



Computed tomography characteristics of acute pancreatitis based on different etiologies at different onset times: a retrospective cross-sectional study

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Background: The clinical characteristics and imaging findings of acute pancreatitis (AP) are different across the various etiologies, the results are conflicting, and their time from symptom onset to imaging varies. The imaging findings of different etiologies at different onset times are unclear. This study aimed to investigate the computed tomography (CT) characteristics of AP based on different etiologies at different onset times.

Methods: Patients who underwent plain and contrast-enhanced computed tomography (CECT) for the first attack of AP in 3 hospitals (Affiliated Hospital of North Sichuan Medical College, Chinese People's Liberation Army Western Theater General Hospital, and Suining Central Hospital) from 2015 to 2019 were recruited. According to the different etiologies of AP, the patients were divided into 5 subgroups: biliary AP (n=591), alcoholic AP (n=267), hypertriglyceridemic AP (n=258), mixed causes subgroups (n=199), and "other/idiopathic" AP (n=545). According to the time from onset to CT examination (e.g., 1–3, 4–7, 8–14, 15–28, and >28 days), the onset time was divided into 5 respective phases (I–V). The CT characteristics and clinical and laboratory features were retrospectively reviewed and compared among the different etiology subgroups and onset time.

Results: The positive rate of CT findings in AP diagnosis based on CECT was 96.7% (1,860/1,924). Necrotizing pancreatitis (NP) occurred in 33.2% (617/1,860) of AP patients with positive CECT findings. Among patients with NP, local complications and severe AP of the modified CT severity index (MCTSI) increased over time in those with biliary AP from 17.1%, 25.2%, and 20.0% in Phase I to 42.9%, 44.0%, and 39.7% in Phase IV [all $P < 0.05$, 95% confidence interval (CI): 0.15 to 0.52, 0.28 to 0.63, and 0.18 to 0.82, respectively]. In contrast, NP, local complications and severe AP of MCTSI in those with hypertriglyceridemic AP decreased over time from 24.3%, 22.5%, and 22.7% in Phase I to 1.3%, 1.2%, and 1.9% in Phase V (all $P < 0.05$, 95% CI: 3.20 to 181.74, 3.31 to 175.74, and 2.00 to 120.78, respectively).

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Conclusions: The proportion of NP was 33.2% of positive CECT findings. There may be differences in the CT and clinical manifestations of the different etiologies, and those differences may be related to the onset time.

Keywords: Acute pancreatitis (AP); etiology; onset time; severity; computed tomography

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Introduction

Acute pancreatitis (AP) is a clinical condition resulting from inflammation of the pancreas and its systemic repercussions (1). The main causes of AP are cholelithiasis (gallstones), alcoholism, high blood triglycerides, high blood calcium, and idiopathic cases (2). Previous studies have shown that the severity, mortality, and prognosis are different across the various etiologies of AP (3-6).

As the first-choice imaging examination to diagnose AP, computed tomography (CT) is suitable to observe the dynamic changes of different etiologies at different onset times (7-9). Previous studies showed that the proportion of necrotizing pancreatitis (NP), imaging scores (such as CT severity index score), and local complications (pancreatic fluid collections) were different across the various etiologies (10-18). The time from symptom onset to imaging of these studies also varied. The imaging characteristics of different etiologies and trends of changes at different onset times of different etiologies remain unclear. Therefore, we conducted this study to investigate the CT characteristics of AP based on different etiologies, including: (I) the CT findings of AP with different etiologies; (II) the CT characteristics for different etiologies at different onset times; and (III) the comparison of CT with clinical characteristics based on different etiologies in different phases of AP. We present the following article in accordance with the STROBE reporting checklist (available at <https://qims.amegroups.com/article/view/10.21037/qims-21-1231/rc>).

Methods

Study design and setting

This is a retrospective cross-sectional study evaluating the CT characteristics of the first attack of AP based on different etiologies at different onset times. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics

Committee of Affiliated Hospital of North Sichuan Medical College (No. 2021ER[A]017), and individual consent for this retrospective analysis was waived.

Identification of patients

Between 1 January 2015 and 31 December 2019, patients with a first episode of AP admitted to 3 tertiary referral centers based in 3 different prefecture-level cities in the province of Sichuan were included. These centers were the Affiliated Hospital of North Sichuan Medical College, Chinese People's Liberation Army Western Theater General Hospital, and Suining Central Hospital.

For the diagnosis of AP, the presence of at least 2 of the following criteria was required: (I) consistent abdominal pain, (II) serum amylase and/or lipase above 3 times the upper limit of normal, and (III) typical imaging findings of AP.

The inclusion criteria of our study were as follows: (I) inpatient, (II) patients diagnosed with primary AP for the first time, (III) patients who underwent both plain and contrast-enhanced CT (CECT), and (IV) patients who had corresponding clinical and laboratory data within 3 days before or after the CT examination to diagnose the clinical severity.

The exclusion criteria were as follows: (I) the age of the patient was less than 18 years; (II) patients with pancreatic carcinoma or any tumor that affects metabolism; (III) patients with AP who presented in combination with chronic liver disease and severe cardiovascular disease; (IV) pregnant patients; and (V) patients with unclear images.

Different disease etiologies were diagnosed according to the following criteria. Biliary AP represents the main etiological background of AP globally and it is diagnosed by imaging techniques (1). Alcoholic AP is caused by excessive alcohol consumption prior to onset or with a clinical history of >5 years and alcohol consumption >50-100 g/day (1). Hypertriglyceridemic AP is related to triglycerides (TGs) over 11.3 mmol/L or above 5.65 mmol/L with emulsion

serum (normal TGs ≤ 1.70 mmol/L) (5,19). Moreover, we grouped patients who had 2 or 3 of the above 3 etiologies as mixed-cause cases. Other causes of AP include endoscopic retrograde cholangiopancreatography, pancreas divisum, genetics, polymorphisms, and drug intake, among others. We grouped the other etiologies and idiopathic etiologies into a subgroup. Therefore, we ultimately included 5 etiology subgroups.

All patients were managed according to the *Evidence-based guidelines for the management of acute pancreatitis* by the International Association of Pancreatology and the American Pancreatic Association working group guidelines of 2013 (20).

Clinical observations

The clinical charts of all cases were reviewed to check age, gender, etiology, length of hospital stay, intensive care unit (ICU) admission, clinical severity using scores according to the 2012 revised Atlanta classification (RAC) (Tables S1,S2) and the Acute Physiology and Chronic Health Evaluation II (APACHE II) score (Table S3) for each patient.

