list-style-type: none"> • Reference standard was unobjective, unblinded, or not independent • Positive and negative tests were verified using separate reference standards • Study was performed in an inappropriate spectrum^d of patients 	Analysis with no sensitivity analysis
5	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or “first principles”	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or “first principles”	Expert opinion without explicit critical appraisal, or based on physiology, bench research, or “first principles”	Expert opinion without explicit critical appraisal, or based on economic theory

1. These levels were generated in a series of iterations among members of the NHS R&D Centre for Evidence-Based Medicine (Chris Ball, Dave Sackett, Bob Phillips, Brian Haynes, and Sharon Straus)

2. Recommendations based on this approach apply to “average” patients and may need to be modified in light of an individual patient’s unique biology (risk, responsiveness, etc.) and preferences about the care they receive

3. Users can add a minus-sign “-” to denote the level that fails to provide a conclusive answer because of:

- EITHER a single result with a wide confidence interval (such that, for example, an absolute risk reduction (ARR) in an RCT is not statistically significant but whose confidence intervals fail to exclude clinically important benefit or harm)
- OR an SR with troublesome (and statistically significant) heterogeneity

⇒ Such evidence is inconclusive, and therefore can only generate grade D recommendations

SR, Systematic review; RCT, randomized controlled trial; CPG, clinical prediction guide

^aBy homogeneity we mean a systematic review that is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need be worrisome, and not all worrisome heterogeneity need be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a “-” at the end of their designated level

^bSee note no. 2 above for advice on how to understand, rate, and use trials or other studies with wide confidence intervals

^cMet when all patients died before the treatment became available, but some now survive on it; or when some patients died before the treatment became available, but none now die on it

^dMet when there are no reports of anyone with this condition ever avoiding (all) or suffering from (none) a particular outcome (such as death)

^eAn “Absolute SpPin” is a diagnostic finding whose Specificity is so high that a Positive result rules-in the diagnosis. An “Absolute SnNout” is a diagnostic finding whose Sensitivity is so high that a Negative result rules-out the diagnosis

^fGood, better, bad, and worse refer to the comparisons between treatments in terms of their clinical risks and benefits

^gBy poor quality cohort study, we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and nonexposed individuals, and/or failed to identify or appropriately control known cofounders, and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study, we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same blinded, objective way in both cases and controls, and/or failed to identify or appropriately control known cofounders

^hBy poor quality prognostic cohort study, we mean one in which sampling was biased in favor of patients who already had the target outcome, or the measurement of outcomes was accomplished in fewer than 80% of study patients, or outcomes were determined in an unblinded, nonobjective way, or there was no correction for confounding factors

Table 2. Grading system for ranking recommendations in clinical guidelines^a

A	Good evidence to support a recommendation for use
B	Moderate evidence to support a recommendation for use
C	Poor evidence to support a recommendation
D	Moderate evidence to support a recommendation against use
E	Good evidence to support a recommendation against use

^aFrom reference 6**Outline of management of acute pancreatitis**

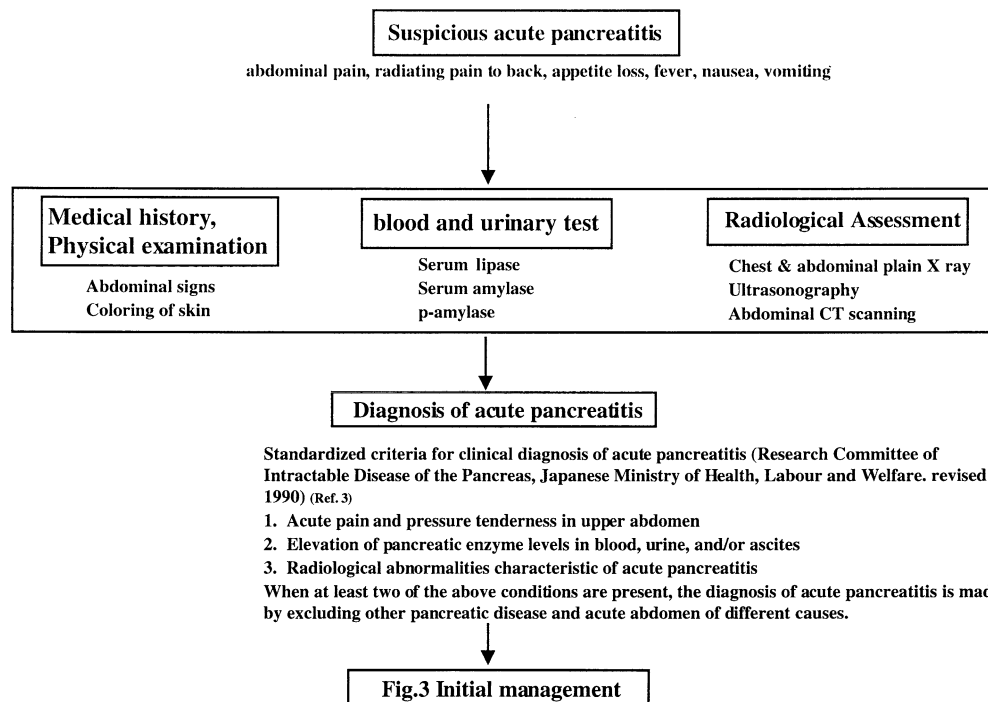
The management of acute pancreatitis is divided into three steps. The first step includes diagnosis and initial management. The second step includes, running simultaneously, severity stratification, management according to disease severity, and etiological assessment. The final step involves the detection and management of complications.

