Assessment of severity of acute pancreatitis according to new prognostic factors and CT grading

Kazunori Takeda · Masamichi Yokoe · Tadahiro Takada · Keisho Kataoka · Masahiro Yoshida ·
Toshifumi Gabata · Masahiko Hirota · Toshihiko Mayumi · Masumi Kadoya · Eigoro Yamanouchi ·
Takayuki Hattori · Miho Sekimoto · Hodaka Amano · Keita Wada · Yasutoshi Kimura · Seiki Kiriyama ·
Shinju Arata · Yoshifumi Takeyama · Morihisa Hirota · Koichi Hirata · Tooru Shimosegawa

Abstract The assessment of severity at the initial medical examination plays an important role in introducing adequate early treatment and the transfer of patients to a medical facility that can cope with severe acute pancreatitis. Under these circumstances, "criteria for severity assessment" have been prepared in various countries, including Japan, and these criteria are now being evaluated. The criteria for severity assessment of acute pancreatitis in Japan were determined in 1990 (of which a partial revision was made in 1999). In 2008, an overall revision was made and the new Japanese criteria for severity assessment of acute pancreatitis were prepared. In the new criteria for severity assessment, the diagnosis of severe acute pancreatitis can be made according to 9 prognostic factors and/or the computed tomography (CT) grades based on contrast-enhanced CT. Patients with severe acute pancreatitis are expected to be transferred to a specialist medical center or to an intensive care unit to receive adequate treatment there. In Japan, severe acute pancreatitis is recognized as being a specified intractable disease on the basis of these criteria, so medical expenses associated with severe acute pancreatitis are covered by Government payment.

K. Takeda (✉)
Department of Surgery, National Hospital Organization
Sendai Medical Center, 2-2-8 Miyagino, Miyagino-ku,
Sendai 983-8520, Japan
e-mail: kktakeda@snh.go.jp

M. Yokoe
General Internal Medicine, Japanese Red Cross Society Nagoya
Daini Hospital, Nagoya, Japan

T. Takada · H. Amano · K. Wada
Department of Surgery, Teikyo University School of Medicine,
Tokyo, Japan

K. Kataoka
Otsu Municipal Hospital, Otsu, Japan

M. Yoshida
Department of Hemodialysis and Surgery,
Clinical Research Center, Kaken Hospital, International
University of Health and Welfare, Chiba, Japan

T. Gabata
Department of Radiology, Graduate School of Medical Science,
Kanazawa University, Ishikawa, Japan

Masahiko Hirota
Department of Surgery, Kumamoto Regional Medical Center,
Kumamoto, Japan

T. Mayumi
Department of Emergency and Critical Care Medicine,
Nagoya University Graduate School of Medicine, Nagoya, Japan

M. Kadoya
Department of Radiology, Shinshu University School
of Medicine, Matsumoto, Japan

E. Yamanouchi
Department of Radiology, St. Marianna University Yokohama
Seibu Hospital, Yokohama, Japan

T. Hattori
Department of Radiology, National Hospital Organization
Disaster Medical Center, Tokyo, Japan

M. Sekimoto
Department of Healthcare Economics and Quality Management,
Kyoto University Graduate School of Medicine, Kyoto, Japan

Introduction

The severity of acute pancreatitis differs widely, ranging
from mild cases in whom short-time remission is achieved
to severe cases that are accompanied by fatal complications
such as shock, organ failure and/or sepsis with infected
pancreatic necrosis. The severity of acute pancreatitis is
also closely associated with the validity of treatment
selection. The assessment of severity at the initial medical
examination plays a useful role in terms of the criteria for
introducing adequate early treatment and for the transfer of
patients to a medical facility that can cope with severe
acute pancreatitis. Under these circumstances, "criteria for
severity assessment" are under preparation in various
countries, including Japan, and these criteria are now being
evaluated. The criteria for severity assessment of acute
pancreatitis in Japan were prepared in 1990 (of which a
partial revision was made in 1999) [1]. In 2008, an overall
revision was made and New Japanese criteria for assess-
ment of severity of acute pancreatitis were prepared. In the
new severity assessment criteria, the diagnosis of severe
acute pancreatitis can be made according to nine prognostic
factors and/or the computed tomography (CT) grade,
determined on the basis of contrast-enhanced CT. Patients
with severe acute pancreatitis are expected be transferred to
a specialist medical center or to an intensive care unit
(ICU) to receive treatment there.

We present below a list of clinical questions (CQ) about
the new criteria together with recommendation levels for
their use.

