abdominal manifestations (from mild tenderness to rebound pain). It is often accompanied by vomiting, fever, tachycardia, and elevated levels of white blood cells and blood or urinary pancreatic enzymes.

Acute edematous pancreatitis (Fig. 1)

Pancreatitis usually results in diffuse or localized enlargement of the pancreas along with inflammation. Although edematous pancreatitis induces necrosis in severe cases, it is defined as that type of pancreatitis not accompanied by necrosis.

Clinical features

Edematous pancreatitis has no area in which there is no infection according to contrast-enhanced CT, although enlargement of the pancreas is observed.

Acute fluid collection (Fig. 2)

Acute fluid collection is defined as exudate collection that often occurs within the pancreas or in the parapancreatic tissue in the early phase of the disease. It may progress as far as the anterior paraphrenic cavity, the mesocolon, and beyond the inferior renal portion. It is also characterized by lack of the fibrous wall.

Clinical features

Although acute exudate collection occurs in 30–50% of patients, spontaneous resolution is achieved in half of them
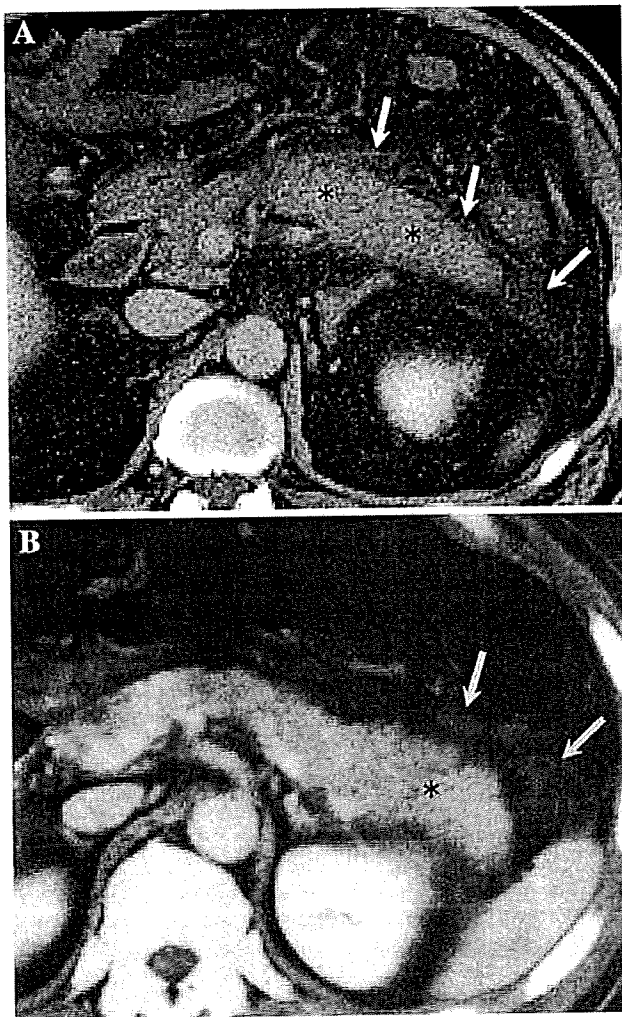

Fig. 1 Acute edematous pancreatitis. Observed are enlargement of the tail of the pancreatic body (a case 1; *asterisks*) and enlargement of the pancreatic tail (b case 2; *asterisks*). It was thought that the evenly visualized tail of the pancreatic body and pancreatic tail shown by contrast-enhanced computed tomography (CT) in both cases suggested the presence of edematous pancreatitis. An increased density of adipose tissue in the parapancreatic tissue (*arrows* in a, b) shows the extension of inflammation as far as the parapancreatic tissue in both cases
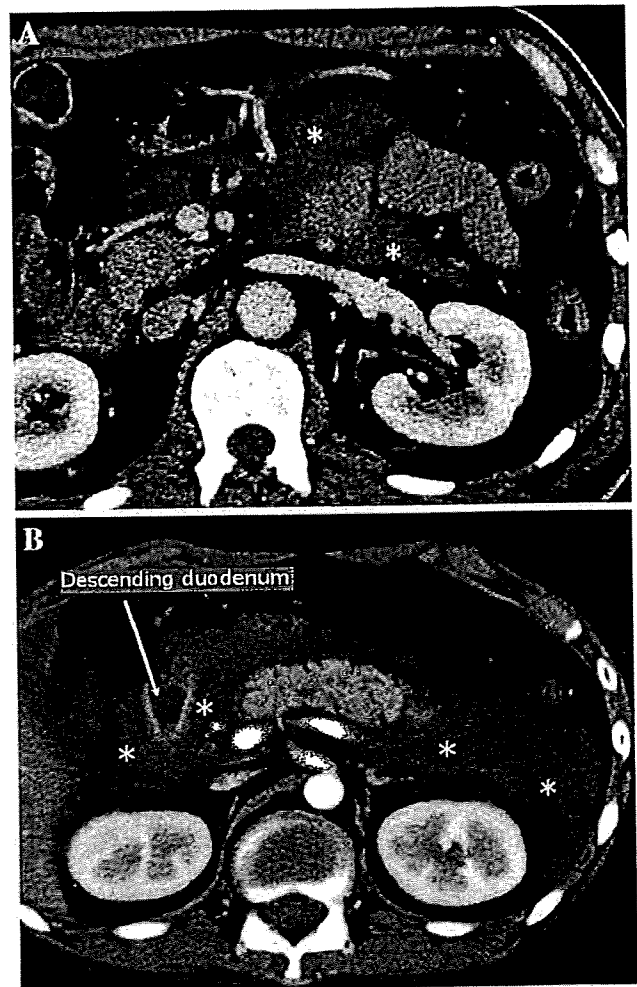

Fig. 2 Acute fluid collection (a case 1, b case 2). Fluid collection (exudate collection; *asterisks*) is observed in the left and right anterior paraphrenic cavities and the transverse mesocolon

(level 4) [12, 13]. Clinical differentiation from pseudocysts is made according to the presence or absence of the cystic wall. Pleural fluid, ascites, and fluid collection as far as the cavity of the omental bursa occur as a reaction against inflammation, so these features are not defined as acute exudate collection.

Necrotizing pancreatitis (Fig. 3)

Pancreatic necrosis is defined as diffuse or localized necrosis of the pancreatic parenchyma and is differentiated from necrosis occurring around the pancreas and that of extrapancreatic adipose tissue [14, 15]. However, pancreatic necrosis is often accompanied by necrosis around the pancreatic adipose tissue. Clinically, in cases of pancreatic necrosis, a poorly visualized area of the pancreatic parenchyma is observed distinctly by contrast-enhanced CT. However, there have been reports in recent years pointing out that the detection of a poorly visualized area by contrast-enhanced CT does not necessarily suggest the presence of necrosis in all the cases involved and that detection of an area that is not visualized, particularly in the acute phase, may suggest the presence of temporary ischemia, which can be reversible [14, 16].

Clinical features

A marked difference is observed in the mortality rate depending upon the presence or absence of infectious

complications in the necrotizing pancreatic tissue (level 4) [17], so the differentiation between infected and noninfected pancreatitis is important.

Infected pancreatic necrosis (Fig. 4)

Infected pancreatic necrosis is the type of necrosis that is complicated by infections such as bacterial infections in the pancreatic parenchyma and parapancreatic tissue [14]. There are not a few cases in which differentiation from noninfected pancreatic necrosis is difficult, so a bacterial culture by fine needle aspiration (FNA) under imaging guidance is required to make the diagnosis of infected pancreatic necrosis.

Clinical features

A marked difference is observed in the mortality rate depending upon the presence or absence of infectious complications in the necrotizing pancreatic tissue (level 4) [17]; the prognosis of necrotizing pancreatitis is reported to be poor when it is accompanied by infections in the necrotic tissue (34–40%) [18, 19].