Table 3. Summary of recommendations

Etiology of acute pancreatitis should be determined in 75%–80% of cases and no more than 25% should be classified as “idiopathic” (grade B).
Lipase is superior to amylase in the diagnosis of acute pancreatitis (grade A).
Chest and abdominal X-rays should be taken in all patients with possible acute pancreatitis (grade A).
Abdominal ultrasonography should be examined in all patients with possible acute pancreatitis on admission (grade A).
Unless diagnosis is determined from clinical signs, laboratory findings, and ultrasonography, or if is not defined, abdominal computed tomography (CT) should be examined (grade A).
Although magnetic resonance imaging (MRI) is not sufficient alone at present, MRI is useful in the diagnosis of acute pancreatitis (grade C).
Unless there is confirmed etiology of acute pancreatitis or gallstone pancreatitis, endoscopic retrograde cholangiopancreatography (ERCP) is not necessary in the diagnosis of acute pancreatitis (grade E).
ERCP is examined in recurrent pancreatitis and possible bile duct stone (grade A).
The use of proteinase inhibitor is recommended with ERCP in acute pancreatitis (grade B).
Severity stratification of acute pancreatitis is necessary to achieve adequate initial management of the disease (grade A).
Although in some cases clinical signs are useful, these are usually used in combination with other data in the stratification of the severity of acute pancreatitis (grade B).
The use of clinical signs only is not sufficient for early stratification of the severity of acute pancreatitis (grade D).
Neither the use of serum amylase nor that of lipase is useful in stratification of the severity of acute pancreatitis (grade D).
Serum C-reactive protein (CRP) at 48h after onset of acute pancreatitis is useful in stratification of the severity of acute pancreatitis (grade A).
Because obesity is a risk factor in the prognosis of acute pancreatitis, body mass index is useful in stratification of the severity of acute pancreatitis (grade B).
Because there is correlation of the severity of acute pancreatitis with both necrosis and the degree of expansion of inflammatory changes, enhanced CT is necessary for the determination of these factors (grade B).
In stratification of the severity of acute pancreatitis, using a scoring system is recommended (grade A).
For a scoring system for the severity of acute pancreatitis, the scoring system of the Japan Ministry of Health, Labour and Welfare and the Acute Physiology and Chronic Health Evaluation (APACHE) II score is recommended within 24h, and the Ranson score and Glasgow score are also useful in 24–48h. Physicians should determine the severity of acute pancreatitis after diagnosis of the disease (grade A).
All patients with severe pancreatitis should be managed in, or referred to, a specialist unit setting with full monitoring and system support and interventional radiological, endoscopic, or surgical procedures (grade B).
In mild to moderate acute pancreatitis, nasogastric tube drainage is not necessary in most cases (grade D).
In severe and possibly severe acute pancreatitis, broadspectrum antibiotics should be used prophylactically (grade A). But in mild to moderate cases, prophylactic antibiotics should not be used (grade D).
High doses of gabexate mesilate may decrease the morbidity of acute pancreatitis (grade B).
The effectiveness of histamine H2 antagonists is not confirmed (grade D).
No efficacy has been confirmed for long-acting formulations of somatostatin (octreotide) in regard to either mortality or morbidity in severe acute pancreatitis (grade D).
No efficacy is proven for octreotide for the prevention of acute pancreatitis after ERCP (grade D).
Although enteral nutrition has not been proven to improve survival in acute pancreatitis, it probably reduces complications.
Enteral nutrition delivered with a jejunal inserted tube should be started early in the course of acute pancreatitis if possible (grade B).
Total parenteral nutrition (TPN) has not been proven efficient in acute (mild to moderate) pancreatitis (grade D).
Selective digestive decontamination (SDD) may decrease infectious complications and mortality in severe acute pancreatitis (grade C).
The efficacy of peritoneal lavage in acute pancreatitis is not proven (grade D).
Early induction of continuous hemodiafiltration (CHDF) in severe acute pancreatitis may prevent multiple organ failure (grade C).
Continuous arterial infusion of proteinase inhibitor and antibiotics may decrease mortality and infectious complications of necrotizing pancreatitis (grade C).