Y. Kimura · K. Hirata
Department of Surgical Oncology and Gastroenterological
Surgery, Sapporo Medical University Graduate School
of Medicine, Sapporo, Japan

S. Kiriyama
Department of Gastroenterology, Ogaki Municipal Hospital,
Ogaki, Japan

S. Arata
Critical Care and Emergency Center, Yokohama City University
Medical Center, Yokohama, Japan

Y. Takeyama
Department of Surgery, Kinki University School of Medicine,
Osaka, Japan

Morihisa Hirota · T. Shimosegawa
Division of Gastroenterology, Tohoku University Graduate
School of Medicine, Sendai, Japan

> **CQ1. Are clinical signs and symptoms, blood tests,
> and BMI useful for severity assessment of acute
> pancreatitis?**

*Clinical signs and symptoms alone are not reliable in
severity assessment and they should be supported by
objective measures (Recommendation A).*

Acute pancreatitis presents with a wide spectrum of clinical
signs and symptoms suggesting dysfunction of the major
organs or abdominal complications. These signs and
symptoms have also been used as factors in severity
assessment in some criteria for reported to date [1–5]. On
the other hand, United Kingdom guidelines (1988) [6]
showed that clinical assessment alone is low in terms of
reliability. The rate of occurrence of wrong assessment
(classification) is about 50%. United Kingdom guidelines
of 2005 also showed that severity assessment should be
supplemented by laboratory data, because of low reliability
of clinical assessment within 24 h following hospitalization
[7]. Comprehensive assessment should be made for
severity classification of acute pancreatitis.

The level of CRP is considered to be a reliable param-
eter that suggests the worsening of pancreatitis (Level 1c–
2b) [8–10]. The Santorini consensus conference (1999)
[11], the World Congress of Gastroenterology guidelines
(2002) [12], and the United Kingdom guidelines (2005) [7]
recommend as a prognostic factor a cut-off level of CRP of
more than 15 mg/dl detected 48 h after onset of the dis-
ease. Also, in the New Japanese criteria for severity
assessment, CRP of more than 15 mg/dl is used as the 7th
prognostic factor (2008). Furthermore, there is a report
showing that a combination of CRP with other types of
diagnostic criteria leads to improvement in the reliability of
severity assessment [8].

The level of procalcitonin (PCT) is a prognostic factor
that is more effective than CRP in predicting the worsening
of acute pancreatitis [13]. On the other hand, it is also
reported (Level 2b) that the level of PCT is a sign that is
particularly effective in predicting the occurrence of pan-
creatic infections [14].

Reports from Western countries show that obesity has a
strong effect on the worsening of acute pancreatitis.
Especially, obesity with a body mass index (BMI; body
weight [kg]/height^2 [m^2]) of 30 kg/m^2 or more is associ-
ated with significantly large numbers of severe cases, cases
of abscess formation, and cases of death compared with
findings in those with a BMI of less than 30 kg/m^2 (Level
2c–4) [15, 16]. Meta-analyses of four prospective studies
showed that obese patient with acute pancreatitis had a
high risk of aggravation of pancreatitis. However, obesity
had no effect on the risk of death in acute pancreatitis [17].
World Congress of Gastroenterology Guidelines (2002)

[12] and the United Kingdom Guidelines (2005) [7] show that obesity is a sign that leads most easily exacerbation of acute pancreatitis. A recent report shows that obese patients with a BMI of 30 Kg/m^2 or more have a tendency to be aggravated easily, resulting in systemic inflammatory response reactions [18]. However, analysis of the national epidemiological survey in Japan conducted in 1999 (Level 3b) [19] showed that there were only a few cases of BMI of 30 kg/m^2 or more (25/852 cases) and that death occurred in only one case; it was noted that no significant difference was found in the number of deaths among these groups and that the absence of this difference in Japan arose from a lack of differences in the type of obesity among people of different ethnicities and in the rate of extreme obesity being low.

CQ2. Are Contrast-enhanced computed tomography (CECT) and magnetic resonance imaging (MRI) useful for the severity assessment of acute pancreatitis?

Accurate diagnosis of the presence and range of pancreatic ischemia or necrosis requires contrast-enhanced CT or contrast-enhanced magnetic resonance imaging (MRI). (Recommendation A)

Because the presence or absence of pancreatic necrosis and the extent of inflammatory changes are closely associated with various types of complications and life-related prognosis, an accurate diagnosis of pancreatic necrosis should be made [20–22]. The assessment of signs including pancreatic enlargement, extension of inflammation to the parapancreatic tissue, fluid collection, pseudocysts, calcified gallstones causing acute pancreatitis, and calcified common bile duct stones can be made using plain CT. However, the diagnosis of pancreatic ischemia or necrosis, as well as the assessment of its extent requires contrast-enhanced CT (Level 1c) [23].

Contrast-enhanced CT is the most useful procedure for the differentiation of necrotized pancreatitis from edematous pancreatitis (Level 1c) [23]. A report from Greece concludes that, irrespective of the early dysfunction of the organ, the risk of death is low even in severe pancreatitis when it is of edematous nature (Level 4) [24].