Pancreatic pseudocyst (Fig. 5)

Irrespective of the presence or absence of a communication between the pseudocyst and the pancreatic duct, pancreatic

Fig. 3 Necrotizing pancreatitis and fat necrosis. The enlarged pancreatic body and tail are seen by plain CT (a, b; *arrows*). Fat necrosis with an increased density than that of fluid collection is observed in the parapancreatic retroperitoneum and in the adipose tissue of the lesser omentum (*asterisks*). The pancreatic tail is visualized by contrast-enhanced dynamic CT (c), but a poorly visualized area (*arrows*) is observed in the enlarged pancreas (d), so the presence of pancreatic necrosis can be strongly suspected. Making a diagnosis of pancreatic necrosis by plain CT is often difficult, so contrast-enhanced CT is required for the accurate assessment of pancreatic necrosis
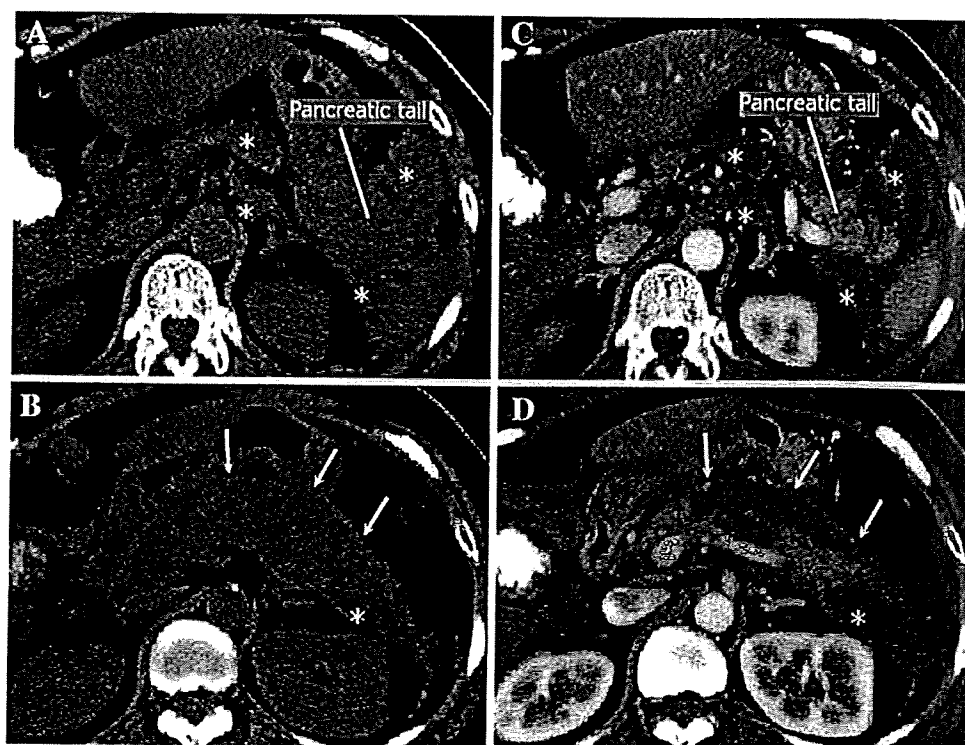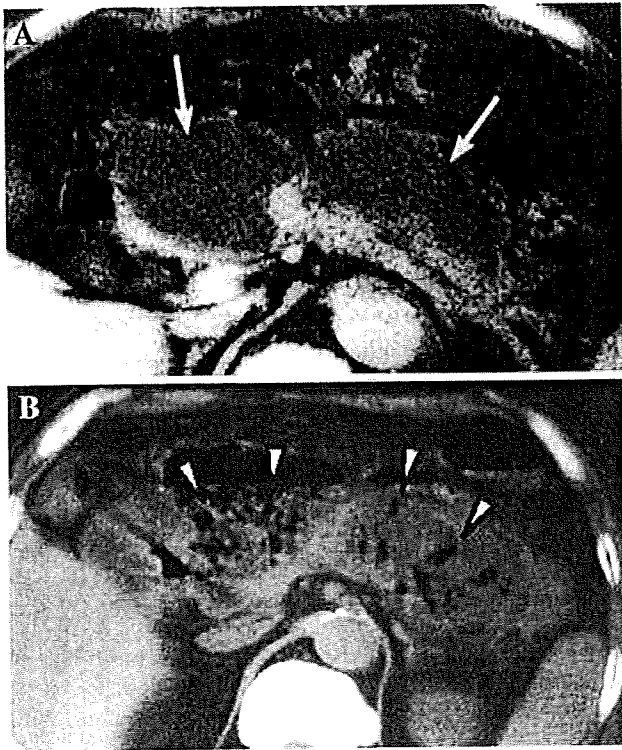
Fig. 4 Infected pancreatic necrosis. The enlarged pancreas and a wide area not stained densely (pancreatic necrosis; *arrows*) are observed in the whole portion of the pancreas by contrast-enhanced CT (**a**) conducted at the time of the onset of acute pancreatitis. Plain CT conducted a week later (**b**) detected the appearance of gas at the necrotic site, so complications of necrotic infection were strongly suspected

Fig. 5 Pancreatic pseudocyst. A cystic tumor (pseudocyst) with a comparatively thick wall at the pancreatic tail is visualized by plain CT (**a**) and contrast-enhanced CT (**b**; *arrows*). The cystic wall is seen to have been stained mildly by contrast-enhanced CT. The high-absorption area within the pseudocyst is assumed to suggest the presence of bleeding (*arrowheads*). Exudate collection accompanied by acute pancreatitis is observed around the pancreas (*asterisks*)

pseudocyst is defined as the type of pseudocyst with a wall structure of granulation or fibrotic tissue. It is accompanied by the collection of pancreatic juice and the tissue of liquefaction necrosis, and often occurs 4 weeks after the onset of acute pancreatitis. It may resolve spontaneously, although it may persist for a long time. It may be complicated by infections or bleeding.

Clinical features

In patients with acute pancreatitis, a pseudocyst can be detected by diagnostic imaging, as well as by palpation. The pseudocyst usually contains large amounts of pancreatic enzymes, although in many cases pseudocysts do not contain bacteria.

Pancreatic abscess (Fig. 6)

Pancreatic abscess is the type of abscess that is accompanied by localized pus collection in the pancreas and adjacent organs. However, there is usually no necrosis within the pancreas, or there is only a small amount if any. Because pancreatic abscess consists of necrotic tissue as
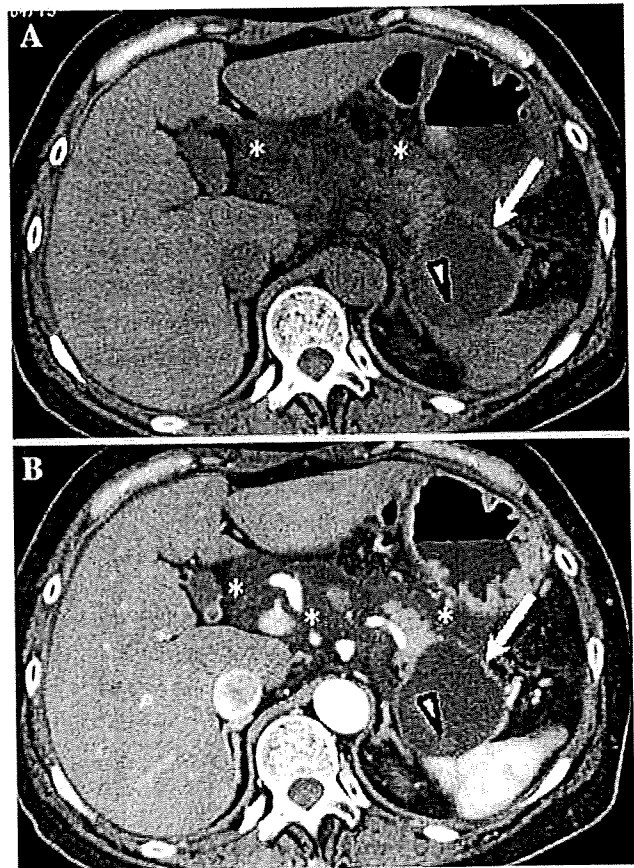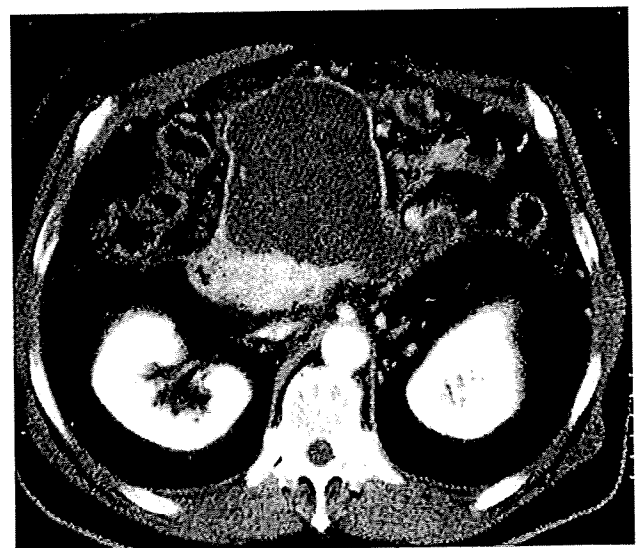

Fig. 6 Pancreatic abscess. Encapsulated fluid collection (abscess) is observed around the pancreatic head

well as liquid components, there are indications that it is induced by the liquefaction of tissue necrosis [14, 15].