CT technique

The CT images were acquired with the patient in the supine position, head advanced, and with a scanning range from the xiphoid process to the iliac crest plane or lower. Patients underwent an abdominopelvic CT study with one of the 5 following multidetector-row CT systems (Table S4): SOMATOM Definition AS + 128 (Siemens Healthineers, Erlangen, Germany), LightSpeed VCT 128 (GE Health care, Boston, MA, USA), Brilliance 64 (Philips Health Care, Amsterdam, The Netherlands), Toshiba Aquilion ONE 320 (Toshiba Medical Systems, Tokyo, Japan), and SOMATOM Definition Flash (Siemens Healthineers, Germany). The acquisition parameters were set at 80–140 kVp; 155–250 mAs; pitch, 0.5–1.0; collimation, 0.625–5 mm; and slice thickness, 1.5–5 mm.

Definition and imaging evaluation

The CT images of all cases were independently reviewed by 2 radiologists (with at least 3 years abdominal CT experience) who were blinded to the patients' clinical and pathological information (including the onset time). The major CT findings were described by using the 2012 RAC, using terms including interstitial edematous

pancreatitis (IEP), NP, subtypes of NP [parenchymal necrosis alone, peripancreatic necrosis alone, and a combined type (peripancreatic and parenchymal necrosis)], and local complications, including acute peripancreatic fluid collections, acute necrotic collections, pancreatic pseudocysts, and walled-off necrosis (21). The severity of AP on CT was graded using the modified CT severity index (MCTSI) score (Table S5) for every AP patient. An MCTSI score was used because it is better than the CT severity index score at avoiding the missed diagnosis of moderate to severe AP (22).

The different phases of AP onset

Onset time was defined as the time from symptoms until CT examination and not the time of admission to the hospital (21). The first symptoms included common abdominal pain, abdominal discomfort, or accompanying symptoms such as nausea and vomiting. Existing research shows that there are several key time points from the onset of AP. Day 3 is when the diagnostic value of CT is still being explored. Assessment within 3 days of symptom onset can provide crucial information about the expected course (23). However, another study pointed the ideal time for assessing severe AP or complications related to AP with CT is after 3 days (7). Day 7 is when the 2012 RAC distinguished the early phase and the late phase of AP onset (21). Day 14 is the time within which half of all deaths occur. These deaths are mainly due to failure of multiple organ systems (1). Day 28 is when local complications of AP begin to differ among patients according to the 2012 RAC (21). Therefore, patients with NP, local complications, and severe disease (graded by MCTSI score, RAC, APACHE II score) were divided into the following 5 phases according to the time points from AP onset to CT examination: Phase I (patients who received CT within 1–3 days after onset), Phase II (patients who received CT within 4–7 days after onset), Phase III (patients who received CT within 8–14 days after onset), Phase IV (patients who received CT within 15–28 days after onset), and Phase V (patients who received CT more than 28 days after onset) (Figure 1). For patients who underwent 2 or more CT examinations, the 2 interobserver values were based on all CT scans until the end-point CT for each patient, and the end result for comparison between patients of different etiology was the value when the clinical features or imaging appearance were most severe.

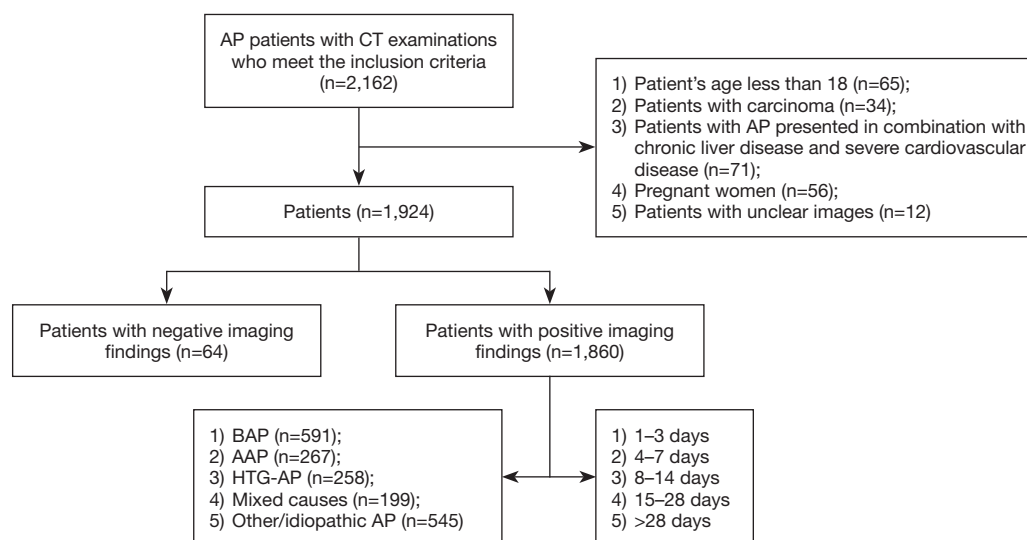


Figure 1 Flow chart illustrating patients with acute pancreatitis recruited in this study. AP, acute pancreatitis; CT, computed tomography; BAP, biliary acute pancreatitis; AAP, alcoholic acute pancreatitis; HTG-AP, hypertriglyceridemic acute pancreatitis.

Data analysis

Statistical analyses were carried out using SPSS 25.0 (IBM Corp., Armonk, NY, USA). Categorical data were reported as n (%), and continuous data were expressed as the median [interquartile range (IQR)] or mean \pm standard deviation (SD). Intragroup correlation coefficients (ICCs) were calculated for the MCTSI score, and kappa statistics were calculated for 2012RAC and necrosis types to evaluate the variability between observers. For the comparison of qualitative variables (necrosis, local complications), grade variable (RAC), and nonnormally distributed data (APACHE II, MCTSI score), the Kruskal–Wallis H test or Bonferroni method were used for etiology subgroups in different phase comparisons. The correlations between clinical and imaging scores were evaluated by Spearman rank correlation tests, and r was used to represent the correlation coefficient. There was a significant difference when $P < 0.05$.

Results

Patient characteristics

This retrospective study included 1,924 AP patients, the average age was 49.97 ± 14.68 years; 58.4% (1,124/1,924) of the patients were men, and 41.6% (800/1,924) were women. The median hospital stay was 12 days (IQR, 8 to 18 days). Only 1.1% (21/1,924) died during the study period, and these deaths all occurred during the first year.