Although there are some experimental reports on the possibility that CT using contrast medium will lead to the exacerbation of acute pancreatitis, this has not been verified in clinical settings [25–28]. In Japan, the use of contrast medium has been contraindicated in principle in patients with acute pancreatitis since 1976; however, there are no reports to date showing that its use has resulted in the worsening of acute pancreatitis. As for circumstances in other countries, there are no countries where the use of

contrast medium is contraindicated on principle in acute pancreatitis, except for Korea, where the use of some types of contrast medium is contraindicated on principle.

CT severity index (Level 2b) [29] is achieved by combining and scoring those factors associated closely with prognosis, including the presence or absence of pancreatic necrosis, the extent of necrosis, and the extent of inflammatory changes around the pancreas. Also in Japan, Matsuno et al. [28] and Takeda and Matsuno [30] proposed a method of severity assessment by contrast-enhanced CT from the same viewpoint and reported its usefulness (Level 2b). The classification of contrast-enhanced CT grade is included in the present revised edition of the Criteria for Severity Assessment of Acute Pancreatitis sponsored by the Japanese Ministry of Health, Labour and Welfare (2008) [45]. However, when contrast-enhanced CT is performed, note should be taken of its side effects. In the new criteria for severity assessment (2008), the classification of the contrast-enhanced CT grade is presented independently of prognostic factors, and severity assessment can be made without using contrast-enhanced CT, which is not indispensable in the early phase of management.

The diagnosis of pancreatic necrosis can be made in almost 100% of cases by performing contrast-enhanced CT 4–10 days after the onset of the disease (Level 1b–2b) [20, 21, 23, 31]. However, several studies conducted in Western countries also show the usefulness of early contrast-enhanced CT performed during the hospital stay (within 36 or 48 h after hospitalization) for the severity assessment of acute pancreatitis (Level 2b) [32, 33]. The use of contrast-enhanced CT is desirable in cases where worsening of pancreatic necrosis is suspected.

Furthermore, similar to contrast-enhanced CT, there are reports showing the usefulness of contrast-enhanced MRI for the detection of pancreatic necrosis and the understanding of the progression of inflammation in the tissue around the pancreas (Level 2b) [34–36]. MRI has benefits in that it can be used without causing exposure to X-rays and because it supplies information about the bile duct and the pancreatic duct. On the other hand, MRI has some weak points in that bringing in metal objects such as an artificial ventilator into the laboratory is prohibited and coping with an emergency examination is difficult.

CQ3. Are severity scoring systems useful for assessing the severity of acute pancreatitis?

The severity scoring system is useful for assessing the severity and for deciding the treatment strategy and the need for transfer to a specialist unit. (Recommendation A)

Symptoms and clinical findings of acute pancreatitis are various and the subjective assessment of its severity is

often difficult. Several forms of severity scoring criteria have been determined for assessing severity to date. Although the severity assessment based on the Ranson score and the Glasgow score requires 48 h, it is reported that prediction of the worsening of the disease can be made in 70–80% of cases by using a scoring system [37–39].

The Acute Physiology and Chronic Health Evaluation (APACHE) II score has been found to be useful for the assessment of acute pancreatitis. In the Atlanta symposium (1992) [5] and the World Congress of Gastroenterology Guidelines (2002) [12], cases with a score of above 8 points are classified into the grade of "severe". In the Santorini consensus conference [11], a score of above 8 points is classified into the grade of "severe". However, it is reported that, when the APACHE II score of above 6 points is classified into the grade of "severe", the sensitivity is assessed as being high (95%), but the positive predictive value is 40% [40]. Larvin has shown that the APACHE II score has a sensitivity of 65% and specificity of 76% during hospital stay, and a sensitivity of 76% and a specificity of 84% at 48 h after hospitalization, and that the difference between the Ranson score and the Glasgow score was not so large [41]. A detailed examination conducted on the basis of the total data of the national epidemiological research in Japan showed that the Japanese criteria have similar assessing ability to that of the Ranson score and the APACHE II score [42].

CQ4. Is the new Japanese severity scoring system useful for assessing the severity of acute pancreatitis?

The new Japanese severity scoring system is useful for assessing the severity of acute pancreatitis (Recommendation A)

The Japanese severity scoring system (1999) and the stage classification have been used widely in Japan because they reflect a good correlation between the classification of stage and the mortality rate. A rapid reduction in the mortality rate of acute pancreatitis has been achieved in recent years; the mortality rate of acute pancreatitis had fallen to 8.9% in the national survey of 2003 compared with 30% in the national survey of 1987 and 22% in the national survey of 1999. In Japan, severe acute pancreatitis is included in the category of a specified intractable disease and the medical expenses of severe acute pancreatitis are covered by government payment. In the Japanese old criteria, there were 18 items in the prognostic factors. This made the assessment based on those criteria extremely complicated and troublesome, which resulted in the overlap of similar prognostic factors. Shortcomings are also pointed out in that the CT grades do not reflect the prognosis of severe acute pancreatitis because the CT grades included in

the prognostic factors were an assessment made by plain CT. For these reasons, the Research Committee for Intractable Disease of the Pancreas made a revision in the severity scoring system.