Clinical features

Pancreatic abscess presents with a wide spectrum of clinical pictures, although it also presents with pictures of infections in many patients. It often occurs 4 weeks after the onset of severe acute pancreatitis. Differentiation between pancreatic abscess and infected pancreatic necrosis is often difficult, and it is reported, according to present knowledge, that their mortality rates are almost the same [20]. An abscess that has occurred following an operation for acute pancreatitis should be assessed as a postoperative abscess and differentiated from an abscess that has occurred while the disease is being managed conservatively.

Alcoholic pancreatitis

Alcoholic pancreatitis is defined as acute pancreatitis associated with alcohol consumption; however, there is no report to date that has defined alcoholic pancreatitis clearly. It is thought that mechanisms involved in its occurrence include contraction of the Oddi sphincter, obstruction of the pancreatic duct due to the sedimentation of an insoluble protein plug, and activated pancreatic protease. Genetic mutation and smoking are also reported to be cofactors that induce pancreatitis [21].

Gallstone-induced pancreatitis

Gallstone-induced pancreatitis is defined as acute pancreatitis caused by gallstones. Although its mechanism is not known, it is assumed that it can be induced by obstruction of the common bile duct and pancreatic duct, which can occur when gallstones are excreted into the duodenum through the common bile duct. Findings that suggest the presence of biliary sludge (obstructive jaundice) are often observed. There can be a complication of cholangitis. Edema of the Vater papilla after gallstones have been excreted, as well as obstruction of the bile duct and pancreatic duct, is also assumed to cause gallstone-induced pancreatitis [22, 23].

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Health insurance and payment systems for severe acute pancreatitis

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Abstract The medical insurance system of Japan is based on the Universal Medical Care System guaranteed by the provision of the Article 25 of the Constitution of Japan, which states that "All the people shall have the right to live a healthy, cultural and minimum standard of life." The health insurance system of Japan comprises the medical insurance system and the health care system for the long-lived. Medical care insurance includes the employees' health insurance (Social Insurance) that covers employees of private companies and their families and community insurance (National Health Insurance) that covers the self-employed. Each medical insurance system has its own medical care system for the retired and their families. The health care system for the long-lived covers people of over 75 years of age (over 65 years in people with a certain handicap). There is also a system under which all or part of

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This article is based on the studies first reported in the JPN guidelines for the management of acute pancreatitis. 3rd ed. JPN Guidelines 2010 (in Japanese). Tokyo: Kanehara; 2009.

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the medical expenses is reimbursed by public expenditure or the cost of medical care not covered by health insurance is paid by the government. This system is referred to collectively as the "the public payment system of medical expenses." To support the realization of the purpose of this system, there is a treatment research enterprise for specified diseases (intractable diseases). Because of the high mortality rate, acute pancreatitis is specified as an intractable disease for the purpose of reducing its mortality rate, and treatment expenses of patients are paid in full by the government dating back to the day when the application was made for a certificate verifying that he or she has severe acute pancreatitis.

Introduction

The average longevity of the Japanese people is 79 years in men and 86 years in women [1]. The long average life span of the Japanese people is a result of support by the Universal Medical Care System based upon the Constitution of Japan along with monetary allowances provided for under this system. No other countries in the world have a medical insurance system comparable to that of Japan which has the two characteristics mentioned above.

Characteristics of the health insurance system of Japan: medical insurance system and health care system for the long-lived

The health insurance system of Japan comprises primarily the medical insurance system and the health care system for the long-lived (also referred to as the health care system for the elderly above 75 years).

The people pay an insurance premium according to their normal level of income. The amount of premium is determined in accordance with their income at the time when the insurance came into effect. Patients pay a part of the cost of medical care that they have received, although a substantial part of it is paid for either by their employers or by public expenditure (tax revenues of national and/or local government). Medical benefit is covered fully by health insurance as needed, irrespective of the amount of the premium that they have paid. A big difference from private insurance is that its resources come entirely from the premium paid by the policy holders.

The medical insurance system of Japan originated with the Health Insurance Law that was enacted in 1922. In 1946, the new Constitution of Japan was promulgated in 1946 after the end of World War II. It stipulates as follows: "All the people shall have the right to live a healthy, cultural and minimum standard of life," and "In all the spheres of life, the State shall make every effort to promote and extend social welfare and social insurance together with public health." The Universal Medical Care System was completed in 1961 when the social security system was put in order on the basis of the provision of the new Constitution,

The health care system comprises Employees' Health Insurance (Social Insurance) that covers employees of private companies and their families and National Health Insurance that covers the self-employed. Each system has its own programs of medical care services for the retired and their families. Currently, the Japanese people under 70 years of age must pay 30% of medical care cost and 70% is paid by the insurance system.

On the other hand, the medical care cost of the elderly over 70 years of age became free of charge in 1973. However, as a result of the extended longevity of the Japanese people and an increase in medical expenses, the Health Care Law for the elderly was enacted in 1983 that introduced a system under which a part of the medical cost is paid by patients. Along with a further decrease in the proportion of the elderly and a decrease in the birth rate in Japan, the proportion of contribution from the revenue of health insurance societies decreased. Also, there is not a small number of the retired who maintain the same level of income as that of the working generation. In consideration of such backgrounds, innovation of the health care system for the elderly is underway, and the health care system for the long-lived was implemented in April 2008 [2]. According to the provision of this system, the elderly of 70–74 years of age are classified into the category of the elderly who are in the early phase of old age (zennki koreisya) and they have to pay 30% of medical care expenses. On the other hand, the elderly of over 75 years of age are classified into the category of the elderly who are in the late phase of old age (koki koreisya) and they have only to pay 10% (30% in the elderly who maintain the same level of income as that of the working generation). Furthermore, it is stipulated that the elderly must also pay a premium regularly, although it is only a small amount.

Payment system of medical expenses

There is also a system under which the government pays all or part of the medical expenses or expenses not covered by medical care insurance (Table 1). This system is called collectively the 'payment system of medical expenses.'

The purpose of providing medical care whose cost is paid by the government lies in the improvement and

Table 1 Public Health insurance and payment systems in Japan

(A) Standard

1. <75 years old

(1) Social Insurance (Employees' Health Insurance) covers employees of private companies and their families

(2) National Health Insurance covers the self-employed and their families.

2. ≥75 years old

The health care system for the long-lived covers the people of over 75 years of age (over 65 years in people with a certain handicap).

(B) The public payment system of medical expenses

All or part of the medical expenses are reimbursed by public expenditure or the cost of medical care not covered by health insurance is paid by the government.

This system was based on the Livelihood Protection Law, the Child Welfare Law, the Maternal and Child Health Law, the Independence Supporting Law, the Infectious Disease Law, the Law Related to Mental Health and Welfare, medical care services for people certified as atomic bomb victims, the Law for Aid to Wounded and Sick-retired Soldiers, Treatment and Research Enterprise for Specified Diseases (45 diseases are specified at present)

development of social welfare and public health. This system is put into practice by the national government or local government on the basis of normal financial resources (including tax revenues) so that medical benefits may be conferred. To be concrete, a diverse range of services is provided for according to this system including payment of medical benefit based on the Livelihood Protection Law, the Child Welfare Law, the Maternal and Child Health Law, the Independence Supporting Law, the Infectious Disease Law, the Law Related to Mental Health and Welfare, medical care services for people certified as atomic bomb victims, the payment of medical benefit based on the Law for Aid to wounded and sick-retired Soldiers. Furthermore, as an enterprise of measures for control of intractable diseases including severe acute pancreatitis, there is a 'Treatment and Research Enterprise for Specified Diseases.'

