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Original Paper

Dual Energy CT for determining the severity of acute pancreatitis

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Abstract

We aimed to quantitatively compare the iodine concentration measured by Dual Energy Computed Tomography (CT) between acute and mild pancreatitis cases and to evaluate the accuracy of the severity assessment of acute pancreatitis using Dual Energy CT. The contrast CT grade based on the guidelines in Japan and definitive diagnoses were evaluated. Iodine concentrations and C-reactive protein (CRP) levels were compared between mild and severe acute pancreatitis. The CECT grading diagnosed five false negative cases out of 41 patients. Only when the CRP reached the highest level, there was a significant difference between severe and mild cases. There were significant differences between the iodine concentration of severe and mild cases. Our results demonstrated measuring iodine concentration using Dual Energy CT is useful for severity assessment of acute pancreatitis.

Key words: Dual Energy CT, Contrast-Enhanced CT, abdomen, pancreatitis, iodine concentration

Introduction

Acute pancreatitis is an acute inflammation of the pancreas that may affect other adjacent and distant organs[1,2]. According to the results of a survey conducted in Japan in 2011, the ratio of the occurrence of mild acute pancreatitis to that of all the severity levels of acute pancreatitis together is 80.3%[3]. Mild acute pancreatitis involves minimal organ and systemic dysfunction. Although patients exhibit pancreatic swelling, enhanced CT images do not depict any poorly contrasted regions[1,3]. Therefore, in several cases, the clinical symptoms of patients with mild acute pancreatitis improve within 1 week[1].

Contrarily, the clinical characteristics of severe acute pancreatitis involve the necrosis of both or either the pancreatic parenchyma and surrounding tissues[3-5]. Patients with severe acute pancreatitis require longer hospital stays and are more prone to developing systemic or organ failures[6,7]. Therefore, an accurate assessment of acute pancreatitis severity is deemed essential for planning the appropriate initial treatment[8-11].

Currently, in Japan, the severity of acute pancreatitis is assessed based on nine prognostic factors, which comprise blood test results (including C-reactive protein, CRP), vital signs, and the CECT-based CT grade classification according to the "guidelines for the management of acute pancreatitis"[3]. Patients are diagnosed with severe acute pancreatitis if they exhibit a total of three or more prognostic factors. The CECT examination results are classified as grades 1 to 3 based on the degree of poor contrast regions in three pancreatic areas (head, body, and tail) and the extent of progression of the inflammation outside the pancreas; grades 2 and above indicate severe acute pancreatitis (Table 1). However, currently, these grades are assigned based on visual assessment. CRP levels are important in determining the severity of acute pancreatitis, and it has been reported that the second day is the most useful time for the measurement of CRP levels to determine the severity of pancreatitis[12].

Dual energy CT (DECT) is based on the principle

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Table 1. JPN Severity Score (JSS)

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 ≦ 3 mEq/l or shock (systolic blood pressure < 80 mmHg)	
2. PaO2 ≦ 60 mmHg (room air) or respiratory failure (respirator management is needed)	
3. BUN ≧ 40 mg/dL (or Cr ≧ 2.0 mg/dl) or oliguria (daily urine output < 400 ml even after IV fluid resuscitation)	
4. LDH ≧ 2 times of upper limit of normal	
5. Platelet count ≦ 100,000/mm^3	
6. Serum Ca ≦ 7.5 mg/dl	
7. CRP ≧ 15 mg/dl	
8. Number of positive measures in SIRS criteria ≧ 3	
9. Age ≧ 70 years	
CT grade by CECT	
1. Extra pancreatic progression of inflammation	
Anterior pararenal space	0 point
Root of mesocolon	1 point
Beyond lower pole of kidney	2 points
2. Hypo enhanced 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 score	
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 is judged as Grade 2 or more, the severity grading is evaluated to be as “severe”.
Measures in SIRS diagnostic criteria: (1) Temperature > 38℃ or < 36℃, (2) Heart rate > 90 beats/min, (3) Respiratory rate > 20 breaths/min or PaCO2 < 32 torr, (4) WBC > 12,000 cells/mm^3, < 4,000 cells/mm^3, or > 10% immature (band) forms

that the mass attenuation coefficient of a substance reflects unique changes depending on the energy of the X-ray photon passed through it to enable substance discrimination and property analysis[13–16]. Interestingly, one of the functions of DECT, three-material decomposition, allows the estimation of the amount of contrast agent present in known substances that are composed of two types of tissues[17–19]. Accordingly, this function can be used to assess the blood volume in the pancreas by measuring the iodine concentration.