Table 3. *Continued*

Urgent ERCP with/without endoscopic sphincterotomy is indicated in gallstone pancreatitis with prolonged biliary obstruction with jaundice, cholangitis, or severe pancreatitis (grade B).
 Suspected infectious necrosis requires evaluation by radiologically guided fine-needle aspiration (grade A).
 In patients with infectious necrosis, necrosectomy is required (grade A).
 Most noninfected necrosis recovers of itself, but if there is progression of organ dysfunction or no signs of improvement, with undeniable evidence of infection, operation is a relative indication (grade B).
 Necrosectomy is the standard operative method for necrotic pancreatitis (grade B).
 Conventional drainage is not recommended after necrosectomy (grade D).
 At present, either continuous closed lavage, open drainage, or another drainage method can be selected, depending on operative findings and operators' experience (grade C).
 In gallstone pancreatitis, after the inflammatory process has subsided, cholecystectomy (with choledochotomy, if necessary) is recommended during the same hospital admission (grade B).
 In mild gallstone pancreatitis without complications, laparoscopic cholecystectomy can be selected (grade B).
 Percutaneous drainage may be effective for some pancreatic abscesses (grade C).
 If percutaneous drainage does not improve clinical signs, open drainage should be performed without delay (grade B).
 Absolute indications for therapeutic intervention for pseudocyst of pancreas are the presence of clinical symptoms, complications, or enlargement of the size of cyst (grade A).
 Relative indication for therapeutic intervention for pseudocyst of pancreas is a diameter of 6 cm or over (grade C).
 If there is no improvement after percutaneous drainage carried out for over 6 weeks, surgical intervention should be considered (grade B).

**Fig. 2.** Diagnosis of acute pancreatitis. CT, Computed tomography

Diagnosis

The diagnosis of acute pancreatitis may be difficult in some cases. The standardized criteria for the clinical diagnosis of acute pancreatitis put forward by the Research Committee of Intractable Disease of the Pancreas, Japanese Ministry of Health, Labour, and Welfare (revised 1990) are usually used in Japan, but these criteria still need the exclusion of other causes of acute abdomen and can not be evaluated in terms of positive

and negative likelihood ratios. However, as there is no gold standard for the diagnosis of acute pancreatitis, these criteria are recommended for diagnosis.

Because the specificity of lipase is superior to that of amylase, with the same sensitivity, measuring lipase is recommended in the diagnosis of acute pancreatitis (level 2a~4; grade A). Abdominal ultrasonography (US) can detect pancreatic swelling and peripancreatic inflammatory change, as well as gallstones, dilatation of the common bile duct, and ascites (level 1b~2b). It is

