

Original Article



Computed Tomography Assessment of Severity of Acute Pancreatitis in Bangladeshi Children

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ABSTRACT


Purpose: Acute pancreatitis (AP) is common among children in Bangladesh. Its management depends mainly on risk stratification. This study aimed to assess the severity of pediatric AP using computed tomography (CT).

Methods: This cross-sectional, descriptive study was conducted in pediatric patients with AP at the Department of Pediatric Gastroenterology and Nutrition, BSMMU, Dhaka, Bangladesh.

Results: Altogether, 25 patients with AP were included, of whom 18 (mean age, 10.27±4.0 years) were diagnosed with mild AP, and 7 (mean age, 10.54±4.0 years) with severe AP. Abdominal pain was present in all the patients, and vomiting was present in 88% of the patients. Etiology was not determined. No significant differences in serum lipase, serum amylase, BUN, and CRP levels were observed between the mild and severe AP groups. Total and platelet counts as well as hemoglobin, hematocrit, serum creatinine, random blood sugar, and serum alanine aminotransferase levels ($p>0.05$) were significantly higher in the mild AP group than in the severe AP group ($p=0.001$). The sensitivity, specificity, positive predictive value, and negative predictive value of CT severity index (CTSI) were 71.4%, 72.2%, 50%, and 86.7%, respectively. In addition, significant differences in pancreatic appearance and necrosis were observed between the two groups on CT.

Conclusion: CT can be used to assess the severity of AP. In the present study, the CTSI effectively assessed the severity of AP in pediatric patients.

Keywords: Pancreatitis; Computed tomography; Bangladeshi; Child

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Conflict of Interest

The authors have no financial conflicts of interest.

INTRODUCTION

Pancreatitis is defined as an inflammation within the parenchyma of the pancreas [1]. It begins with the activation of zymogens within acinar cells, resulting in acinar cell injury [2]. In most cases, parenchymal inflammation is mild and self-limiting. However, few patients have severe inflammation, known as severe acute pancreatitis (SAP) [3]. Acute pancreatitis (AP) is the sudden onset of severe upper abdominal pain radiating to the back, and is often associated with nausea, vomiting, and epigastric tenderness [4]. The causes of pancreatitis in children are idiopathic, biliary, drug-induced, systemic diseases, trauma, infections, and metabolic and hereditary predispositions. AP is diagnosed in children based on at least two of the following criteria: sudden onset of abdominal pain compatible with AP, elevation of serum amylase and/or serum lipase levels to more than three times the upper limit of the normal level, and characteristic imaging findings compatible with AP [5]. Characteristic imaging findings include pancreatic edema, fat stranding, peripancreatic fluid collection, and necrosis on abdominal imaging [6].

The incidence of AP in children has increased over the last two decades [7], ranging from 3.6 to 13.2 cases per 100,000 children [8]. Although most patients have favorable outcomes, 15–20% of patients may develop severe complications, with a mortality rate of 4–10% [8,9].

Up to 25% of AP cases in children may have complications, in which early systemic complications include respiratory distress syndrome, pleural effusion, pneumonia, shock, and acute renal insufficiency [1]. Meanwhile, pancreatic necrosis, pseudocyst, and abscess are late complications. The North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition Pancreas Committee (NASPGHAN) classifies AP as mild, moderately severe, or severe. Early identification and aggressive management are recommended for patients at a higher risk of SAP [5]. No single parameter is suitable for the early prediction of acute inflammation or necrosis [10].

Disease severity of AP at presentation can be demonstrated based on radiological findings. The computed tomography severity index (CTSI) was developed based on pancreatic morphology and extended necrosis by Balthazar et al. [11,12]. Computed tomography (CT) can be used to identify local complications associated with AP early and accurately. Previous studies have demonstrated that CT has advantages over clinical scoring systems in risk identification and stratification [9].

Contrast-enhanced CT can be used to predict major complications in patients with AP [9]. Small-scale studies have been conducted in Bangladesh on different aspects of pancreatitis in children; however, to date, no study has been conducted to assess the usefulness of the CT scan index in assessing the severity of AP. Therefore, this study was conducted to identify the severity of AP in children in a tertiary care center using CT. Early risk stratification may help initiate aggressive management and decrease complication and mortality rates.