In this study, we evaluated pancreatic ischemia leading to pancreatic necrosis via quantitative evaluation of the iodine concentration in the pancreas based on a CE-DECT examination and examined the efficacy of DECT as a new diagnostic modality for acute pancreatitis.

Methods

1. Ethics

This study was designed as a retrospective study. Any personal information included among all the data of the subjects in this study was anonymized, and the study was approved in advance by the ethics committee of Showa University Hospital (approval date: March 26, 2018; approval No: 2495).

2. Equipment used

CT data were acquired using a SOMATOM Force CT system (manufactured by Siemens Healthcare, Forchheim, Germany), and the iodine concentration was measured using the Syngo.via software version

6.4 (manufactured by Siemens Healthcare, Forchheim, Germany).

3. Subjects

Consecutive patients who underwent a contrast-enhanced CT examination for acute pancreatitis between December 2015 and March 2018 were retrospectively reviewed.

3.1 Consistency between the contrast CT grade and definitive diagnosis

Patients who were suspected of suffering from acute pancreatitis underwent a contrast-enhanced CT scan upon admission and were evaluated as mild/severe based on the contrast-enhanced CT grade which is a visual assessment in accordance with the "guidelines for the management of acute pancreatitis."

This study investigated the consistency between the severity assessment alone based on the CECT grade and the definitive diagnosis based on the results of the nine prognostic factors (Table 1). Suspected cases of acute pancreatitis were subjected to a CECT scan upon admission and were designated as mild/severe based on the CECT grade determined based on the visual assessment as outlined in the "guidelines for the management of acute pancreatitis"[3].

The imaging parameters used for CECT examination were: tube voltage=80 kV/Sn, 150 kV; tube current=automatic exposure control (AEC); X-ray tube rotation time=0.5 s/rotation; collection detector=Acq.128* 0.6 mm; pitch factor=0.6; image reconstruction function =Bv40 (soft abdominal region standard function); and reconstruction slice thickness=5 mm. The following contrast conditions were used: intravenous administration using a 22 or 20-gage needle, iodine amount=540 mgI/kg, and injection time=30 s. The images were captured via dynamic shooting using the fixed time method (plain, after 30 s, and after 60 s).

3.2 Measurement of iodine concentration in the three areas of the pancreas

A region of interest (ROI) was set for the head, body, and tail of the pancreas of each patient (Figure 1), and the iodine concentration was measured by a radiology technologist (H.H.) with five years of experience. The ROI size was unified to 1 cm^2. The ROIs were set at positions in which each of the three pancreatic sections could be observed in the widest range. To evaluate the decrease in contrast enhancement resulting from pancreatic necrosis, the representative value was set to the minimum value of the iodine concentration in the three pancreatic sections. The iodine concentration of