In the 1,924 patients with AP, the etiologies included biliary AP in 32.1% of patients (618/1,924), alcoholic AP in 14.3% of patients (276/1,924), hypertriglyceridemic AP in 13.7% of patients (264/1,924), mixed cause AP in 10.4% of patients (201/1,924), and “other/idiopathic” AP in 29.4% of patients (565/1,924).

The clinical characteristics of patients with AP of different etiologies are shown in *Table 1*. The average age in the biliary AP group was 56.72 ± 15.39 years, which was older than that in other etiology subgroups with an average age of 40–50 years ($P < 0.05$). The median age in the hypertriglyceridemic AP group was 41.94 ± 10.34 years, which was similar to that in the alcoholic AP group and lower than that in the other 3 etiology subgroups ($P < 0.05$).

There was a significant difference in etiology distribution between the male group and the female group ($P < 0.05$). The proportion of male patients was the highest in the alcoholic AP subgroup (97.5%, 267/276), while the proportion of female patients was highest in the biliary AP subgroup (62.0%, 383/618). Regarding the length of hospital stay during the index admission, among the 5 etiology subgroups, the median length of hospital stay for patients with biliary AP was 14 days (IQR, 10 to 19 days), which was longer than that for patients with alcoholic AP (11 days), hypertriglyceridemic AP (12 days), and “other/idiopathic” AP (11 days) ($P < 0.05$). There were 8.4% (162/1,924) of AP patients admitted to the ICU. Patients with mixed cause AP (11.9%, 24/201) were more likely to

Table 1 Patient characteristics based on different etiologies (n=1,924 AP patients)

Characteristics	All patients (n=1,924)	BAP (n=618)	AAP (n=276)	HTG-AP (n=264)	Mixed causes (n=201)	Other/idiopathic AP (n=565)	P value
Age, average (SD), year	49.97 (14.68)	56.72 (15.39)	45.49 (11.97)	41.94 (10.34)	46.91 (11.74)	49.61 (14.62)	0.00
Gender (male), n (%)	1,124 (58.4)	235 (38.0)	267 (97.5)	173 (65.5)	182 (90.5)	267 (47.3)	0.00
Hospital stay [IQR], d	12 [8, 18]	14 [10, 19]	11 [7, 16]	12 [8, 18]	13 [9, 18.5]	11 [8, 17]	0.00
Patients in intensive care unit, n (%)	162 (8.4)	61 (9.9)	16 (5.8)	23 (8.7)	24 (11.9)	38 (6.7)	0.05

SD, standard deviation; IQR, interquartile range; AP, acute pancreatitis; BAP, biliary acute pancreatitis; AAP, alcoholic acute pancreatitis; HTG-AP, hypertriglyceridemic acute pancreatitis.

be admitted to the ICU than the other 4 etiology subgroups ($P<0.05$). Patients with alcoholic AP (5.8%, 16/276) were less likely to be admitted to the ICU than those with biliary AP (9.9%, 61/618) ($P<0.05$).

The positive rate of CT for AP diagnosis and interobserver agreement

Of the 1,924 patients who met the criteria of AP, 96.7% (1,860/1,924) had positive CT findings as well as at least 1 of the other 2 criteria, and 3.3% (64/1,924) of patients met the first 2 criteria for AP diagnosis only, meaning that these patients had negative imaging findings. Among the 1,860 AP patients with positive CT findings, the etiologies included biliary AP in 31.8% (591/1,860), alcoholic AP in 14.4% (267/1,860), hypertriglyceridemic AP in 13.9% (258/1,860), mixed cause AP in 10.7% (199/1,860), and “other/idiopathic” AP in 29.3% (545/1,860).

As the 2012RAC includes the evaluation standard for local complications on imaging, based on the same clinical information, we used the 2012RAC to compare the endpoint of the total value of mild, moderately severe, and severe AP. Interobserver agreement was excellent for the 2012 RAC [*Kappa*, 0.939; 95% confidence interval (CI): 0.925 to 0.953], MCTSI score (ICC, 0.909; 95% CI: 0.901 to 0.916), NP (*Kappa*, 0.915; 95% CI: 0.897 to 0.933), and necrotizing subtypes (*Kappa*, 0.899; 95% CI: 0.763 to 0.811) ($P<0.001$).

The CT findings

The CT findings of AP based on different etiologies

Among the 1,860 AP patients with positive CT findings, 66.8% (1,243/1,860) had IEP, and 33.2% (617/1,860) had NP. The prevalence of IEP for hypertriglyceridemic AP

patients (72.5%, 187/258) was higher than that for those with alcoholic AP (63.7%, 170/267) and “other/idiopathic” AP (62.9%, 343/545) ($P<0.05$). Among the 617 NP patients, the proportion of the combined type (peripancreatic and parenchymal necrosis) (63.7%, 393/617) was higher than that of peripancreatic necrosis alone (28.4%, 175/617) and parenchymal necrosis alone (7.9%, 49/617).

Among the 1,860 AP patients, the prevalence of NP in “other/idiopathic” AP patients was 37.1% (202/545), which was higher than that of those with biliary AP (31.0%, 183/591) and hypertriglyceridemic AP (27.5%, 71/258) ($P<0.05$). However, the prevalence of NP was not significantly different among patients with alcoholic AP (36.3%, 97/267), biliary AP (31.0%, 183/591), hypertriglyceridemic AP (27.5%, 71/258), and mixed causes (32.3%, 64/199) ($P>0.05$). The proportion of those 3 necrotic subtypes had no significant differences in etiology distribution ($P>0.05$; *Figure 2*).

There were 617 NP patients among the 1,860 AP patients with positive CT examinations. In the 617 NP patients, “other/idiopathic” AP and biliary AP were more common, accounting for 32.7% (202/617) and 29.7% (183/617), respectively. Alcoholic AP, hypertriglyceridemic AP, and mixed causes accounted for 15.7% (97/617), 11.5% (71/617), and 10.4% (64/617), respectively.

Among the 617 NP patients, the percentage of biliary AP increased from Phase I (17.1%, 19/111) to Phase IV (42.9%, 42/98) ($P<0.05$). However, the percentage of hypertriglyceridemic AP decreased from Phase I (24.3%, 27/111) to Phase V (1.3%, 1/76), and the percentage of mixed causes decreased from Phase I (18.0%, 200/111) to Phase III (6.3%, 13/206) ($P<0.05$). There was no significant difference in the percentage of alcoholic AP and “other/idiopathic” AP among Phases I–V NP patients ($P>0.05$; *Table 2*).