MATERIALS AND METHODS

This descriptive cross-sectional study was conducted at the Pediatric Gastroenterology and Nutrition Department of Bangabandhu Sheikh Mujib Medical University (BSMMU) in Dhaka, Bangladesh from May 2019 to October 2020. Study approval was obtained from the institutional ethics committee of BSMMU (approval No. BSMMU/2019/5708, date 09-05-2019).

Study population

Children aged <18 years with abdominal pain admitted to the Pediatric Gastroenterology and Nutrition Department of BSMMU, and diagnosed with AP as per the International Study Group of Pediatric Pancreatitis: In Search for a Cure (INSPPIRE) criteria were included in this study.

Inclusion criteria

The inclusion criteria were children of either sex, age of <18 years, and diagnosis of AP due to any etiology.

AP was clinically defined according to the INSPPIRE criteria.

Exclusion criteria

The exclusion criteria were as follows: acute recurrent pancreatitis; chronic pancreatitis; abdominal pain due to other causes; and refusal of the parents to provide consent.

Operational definitions

According to the INSPPIRE definitions, AP is diagnosed when two or more of the following three criteria are met [13]: clinical symptoms of typical (acute onset of severe agonizing pain, commonly epigastric) abdominal pain; serum amylase and/or lipase levels that are ≥ 3 times the upper limit of normal levels; and imaging evidence of AP on ultrasound or CT.

Severity of pancreatitis in children

According to the NASPGHAN, AP is classified as follows [5]:

Pediatric mild AP is AP that is not associated with organ failure or local or systemic complications and generally resolves within the first week after presentation. It is the most common form of pediatric AP. Pediatric moderately SAP is defined as AP with either the development of transient organ failure/dysfunction (not lasting >48 hours) or local or systemic complications. Local complications include the development of (peri) or pancreatic complications such as fluid collection and necrosis. Systemic complications include the exacerbation of previously diagnosed comorbid diseases (such as lung or kidney disease). Pediatric SAP is AP with organ dysfunction persisting for >48 hours. Persistent organ failure (POF) may be single or multiple, and may develop beyond the first 48 hours of presentation.

For this study, we grouped patients with moderately SAP and SAP, as defined by the NASPGHAN guidelines, into the SAP group.

CTSI

CT findings were graded as follows: normal (grade A, 0 point), focal or diffuse pancreatic enlargement (grade B, 1 point), peripancreatic inflammation or gland abnormalities (grade C, 2 points), single-fluid collection (grade D, 3 points), and two or more fluid collections or adjacent gas bubbles (grade E, 4 points). Necrosis was graded as follows: no necrosis, 0 point; 0–30% necrosis, 2 points; 30–50% necrosis, 4 points; and >50% necrosis, 6 points [9].

Study procedure

After patient enrollment, medical history was first obtained directly from the patients/parents/caregivers, and a physical examination of all the patients was performed by the researcher on the day of admission under the supervision of a guide. Venous blood

(approximately 5 mL) was drawn aseptically for laboratory workup. Complete blood count (CBC) reports included hemoglobin and white blood cell (WBC) counts with differentials, platelets, and hematocrit. CBC was performed using a Sysmex autoanalyzer (model XN 2000) in the Department of Hematology, BSMMU. Other laboratory tests including serum amylase, lipase, calcium, blood urea nitrogen (BUN), fasting serum glucose, and C-reactive protein (CRP) levels were assessed by the Department of Biochemistry, BSMMU using an autoanalyzer. Serum amylase and lipase levels were measured using a Siemens Dimension Flex, 2016-02 version. Serum calcium and creatinine levels were estimated using a Siemens Dimension RXL. When the patient was hemodynamically stable, a CT scan of the pancreas was sent to the Radiology and Imaging Department, and the report was assessed by one operator. CT scans were performed using the SOMATOM definition AS (Siemens) 128 slice CT scan machine in the Radiology and Imaging Department of BSMMU. After CT, CTSI grading was performed by a single operator in every case.

Data collection instrument

A pre-designed questionnaire was used to collect sociodemographic data, history of illness, examination findings, and investigation findings and was completed for each case, which included all the variables of interest.