In the New Japanese criteria, prognostic factors and the contrast-enhanced CT grade are prepared so that severity assessment can be made according to both criteria (Table 1). Prognostic factors consist of the following 9 items: (1) base excess (BE) $\leqq -3$ mEq/L or shock: (systolic blood pressure <80 mmHg), (2) PaO_2 $\leqq 60$ mmHg (room air) or requiring respirator management, (3) blood urea nitrogen (BUN) $\geqq 40$ mg/dl (or creatinine [Cr] $\geqq 2.0$ mg/dl) or oliguria after fluid replacement, (4) lactic dehydrogenase (LDH) $\geqq 2$ times of upper limit of normal, (5) platelet count $\leqq 10 \times 10^4/mm^3$, (6) Ca $\leqq 7.5$ mg/dl, (7) CRP $\geqq 15$ mg/dl, (8) number of positive measures in SIRS criteria $\geqq 3$, and (9) age $\geqq 70$ years. Patients who satisfy more than 3 of the above 9 items are assessed as having severe acute pancreatitis. The contrast-enhanced CT grade is a classification for severity assessment made by the combination of 2 factors: the degree of extrapancreatic progression of inflammation and the extent of the poorly enhanced area that suggests the presence of pancreatic ischemia or necrosis, and cases of grade 2 or more are assessed as being severe (Table 1; Figs. 1, 2, 3).

A detailed examination of the new criteria conducted in 2006 according to the total data of the national survey of acute pancreatitis (including the data of cases from 1995 to 1998)found that the mortality rate was 29.3% in cases with a prognostic score of more than 3 points while it was 1.8% in cases with a prognostic score of under 2 points; a distinct difference was observed between the two categories. Furthermore, according to a report that assessed and examined the usefulness of the new assessment criteria by determining the area under curve by means of a receiver operating (ROC) analysis that used the mortality rate as a parameter, the new criteria (prognostic factors) were largely as useful as the old criteria, the Ranson Score, and the APACHE II score for severity assessment [43]. According to an examination of contrast-enhanced CT and the prognosis associated with its use, the mortality rate was 3.3% in cases of CT grade 1, 21.9% in cases of CT grade 2, and 33.3% in cases of CT grade 3 [44]. A prospective study conducted in 2007 showed that the mortality rate was 0% in cases with a prognostic score of under 2 points and 19.1% in cases with a prognostic score of more than 3 points. For contrast-enhanced CT, the mortality rate was 0% in cases of CT grade 1, 14.3% in cases of CT grade 2, and 15.4% in cases of CT grade 3. For complications of organ disorders, the rate was 4.3% in cases of CT grade1, 42.9% in cases of CT grade 2, and 46.2% in cases of CT grade 3. The mortality rate of cases that satisfied both the prognostic factors of more than 3 points and grade 2 of

Table 1 The severity scoring system of acute pancreatitis of the Japanese Ministry of Health, Labour and Welfare (2008)

Prognostic factors (1 point for each factor)	
1. Base Excess $\leqq 3$ mEq/L or shock (systolic blood pressure <80 mmHg)	
2. PaO_2 $\leqq 60$ mmHg (room air) or respiratory failure (respirator management is needed)	
3. BUN $\geqq 40$ mg/dL (or Cr $\geqq 2.0$ mg/dL) or oliguria (daily urine output <400 mL even after IV fluid resuscitation)	
4. LDH $\geqq 2$ times of upper limit of normal	
5. Platelet count $\leqq 100,000/mm^3$	
6. Serum Ca $\leqq 7.5$ mg/dL	
7. CRP $\geqq 15$ mg/dL	
8. Number of positive measures in SIRS criteria $\geqq 3$	
9. Age $\geqq 70$ years	
CT Grade by CECT	
1. Extrapancreatic progression of inflammation	
Anterior pararenal space	0 point
Root of mesocolon	1 point
Beyond lower pole of kidney	2 points
2. Hypoenhanced lesion of the pancreas	
The pancreas is conveniently divided into three segments (head, body, and tail).	
Localized in each segment or only surrounding the pancreas	0 point
Covers 2 segments	1 point
Occupies entire 2 segments or more	2 points
1 + 2 = Total scores	
Total score = 0 or 1	Grade 1
Total score = 2	Grade 2
Total score = 3 or more	Grade 3
Assessment of severity	

(1) If prognostic factors are scored as 3 points or more, or (2) If CT Grade grade is judged as Grade grade 2 or more, the severity grading is evaluated to be as "severe".