The local complications

Among the 1,860 AP patients with positive CT findings, 64.6% (1,202/1,860) had local complications. Among the 1,202 patients with local complications, the acute peripancreatic fluid collections (52.7%, 634/1,202) was more common than acute necrotic collections (39.7%, 477/1,202), walled-off necrosis (15.2%, 183/1,202), and pancreatic pseudocysts (0.2%, 3/1,202).

Among the 1,860 patients with positive CT findings,

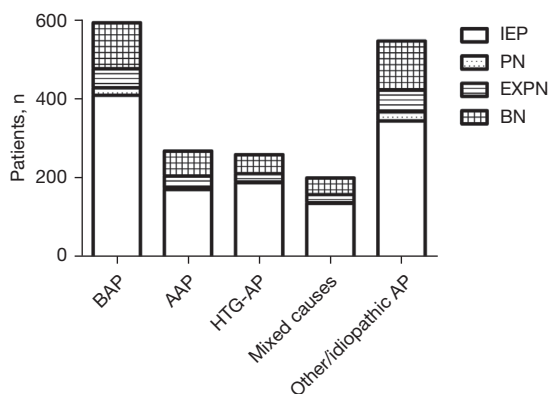


Figure 2 The types and subtypes of acute pancreatitis in the different etiological subgroups. BAP, biliary acute pancreatitis; AAP, alcoholic acute pancreatitis; HTG-AP, hypertriglyceridemic acute pancreatitis; IEP, interstitial edematous pancreatitis; PN, parenchymal necrosis alone; EXPN, peripancreatic necrosis alone; BN, peripancreatic and parenchymal necrosis.

according to the etiology of AP, the prevalence of local complications in mixed causes (71.9%, 143/199), hypertriglyceridemic AP (69.0%, 178/258), and alcoholic AP (68.2%, 182/267) patients was higher than that in biliary AP patients (59.7%, 353/591; $P < 0.05$).

There were 1,202 patients with local complications in the 1,860 patients with positive CT examinations. Among the 1,202 patients, the percentage of biliary AP increased from Phase I (25.2%, 102/404) to Phase IV (44.0%, 55/125) ($P < 0.05$). However, the percentage of hypertriglyceridemic AP decreased from Phase I (22.5%, 91/404) to Phase V (1.2%, 1/84) ($P < 0.05$). There was no significant difference in the percentage of alcoholic AP, “other/idiopathic” AP, or mixed causes among Phases I–V patients with local complications ($P > 0.05$; Table 3).

The MCTSI score

Among the 1,860 AP patients, the average MCTSI score was 5.41 ± 2.38 points. According to the etiology of AP, the MCTSI score was 5.45 ± 2.47 points in alcoholic AP, 5.45 ± 2.42 points in biliary AP, 5.45 ± 2.29 points in the mixed causes subgroup, 5.39 ± 2.42 points in “other/idiopathic” AP, and 5.27 ± 2.17 points in hypertriglyceridemic AP. However, there was no significant difference in etiology distribution in the MCTSI score ($P > 0.05$).

Among the 1,860 patients with positive CT examinations, 391 patients had severe AP graded by the MCTSI score (8–10 points). The percentages of biliary AP in Phases I–V were 20.0%, 25.3%, 34.9%, 39.7%, and

Table 2 The percentages of NP on CT for different etiologies at different onset times (n=617 patients)

Groups	All patients	1–3 days	4–7 days	8–14 days	15–28 days	>28 days	P value [†]
All patients (n)	617	111	126	206	98	76	
BAP	29.7% (183/617)	17.1% (19/111)	23.0% (29/126)	31.1% (64/206)	42.9% (42/98)	38.2% (29/76)	<0.05*
AAP	15.7% (97/617)	12.6% (14/111)	14.3% (18/126)	17.5% (36/206)	15.3% (15/98)	18.4% (14/76)	>0.05
HTG-AP	11.5% (71/617)	24.3% (27/111)	17.5% (22/126)	7.8% (16/206)	5.1% (5/98)	1.3% (1/76)	<0.05**
Mixed causes	10.4% (64/617)	18.0% (20/111)	15.1% (19/126)	6.3% (13/206)	8.2% (8/98)	5.3% (4/76)	<0.05***
Other/idiopathic AP	32.7% (202/617)	27.9% (31/111)	30.2% (38/126)	37.4% (77/206)	28.6% (28/98)	36.8% (28/76)	>0.05

[†], the Bonferroni-adjusted P value. *, the Bonferroni method showed significant difference between 1–3 and 15–28 days ($P < 0.05$, 95% CI: 0.15–0.52), 1–3 and >28 days ($P < 0.05$, 95% CI: 0.17–0.66), 4–7 and 15–28 days ($P < 0.05$, 95% CI: 0.22–0.71). **, the Bonferroni method showed significant difference between 1–3 and 8–14 days ($P < 0.05$, 95% CI: 1.95–7.46), 1–3 and 15–28 days ($P < 0.05$, 95% CI: 2.20–16.23), 1–3 and >28 days ($P < 0.05$, 95% CI: 3.20–181.74), 4–7 and 15–28 days ($P < 0.05$, 95% CI: 1.43–10.81), 4–7 and >28 days ($P < 0.05$, 95% CI: 2.10–120.31). ***, the Bonferroni method showed significant difference between 1–3 and 8–14 days ($P < 0.05$, 95% CI: 1.56–6.85), 4–7 and 8–14 days ($P < 0.05$, 95% CI: 1.25–5.55). NP, necrotizing pancreatitis; CT, computed tomography; BAP, biliary AP; AAP, alcoholic AP; HTG-AP, hypertriglyceridemic AP; AP, acute pancreatitis.