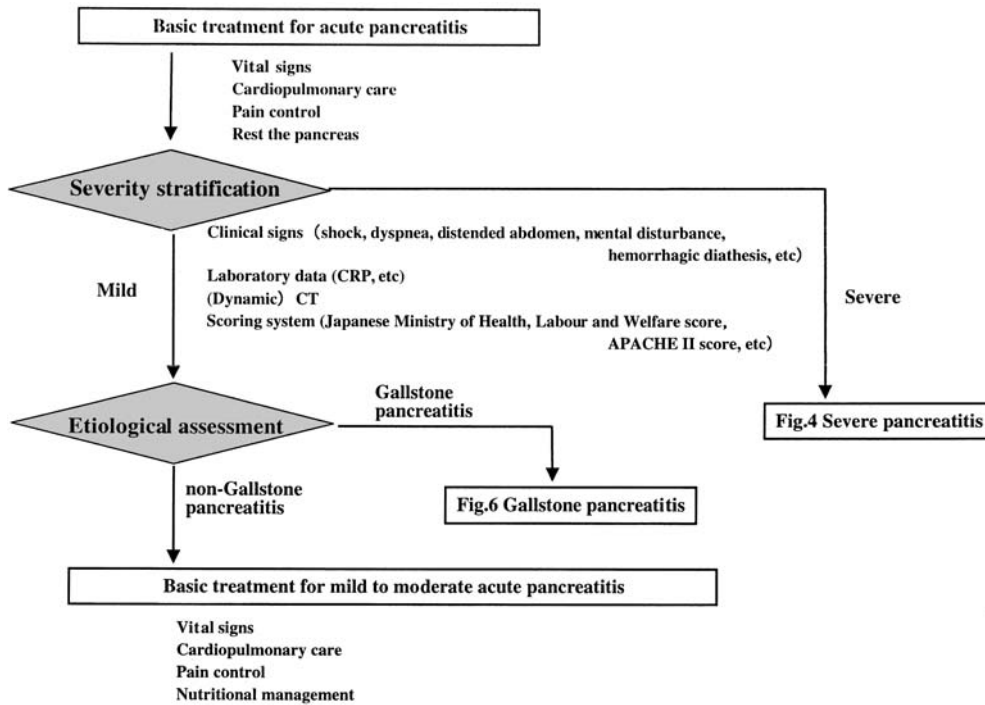


Fig. 3. Initial management of acute pancreatitis. *CRP*, C-reactive protein; *CT*, computed tomography

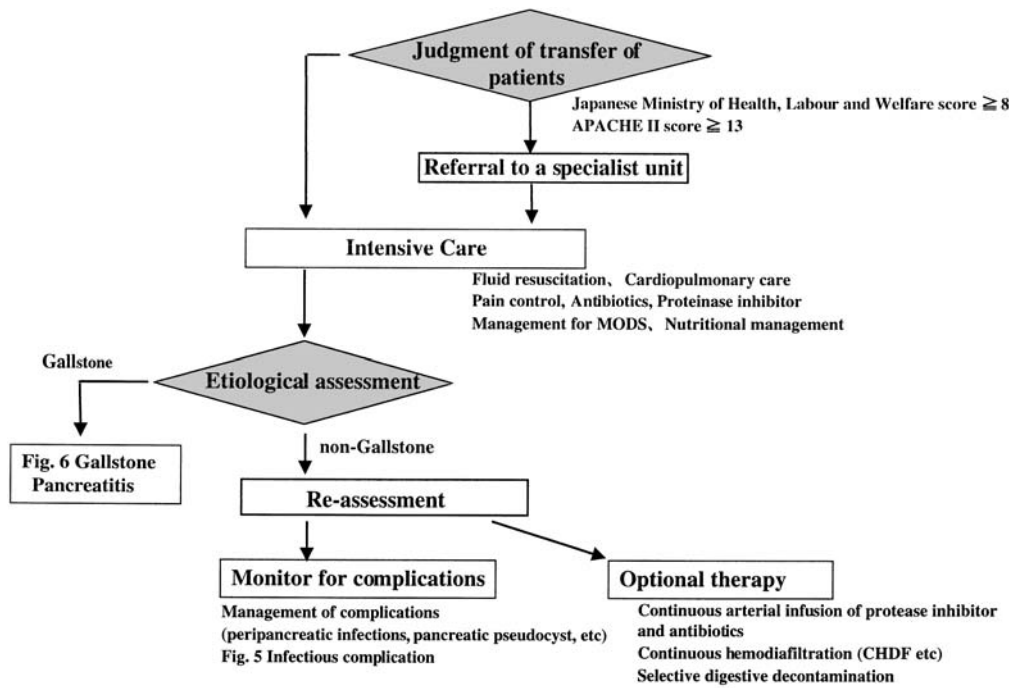


Fig. 4. Management of severe acute pancreatitis. *MODS*, Multiple organ dysfunction syndrome

also useful to exclude other causes of acute abdomen, such as abdominal aortic aneurysm. US findings should be examined in all patients with possible acute pancreatitis on admission (grade A). On the other hand, although abdominal computed tomography (CT) is useful in the assessment of severity, it is not necessary for the diagnosis itself of acute pancreatitis. In cases of diagnostic doubt, particularly those with atypical presentation

or unknown etiology, abdominal CT should be examined (grade A).