Measures in SIRS diagnostic criteria: (1) Temperature >38°C or <36°C, (2) Heart rate >90 beats/min, (3) Respiratory rate >20 breaths/min or $PaCO_2$ <32 torr, (4) WBC >12,000 cells/mm^3, <4,000 cells/mm^3, or >10% immature (band) forms

contrast-enhanced CT was very high (30.8%) [45]. A prognostic score of 3 points in the new criteria is equivalent to that of 6–8 points in the old criteria [46]. The use of the new criteria for severity assessment resulted in a decrease by half in the number of cases of severe acute pancreatitis for which medical expenses are covered by Government payment [45, 46].

The new guidelines recommend that severity assessment is made at first on the basis of the prognostic factors that can be assessed at any time and everywhere, and that contrast-enhanced CT is performed in cases in which pancreatic necrosis is suspected by plain CT. It is also recommended that, in cases in which worsening of the disease is suspected, contrast-enhanced CT is performed even if the prognostic factor score is less than 2 points. Concerning advanced medical facilities that provide treatment for acute severe pancreatitis, it is recommended that the treatment policy is determined based on the

understanding of the extent of the progress of inflammation and severity assessment.

> **CQ5. What are the indications for transferring patients with severe acute pancreatitis to a specialist unit?**

Patients with severe acute pancreatitis (prognostic factor $\geqq 3$) assessed by the new Japanese criteria should be transferred promptly to a specialist medical institution.

As soon as the diagnosis of acute pancreatitis has been made, monitoring and fundamental treatment including adequate fluid replacement should be initiated. According to the guidelines of the British Society of Gastroenterology (1998) [6], when pancreatic necrosis of more than 50% or acute exudate collection is observed in multiple sites by contrast-enhanced CT, or when there is a complication of