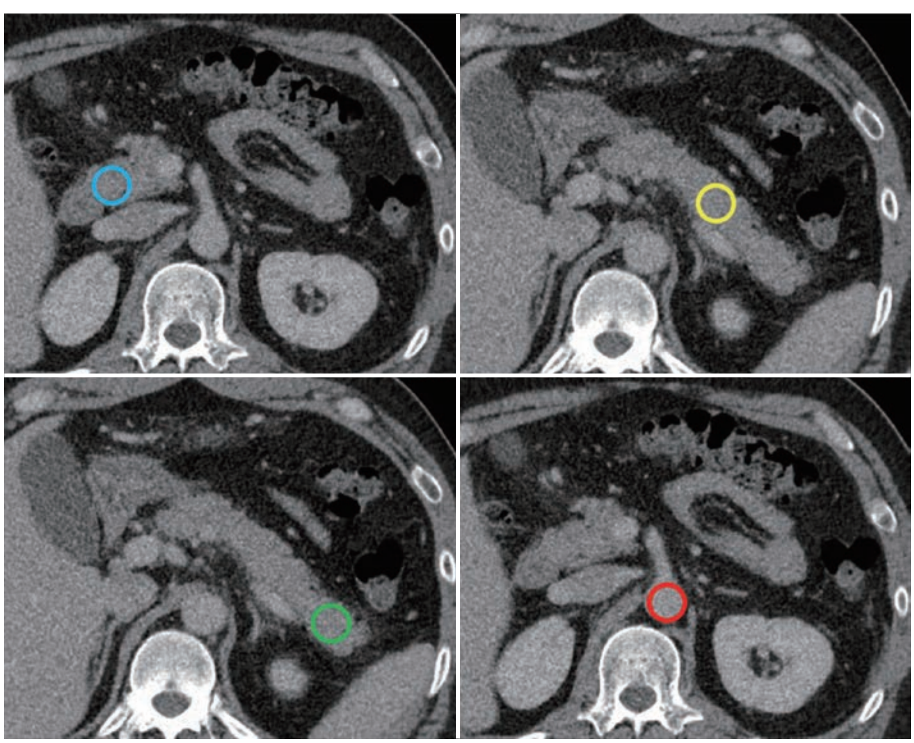

Fig. 1. Axial contrast-enhanced CT images of a patient with pancreatitis. Iodine concentrations were measured in the pancreatic head (blue), pancreatic body (yellow), pancreatic tail (green), and in the aorta at the celiac artery level (red) for normalization.

the pancreas was divided by the iodine concentration in the aorta for normalization.

3.3 Comparison of iodine concentrations in mild and severe acute pancreatitis

We compared the iodine concentrations in the pancreas of 20 patients with mild acute pancreatitis and 21 patients with severe acute pancreatitis.

3.4 Transition in the CRP level in acute pancreatitis

We also investigated the maximum CRP value and number of days to reach the maximum value during the hospital visits of 20 patients with mild acute pancreatitis and 21 patients with severe acute pancreatitis.

3.5 Receiver operating characteristic analysis of iodine concentration

Using mild acute pancreatitis as the negative outcome and severe acute pancreatitis as the positive one, we conducted a receiver operating characteristic (ROC) analysis to verify whether the severity of acute pancreatitis can be determined by measuring the iodine concentration and calculated the cutoff values for this iodine concentration.

Statistical analysis

The iodine concentrations between mild and severe acute pancreatitis were using the Wilcoxon test ($\alpha = 5\%$). The JMP PRO 13 software (SAS Institute, North Carolina, U.S.) was used for statistical analysis.

Results

1. Patient demographics

Records of 46 patients with acute pancreatitis were reviewed from our database. Patients with poor image quality (n=3) and with recurrence of the disease (n=2) were successively excluded. Finally, 41 eligible patients (29 males and 12 females; mean age =54.7 ± 20.2 years) were identified for analysis.

2. Consistency between the contrast CT grade and definitive diagnosis

Based on the CECT grade classification performed at the time of the initial visit, 25 patients had mild acute pancreatitis and 16 had the severe cases. Whereas, the severity determined via definitive diagnosis based on other prognostic factors (Table 1) classified the cases into 20 mild cases and 21

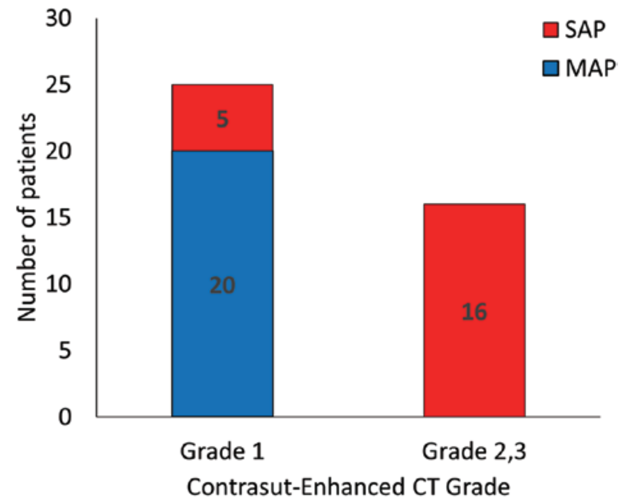

Fig. 2. The graph shows the number of patients based on the contrast-enhanced CT grade. The red numbers on the bar chart represent patients with severe acute pancreatitis (SAP) based on definitive diagnoses, and the blue numbers represent mild acute pancreatitis (MAP) patients identified by definitive diagnoses.

severe cases (Figure 2). The CECT-based grading demonstrated 76.2% sensitivity, 100% specificity, and 87.8% accuracy.

3. Comparison of iodine concentrations in mild and severe acute pancreatitis

The iodine concentrations in all cases of mild and severe acute pancreatitis are presented in Table 2. Patients with severe acute pancreatitis had significantly lower iodine concentrations than those with mild acute pancreatitis ($p < 0.05$) (Figure 3).