A research enterprise of treatment of specified diseases including acute severe pancreatitis

In 1973, a research enterprise of treatment of specified diseases including acute severe pancreatitis was initiated as one of the enterprises of measures for control of intractable diseases. As mentioned above, a substantial proportion of overall medical expenses are to be borne by the insurance system. However, in intractable or severe diseases, the cost of medical care may amount to a large sum even if patients pay a small proportion of it. The purpose of this system is to reduce the cost of medical care to be borne by patients

themselves with serious and/or rare intractable diseases (45 diseases are specified at present) including severe acute pancreatitis. For such diseases, the total amount of treatment cost is reimbursed from the public expenditure dating back to the day when the application was made for a certificate to receive treatment of serious and/or rare intractable diseases.

The application for receiving payment should be made by patients themselves or their families to their public health office or prefectural government (depending upon the area in which they live) by submitting: an application form for a certificate to receive treatment for a specified disease and a resident card together with a clinical examination record prepared by their physicians. Once a patient has been proven to have a specific disease, medical expenses paid by the patient will be borne, on principle, by the national and local (prefectural) government on the basis of 50/50 for a period of 6 months (or longer, if severe acute pancreatitis persists) from the date when the application was made for receiving payment. Note should be taken that the payment of medical care expenses starts on the date of the application for receiving payment, so the application should be made as soon as possible. Also, it should be noted that the definition of severe acute pancreatitis under this system is based on the criteria for severity assessment established under the sponsorship of the Ministry of Health, Labour and Welfare.

The homepage website of the Japan Disease Center (http://www.nanbyo.or.jp) provides patients and their families with information on subjects such as "Severity Assessment Criteria" and the "Clinical Examination Record". The information is prepared by the Research Group for Specific Intractable Pancreatic Diseases under the sponsorship of the Japanese Ministry of Health, Labour and Welfare.

Specific medical checkup and specific health guidance

Along with changes in lifestyle and dietary habits of the Japanese, there is an increase in lifestyle-related diseases such as obesity, diabetes, hypertension and metabolic syndrome. Also, diseases induced by the conditions mentioned above (or aggravation factors) are increasing currently. Under these circumstances, large-scale preventive measures including specific medical checkup and specific health guidance were implemented in April 2008 in Japan.

Specific medical checkup is conducted for all the Japanese people of 40–74 years of age by focusing on examinations of metabolic syndrome in particular. Included in the examinations are history taking (use of medication, smoking habit, etc.), physical measurement (height, abdominal circumference and BMI: body mass index),

blood pressure, physical examination, urinalysis (urine sugar and urine protein) and blood test (lipid, sugar and liver function).

Medical checkup is optional and expenses are paid primarily by health insurance companies. Patients will get feedback on test results and information on appropriate guidance in about a month.

In those people who have been assessed as having a high risk of developing lifestyle-related diseases and requiring guidance, health care guidance for improvement in dietary and exercise habits is provided for by physicians, public health nurses and nutritional managers. The contents of guidance include support for motivation and active support, and more active support is provided for those with a higher risk. The assessment of the improvement in a dietary habit is to be conducted in 6 months.

Ten months have passed since the implementation of this system, and there is a report of news coverage from the overseas governments and media [3].

It is expected that such national-scale efforts as these will result in a reduction in the occurrence of severe acute pancreatitis or its aggravation in future.

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Changes in management of acute pancreatitis before and after the publication of evidence-based practice guidelines in 2003

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Abstract

Background The Japanese Guidelines for the Management of Acute Pancreatitis was published in 2003. However, the impact of the guidelines on physicians' practice patterns has not been well known.

This article is based on the studies first reported in the JPN guidelines for the management of acute pancreatitis. 3rd ed. JPN Guidelines 2010 (in Japanese). Tokyo: Kanehara; 2009.

Methods To examine the current clinical practices in the management of acute pancreatitis, we conducted a questionnaire survey with members of three societies involved in the treatment of pancreatic diseases and abdominal emergency medical care. Questions included diagnostic and treatment processes considered important in the management of acute pancreatitis in addition to demographic data, experience in medical care, and areas of specialty of respondents. We also examined changes in the treatment of

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acute pancreatitis before and after publication of the Guidelines.

Results Of 1,000 society members to whom questionnaires were mailed, 590 responded. Respondents who had read the Guidelines also handled significantly more cases in the most recent 3 years. A variety of changes were observed in the performance of clinical practices before and after publication of the Guidelines. The use of amylase in the assessment of severity decreased significantly, while its use for determination of severity scores increased significantly after publication of the Guidelines. In treatment, use of a nasogastric tube in mild and moderate cases deceased after the Guidelines. The frequency of prophylactic use of antibiotics decreased with mild pancreatitis after publication of the Guidelines.

Conclusions Although it is difficult to attribute these changes to the direct influence of the Guidelines, several changes were observed in performance of clinical practices in accordance with recommendations of the Guidelines.

Keywords Acute pancreatitis · Clinical practice guidelines · Physicians' practice pattern · Questionnaire survey

Introduction

Acute pancreatitis is a relatively common disease that occurs in 50 ~ 80 cases/100,000 population annually [1–8]. In recent years, the overall mortality rate of this disease has ranged from 2.9 to 7.8% in Japan [9–11]. However, the mortality rate of severe acute pancreatitis is more than 30% even today [12]. Therefore, improvement in its prognosis is an important problem that needs to be addressed. To improve the outcome of patients with acute pancreatitis, guidelines for its management have been drafted based on results from current clinical studies [13–16]. The Japanese Guidelines for the Management of Acute Pancreatitis [17] (hereafter, "Guidelines"), published in 2003, had a substantial impact on subsequent preparation of guidelines within the country.

Diffusion of effective treatments via guidelines is likely to have a major impact on patient outcomes. However, a number of studies have shown that guideline adherence is not necessarily satisfactory [18]. Without effective use, the presence of guidelines, even if its preparation required substantial manpower and expenses, would be meaningless. To examine the contents of current medical care with respect to the degree of guideline adherence, we conducted a questionnaire survey with members of three societies involved in the treatment of pancreatic diseases and abdominal emergency medical care. Furthermore, we examined changes in the treatment of acute pancreatitis before and after publication of the Guidelines.

Methods

We conducted a descriptive study using questionnaires with approximately 1,000 participants, including councilors and members of the Japanese Society of Abdominal Emergency Medicine, the Japan Pancreas Society, and the Japanese Society of Hepato-Biliary-Pancreatic Surgery. Participants were randomly selected from members of these societies at the rate of 1 of 3 members, and questionnaires were mailed together with a self-addressed return envelope. Details of the survey are shown in Table 1. Questions included diagnostic and treatment processes considered important in the management of acute pancreatitis in addition to demographic data, experience in medical care, and areas of specialty of respondents. First, we divided respondents by whether they had read the Guidelines or not. Respondents who replied "I read the text," "I only read the recommendations," and/or "I read the flow charts" were considered to have read the Guidelines. To document changes in clinical practice within these groups before and after publication of the Guidelines in July 2003 between the two groups, we compared the proportions of respondents who performed clinical practices in accordance with the Guidelines using Chi-square tests.

Next, we determined whether there were changes in clinical practices before and after publication of the Guidelines in each respondent. Based on changes before and after publication of the Guidelines, respondents were divided into the following three groups: those who did not perform the clinical practice in the past but who perform it now, those who performed the practice in the past but do not perform it now, and those for whom no changes were observed or who did not provide an answer. Differences in clinical practice changes between the two groups were examined using Mann–Whitney U tests.

Medical facilities in which chief physicians in charge of medical care were members of the societies were asked about the number of cases with acute pancreatitis that respondents handled over the period of 3 years between 2002 and 2004, as well as patient outcomes based on severity.