Statistical analysis

Data were analyzed using the SPSS software for Windows version 25.0 (IBM Co.). Categorical variables were analyzed using the chi-square or Fisher's exact tests. All continuous variables that followed a normal distribution are reported as means and standard deviations, and were compared using a two-sample *t*-test. All continuous variables that did not follow a normal distribution are reported as medians and interquartile ranges (IQR), and were compared using the Mann-Whitney U-test. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of the CTSI were compared with those of the NASPGHAN guidelines for mild AP and SAP. Statistical significance was set at $p < 0.05$.

RESULTS

Among the included patients, 13 (52%) were aged >10 years, 9 (36%) were within the age group of 5–10 years, and 3 (12%) were aged <5 years. More than half or 14 (56%) of the patients were male, and the remaining 11 patients (44%) were female (**Table 1**).

In our study ($n=25$), 18 (72%) cases were mild, and 7 (28%) had SAP according to the NASPGHAN classification. Most of the patients ($n=10$, 40%) were suffering from sharp pain, whereas six patients (24%) experienced diffuse pain. The epigastric region was the main location of pain in 14 patients (56%), whereas six patients (24%) had pain in the hypochondriac region (**Table 1**). No significant differences in total and platelet counts as well as hemoglobin, hematocrit, serum creatinine, random blood sugar (RBS), and serum alanine aminotransferase levels were observed between the mild AP and SAP groups ($p > 0.05$); however, serum calcium levels were significantly higher in the mild AP group than in the SAP group ($p=0.001$) (**Table 2**). No significant differences in serum lipase, amylase, BUN, and CRP levels were observed between the mild AP and SAP groups ($p > 0.05$) (**Table 3**). Of 18 patients in the mild AP group, 6 patients (33.3%) had a normal pancreas, and another 6 had focal or diffuse enlargement, although none in the SAP group ($n=7$) had these findings. Meanwhile, 6 patients (85.7%) in the SAP group had either single or multiple fluid collections, whereas

Table 1. Characteristics and location of abdominal pain in the study population (n=25)

Variables	No (%)
Age group (yr)	
<5 yr	3 (12)
5–10 yr	9 (36)
>10 yr	13 (52)
Sex	
Male	14 (56)
Female	11 (44)
Severity of pancreatitis	
Mild	18 (72)
Severe	7 (28)
Pattern of pain	
Diffuse	6 (24)
Colicky	5 (20)
Sharp	10 (40)
Dull	2 (8)
Localized	2 (8)
Location of pain	
Epigastric	14 (56)
Hypochondriac	6 (24)
Whole abdomen	5 (20)

Table 2. Comparison of hematological and biochemical parameters between the mild AP and SAP groups (n=25)

Variable	Total (n=25)	Mild AP (n=18)	SAP (n=7)	p-value
Hemoglobin (g/dL)	11.48±1.83	11.91±1.37	10.38±2.48	0.060
Total count (K/mm ³)	12.71±5.63	11.77±2.48	15.14±9.99	0.862
Platelet (lac/mm ³)	3.22±1.14	3.02±0.94	3.73±1.47	0.164
Hematocrit (%)	35.38±5.51	36.56±4.07	32.37±7.71	0.088
Serum creatinine (mg/dL)	0.65±0.56	0.53±0.14	0.98±1.01	0.070
RBS (mmol/L)	5.25±1.25	5.25±1.11	5.25±1.67	0.990
Serum ALT (IU/L)	29.28±23.31	26.00±17.03	37.71±35.10	0.268
Serum calcium (mg/dL)	9.20±0.82	9.52±0.68	8.40±0.59	0.001*

Values are presented as mean±standard deviation.

An independent sample t-test was used to analyze data.

AP: acute pancreatitis, SAP: severe acute pancreatitis, RBS: random blood sugar, ALT: alanine aminotransferase.

*Significant.

Table 3. Comparison of biochemical markers between the mild AP and SAP groups (n=25)

Variable	Mild AP (n=18)	SAP (n=7)	p-value
Lipase (U/L)	708 (309.75–2,599.50)	886 (548–2,738)	0.657
Amylase (U/L)	474 (272.25–1,053.00)	1,471 (112–2,080)	0.574
BUN (mg/dL)	9.13 (7.37–15.00)	8.0 (5.90–10.00)	0.270
CRP (mg/L)	16.36 (4.12–35.35)	40.52 (10.82–55.19)	0.220

Values are presented as median (interquartile range).