Table 3 The percentages of local complications on CT based on different etiologies at different onset times (n=1,202 patients)

Groups	All CTs	1–3 days	4–7 days	8–14 days	15–28 days	>28 days	P value [†]
All CTs (n)	1,202	404	299	290	125	84	
BAP	29.4% (353/1,202)	25.2% (102/404)	26.1% (78/299)	29.3% (85/290)	44.0% (55/125)	39.3% (33/84)	<0.05 [†]
AAP	15.1% (182/1,202)	13.4% (54/404)	13.4% (40/299)	18.3% (53/290)	16.8% (21/125)	16.7% (14/84)	>0.05
HTG-AP	14.8% (178/1,202)	22.5% (91/404)	17.1% (51/299)	9.7% (28/290)	5.6% (7/125)	1.2% (1/84)	<0.05 ^{**}
Mixed causes	11.9% (143/1,202)	26.5% (50/404)	29.1% (43/299)	32.4% (30/290)	22.4% (14/125)	35.7% (6/84)	>0.05
Other/idiopathic AP	28.8% (346/1,202)	12.4% (107/404)	14.4% (87/299)	10.3% (94/290)	11.2% (28/125)	7.1% (30/84)	>0.05

[†], the Bonferroni-adjusted P value. *, the Bonferroni method showed significant difference between 1–3 and 15–28 days (P<0.05, 95% CI: 0.28–0.63), 4–7 and 15–28 days (P<0.05, 95% CI: 0.17–0.66), 8–14 and 15–28 days (P<0.05, 95% CI: 0.34–0.82). **, the Bonferroni method showed significant difference between 1–3 and 8–14 days (P<0.05, 95% CI: 1.73–4.29), 1–3 and 15–28 days (P<0.05, 95% CI: 2.21–10.88), 1–3 and >28 days (P<0.05, 95% CI: 3.31–175.74), 4–7 and 15–28 days (P<0.05, 95% CI: 0.77–4.24), 4–7 and >28 days (P<0.05, 95% CI: 1.19–66.19). CT, computed tomography; BAP, biliary AP; AAP, alcoholic AP; HTG-AP, hypertriglyceridemic AP; AP, acute pancreatitis.

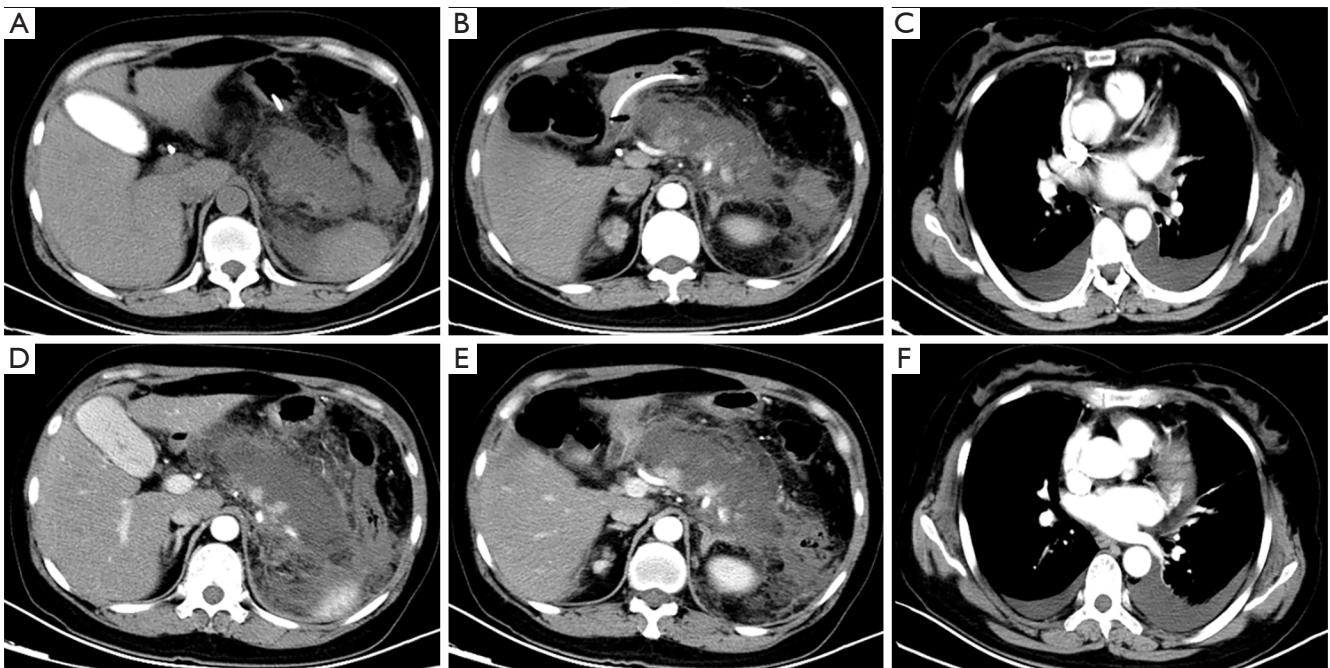


Figure 3 The severity of biliary AP graded by the MCTSI score in the different phases. A 46-year-old woman with biliary AP. (A–C) Four days after onset, NP and acute necrotic collections involving the pancreatic parenchyma and peripancreatic tissues were observed. (A) Positive gallstone in biliary. (B) Heterogeneous collection in the region of the body and tail of the pancreas and peripancreatic tissues. (C) Bilateral pleural effusion. MCTSI, 10 points. (D–F) Nine days after onset, the size of necrotic and acute necrotic collections increased; bilateral pleural effusion was not obviously decreased. MCTSI, 10 points. AP, acute pancreatitis; MCTSI, modified CT severity index; NP, necrotizing pancreatitis.

40.7%, respectively, which showed an increasing trend from Phase I to Phase V (P<0.05; *Figure 3*). However, the percentage of hypertriglyceridemic AP decreased from Phase I to Phase V, and the percentages were 22.7%, 17.3%,

7.8%, 6.9%, and 1.9%, respectively (P<0.05; *Figure 4*). There were no significant differences in the percentage of alcoholic AP, “other/idiopathic” AP, or mixed causes among Phases I–V of severe AP graded by the MCTSI score (P>0.05).