Results

Respondents

Of 1,000 society members to whom questionnaires were mailed, 590 responded (response rate, 59%). Respondents were divided into the following two groups based on their recognition of the Guidelines: (1) those who had read the Guidelines ($N = 463$) and (2) those who had not read the

Table 1 Recognition of the Guidelines and respondent characteristics

Item	Respondents who have read the Guidelines N (%)	Respondents who have not read the Guidelines N (%)	P value
Age (years)			
20–30	65 (22)	56 (21)	0.78
40–49	126 (43)	124 (46)	
50–59	73 (25)	71 (26)	
60–69	26 (9)	19 (7)	
Clinical practices setting			
University hospital	123 (42)	103 (38)	0.42
Designated hospital for clinical training	237 (81)	208 (76)	0.12
Clinical practices department			
Gastrointestinal medicine	56 (19)	19 (7)	<0.001
Other internal medicine	15 (5)	11 (4)	
Gastrointestinal surgery	142 (48)	127 (47)	
Other surgery	41 (14)	85 (31)	
Emergency care	21 (7)	6 (2)	
Others or no response	18 (6)	24 (9)	
Area of specialty			
Hepato-biliary pancreatic diseases	206 (70)	162 (60)	0.02
Case numbers for 3 years			
0 or no response	49 (17)	131 (48)	<0.001
<10 cases	136 (46)	113 (42)	
11–20 cases	60 (20)	17 (6)	
>21 cases	48 (16)	11 (4)	

Guidelines ($N = 127$). Respondents who answered that they only read the recommendations and those who answered that they only read the flow charts were included in the group of respondents who read the Guidelines. Those who did not answer to the question were included in the group that did not read the Guidelines. Table 1 summarizes the details of the respondents. Of those that read the "Guidelines", the proportion of respondents specializing in gastrointestinal diseases was high and that of general surgeons was low compared those who did not read the "Guidelines". Also, the proportion of respondents specializing in hepato-biliary pancreatic diseases was significantly higher (70 vs. 60%; $P = 0.02$) in the group that read the Guidelines. Respondents who had read the Guidelines also handled significantly more cases for 3 years.

Changes in the performance of medical care before and after publication of the Guidelines

Changes in performance of medical care before and after publication of the Guidelines are shown in Table 2. Changes were observed in diagnosis, severity assessment, treatment, nutrition support, and specific therapy. Before

publication of the Guidelines, there were more respondents who used amylase to diagnose acute pancreatitis than those who used lipase. However, following publication of the Guidelines, these numbers became almost equal between the groups. In contrast, frequency of the use of amylase in the assessment of severity decreased significantly, while its use for determination of severity scores increased significantly after publication of the Guidelines.

In treatment, use of a nasogastric tube in mild and moderate cases deceased after the Guidelines. The frequency of prophylactic use of antibiotics decreased with mild pancreatitis after publication of the Guidelines, although more than 40% of respondents replied that they used antibiotics for prophylactic purposes. In contrast, it was found that prophylactic antibiotics were in use in moderate and/or severe pancreatitis at a high proportion. Furthermore, the use of protease inhibitors decreased in mild pancreatitis cases after publication of the Guidelines, although no changes were observed in the proportion of its use in moderate and severe pancreatitis. With respect to H_2 receptor antagonists, the proportion of their use increased in mild cases and decreased in moderate and severe cases after publication of the Guidelines (21 vs. 30%, $P = 0.002$).

Table 2 Changes in performance of clinical practices after publication of the Guidelines (all respondents)

Item	Before publication of the Guidelines N (%)	After publication of the Guidelines N (%)	P value
Diagnosis of acute pancreatitis			
Amylase	414 (97)	407 (96)	0.18
Lipase	268 (63)	320 (75)	<0.001
Decision on diagnosis			
Amylase	203 (52)	165 (41)	0.002
Lipase	121 (31)	191 (47)	<0.001
Severity assessment			
Amylase	116 (28)	91 (22)	0.045
Lipase	51 (12)	49 (12)	0.83
CRP	147 (36)	149 (36)	0.94
Severity score (either)	373 (90)	399 (96)	<0.001
Score of the Ministry of Health, Labour and Welfare	230 (56)	238 (57)	0.73
Contrast-enhanced CT	351 (83)	386 (91)	<0.001
Treatment			
Nasogastric tube (mild and moderate)	156 (38)	87 (21)	<0.001
Prophylactic antibiotic administration			
Mild	248 (59)	176 (43)	<0.001
Moderate	377 (91)	354 (86)	0.06
Severe	402 (98)	402 (99)	0.60
Protease inhibitors			
Mild	357 (86)	328 (80)	0.026
Moderate	404 (98)	397 (96)	0.222
Severe	408 (99.8)	411 (100)	0.499
H$_2$ receptor antagonists			
Mild	85 (21)	126 (30)	0.002
Moderate	351 (86)	307 (74)	<0.001
Severe	399 (98)	382 (92)	0.001
Nutrition			
Parenteral nutrition/enteral feeding (mild cases)	101 (25)	111 (28)	0.338
Enteral feeding (severe cases)	37 (9)	113 (28)	<0.001
Specific treatment for severe cases			
Selective digestive decontamination	85 (24)	128 (35)	0.001
Blood purification therapy	239 (66)	274 (74)	0.023
Intra-arterial infusion of protease inhibitors and antibiotics	259 (72)	295 (80)	0.012

Although no changes were observed in nutritional support (parenteral nutrition and enteral feeding) before and after publication of the Guidelines, the proportion of enteral feeding increased significantly in severe pancreatitis cases after publication (9 vs. 28%, $P < 0.001$). An increase in the proportion of all forms of specific treatment was observed, including selective digestive decontamination (24 vs. 35%, $P = 0.001$), blood purification therapy (66 vs. 74%, $P = 0.02$), and intra-arterial infusion of protease inhibitors and antibiotics (72 vs. 80%, $P = 0.01$).

Changes in performance of medical care and recognition of the Guidelines

The relationship between those who read the Guidelines or those who did not with changes in performance of medical care after publication of the Guidelines is summarized in Table 3. We first compared whether there was a difference in the proportion of respondents who read or did not read the Guidelines with respect to the performance of clinical practices prior to publication of the Guidelines.

Table 3 Changes in performance of clinical practices before and after reading the Guidelines and changes before and after its publication

Item	Respondents who read the Guidelines (N = 463)				Respondents who have not read the Guidelines (N = 127)				P value
	Numbers of respondents	Baseline (%)	+ (%)	− (%)	Numbers of respondents	Baseline (%)	+ (%)	− (%)	
Diagnosis of acute pancreatitis									
Amylase	368	97.3	0	0.6	57	98.2	0	2.4	0.09
Lipase	368	64.1	11.4	1.1	57	56.1	2.4	0.8	0.06
Decision on diagnosis									
Amylase	368	51.6	0.2	6.9	57	51.9	0.0	4.7	0.43
Lipase	368	24.6	14.9	0.9	57	5.5	4.7	0.8	0.00
Severity assessment									
Amylase	360	26.9	0.2	4.8	53	35.8	0	2.4	0.29
Lipase	360	12.5	1.7	1.7	53	11.3	0	0	0.99
CRP	360	35.0	1.7	1.7	53	39.6	0	0	0.96
Severity score (either)	360	90.8	5.0	0.2	53	86.8	3.1	0	0.45
Score of the Ministry of Health, Labour, and Welfare	360	55.6	3.2	1.7	53	56.6	3.1	0	0.45
APACHE score	360	3.1	0.4	0.4	53	1.9	0	0	0.98
Contrast-enhanced CT	368	83.7	7.6	0.6	55	78.2	3.1	0.8	0.08
Treatment									
Nasogastric tube (mild and moderate)	362	36.7	1.9	14.5	54	42.6	1.6	8.7	0.13
Prophylactic antibiotic administration									
Mild	363	61.2	1.1	14.7	54	48.1	0	5.5	0.02
Moderate	364	90.4	2.4	5.6	52	92.3	1.6	3.1	0.53
Severe	360	97.5	0.9	0.2	51	100	0	0	0.48
Protease inhibitors									
Mild	360	87.2	0.9	6.3	55	78.2	0.0	0.8	0.05
Moderate	360	97.8	0.6	1.5	53	98.1	0.0	0.8	0.96
Severe	358	99.7	0.2	0.0	51	100	0.0	0.0	0.60
H$_2$ receptor antagonists									
Mild	360	21.1	11.2	5.2	49	23.5	4.9	2.0	0.42
Moderate	360	86.4	1.5	11.4	49	85.3	2.0	3.9	0.03
Severe	360	98.1	0.2	4.8	49	91.2	1.0	2.0	0.13
Nutrition									
Parenteral nutrition/enteral feeding (mild cases)*	363	21.8	3.5	0.9	54	52.6	2.0	0.0	0.76
Enteral feeding (severe cases)	364	9.6	16.0	0.2	51	2.9	2.9	0.0	0.00
Specific treatment for severe cases									
Selective digestive decontamination	318	23.3	9.1	1.3	42	22.2	0.0	0.0	0.87
Blood purification therapy	318	65.4	8.0	2.2	42	70.4	2.0	1.0	0.11
Intra-arterial infusion of protease inhibitors and antibiotics	318	73.0	7.6	2.4	42	66.7	3.9	2.9	0.32

Baseline shows the proportion of performance before and after publication of the Guidelines

+, Proportion of respondents who did not perform clinical practices before publication of the Guidelines but began after its publication

−, Proportion of respondents who performed clinical practices before publication of the Guidelines but discontinued after its publication

* A significant difference (P < 0.05) in the performance of clinical practices among those who read the Guidelines and those who did not

A significant difference was observed between the two groups only in the proportion of respondents who answered that they used lipase for decision on diagnosis (24.6 vs. 5.5%, P < 0.001) and those who answered that they used parenteral nutrition or enteral feeding in mild pancreatitis cases (21.8 vs. 52.6%, P = 0.002).