Mann-Whitney U-test.

AP: acute pancreatitis, SAP: severe acute pancreatitis, BUN: blood urea nitrogen, CRP: C-reactive protein.

only one patient had a fluid collection in the mild AP group. This difference was statistically significant ($p=0.002$). No necrosis in the parenchyma was detected in 12 patients (66.7%) in the mild AP group, and 5 of 7 patients (71.4%) in the SAP group had up to 50% necrosis ($p=0.024$), which was also significant (**Table 4**). A comparison of the SAP and mild AP groups based on the CTSI revealed that 5 patients (71.4%) in the SAP group (n=7) had CTSI scores of ≥ 4 , whereas 5 patients (27.8%) in the mild AP group (n=18) had CTSIs score of ≥ 4 , and the difference was statistically significant ($p=0.045$) (**Table 5**). Significant differences in pancreatic appearance and total CTSI score were observed between the mild AP and SAP groups ($p<0.05$); however, pancreatic necrosis was not significantly different between the two groups ($p>0.05$) (**Table 6**). Diagnostic statistical analysis revealed that the sensitivity,

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Table 4. Comparison of computed tomography scan findings between the mild AP and SAP groups (n=25)

	Mild AP	SAP	p-value
Pancreatic appearance			0.002*
Normal pancreas (grade A=0)	6	0	
Focal or diffuse enlargement of the pancreas (grade B=1)	6	0	
Pancreatic gland abnormalities associated with peripancreatic inflammation (grade C=2)	5	1	
Fluid collection in a single location (grade D=3)	0	3	
Two or more fluid collections and/or gas in or adjacent to the pancreas (grade E=4)	1	3	
Parenchymal necrosis			0.024*
No necrosis (point=0)	12	2	
Necrosis 0–30% of the parenchyma (point=2)	5	2	
Necrosis 30–50% of the parenchyma (point=4)	0	3	
Necrosis >50% of the parenchyma (point=6)	1	0	

Exact chi-square test.

AP: acute pancreatitis, SAP: severe acute pancreatitis.

*Significant.

Table 5. Comparison of CTSI scores between the mild AP and SAP groups (n=25)

Severity by CTSI score	Severity of acute pancreatitis based on the NASPGHAN criteria			p-value
	Severe	Mild	Total	
Severe (score≥4)	5	5	10	0.045*
Mild (score<4)	2	13	15	
Total	7	18	25	

Fisher's exact test.

CTSI: computed tomography severity index, AP: acute pancreatitis, SAP: severe acute pancreatitis, NASPGHAN: The North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition Pancreas Committee.

*Significant.

Table 6. Comparison of mean of CTSI between the mild AP and SAP groups (n=25)

	NASPGHAN severity		p-value
	Mild (n=18)	Severe (n=7)	
Pancreatic appearance	1.11±1.08	3.29±0.76	0.0001*
Pancreatic necrosis	0.89±1.57	2.29±1.79	0.067†
CTSI score total	2.00±2.54	5.57±2.22	0.004*

Values are presented as mean±standard deviation.

Independent sample t-test.

CTSI: computed tomography severity index, AP: acute pancreatitis, SAP: severe acute pancreatitis.

*Significant, †not significant.

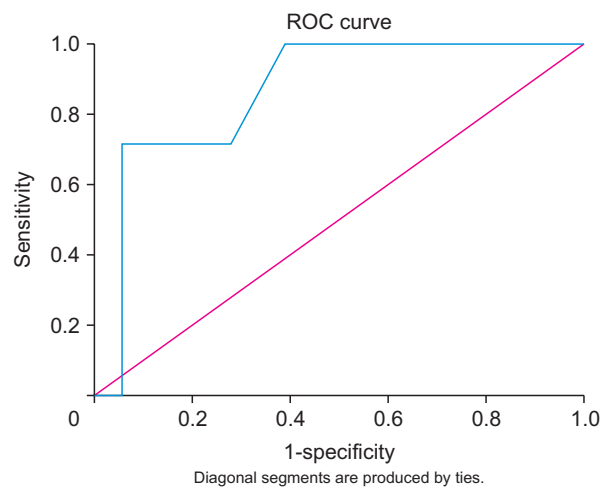


Fig. 1. Receiver operator characteristic (ROC) curve of computed tomography severity index for predicting severity of pediatric acute pancreatitis.