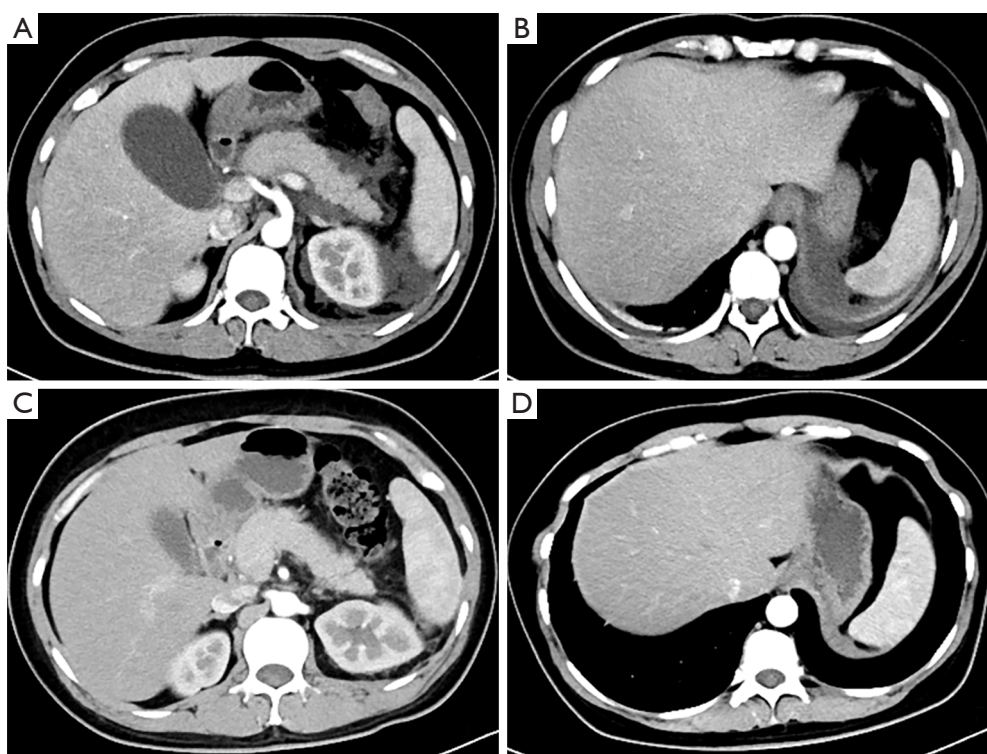


Figure 4 The severity of hypertriglyceridemic AP graded by the MCTSI score in the different phases. A 39-year-old woman with hypertriglyceridemic AP. (A,B) Three days after onset, acute interstitial edematous pancreatitis and acute peripancreatic fluid collection were observed. (A) The pancreatic parenchyma was homogeneous after enhancement, acute peripancreatic fluid collections around the tail of pancreas and left paracolic sulcus. (B) Small bilateral pleural effusion. MCTSI, 6 points. (C,D) Nineteen days after onset. (C) The size of acute peripancreatic fluid collections decreased. (D) Bilateral pleural effusion was absorbed. MCTSI, 4 points. AP, acute pancreatitis; MCTSI, modified CT severity index.

Clinical characteristics

Time from onset of symptoms to discharge

Among the 1,860 AP patients, for the time from onset of symptoms to clinical discharge, among the 5 etiology subgroups, the median days for biliary AP was 18 days (IQR, 13 to 28 days), which was longer than that of the other 4 subgroups ($P < 0.05$). The median days for hypertriglyceridemic AP was 13 days (IQR, 10 to 19.25 days), which was shorter than that for the biliary AP (18 days), “other/idiopathic” AP (16 days), and mixed causes subgroups (16 days) ($P < 0.05$).

The severity of AP graded by the 2012 RAC

Among the 1,860 AP patients, moderately severe AP (MSAP) (63.8%, 1,187/1,860) was more common than mild AP (MAP) (27.2%, 506/1,860) and severe AP (SAP) (9.0%, 167/1,860) as graded by the 2012 RAC. According to the etiology of AP,

the percentage of SAP was 8.3% (49/591) in the biliary AP subgroup, 9.0% (24/267) in the alcoholic AP subgroup, 9.3% (24/258) in the hypertriglyceridemic AP subgroup, 12.6% (25/199) in the mixed causes subgroup, and 8.3% (45/545) in the “other/idiopathic” AP subgroup. There were no significant differences in etiology distribution in the severity of AP graded by the 2012 RAC ($P > 0.05$; *Figure 5*).

There were 167 patients with SAP among the 1,860 patients with positive CT examinations. Among these 167 patients, biliary AP and “other/idiopathic” AP were more common, with percentages of 29.3% (49/167) and 26.9% (45/167), while alcoholic AP, hypertriglyceridemic AP, and mixed causes accounted for 14.4% (24/167), 14.4% (24/167), and 15.0% (25/167), respectively.

Among the 167 patients with SAP, the clinical trend of the percentage of hypertriglyceridemic AP decreased from Phase I (34.4%, 11/32) to Phase V (0.0%, 0/15) ($P < 0.05$). There was no significant difference in the percentage of

alcoholic AP, biliary AP, “other/idiopathic” AP, and mixed causes among Phases I–V of severe AP graded by the 2012RAC ($P>0.05$; Table 4).

The APACHE II scores

Among the 1,860 AP patients, the average APACHE II score was 4.95 ± 3.50 points. According to the etiology of AP, the average APACHE II score was higher in the biliary AP (5.98 ± 3.42 points) than in those with “other/idiopathic” AP (4.88 ± 3.28 points), mixed causes (4.65 ± 3.16 points), alcoholic AP (4.11 ± 4.76 points), and hypertriglyceridemic AP (3.84 ± 2.91 points; $P<0.05$).

There were 387 patients with severe AP graded by

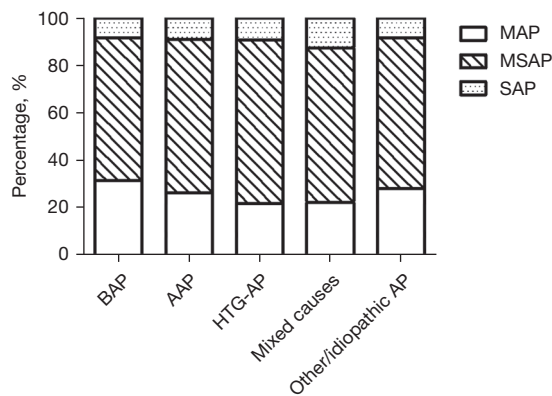


Figure 5 The severity of acute pancreatitis graded by the 2012 revised Atlanta classification in the different etiological subgroups. BAP, biliary acute pancreatitis; AAP, alcoholic acute pancreatitis; HTG-AP, hypertriglyceridemic acute pancreatitis; MAP; mild acute pancreatitis; MSAP; moderately severe acute pancreatitis; SAP; severe acute pancreatitis.

APACHE II score (at least 8 points) among the 1,860 patients with positive CT examinations. Among the 387 patients, the percentage of hypertriglyceridemic AP in Phases I–V was 17.6%, 5.4%, 1.1%, 5.3%, and 0.0%, respectively, and the trend of the percentage of hypertriglyceridemic AP decreased from Phase I to Phase V ($P<0.05$). There was no significant difference in the percentage of alcoholic AP, biliary AP, “other/idiopathic” AP, or mixed causes among Phases I–V of severe AP graded by APACHE II score ($P>0.05$).