Fig. 1 Degree of extrapancreatic progression of inflammation in acute pancreatitis based on contrast-enhanced computed tomography. **a** Progression within anterior pararenal space (0 point), **b** progression to root of mesocolon (1 point), **c** progression to retroperitoneal space beyond lower pole of kidney (2 points)
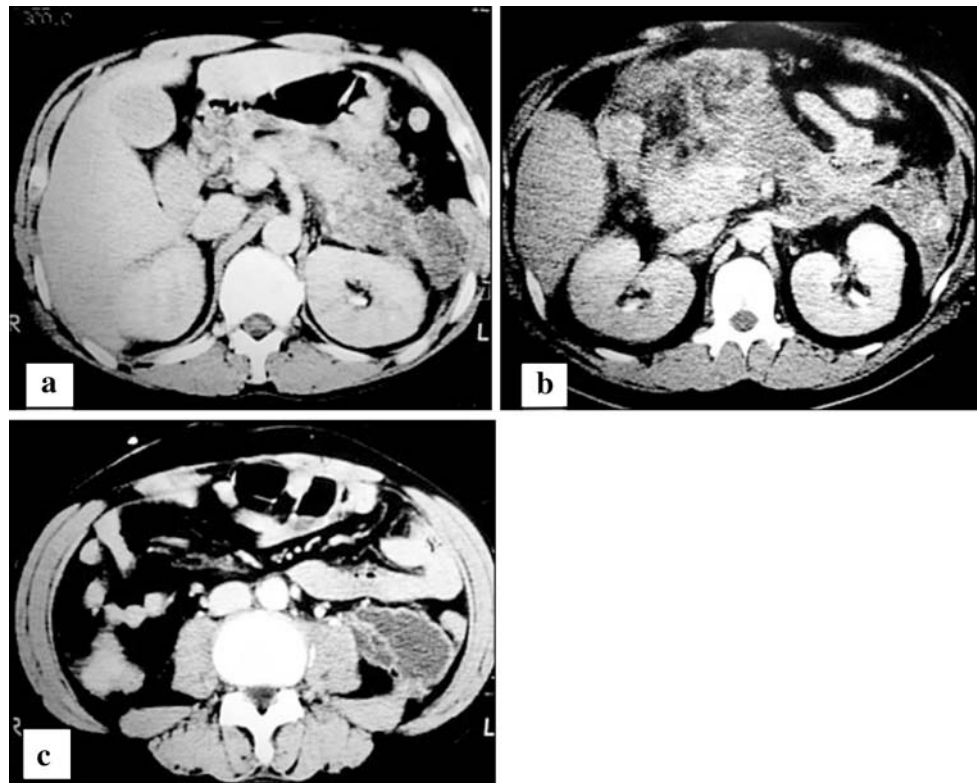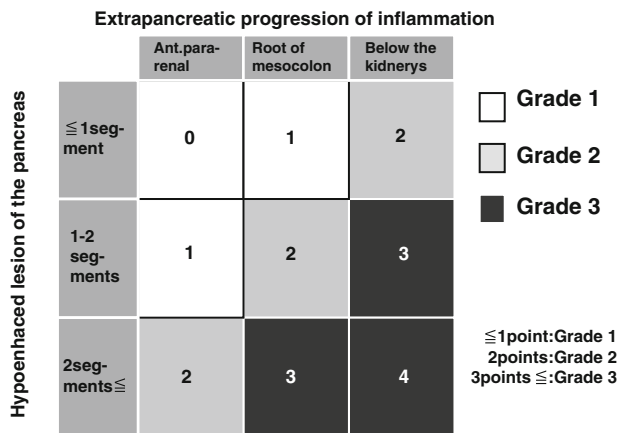
Fig. 2 Extent of hypoenhanced lesion of the pancreas based on contrast-enhanced computed tomography (*CT*). **a** Hypoenhanced lesion is localized in the tail of the pancreas (0 point), **b** hypoenhanced lesion is localized in the entire tail and part of the body of the pancreas (1 point), **c** hypoenhanced lesion is localized in the entire gland, except for part of the tail of the pancreas (2 points)
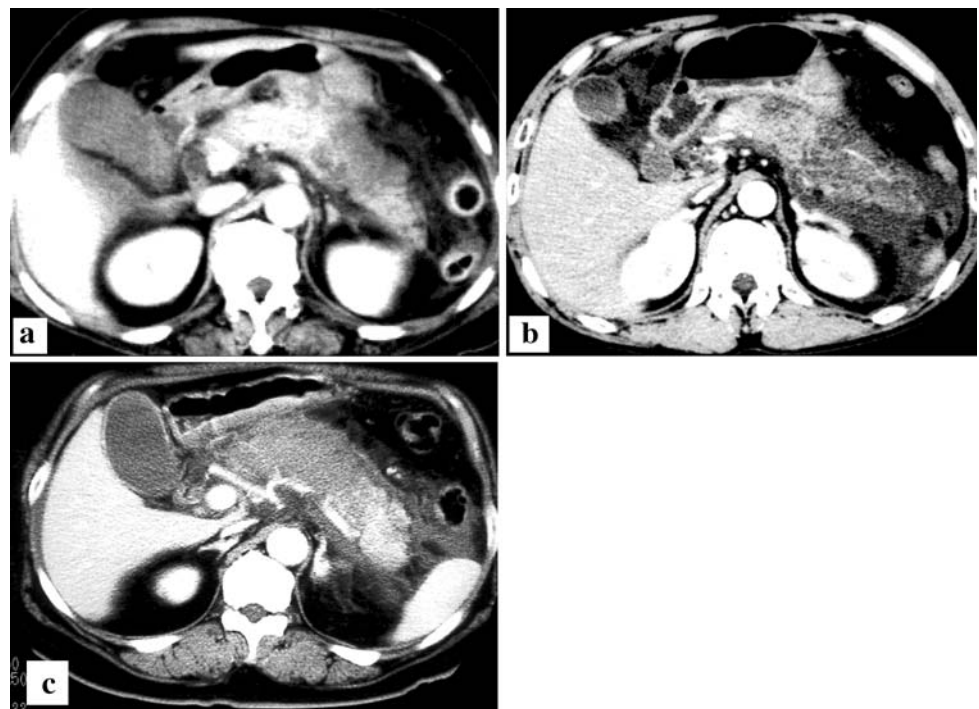
organ dysfunction, it is recommended that these criteria become criteria for patient transfer to a specialist medical facility.

The Santorini consensus conference (1999) [11] determined obesity (BMI >30 kg/m^2), collection of pleural effusion, APACHE II score of more than 6, APACHE O

Extrapancreatic progression of inflammation

Fig. 3 Schematic matrix of progression of acute pancreatitis. CT Grade is a classification of severity assessment made by combining two factors: the degree of extrapancreatic progression of inflammation and the extent of hypoenhanced lesion of the pancreas based on contrast-enhanced CT. *Ant.,* Anterior

score (1 point is added to the APACHE II in cases of BMI of 25–30 kg/m^2 and 2 points in cases of BMI >30 kg/m^2, respectively) of more than 6, and CRP more than 15 mg/dL as the severity criteria and recommended these as the transfer criteria. The Practice Guidelines in Acute Pancreatitis (2006) [47] consider organ dysfunction as the most important reason for transfer and assess that patients with decreased blood pressure and renal failure(Cr >2.0 mg/dL)who show no response to hypoxia in particular and the initial fluid replacement should be transferred to the ICU immediately. In cases of acute pancreatitis in elderly patients with cardiac failure that require accurate determination of the fluid replacement dosage the Practice Guidelines also assess that those patients are indicated for transfer to achieve improvement in hemodynamic derangement. The Guidelines put forward ① BMI more than 30 kg/m^2, ② oliguria (<50 ml/h), ③ tachycardia (heart rate [HR], >120 bpm), ④ encephalopathy, and ⑤ increased dosage of sedatives as conditions that require attention, although emergency transfer is not needed.