Initial management

In the initial management of acute pancreatitis, monitoring of temperature, pulse, blood pressure, and urine output; cardiopulmonary care with sufficient fluid re-

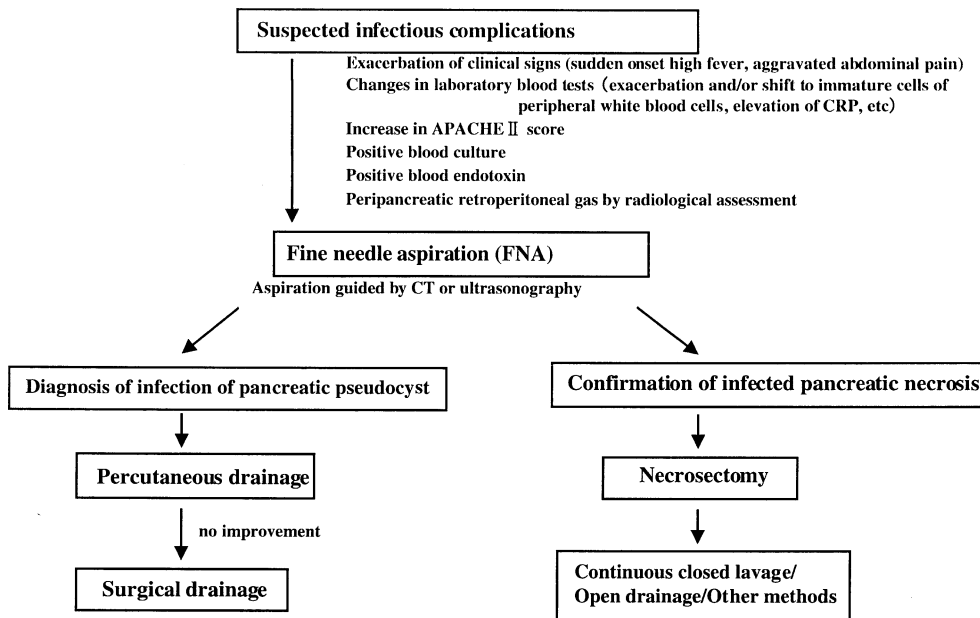


Fig. 5. Management of infectious complications of acute pancreatitis. *CT*, Computed tomography