Correlation between the clinical and imaging characteristics

Among the 1,860 AP patients with positive CT findings, according to Spearman’s rank correlation coefficients, the MCTSI score showed positive correlations with the 2012 RAC and APACHE II score. The correlation coefficients between the MCTSI and RAC were higher than those between the MCTSI and APACHE II score (Table 5).

The correlation coefficient between the MCTSI and RAC was the highest in Phase I ($r=0.665$) and the lowest in Phase IV ($r=0.463$). The correlation coefficient between the MCTSI and RAC was the highest in alcoholic AP ($r=0.653$) and the lowest in hypertriglyceridemic AP ($r=0.584$) among the 5 etiological subgroups. For each etiology-subgroup, the correlation coefficient between MCTSI and RAC was the highest in Phase I for “other/idiopathic” AP ($r=0.741$), Phase II for alcoholic AP ($r=0.784$), Phase III for hypertriglyceridemic AP ($r=0.592$) and mixed causes AP ($r=0.730$), and Phase V for biliary AP ($r=0.663$). This shows that the correlation between MCTSI and RAC in different etiological subgroups reached its highest at different phases

Table 4 The percentages of SAP graded by RAC based on different etiologies at different onset times ($n=167$ patients)

Groups	All CTs	1–3 days	4–7 days	8–14 days	15–28 days	>28 days	P value [†]
All patients (n)	167	32	53	41	26	15	
BAP	29.3% (49/167)	21.9% (7/32)	22.6% (12/53)	34.1% (14/41)	30.8% (8/26)	53.3% (8/15)	>0.05
AAP	14.4% (24/167)	6.3% (2/32)	11.3% (6/53)	14.6% (6/41)	26.9% (7/26)	20.0% (3/15)	>0.05
HTG-AP	14.4% (24/167)	34.4% (11/32)	15.1% (8/53)	9.8% (4/41)	3.8% (1/26)	0.0% (0/15)	<0.05*
Mixed causes	15.0% (25/167)	25.0% (8/32)	20.8% (11/53)	4.9% (2/41)	11.5% (3/26)	6.7% (1/15)	>0.05
Other/idiopathic AP	26.9% (45/167)	12.5% (4/32)	30.2% (16/53)	36.6% (15/41)	26.9% (7/26)	20.0% (3/15)	>0.05

[†], the Bonferroni-adjusted P value. *, the Bonferroni method showed significant difference between 1–3 and 4–7 days ($P<0.05$, 95% CI: 1.03–8.40), 1–3 and 8–14 days ($P<0.05$, 95% CI: 1.37–17.14), 1–3 and 15–28 days ($P<0.05$, 95% CI: 1.56–109.95). SAP, severe AP; RAC, revised Atlanta classification; BAP, biliary AP; AAP, alcoholic AP; HTG-AP, hypertriglyceridemic AP; AP, acute pancreatitis.

Table 5 The correlations among the RAC, APACHE II score, and MCTSI score based on the etiological subgroups at different onset times (n=1,860 patients)

Groups	Overall	1–3 days	4–7 days	8–14 days	15–28 days	>28 days
All patients (n)	1,860	654	500	414	169	123
MCTSI/RAC						
All patients	0.620	0.665	0.607	0.598	0.463	0.604
BAP	0.615	0.622	0.543	0.624	0.623	0.663
AAP	0.653	0.740	0.784	0.469	–*	–*
HTG-AP	0.584	0.565	0.585	0.592	–*	–*
Mixed causes	0.603	0.625	0.539	0.730	–*	0.714
Other/idiopathic AP	0.634	0.741	0.600	0.603	0.426	0.444
MCTSI/APACHE II						
All patients	0.167	0.199	0.157	0.210	–*	–*
BAP	0.150	–*	0.187	0.300	–*	–*
AAP	0.128	–*	–*	–*	–*	–*
HTG-AP	0.239	0.243	0.243	–*	–*	–*
Mixed causes	0.286	0.274	0.274	–*	–*	–*
Other/idiopathic AP	0.204	0.276	0.276	0.261	–*	–*

* , spearman rank correlation tests showed no correlation ($P>0.05$). RAC, revised Atlanta classification; APACHE II, acute Physiology and Chronic Health Evaluation II; MCTSI, modified CT severity index; BAP, biliary AP; AAP, alcoholic AP; HTG-AP, hypertriglyceridemic AP; AP, acute pancreatitis.

following the different onset times of the disease.

Discussion

In this study, 96.7% of AP patients with CECT examinations had positive CT findings. We found that biliary AP was the most common etiology of AP, which is consistent with the results of previous studies (24,25). The proportion of “other/idiopathic” AP in the present study was 29.4%, which is higher than that in present studies in China that range from 17% to 24% (3,26–28). A possible reason for this is that our results were based on CT and did not include all clinical AP patients. Clinically, some patients with mild AP were not diagnosed by CT, and the proportion of the etiology of these patients was uncertain.

We observed NP in 33.2% of AP patients with positive CECT findings and it was mostly seen in “other/idiopathic” AP patients, while IEP was most common in hypertriglyceridemic AP patients. Biliary AP showed an increasing percentage, while hypertriglyceridemic AP showed a decreasing percentage of NP on CT from

Phase I to Phase IV. There were 64.6% of AP patients with local complications as shown by CT. Compared with parenchymal necrosis, local peri-pancreatic complications occurred more frequently in non-biliary disease. Biliary AP showed an increasing percentage of local complications, while hypertriglyceridemic AP showed a decreasing percentage from Phase I to Phase IV. Biliary AP and hypertriglyceridemic AP also showed changes of severe AP graded by MCTSI scores. For severe AP graded by RAC and APACHE II scores, only hypertriglyceridemic AP showed a decreasing percentage from Phase I to Phase V. The correlation coefficients between MCTSI and RAC were higher than those between the MCTSI and APACHE II score. Our results may serve to renew some basic data about CT characteristics according to the 2012 RAC and provide evidence for different rules for CT features based on the common etiologies of AP at different onset times. This may be helpful for the accurate recognition and management of AP.

In this study, 96.7% of patients with AP had positive CT findings based on CECT, and this percentage was

higher than that of a previous study in 2006 (29). This may be because the current imaging methods available are better than those used previously, and pancreatologists and radiologists have reached a new consensus and understanding about AP after publication of the 2012 RAC (21). Hence, we can better observe the abnormality on images and use clearer definitions.