4. Transition in the CRP level in acute pancreatitis

The CRP levels at the first hospital visit and the highest CRP values in the mild and severe acute pancreatitis patients are presented in Figure 4. There was no significant difference between the two groups in terms of the CRP levels at the time of the initial visit. However, the highest CRP value in the severe acute pancreatitis patients was significantly greater than that in the mild acute pancreatitis patients ($p < 0.05$).

It took a median of 2 days for the CRP levels to peak; the shortest duration was on the same day, while the longest was 4 days to reach the higher CRP levels.

Table 2. Iodine concentration in three segments (head, body, and tail) of the pancreas in patient with Acute Pancreatitis

Mild Acute Pancreatitis					Severe Acute Pancreatitis				
No	head (%)	body (%)	tail (%)	minimum (%)	No	head (%)	body (%)	tail (%)	minimum (%)
1	55.2	50.9	47.1	47.1	1	22.9	26.1	13.5	13.5
2	47.7	40.9	42	40.9	2	40.6	39.3	38.4	38.4
3	30.2	36.2	33	30.2	3	32.7	37.5	46.7	32.7
4	46.7	48.2	41.7	41.7	4	31.2	35.1	27.3	27.3
5	31.8	36.5	42.2	31.8	5	18.1	15.3	22.6	15.3
6	49.5	35.4	65.2	35.4	6	39.4	48.2	53.2	39.4
7	45.4	45.4	48.5	45.4	7	59.5	14.1	16.9	14.1
8	75.3	66.2	53.3	53.3	8	49	44.8	38.8	38.8
9	42.8	48.5	46.7	42.8	9	42.8	53	46.6	42.8
10	56.7	49	45.3	45.3	10	54.4	39.4	39.5	39.4
11	43.7	43.8	41.6	41.6	11	34.8	21	37.6	21
12	70.1	60.1	51.1	51.1	12	39	51.4	42.3	39
13	68.8	72.8	77.7	68.8	13	14.5	23.8	36.4	14.5
14	70.9	60.5	56.3	56.3	14	32.7	37.3	35	32.7
15	65.6	47.7	48.2	47.7	15	36.9	54	55.5	36.9
16	40.8	41.5	45	40.8	16	38.5	36.3	59.2	36.3
17	56.4	41	42.1	41	17	42.1	37.1	54.8	37.1
18	54.4	59.8	54.1	54.1	18	38.5	35.4	36.5	35.4
19	53.6	49	60.7	49	19	37	31.8	40.6	31.8
20	56.2	53.9	54.7	53.9	20	49.5	25.6	13.1	13.1
					21	50.6	39.2	48	39.2

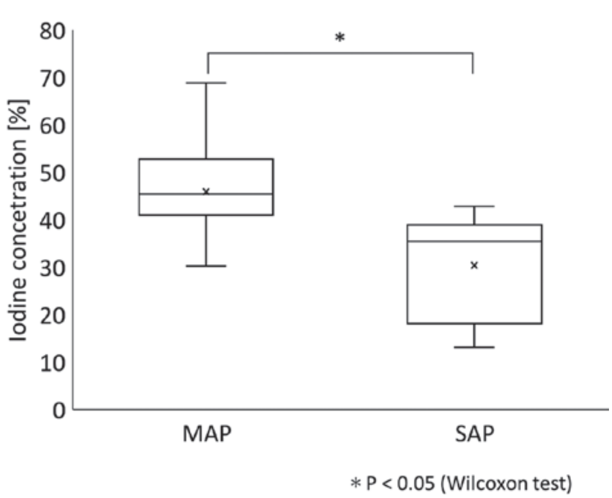

Fig. 3. The box plots depict the measured iodine concentration in mild acute pancreatitis (MAP) and severe acute pancreatitis (SAP). The horizontal line in the box represents the median. The top and bottom of the box depict the quartiles. The mark (×) in the box represents the average.

5. ROC analysis

The ROC analysis revealed the area under the curve as 0.89 given the cutoff value of the iodine concentration was 39.4%, sensitivity was 95.7%, and specificity was 85% (Figure 5). Examples of CT images of a patient with false negative results, including the iodine concentration, are shown in Figure 6. Although this case did not involve pancreatic ischemia, increased CT values were seen in the adipose tissues due to an inflammatory reaction that extended beyond the inferior pole of the kidney. This cutoff value enabled the diagnosis of severe acute pancreatitis in the five cases involving false negative results, which are described in subsection 2 of the results.