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In contrast, significant differences were observed in the following items with respect to changes in performance of clinical practices before and after publication of the Guidelines: (1) lipase measurements for diagnostic decisions, (2) prophylactic antibiotic administration in mild cases, (3) prophylactic use of protease inhibitors in mild cases, (4) use of H_2 receptor antagonists in moderate cases, and (5) use of enteral feeding in severe cases. For those who read the Guidelines, the proportion of those who measured lipase to determine diagnosis was high before publication; the proportion of respondents who started measurements after publication was also high. No difference was observed between the two groups in the proportions of those who used antibiotics for mild cases and those who used H_2 receptor antagonists in moderate cases. However, the proportion of respondents who discontinued prophylactic use of antibiotics and H_2 receptor antagonists was high among those who read the Guidelines. There was no difference between groups with respect to the use of enteral feeding in severe cases, although the proportion of respondents who began enteral feeding was high among those who read the Guidelines. With respect to severity assessment, there was no difference in the use of any of the parameters between both groups before and after publication of the Guidelines.

Discussion

In this study, we conducted a questionnaire survey with members of major societies in Japan who are involved in pancreatic disease treatment and abdominal emergency clinical practices. The response rate (59%) was relatively high. It is likely that respondents have many opportunities to get involved with patients with acute pancreatitis compared to non-respondents. Thus, respondents are likely to have a deep interest in the treatment of pancreatitis and care of patients afflicted with this disease. Accordingly, our results likely reflect a higher level of acute pancreatitis management than actually exists.

Our data demonstrated that acute pancreatitis management as recommended by the Guidelines is not adhered to as widely as expected. Almost all respondents replied that they measure amylase levels, while only 75% of the respondents measure lipase levels. It comes partly from the accessibility issues of lipase measurement in Japan that lipase is not measurable after and/or even in daily hours in some hospitals. Approximately 90% of respondents answered that they conduct contrast-enhanced CT, although the proportion of respondents who answered that they used the score system created by the Ministry of Health, Labour, and Welfare (MHLB) was less than 60%. The proportion of respondents who answered that they used CRP as the single marker for severity assessment was 36%. Although the

Guidelines recommend against the usage of a nasogastric tube, parenteral nutrition, and prophylactic antibiotics in mild cases, the proportion of respondents who used these was relatively high. Furthermore, while the Guidelines recommend that protease inhibitors be used only in severe cases, we found that they are widely used in patients irrespective of severity. Despite recommendations against the use of H_2 receptor antagonists based on severity, 92% of respondents indicated their use in 30% of mild cases, 74% of moderate cases, and up to 92% of severe cases.

Changes were also observed in the performance of clinical practices after publication of the Guidelines. A substantial portion of these changes occurred in accordance with its recommendations. With respect to the decision on diagnosis, measurement of amylase decreased (52 vs. 41%, $P = 0.002$), whereas that of lipase increased (31 vs. 47%, $P < 0.001$). The proportion of respondents who use contrast-enhanced CT for severity assessment increased (83 vs. 92%, $P < 0.001$). With respect to individual treatment processes, use of a nasogastric tube in mild and moderate cases and administration of prophylactic antibiotics and protease inhibitors in mild cases deceased. Use of H_2 receptor antagonists decreased in mild cases and increased in moderate and severe cases. With respect to nutrition support, there were no changes in those who answered that they conduct parenteral nutrition or enteral feeding before or after publication of the Guidelines, while those who answered that they use enteral feeding in severe cases significantly increased (9 vs. 28%, $P < 0.001$). The proportion of the use of specific treatments in severe cases increased in both forms of nutrition support after publication of the Guidelines.

Discussing the impact of the Guidelines on performance of clinical practices is generally difficult. In the present study, a variety of changes were observed in the performance of clinical practices before and after publication of the Guidelines, so the influence of secular trends as a factor responsible for the changes should be considered. Respondents were divided into two groups based on whether they read the Guidelines or not. No significant difference was found in the age of respondents and the medical facilities at which they work, potentially due to differences in their areas of speciality and the annual number of cases associated with their medical institutions. In contrast, a significant difference was observed between the two groups in the performance of some clinical practices' activities after publication of the Guidelines, while no difference was observed in the performance of others. These results suggest that only a few changes were observed in performance of clinical practices in accordance with recommendations of the Guidelines, but it is difficult to attribute these changes to the direct influence of the Guidelines. With respect to the number of respondents who have read the Guidelines, more specialize in gastrointestinal diseases compared to those

who have not read the Guidelines; the former also see patients with acute pancreatitis more frequently than the latter. Accordingly, those who have read the Guidelines are likely more frequently exposed to recent information on acute pancreatitis.

Reasons for lack of adherence to the Guidelines are diverse. According to a systematic review of articles by Cabana et al., 46 articles discussed "insufficient recognition of guidelines" and 31 discussed "unfamiliarity with the contents of guidelines" as factors that obstruct guideline adherence. Other factors mentioned were the "inability to agree with guidelines," "lack of results to be expected by following guidelines," "lack of ability to put into practice recommendations of guidelines," "lack of volition," and "inability to break habits." External obstacles were "lack of patients' agreement," "presence of contents opposed to existing opinions," "presence of restrictions by an organization or the medical system," "not covered by medical insurance," and "concerns about a possible increase in medical lawsuits" [18]. The rate of adherence to the Guidelines in the present study was by no means high. The following factors may have contributed to the low adherence rate in the present study: lack of knowledge about the Guidelines, inability to agree with contents of the Guidelines, and inability to break habits in clinical practices. We speculate that many of the non-respondents have no knowledge of or no interest in the Guidelines. With the exception of one item, there was no substantial change in performance of clinical practices even among those who read the Guidelines. Such a lack of change might be due to the inability to agree with contents of the Guidelines and inability to break habits in clinical practices. Changes in performance of clinical practices in accordance with recommendations observed among those who had not read the Guidelines suggest that clinical practices for acute pancreatitis are improving. These may come from the situations that brochures and handouts of the guidelines were distributed and symposiums of the Guidelines were taken place several times in many conferences.

Conclusions

We found that the Guidelines are being read more frequently by physicians who specialize in gastrointestinal diseases and hepato-biliary pancreatic diseases, as well as those who treat patients with acute pancreatitis. An improvement in adherence rate was observed with respect to several clinical practices recommended by the Guidelines. Such an improvement in adherence was observed in physicians who had read the Guidelines and those who had not.