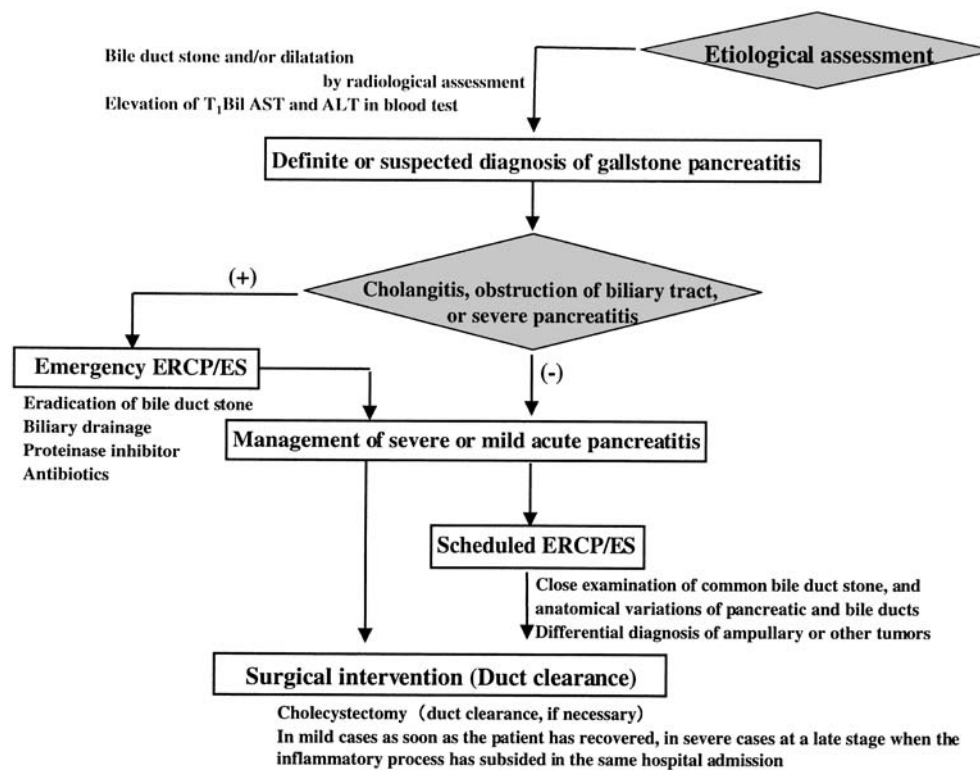


Fig. 6. Management of acute pancreatitis due to gallstone. *ERCP/ES*, Endoscopic retrograde cholangiopancreatography with or without endoscopic sphincterotomy; *AST*, aspartate aminotransferase; *ALT*, alanine aminotransferase

suscitation; pain control; and resting the pancreas are needed.

Severity stratification

Mild acute pancreatitis runs an uneventful self-limiting course, but severe pancreatitis needs intensive monitor-

ing and management, and still shows 20%–30% mortality rates^{3,4} (levels 3b). Therefore, early assessment of the severity of acute pancreatitis is needed in all patients (grade A). *CT*, especially enhanced *CT*, is useful in the assessment of severity of the disease to evaluate the degree of pancreatic necrosis and expansion of inflammation⁷ (level 1c, grade B).

Table 4. Severity scores and stages of the Japanese Ministry of Health and Welfare; and mortality rates^a

Severity score	Stage	Mortality (%)
0	0 (Mild)	0/22 (0)
1	1 (Moderate)	0/13 (0)
2–8	2 (Severa I)	2/34 (6)
9–14	3 (Severe II)	7/16 (44)
15 or over	4 (Severe III)	5/5 (100)

^aFrom Ogawa et al.⁸

A scoring system has the potential to provide improved measurements of the severity and outcome of acute pancreatitis. Not only clinical signs, with laboratory data such as C-reactive protein (CRP), and radiological assessment, but also a scoring system, such as that of the Japanese Ministry of Health and Welfare (JMHW) and the Acute Physiology and Chronic Health Evaluation (APACHE) II should be used in the assessment of severity in the early stage of the disease^{8,9} (grade A). Table 4 shows the mortality of acute pancreatitis according to the severity score and the stages of the JMHW, which are well correlated (level 3b).⁸ Those patients with predicted severe pancreatitis, with a JMHW score of 8 or over or an APACHE II score of 13 or over need to be transferred to a specialist unit for management (grade B).

Etiological assessment and management

Because the etiology of an attack of acute pancreatitis affects decision-making and further therapeutic interventions, etiological assessment is needed in all patients. Early abdominal US is recommended in all patients to detect gallstones and dilation of the bile duct (grade A). In complicated gallstone pancreatitis, urgent endoscopic retrograde cholangiopancreatography (ERCP) with/without endoscopic sphincterotomy is proven to decrease complications and mortality^{10–13} (level 1b). Therefore, in severe gallstone pancreatitis or gallstone pancreatitis with cholangitis or obstruction of the biliary tract, emergent ERCP is recommended (grade B).

Management of acute pancreatitis

In mild to moderate acute pancreatitis, nasogastric tube drainage is not necessary in most cases (level 1b; grade D). In severe and possibly severe acute pancreatitis, broadspectrum antibiotics should be used prophylactically¹⁴ (level 1a; grade A). But in mild to moderate cases, prophylactic antibiotics should not be used (level 1a; grade D).

Continuous infusion of high doses of gabexate mesilate does not affect mortality, but significantly re-

duces the incidence of complications requiring surgery and the incidence of complications in general (level 1a).^{15,16} Therefore, gabexate mesilate is recommended in severe pancreatitis (grade B). Several randomized controlled trials (RCTs) of H₂ receptor antagonists failed to show any clinical benefit (levels 1b; grade D).