Table 7. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of CTSI in determining severity of acute pancreatitis

Statistics	Formula	Value (%)
Sensitivity	a	71.4
	a+c	
Specificity	d	72.2
	b+d	
Positive predictive value	a	50.0
	a+b	
Negative predictive value	d	86.7
	c+d	
Diagnostic accuracy	a+d	72.0
	a+b+c+d	

True positive (a)=5; false positive (b)=5; false negative (c)=2; true negative (d)=13.
CTSI: computed tomography severity index.

specificity, PPV, NPV, and accuracy of CTSI in predicting SAP were 71.4%, 72.2%, 50%, 86.7%, and 72%, respectively (**Table 7**). Using the SPSS 25 version, a receiver operating characteristic (ROC) curve analysis revealed that the area under the curve (AUC) of the CTSI was 0.865 (95% confidence interval [CI], 0.715–1.00), with a CTSI cutoff value of 5.00 for sensitivity at 71.4% and specificity at 94.4% (**Fig. 1**).

DISCUSSION

AP is common in pediatric gastroenterology departments. Predicting severity at the time of admission results in better management and outcomes; however, this is not an easy task. The CTSI may help in distinguishing patients with severe disease.

In our study, most cases were observed in the >10 years age group (52%), followed by 5–10 years (36%), and 12% belonging to those <5 years. Nydegger et al. [14] have reported similar results in their study, 43.7% in the 10–15-year age group, 31.9% in the 5–10-year group, and 24.4% were aged <5 years. The mean age in our study was 10.35±3.28 years, which was similar to the study conducted previously in the same center by Musabbir et al. [15].

Of 25 patients, 14 (56%) in our study were male. Vitale et al. [16] have reported that 62 of the 118 patients in their study were male. In many other studies, a slight female preponderance was noted [17]. This supports the findings of Lankisch et al. [2] that sex is not an independent risk factor for the severity and outcome of AP.

Among 25 cases, 72% were in the mild group, and 28% in the severe group. No significant difference in age was observed between the mild AP group and SAP group ($p=0.86$). Vitale et al. [16] have also identified no significant differences in age ($p=0.96$), which is consistent with the results of our study. However, Galai et al. [17] in their study, identified a statistically significant ($p=0.01$) difference in the mean age among patients with mild AP (13.8 years) and SAP (8.3 years). In our study, most of the patients (40%) were suffering from sharp pain, whereas 24% experienced diffuse pain. The epigastric region was the primary site of pain (56%). In another study conducted at the same center, 81.3% of patients experienced sharp, agonizing pain, and among them, 77% of patients had pain in the epigastric region [15]. Apart from abdominal pain, 88% of the patients were suffering from vomiting, and loss of appetite was observed in 64% of patients. In Musabbir et al. [15], 72% of patients suffered from vomiting. In this study, 23 of 25 patients (92%) had abdominal tenderness, 44% of

patients had anemia, 20% had ascites, and 16% had hepatomegaly. Musabbir et al. [15] have reported that 82% had abdominal tenderness, and 12% had ascites, a finding with is consistent with that in our study.

Moreover, the causes of pancreatitis in this study were idiopathic in 80% of the cases. Musabbir et al. [15] have reported that in 82% of cases, no underlying causes were determined, which is consistent with our study. Pezzilli et al. [18] have also reported unknown cause as the most common (34%) etiology. However, Nydegger et al. [14] have determined the primary cause as traumatic (36.3%). In our study, we did not identify any statistically significant differences WBC and platelet count as well as hemoglobin, hematocrit, serum creatinine, RBS, or serum ALT levels between the mild AP and SAP groups. Previous studies have not identified any differences in the values of these hematological parameters between mild and severe cases [19].

Serum calcium values were significantly different ($p=0.001$) between the mild AP (9.5 ± 0.68 mmol/L) and SAP (8.4 ± 0.59 mmol/L) groups. Peng et al. [20] have reported that compared to patients without POF, those with POF had a significantly lower serum calcium values on admission (2.11 ± 0.46 vs. 1.55 ± 0.36 mmol/L, $p<0.001$). Serum calcium levels decrease in critically ill patients. Hypocalcemia is significantly more frequent in patients with SAP; hence, hypocalcemia may serve as a potential prognostic factor [20].