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New diagnostic criteria of acute pancreatitis

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Abstract Practical guidelines for the diagnosis of acute pancreatitis are presented so that a rapid and adequate diagnosis can be made. When acute pancreatitis is suspected in patients with acute onset of abdominal pain and tenderness mainly in the upper abdomen, the diagnosis of acute pancreatitis is made on the basis of elevated levels of pancreatic enzymes in the blood and/or urine. Furthermore, other acute abdominal diseases are ruled out if local findings associated with pancreatitis are confirmed by diagnostic imaging. According to the diagnostic criteria established in Japan, patients who present with two of the following three manifestations are diagnosed as having acute pancreatitis: characteristic upper abdominal pain, elevated levels of pancreatic enzymes, and findings of

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ultrasonography (US), CT or MRI suggesting acute pancreatitis. Detection of elevated levels of blood pancreatic enzymes is crucial in the diagnosis of acute pancreatitis. Measurement of blood lipase is recommended, because it is reported to be superior to all other pancreatic enzymes in terms of sensitivity and specificity. For measurements of the blood amylase level widely used in Japan, it should be cautioned that, because of its low specificity, abnormal high values are also often obtained in diseases other than pancreatitis. The cut-off level of blood pancreatic enzymes for the diagnosis of acute pancreatitis is not able to be set because of lack of sufficient evidence and consensus to date. CT study is the most appropriate procedure to confirm image findings of acute pancreatitis. Elucidation of the etiology of acute pancreatitis should be continued after a diagnosis of acute pancreatitis. In the process of the etiologic elucidation of acute pancreatitis, judgment whether it is gallstone-induced or not is most urgent and crucial for deciding treatment policy including the assessment of whether endoscopic papillary treatment should be conducted or not. The diagnosis of gallstone-induced acute pancreatitis can be made by combining detection of elevated levels of bilirubin, transamylase (ALT, AST) and ALP detected by hematological examination and the visualization of gallstones by US.

Keywords Acute pancreatitis · Guidelines · Diagnostic criteria · Etiology · Gallstone pancreatitis · Clinical indicators

Introduction

The diagnosis of acute pancreatitis is determined on the basis of acute onset of abdominal pain and tenderness mainly in the upper abdomen, elevated levels of pancreatic enzymes in the blood and/or urine and findings of pancreatitis detected by diagnostic imaging such as ultrasonography (US) and CT. Other abdominal diseases should be ruled out. After the diagnosis of acute pancreatitis has been made, its etiology should be made clear to decide treatment policy of acute pancreatitis or to prevent the recurrence of pancreatitis.

The diagnostic criteria established by the Japanese Ministry of Health, Labour, and Welfare were revised in part in 2008. The present article shows a detailed description of the new diagnostic criteria. Based on up-to-date evidence, also reviewed are hematological examination, urinalysis, and various types of diagnostic imaging in the diagnosis of acute pancreatitis, and the clinical significance of etiological search.

Diagnostic criteria

CQ1 What are the diagnostic criteria for acute pancreatitis?

1. Acute abdominal pain and tenderness in the upper abdomen.

2. Elevated levels of pancreatic enzymes in the blood or urine.

3. Abnormal findings of acute pancreatitis detected by US, CT or MRI.

Patients who present with at least two of the above three manifestations and in whom other pancreatic diseases and acute abdomen have been ruled out are diagnosed as having acute pancreatitis. However, acute aggravation in chronic pancreatitis should be included as the category of acute pancreatitis.

Note: Measurement of pancreatic enzymes (such as pancreatic amylase and lipase) with high specificity for the pancreas is desirable.

In the diagnostic criteria of acute pancreatitis established by the Japanese Ministry of Health, Labour, and Welfare 2008 [1], a diagnosis of acute pancreatitis is made if the patient presents with at least two of the following three manifestations: acute attack of abdominal pain and tenderness in the upper abdomen, elevated levels of pancreatic leaking enzymes and findings of the pancreas detected by US, CT or MRI. Because individual cut-off levels differ depending upon reports (Table 1) [2–13], at present there is neither sufficient evidence nor consensus to support the setting of cut-off levels.

Indicated for differential diagnosis is acute abdomen causing abdominal pain, which also arises from perforation of the alimentary tract, acute cholecystitis, ileus, mesenteric artery occlusion and acute aortic dissection.

Clinical symptoms and signs

CQ2 What are clinical symptoms and signs in patients in whom acute pancreatitis is suspected?

Acute pancreatitis should be differentiated from other abdominal diseases in patients who have acute onset of abdominal pain and tenderness mainly in the upper abdomen (Recommendation A)

It is reported that more than 90% of patients with acute pancreatitis complain of abdominal pain (Table 2) (Level 3b–5) [14–16]. Clinical symptoms and signs most characteristic of acute pancreatitis are acute attack of abdominal pain and tenderness in the upper abdomen. It is reported that abdominal pain occurs most frequently in the upper abdomen followed by the whole abdomen, while tenderness occurs most frequently in the whole abdomen followed by the upper abdomen and the right

Table 1 Diagnostic ability of pancreatic enzyme measurements for acute pancreatitis

Author	Year	n (AP)	Methodology	Upper limit of normal	Cut-off values	Sensitivity	Specificity	PPV	NPV	PLR	NLR	AUC
Lipase												
Steinberg et al. [2]	1985	163 (39)	Turidimetric	72	75	86.5	99.0	97.0	95.1	86.50	0.14	
Ventrucci et al. [3]	1986	189 (12)	ELISA	62	62	91.7	84.7	42.3	98.9	5.99	0.10	
Thomson et al. [4]	1987	168 (×)	Seragen-lipase	68	68	100.0	96.0	85.0	100.0	25.00	0.00	
Jang et al. [5]	2007	193 (17)	Turbidimetric	100.0	300.0	53.0	99.0				9.00	0.05
Petrov et al. [6]	2007	178 (64)	Turbidimetric	60.0	180.0	92.0	94.0	89.0	95.0			0.960
Sáezet al. [7]	2005	72 (50)	Turbidimetric	60.0	180.0	84.0	85.7	93.4	72.0	5.87	0.19	
Chenet al. [8]	2005	165 (98)	Turbidimetric	190.0	570.0	94.0	92.9	90.0	95.8	13.24	0.06	
Kylänpää-Bäck et al. [9]	2002	237 (29)	Turbidimetric	200.0	200.0	79.0	88.0	49.0	97.0	6.58	0.24	
					600.0	55.0	99.0	84.0	94.0	55.00	0.45	
Wilson et al. [10]	2005	188 (29)	Turbidimetric	190.0	570.0	100.0	99.0	97.0	100.0	100.00	0.00	
Amylase												
Steinberg et al. [2]	1985	163 (39)	Phadebas	326	326	94.9	86.0	75.5	97.4	6.78	0.06	
					600	92.3	100.0	100.0	96.6	ND	0.08	
Pace et al. [11]	1985	121 (21)	Phadebas	300	300	100.0	71.6	15.6	100.0	3.52	0.00	
Ventrucci et al. [3]	1986	189 (12)	Phadebas	377	377	91.7	77.8	35.5	98.6	4.13	0.11	
Thomson et al. [4]	1987	168 (×)	Phadebas	316	316	95.6	97.6	91.7	98.8	39.83	0.05	
					1000	60.9	100.0	100.0	90.4	∞	0.39	
Jang et al. [5]	2007	192 (17)	Turbidimetric	100.0	570.0	100.0	99.0	97.0	100.0	100.00	0.00	
Raty et al. [12]	2007	51 (13)	Turbidimetric		300.0	41.0	95.0			1.40	0.09	0.731
					×2 (Upper limit of normal)							0.654
Petrov et al. [6]	2007	177 (64)	Turbidimetric	100.0	×3 (Upper limit of normal)							0.910
Sáez et al. [7]	2005	72 (50)	Turbidimetric	100.0	300.0	77.0	95.0	89.0	87.0			
Chen et al. [8]	2005	165 (98)	Turbidimetric	190.0	330.0	74.0	86.4	92.5	59.3	5.44	0.30	
Wilson et al. [10]	2005	188 (29)	Turbidimetric	108.0	570.0	94.9	91.4	86.9	88.5	11.03	0.06	
p-Amylase												
Koehler et al. [13]	1982	37 (×)	Cellulose Electropheresis	52	324.0	63.0	99.0	95.0	93.0	63.00	0.37	
Steinberg et al. [2]	1985	163 (39)	Wheat Protein Inhibitor	181	181	92.3	85.1	73.5	96.1	6.19	0.09	
					375	84.0	96.5	91.7	93.3	24.00	0.17	
Pace et al. [11]	1985	121 (21)	Cellulose Electropheresis	120	225	100.0	48.9	17.9	100.0	1.96	0.00	
Ventrucci et al. [3]	1986	189 (12)	Phadebas	220	220	100.0	84.4	46.2	100.0	6.41	0.00	
Elastase-1												
Wilson et al. [10]	2005	188 (29)	ELISA	3.5	3.5	80.0	96.0	80.0	96.0	20.00	0.21	

PLR = Sensitivity/(100 − Specificity)

NLR = (100 − Sens)/Spec

AP Acute pancreatitis, *PPV* positive predictive value, *NPV* negative predictive value, *PLR* positive likelihood ratio, *NLR* negative likelihood ratio, *AUC* area under the curve, *ND* not determined

upper abdomen (Table 3) (Level 4) [17]. There are cases in which acute pancreatitis is not accompanied by abdominal pain, although this occurs very rarely (Level 2b) [18]. Of all the patients with abdominal pain, the rate of acute pancreatitis is reported to be 0.9% ($n = 1000$) (Level 2b) [19] and that the rate of acute pancreatitis is 1.6% ($n = 6317$) when there is abdominal pain of acute onset in patients under 50 years of age and 7.3% ($n = 2406$) in patients over 50 years of age (Level 4) [20]. On the other hand, it is reported that the rate is 2–3% in the case of acute abdomen (Level 2b, 5) [21, 22]. Except for abdominal pain, symptoms and signs observed frequently include pain radiating to the back, anorexia, fever, nausea and vomiting, and decreased bowel sound (Table VI-1, 2) (Level 3b–5) [14–16].