Although enteral nutrition was not proven to improve survival in acute pancreatitis, it was proven to reduce complications^{17–19} (level 1b). Enteral nutrition delivered with a jejunal inserted tube should be started early in the course of acute pancreatitis if possible (grade B). On the other hand, total parenteral nutrition (TPN) has not proven to be effective in acute (mild-to-moderate) pancreatitis^{17–20} (level 1b; grade D).

Selective digestive decontamination (SDD) was reported to decrease infectious complications and mortality in severe acute pancreatitis in one RCT²¹ (level 1b). Although this procedure still needs large and good quality studies, it may be used in severe cases (grade C).

The efficacy of peritoneal lavage in acute pancreatitis is not proven (grade D). In Japan, continuous hemodiafiltration (CHDF) and the continuous arterial infusion of proteinase inhibitor and antibiotics are used in some patients with severe pancreatitis. Although there are many case reports that show the efficacy of these therapies, good quality RCTs have not been performed (level 3b–4). Early induction of CHDF in severe acute pancreatitis, and the continuous arterial infusion of proteinase inhibitor and antibiotics in necrotizing pancreatitis may decrease mortality and infectious complications (grade C).

Surgical intervention

If patients with severe acute pancreatitis have exacerbation of clinical signs (sudden onset of high fever, aggravated abdominal pain, etc), laboratory blood test changes (such as exacerbation or shift to immature cells in peripheral white blood cells, elevation of CRP, etc), increased APACHE II score, or a positive blood culture or endotoxin, image-guided fine-needle aspiration should be done for the diagnosis of infectious pancreatic necrosis (level 2b; grade A). If the finding is positive, necrosectomy should be done, which is the standard operative method for necrotic pancreatitis (grade A).

Indications for surgical intervention in noninfected necrosis are still controversial. Because most noninfected necrosis recovers of itself (levels 2c–3b), indication for operation is limited to patients with progression of organ dysfunction or no signs of improvement (grade B).

Both continuous closed lavage and open drainage are reported to be superior to conventional closed catheter drainage in terms of survival (level 2a). Conventional

drainage is not recommended after necrosectomy (grade D). At present, either continuous closed lavage, open drainage, or an other drainage method can be selected, depending on operative findings and operators' experience (grade C).

In gallstone pancreatitis, recurrence of pancreatitis occurs frequently. After the inflammatory process has subsided, cholecystectomy (with choledochotomy, if necessary) is recommended during the same hospital admission (grade B). In mild gallstone pancreatitis without complications, laparoscopic cholecystectomy can be selected (grade B).

Percutaneous drainage may be effective in some pancreatic abscesses (grade C). But if percutaneous drainage does not improve the clinical signs, open drainage should be performed without delay (grade B).

Absolute indications for therapeutic intervention for pseudocyst of the pancreas are the presence of clinical symptoms, complications, or enlargement of the size of the cyst (grade A). Relative indication for therapeutic intervention for pseudocyst of the pancreas is a diameter of 6cm or over (grade C). If there is no improvement after percutaneous drainage performed for over 6 weeks, surgical intervention should be considered (grade B).

Conclusions

Evidence-based practice guidelines for acute pancreatitis have been developed by the Japanese Society of Emergency Abdominal Medicine. The guidelines depend on a systematic review to collect the most reliable evidence. The strength of evidence and the recommendations for various interventions are stated. The Working Group has summarized the evidence for important interventions in a manner that allows practitioners to make more well-informed decisions about which treatment to offer to their patients. Although the guidelines are still under development, it is hoped the practice guidelines for acute pancreatitis will provide useful information for physicians to manage the disease.