Patients who have been assessed as having a prognostic score of more than 3 points (severe cases) according to the new Japanese criteria should be transferred to a medical facility or to an ICU that is in a position to cope with acute severe pancreatitis by providing ICU management, interventional radiology (IVR), continuous hemodiafiltration (CHDF), and/or endoscopic sphincterotomy (EST).

Because cases with a prognostic score of 2 points or less at the time of hospitalization often become worse depending upon the clinical course, those cases that have been assessed as being severe after repeated assessment of the prognostic score on the basis of the criteria for severity assessment, while receiving a sufficient dosage of fluid replacement and careful follow up, are indicated for

transfer. Decision on the necessity for transfer should be made by taking into consideration the influence on the disease of the time spent for transfer.

References

1. Ogawa M, Hirota M, Hayasaka T, et al. Development and use of a new staging system for severe acute pancreatitis based on a nationwide survey in Japan. Pancreas. 2002;25:325–30.
2. Forell MM. Die konservative Behandulung der Pankreaserkrankungen. Der Internist. 1964;5:453–7.
3. Bank S, Wise L, Gersten M. Risk factors in acute pancreatitis. Am J Gastroenterol. 1983;78:637–40.
4. Imrie CW, Benjamin IS, Ferguson JC, et al. A single-centre double-blind trial of Trasylol therapy in primary acute pancreatitis. Br J Surg. 1978;65:337–41.
5. Bradley EL III. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. Arch Surg. 1993;128:586–90.
6. British Society of Gastroenterology. United Kingdom guidelines for the management of acute pancreatitis. Gut. 1998; 42 S2:1S–13S.
7. UK Working Party on Acute Pancreatitis. UK guidelines for the management of acute pancreatitis. Gut. 2005;54 Suppl III: iii1–iii9.
8. Viedma JA, Perez MM, Agullo J, et al. Inflammatory response in the early prediction of severity in human acute pancreatitis. Gut. 1994;35:822–7.
9. Pezzilli R, Billi P, Miniero R, et al. Serum interleukin-6, interleukin-8, and beta 2-microglobulin in early assessment of severity of acute pancreatitis. Comparison with serum C-reactive protein. Dig Dis Sci. 1995;40:2341–8.
10. Uchikov PA, Sirakova IP, Murdjeva MA, Uchikov AP. Changes in plasma levels of acute phase proteins in pancreatitis. Folia Med (Plovdiv). 2000;42:23–30.
11. Dervenis C, Johnson CD, Bassi C, et al. Diagnosis, objective assessment of severity, and management of acute pancreatitis. Santorini Consensus Conference. Int J Pancreatol. 1999;25:195–210.
12. Toouli J, Brooke-Smith M, Bassi C, et al. Working party of the program committee of the Bankok World Congress of Gastroenterology 2002. Guidelines for the management of acute pancreatitis. J Gastroenterol Hepatol. 2002;17(Suppl):S15–39.
13. Skipworth RA, Pereira SP. Acute pancreatitis. Curr Opin Crit Care. 2008;14:172–8.
14. Rau BM, Kemppainen EA, Gumbs A, et al. Early assessment of pancreatic infections and overall prognosis in severe acute pancreatitis by procalcitonin (PCT): a prospective international multicenterstudy. Ann Surg. 2007;245:745–54.
15. Funnell IC, Bornman PC, Weakley SP, et al. Obesity: an important prognostic factor in acute pancreatitis. Br J Surg. 1993;80:484–6.
16. Martinez J, Sanchez PJ, Palazon JM, et al. Obesity: a prognostic factor of severity in acute pancreatitis. Pancreas. 1999;19:15–20.
17. Martinez J, Sanchez-Paya J, Palazon JM, et al. Is obesity a risk factor in acute pancreatitis? A meta-analysis. Pancreatology. 2004;4:42–8.
18. Sempere L, Martinez J, de Madaria E, et al. Obesity and fat distribution imply a greater systemic inflammatory response and a worse prognosis in acute pancreatitis. Pancreatology. 2008;8:257–64.

19. Hirota M, Ogawa M. Obesity in acute pancreatitis. Kan-Tan-Sui. 2001;42:53–6. (in Japanese).

20. Vesentini S, Bassi C, Talamini G, et al. Prospective comparison of C-reactive protein level, Ranson score and contrast-enhanced computed tomography in the prediction of septic complications of acute pancreatitis. Br J Surg. 1993;80:755–7.

21. Kemppainen E, Sainio V, Haapiainen R, et al. Early localization of necrosis by contrast-enhanced computed tomography can predict outcome in severe acute pancreatitis. Br J Surg. 1996;83:924–9.

22. Bradley EL III, Murphy F, Ferguson C. Prediction of pancreatic necrosis by dynamic pancreatography. Ann Surg. 1989;210:495–503.

23. Larvin M, Chalmers AG, McMahon MJ. Dynamic contrast enhanced computed tomography: a precise technique for identifying and localizing pancreatic necrosis. BMJ. 1990;300:1425–8.