The median value (IQR) for S. Lipase, serum amylase, and BUN were not statistically significant ($p=0.657$, 0.574 , and 0.270 , respectively) in the current study. Galai et al. [17] have reported that the median value of serum lipase levels was not significant ($p=0.27$), which is similar in our study. Vitale et al. [16] have observed no significant differences in serum amylase levels ($p=0.35$). However, in their study, the median BUN value (median) was significantly different ($p=0.0007$) between the mild AP and SAP groups (10 mg/dL vs. 20 mg/dL). Although some previous studies [16] on AP have reported that CRP has a discriminating value between mild AP and SAP, we did not observe any significant difference ($p=0.220$) in CRP values, similar to Izquierdo et al. [21].

In our study, the CT findings showed a statistically significant ($p=0.002$) difference in pancreatic appearance between the mild AP and SAP groups. The appearance of the pancreas in the mild AP group was grades A and B in 33.33% each, grade C in 27.78%, and grade E in 5.56%. In the SAP group, grade C was observed in 14.29%, and grades D and E were observed in 42.86% each. Using Balthazar scoring system, Lautz et al. [22] identified that in mild AP, pancreatic appearance was grade A in 14.9%, grade B in 17.0%, grade C in 29.8%, grade D in 23.4%, and grade E in 14.9% of the cases. By contrast, SAP in patients was graded A or B in 0%, grade C in 5.9%, grade D in 29.4%, and grade E in 64.7% of the patients.

A significant difference was observed in pancreatic necrosis between the two groups ($p=0.024$). No necrosis in 66.67%, 0–30% necrosis in 27.78%, and >50% in 5.56% of the cases were observed in the mild AP group. Meanwhile, no necrosis and 0–30% necrosis were observed in 28.5% of each group, and 30–50% of necrosis was noted in 42.86% of the SAP group. Using the Balthazar scoring system, Lautz et al. [22] have reported that in the mild group, no necrosis occurred in 91.5% of the patients, whereas no necrosis in 41.2%, <30% necrosis in 5.9%, 30–50% necrosis in 5.9%, and >50% necrosis in 47.1% of the patients with SAP were observed. The mean CTSI was 2.00 ± 2.54 in the in the mild AP group and 5.57 ± 2.22 in the in the SAP group, with a significant difference ($p=0.004$). The ROC curve analysis

showed an AUC of 0.865 (95% CI, 0.715–1.00). CTSI in the mild group was significantly lower than that in the severe group (2.4 ± 2.0 vs. 6.8 ± 3.3 ; $p < 0.001$) in the study of Lautz et al. [22]. Our findings are consistent with those of a previous study.

In this study, the sensitivity, specificity, PPV, and NPV of the CTSI in predicting SAP were 71.4%, 72.2%, 50%, and 86.7%, respectively. Fabre et al. [23] have reported the sensitivity and specificity of CTSI as 80% and 85.71%, respectively. These findings are consistent with those of the present study. Balthazar score has sensitivity, specificity, PPV, and NPV of 81%, 76%, 62%, and 90%, respectively [22]. In 2012, Lautz et al. [9] reported the sensitivity and specificity of CTSI score as 81% and 76%, respectively, with a CTSI cutoff value of 4 to differentiate mild AP and SAP, whereas our study used a CTSI cutoff value of 5.00 with sensitivity of 71.4% and specificity of 94.4% (**Fig. 1**).

In 2016, Hashimoto et al. [24] reported the sensitivity and specificity of CTSI as 50.0% and 76.9%, respectively. In our study, we examined the CTSI and revealed that it had acceptable sensitivity and accurately delineated local complications.

Conclusion

In this study, a CT scan showed promising results with a CTSI cutoff value of 5.00, with a sensitivity of 71.4% and specificity of 94.4%. Moreover, a CT scan is useful and effective in the early detection of local complications, including pancreatic necrosis, ascites, pleural effusion, and pancreatic pseudocysts of AP.

Limitations

Owing to limited resources, the coronavirus disease 2019 pandemic situation, and the small sample size, our conclusions are limited.

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