References

1. British Society of Gastroenterology (1998) United Kingdom Guidelines for the Management of Acute Pancreatitis. *British Society of Gastroenterology*. *Gut* 42: Suppl 2:S1-13
2. Dervenis C, Johnson CD, Bassi C, Bradley E, Imrie CW, McMahon MJ, Modlin I (1999) Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini consensus conference. *Int J Pancreatol* 25:195-210
3. Yamamoto M, Saitoh Y (1996) Severe acute pancreatitis in Japan. *J Hepatobiliary Pancreat Surg* 3:203-209
4. Lin Y, Takamoshi A, Ohno Y, Kawamura T, Ogawa M, Hirota M (2000) Nationwide epidemiological survey of acute pancreatitis in Japan. In: Annual Report of Research Committee on Epidemiology of Intractable Diseases (in Japanese). The Ministry of Health and Welfare of Japan, Tokyo, pp 72-78
5. Oxford Centre for Evidence-based Medicine (1999) Levels of evidence and grades of recommendations. (<http://cebm.jr2.ox.ac.uk/docs/levels.html>) November 23, 1999
6. Kish MA (2001) Guide to development of practice guidelines. *Clin Infect Dis* 32:851-854
7. Larvin M, Chalmers AG, McMahon MJ (1990) Dynamic contrast enhanced computed tomography: a precise technique for identifying and localising pancreatic necrosis. *BMJ* 300:1425-1428
8. Ogawa M, Hirota M, Hayakawa T, Matsuno M, Watanabe S, Atomi H, Otsuki M, Kashima T, Koizumi M, Harada H, Yamamoto M, Nishimori I (1999) Stages of severity stratification for acute pancreatitis (in Japanese). In: Ogawa M (ed) Annual report of Research Committee on Intractable Pancreatic Diseases, Division of Gastrointestinal Diseases, The Ministry of Health and Welfare of Japan, pp 19-22
9. Larvin M (1997) Assessment of severity and prognosis in acute pancreatitis. *Eur J Gastroenterol Hepatol*, 9:122-130
10. Neoptolemos JP, Carr LD, London NJ, Bailey IA, James D, Fossard DP (1988) Controlled trial of urgent endoscopic retrograde cholangiopancreatography and endoscopic sphincterotomy versus conservative treatment for acute pancreatitis due to gallstones. *Lancet* II:979-983
11. Fan ST, Lai EC, Mok FP, Lo CM, Zheng SS, Wong J (1993) Early treatment of acute biliary pancreatitis by endoscopic papillotomy. *N Engl J Med* 328:228-232
12. Nowak A, Nowakowska-Dulawa E, Marek T, Rybicka J (1995) Final results of the prospective, randomized, controlled study on endoscopic sphincterotomy versus conventional management in acute biliary pancreatitis (abstract). *Gastroenterol* 108:380
13. Folsch UR, Nitsche R, Ludtke R, Hilgers RA, Creutzfeldt W (1997) Early ERCP and papillotomy compared with conservative treatment for acute biliary pancreatitis. The German Study Group on Acute Biliary Pancreatitis. *N Engl J Med* 336:237-242
14. Golub R, Siddiqi F, Pohl D (1998) Role of antibiotics in acute pancreatitis: A meta-analysis. *J Gastro Surg* 2:496-503
15. Messori A, Rampazzo R, Scroccaro G, Olivato R, Bassi C, Falconi M, Pederzoli P, Martini N (1995) Effectiveness of gabexate mesilate in acute pancreatitis. A metaanalysis. *Dig Dis Sci* 40:734-738
16. Andriulli A, Leandro G, Clemente R, Festa V, Caruso N, Annese V, Lezzi G, Lichino E, Bruno F, Perri F (1998) Meta-analysis of somatostatin, octreotide and gabexate mesilate in the therapy of acute pancreatitis. *Aliment Pharmacol Ther* 12:237-245
17. McClave SA, Greene LM, Snider HL, Makk LJ, Cheadle WG, Owens NA, Dukes LG, Goldsmith LJ (1997) Comparison of the safety of early enteral vs parenteral nutrition in mild acute pancreatitis. *JPEN* 21:14-20
18. Windsor AC, Kanwar S, Li AG, Barnes E, Guthrie JA, Spark JI, Welsh F, Guillou PJ, Reynolds JV (1998) Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. *Gut* 42:431-435
19. Kalfarentzos F, Kehagias J, Mead N, Kokkinis K, Gogos CA (1997) Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial. *Br J Surg* 84:1665-1669
20. Sax HC, Warner BW, Talamini MA, Hamilton FN, Bell RJ, Fischer JE, Bower RH (1987) Early total parenteral nutrition in acute pancreatitis: lack of beneficial effects. *Am J Surg* 153: 117-124
21. Luiten EJ, Hop WC, Lange JF, Bruining HA (1995) Controlled clinical trial of selective decontamination for the treatment of severe acute pancreatitis. *Ann Surg* 222:57-65