Representative images of patients with severe acute pancreatitis captured via DECT are presented in Figure 7. A visual assessment of these images did not reveal unevenness or decrease in the pancreatic

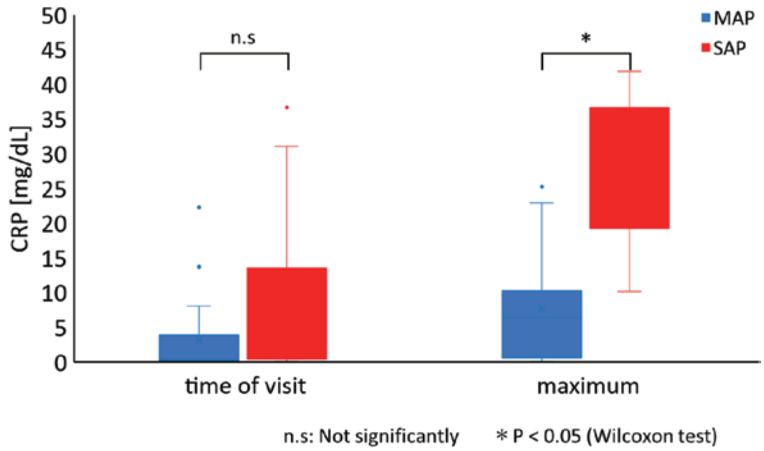

Fig. 4. These graphs present the C-reactive protein (CRP) values in mild acute pancreatitis (MAP) and severe acute pancreatitis (SAP) at the time of the visit and the maximum level. The horizontal line in the box represents the median. The top and bottom of the box depict the quartiles. The mark (×) in the box indicates the average.

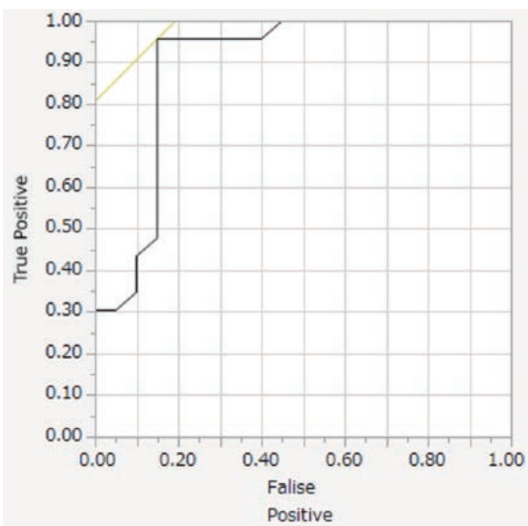

Fig. 5. A receiver operand characteristic (ROC) curve for using the iodine concentration to determine the severity of acute pancreatitis.

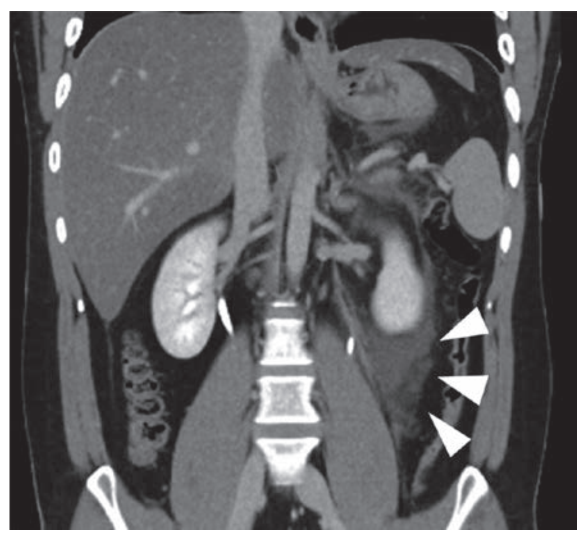

Fig. 6. A coronal view image of a 21-year-old man with severe acute pancreatitis whose pancreatic iodine concentration was higher than the cutoff value.