24. Lytras D, Manes K, Triantopoulou C, et al. Persistent early organ failure defining the high-risk group of patients with severe acute pancreatitis? Pancreas. 2008;36:249–54.

25. Carmona-Sanchez R, Uscanga L, Bezaury-Rivas P, et al. Potential harmful effect of Iodinated intravenous contrast medium on the clinical course of mild acute pancreatitis. Arch Surg. 2000;135:1280–4.

26. Hwang TL, Chang KY, Ho YP. Contrast-enhanced dynamic computed tomography does not aggravate the clinical severity of patients with severe acute pancreatitis. Reevaluation of the effect of intravenous contrast medium on the severity of acute pancreatitis. Arch Surg. 2000;135:287–90.

27. Uhl W, Roggo A, Kirschstein T, et al. Influence of contrast-enhanced computed tomography on course and outcome in patients with acute pancreatitis. Pancreas. 2002;24:191–7.

28. Matsuno S, Ogawa M, Takeda K et al. Annual report, 2001, Committee of Intractable Disease of the Pancreas, Japanese Ministry of Health, Labor and Welfare; 2001. p. 19–26 (in Japanese).

29. Balthazar EJ, Robinson DL, Megibow AJ, Ranson JH. Acute pancreatitis: value of CT in establishing prognosis. Radiology. 1990;174:331–6.

30. Takeda K, Matsuno S. Management of acute necrotizing pancreatitis based on CT grading. J Abdom Emerg Med. 1998;18:961–5. (in Japanese).

31. London NJ, Leese T, Lavelle JM, et al. Rapid-bolus contrast-enhanced dynamic computed tomography in acute pancreatitis: a prospective study. Br J Surg. 1991;78:1452–6.

32. Clavien PA, Hauser H, Meyer P, Rohner A. Value of contrast-enhanced computerized tomography in the early diagnosis and prognosis of acute pancreatitis. Am J Surg. 1988;155:457–66.

33. Rotman N, Chevret S, Pezet D, et al. Prognostic value of early computed tomographic scans in severe acute pancreatitis. J Am Coll Surg. 1994;179:538–44.

34. Hirota M, Kimura Y, Ishiko T, et al. Visualization of the heterogenous internal structure of so-called pancreatic necrosis by magnetic resonance imaging. Pancreas. 2002;25:63–7.

35. Ward J, Chalmers AG, Guthrie AJ, et al. T2-weighted and dynamic enhanced MRI in acute pancreatitis: comparison with contrast enhanced CT. Clin Radiol. 1997;52:109–14.

36. Lecesne R, Taourel P, Bret PM, et al. Acute pancreatitis: interobserver agreement and correlation of CT and MR cholangiopancreatography with outcome. Radiology. 1999;211:727–36.

37. Blamey SL, Imrie CW, O'Neill J, et al. Prognostic factors in acute pancreatitis. Gut. 1984;25:1340–6.

38. Ranson JHC, Rifkind KM, Turner JW. Prognostic signs and nonoperative peritoneal lavage in acute pancreatitis. Surg Gynecol Obstet. 1976;143:209–19.

39. Leese T, Shaw D. Comparison of three Glasgow multifactor prognostic scoring system in acute pancreatitis. Br J Surg. 1988;75:460–2.

40. Wilson C, Heath DI, Imrie CW. Prediction of outcome in acute pancreatitis: a comparative study of APACHE II, clinical assessment and multiple factor scoring systems. Br J Surg. 1990;77:1260–4.

41. Larvin M. Assessment of severity and prognosis in acute pancreatitis. Eur J Gastroenterol Hepatol. 1997;9:122–30.

42. Kitagawa M, Naruse T, Hayakawa T, et al. Prediction of exacerbation of acute pancreatitis. Suizou. 2005;20:17–30. (in Japanese).

43. Matsuno S, Takeda K, Kitagawa M et al. Annual report, 2005, Committee of Intractable Disease of the Pancreas, Japanese Ministry of Health, Labor and Welfare; 2005. p. 32–8 (in Japanese).

44. Matsuno S, Takeda K, Ogawa M, et al. Re-evaluation of CT Grade in acute pancreatitis. Suizou. 2002;7:93–9. (in Japanese).

45. Takeda K, Ootsuki M, Kihara Y et al. Annual report, 2008, Committee of Intractable Disease of the Pancreas, Japanese Ministry of Health, Labor and Welfare; 2008. p. 43–7 (in Japanese).

46. Yokoe M, Mayumi T, Hayashi K. Clinical evaluation of the revised staging system for acute pancreatitis in Japan. Suizou. 2009;24:140–6. (in Japanese).

47. Bank PA, Freeman ML. Practice guidelines in acute pancreatitis. Am J Gastroenterol. 2006;101:2379–400.