Hematological examination and urinalysis

> CQ3   Which pancreatic enzyme measurements are important in making a diagnosis of acute pancreatitis?

Measurement of blood lipase is most useful for the diagnosis of acute pancreatitis (Recommendation A)

Table 2 Clinical symptoms and findings of acute pancreatitis

Symptoms[a]	Frequency of occurrence frequency (%)	Symptoms[b]	Frequency (%)
Abdominal pain	90	Abdominal pain	95
Muscular defense	80	Radiating pain to the back	
Nausea, vomiting	70	Anorexia	85
Meteorism	60	Nausea, vomiting	75
Ileus	55	Decreased sound of intestinal peristalsis	60
Jaundice	30	Fever	60
Shock	20	Muscular defense	50
Neurological findings	10	Shock	15
		Jaundice	15
		Hematemesis	10

[a] From Ref. [14]

[b] From Ref. [15] with partial alterations

When the measurement of blood lipase is difficult, blood amylase (pancreatic amylase) should be measured (Recommendation A)

Detection of elevated levels of blood pancreatic enzymes is crucial in the diagnosis of acute pancreatitis. The diagnostic ability of measurements of various types of pancreatic enzymes is listed in Table 1.

Among several pancreatic enzymes, blood amylase is used most widely because it can be measured rapidly. However, blood lipase is reported to be superior to blood amylase in terms of sensitivity and specificity [23–27] (Level 3b, 5). By comparison of values of various pancreatic enzymes for diagnosing acute pancreatitis (Level 2a) [28, 29], blood lipase has similar sensitivity to blood amylase but with superior specificity (Tables 4, 5), so measurement of blood lipase is recommended rather than blood amylase for the diagnosis of acute pancreatitis. Addition of measurements of blood amylase to blood lipase resulted in no improvement in the diagnostic ability of acute pancreatitis [30].

Blood lipase

The sensitivity and specificity of blood lipase in a diagnosis of acute pancreatitis are reported to be 85–100 and 84.7–99.0%, respectively (Level 2a) [28] and blood lipase is shown to be more sensitive than blood amylase (Level 2b–3b) [4, 31, 32] (Table 1). Abnormal values of blood lipase last longer than those of blood amylase (Level 2b) [33], so blood lipase is useful in a diagnosis of acute pancreatitis when blood amylase level is normal. Also, blood lipase has almost equal diagnostic value as that of blood p-amylase (Level 2b) [32]. Blood lipase is also reported to be useful because of its high sensitivity in a diagnosis of alcohol-induced acute pancreatitis (Level 2b) [34].

Blood amylase (total blood amylase)

The sensitivity and specificity of blood amylase in a diagnosis of acute pancreatitis are not constant because of the difference in the diagnostic grounds of acute pancreatitis and the cutoff level that has been set. When the cutoff blood amylase level is set at the upper limit of normal, its sensitivity and specificity are 91.7–100 and 71.6–97.6%,

Table 3 Abdominal pain, site of tenderness (%)

	RUQ	LUQ	RLQ	LLQ	Upper half	Lower half	Right half	Left half	Central	General
Site of abdominal pain	6		2	2	38	6		2	14	29
Site of tenderness	14	6			16		8	4		48

From Ref. [18]

Table 4 Diagnostic ability of measurements of blood amylase, *p*-amylase and lipase in acute pancreatitis

Lipase	Total amylase	Pancreatic amylase
Sensitivity		
Very good	Very good	Good
90–100%	95–100%	84–100%
Specificity		
Very good	Low	Good
99%	70%	40–97%
At upper limit of normal	Influenced by "cut-off level"	Influenced by "cut-off level"
Positive predictive value (PPV)		
Very good	Very low	50–96%
90%	15–72%	
Negative predictive value (NPV)		
95–100%	97–100%	70–100%
Reliability		
Good	Good	Poor

From Ref. [28] with partial alterations

Table 5 Sensitivity and specificity of main blood pancreatic enzymes

	Sensitivity (%)	Specificity (%)
Lipase	82–100	82–100
Total amylase	67–100	85–98
Pancreatic amylase	67–100	83–98
Trypsin	89–100	79–83
Elastase 1	97–100	79–96

From Ref. [29] with partial alterations

respectively. On the other hand, when the cutoff level is set higher, specificity improves but sensitivity decreases. It is shown that at the cutoff level of 1000 IU/L, specificity rises up to 100% while sensitivity goes down to 60.9% (Level 2a–3b) [2, 3, 8–11, 13, 25, 28, 35] (Table 1).

There are the following factors contributing to decreased blood amylase sensitivity. Blood amylase levels do not increase in many cases of alcohol-induced acute pancreatitis, especially when chronic pancreatitis is present in the background (Level 2b) [31, 36]. Compared with other pancreatic enzymes, blood amylase levels decrease soon after the onset of the disease and an abnormal high level lasts for only a short time. Therefore, if the passage of time from the onset of the disease to the hospital visit is long, the level may return to normal (Level 3b) [37, 38]. There is also a report showing that blood amylase levels seldom rise in the case of acute pancreatitis caused by hyperlipidemia (Level 3b) [39].

Table 6 Condition causing hyperamylasemia

Pancreatic diseases	Neoplastic lesion other than pancreatitis
Pancreatitis	Ovary prostate lung esophagus solid tumor of the thymus
Complications in pancreatitis (pancreatic pseudocysts, pancreatic abscess)	Multiple osteoma
	Pheochromocytoma
Trauma (surgery and ERCP included)	Others
Pancreatic obstruction	Renal failure
Pancreatic tumor	Renal transplantation
Cystic fibrosis	Macroamylasemia
Salivary disease	Burns
Infection (mumps)	Acidosis (ketotic non-ketotic)
Trauma (surgery included)	Pregnancy
X-rays irradiation	Head injury
Ductal stenosis	Drug-induced (morphine diuretic steroid)
Gastrointestinal disease	Acute aortic dissection
Penetration or perforation in gastrointestinal ulcer	Postoperative (except for trauma)
Intestinal penetration or perforation	Anorexia nervosa
Obstruction of mesenteric artery	Atopic
Appendicitis	
Liver disease(hepatitis cirrhosis)	
Gynecological disorder	
Rupture of ectopic pregnancy	
Ovarian cystoma	
Pelvic infection	

From Ref. [40]

A hole regarding blood amylase levels in a diagnosis of acute pancreatitis is that an abnormal high level is often detected in diseases other than pancreatic diseases (Table 6) and that blood amylase has poor specificity for diagnosis (Level 2a) [30].

p-Amylase (amylase isozyme)

There is a study reporting that, by measuring the blood *p*-amylase level, a differential diagnosis of hyperamylasemia not associated with pancreatic diseases was made in 83% (19/23 cases) of patients with hyperamylasemia (Level 4) [40]. On the other hand, there are reports showing that the differential ability of measurements of blood *p*-amylase was 20–44% (Level 3b) [11, 13]. According to another report, no improvement was observed in sensitivity and specificity compared with blood amylase and other blood pancreatic enzymes (Level 2b) [2] (Table 1). The usefulness of blood *p*-amylase in making a diagnosis of acute pancreatitis is therefore not certain.