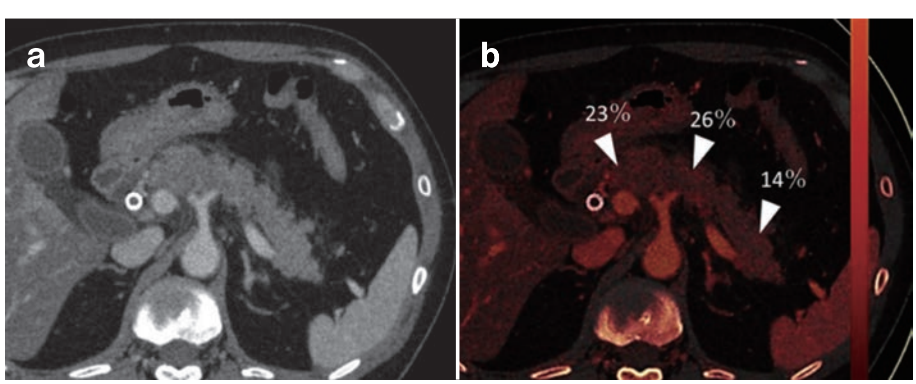

Fig. 7. CT images of a 64-year-old man with severe acute pancreatitis. A transverse (a) contrast-enhanced CT image and (b) iodine map from a dual energy CT scan.

contrast effect, indicating that the entire pancreas contained an even concentration, indicative of a diagnosis of mild acute pancreatitis. However, the iodine concentration was found to be 23% in the pancreatic head, 26% in the pancreatic body, and 14% in the pancreatic tail. All of these were lower than the cutoff value of 39.4%, indicating overall ischemia.

Discussion

Typically, acute pancreatitis presents as ischemia of the pancreatic parenchyma on CT. In this study, we specifically monitored changes in the contrast enhancement effects resulting from ischemia of the pancreatic parenchyma and quantitatively analyzed the iodine concentration in the pancreatic parenchyma of patients with acute pancreatitis. The severity of acute pancreatitis is graded by visual assessment of the CECT image to assess the degree of ischemia in the pancreatic parenchyma[3]. In the case of significant local ischemia, contrast is observed on enhanced CT images, and it is easy to identify the ischemic sites. However, this is not limited to the abovementioned cases. Determining the severity of the condition by visual evaluation depends upon the experience and ability of the image interpreter. As outlined in section 3.2., the severity assessment based on the conventional CECT grading indicated five false negative cases, suggesting that appropriate treatment may not have been initiated for severe acute pancreatitis and requires immediate treatment. On the other hand, a comparison of the iodine concentrations between severe and mild cases indicated a significant difference between the two groups, suggesting the possibility of an accurate severity assessment.

Although peak CRP levels are more useful in determining the severity of acute pancreatitis compared to those at the time of admission, our study revealed that it took a median of 2 days for the CRP levels to peak. Therefore, measuring the iodine concentration may offer an early and accurate way for severity assessment using the standard CECT examination performed during hospital visits.

The ROC analysis revealed a cutoff value of 39.4% for the iodine concentration with a sensitivity of 95.7% and a specificity of 85%. A survey conducted in Japan in 2011 identified a 2.1% mortality rate among all cases of acute pancreatitis and 10.1% among severe cases[3]. Therefore, in addition to the basic treatment, severe cases require intensive care measures, such as organ failure countermeasures, infusion management, nutritional management (early enteral nutrition), infection prevention, and measures to prevent abdominal compartment syndrome[20–22]. We believe the iodine concentration cutoff values obtained in this study could help in determining the most appropriate initial treatment modality.

In this study, three cases that were initially considered to be mild were identified as being severe. These cases involved mild acute pancreatitis associated with pancreatic cancer. Therefore, a decrease in the pancreatic iodine concentration in these patients was thought to be due to the hypovascularity caused by pancreatic cancer and not by pancreatitis itself. On the other hand, one severe case failed to be classified as severe. Therefore, we believe that a quantitative evaluation of the iodine concentration along with the existing conventional guidelines would enable a more accurate severity assessment. Moreover, all five false negative cases, that were diagnosed as mild based on the CECT grading assigned via a visual evaluation performed by the doctors, were accurately diagnosed as severe. In this regard, we believe that the quantitative evaluation of the iodine concentration allows an objective determination of acute pancreatitis even in patients in whom visual differentiation is difficult.

The study had a limitation. It is known that the accuracy of material decomposition with DECT is changed by a combination of tube voltage. Therefore, the cutoff value of iodine concentration for the severity assessment of acute pancreatitis may vary with the CT machine used.

In conclusion, the results of this study suggest that a quantitative evaluation of iodine concentration can be performed using DECT which makes it useful as a new diagnostic method for determining the severity of acute pancreatitis.

Conflicts of interest disclosure

There is no potential conflict of interest to disclose.

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