A study in 2019 suggested that up to 10–20% of patients with AP also had NP (30). However, in our study, that proportion was 33.2%. The possible reason for this is that the identification of necrosis has become more accurate with advances in imaging technology (31). For example, previously, patients with peripancreatic necrosis alone were likely to be categorized as having pancreatic fluid collections (32). Furthermore, the 33.2% proportion was based on patients with positive CT findings, but some patients with mild AP or IEP did not undergo any CT scan, which may also have contributed to the high proportion of NP results.

Consistent with Huang *et al.* (33), IEP was the most common in hypertriglyceridemic AP patients. A meta-analysis pointed out that NP was more common in alcoholic AP than biliary AP (10), which contradicted the results of Hughey *et al.* (12). In our results, the prevalence of NP in alcoholic AP was higher than that in biliary AP but with no significant difference, which is consistent with a previous study (34). This may be because some studies that conducted meta-analysis included not only primary AP but also recurrent AP (10). A study indicated that the recurrence rate was approximately 38% for alcoholic AP and 17% for biliary AP (35).

Patients with NP usually have a protracted and variable disease course because pancreatic and peripancreatic necrosis may liquefy or remain solid, become infected or remain sterile, or persist or disappear over time (21,36). In our results, biliary AP showed an increasing percentage of NP on CT from Phase I to Phase IV, while hypertriglyceridemic AP showed a decreasing percentage from Phase I to IV. Our results indicate that compared with other etiological subgroups, biliary AP has a longer time from onset to discharge, while hypertriglyceridemic AP has a shorter time.

In this study, CT showed that 64.6% of AP patients had local complications, which was relatively higher than that of previous studies (15,37). This may be because of the recent development of imaging modalities that enabled us to closely observe fluid collections in this study. Previous studies have reported that alcoholic AP is closely related to

the development of local complications, including walled-off necrosis and pancreatic pseudocysts (15,37,38). Our study also found that the prevalence of local complications in alcoholic AP was higher than that in biliary AP.

Biliary AP is an inflammation of the pancreas that occurs due to obstruction of the common channel that drains both the biliary and pancreatic ducts (1). The symptoms of older biliary AP patients may be far less obvious in their respective manifestations (39), the admission time will be postponed, and persistent inflammatory stimulation results in slow improvement or stops the local morphological changes around the pancreas. This may be why CT showed that the local complications of biliary AP recovery were slower.

In this study, we found that hypertriglyceridemic AP patients recovered faster than others regardless of CT or clinical examination. The reason for this may be because hypertriglyceridemia dose aggravates the severity and related local complications of AP, and TG levels are high in the early stage but decrease significantly in the late stage, as many hypertriglyceridemic AP patients receive aggressive intravenous fluid administration and have compromised caloric intake (40–42). However, biliary AP patients are often older and have many systemic complications, and those factors would not change with onset time, which may explain why biliary AP patients have a high APACHE II score and the percentage of biliary AP was not significantly different at different phases of SAP graded by the RAC and APACHE II score.

Some studies have shown that there is no correlation between imaging scores (CTSI, MRSI score) and the APACHE II score (7,43). However, Zhou *et al.* (32) demonstrated that extrapancreatic inflammation on CT scores have weak positive correlations with the APACHE II score. In addition, Peng *et al.* (44) reported that the pleural effusion volume was correlated with the APACHE II score, and Jiang *et al.* (45) found a significant correlation between the incidence of vascular involvement and AP severity on the basis of APACHE II score. In our study, the MCTSI score had a positive correlation with the RAC and APACHE II score. The possible reason may be that the previous studies only scored imaging in the early phase of the disease (usually within 72 h) when necrotic tissues were not yet clearly visible.

Our study had some limitations. First, this study used retrospective data collection, and partial information could not be collected for the clinical and imaging characteristics at the same time, which might have led to the loss of data and affected the results. Second, the patients were divided

into 5 phases, and the patients in each subgroup were observed together, which was an ideal state. However, some patients had individual differences leading to errors, so it is worthwhile to conduct a prospective study to investigate the dynamic course of disease in the same patient in the future.

Conclusions

The AP patients in this study had a very high rate of positive CECT findings, and the proportion of NP shown on CT was as high as 33.2% of positive CECT findings. Biliary AP recovery was slower, while hypertriglyceridemic AP recovery was faster on CT than in other etiological subgroups. There may be differences in the imaging and clinical manifestations of different etiologies of AP, and these may be related to the onset time of AP symptoms.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://qims.amegroups.com/article/view/10.21037/qims-21-1231/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Affiliated Hospital of North Sichuan Medical

College (No. 2021ER[A]017), and individual consent for this retrospective analysis was waived.

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Table S1 Modified Marshall scoring system for organ dysfunction Score (1)

Organ system	Score				
	0	1	2	3	4
Respiratory (PaO ₂ /FiO ₂)	>400	301–400	201–300	101–200	≤101
Renal*					
(serum creatinine, mmol/l)	≤134	134–169	170–310	311–439	>439
(serum creatinine, mg/dl)	<1.4	1.4–1.8	1.9–3.6	3.6–4.9	>4.9
Cardiovascular (systolic blood pressure, mm Hg) [†]	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH<7.3	<90, pH<7.2
For non-ventilated patients, the FiO ₂ can be estimated from below:					
Supplemental oxygen (l/min)	FiO ₂ (%)				
Room air	21				
2	25				
4	30				
6–8	40				
9–10	50				

A score of 2 or more in any system defines the presence of organ failure. *A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥134 μmol/l or ≥1.4 mg/dL. [†]Off inotropic support.

Table S2 The grades of severity according to the 2012 revised Atlanta classification (1)

The grades of severity	define
Mild acute pancreatitis	No organ failure No local or systemic complications
Moderately severe acute pancreatitis	Organ failure that resolves within 48 h (transient organ failure) and/or Local or systemic complications without persistent organ failure
Severe acute pancreatitis	Persistent organ failure (>48 h) –Single organ failure –Multiple organ failure

Table S3 Acute Physiology and Chronic Health Evaluation II score, APACHE II score (2)

A. age	≤44,0	45-54, 2	55-64, 3	65-74, 5	≥75,6					A point	
B. Past health score: patients with severe organ system dysfunction or immune damage.	Non-operative or after elective surgery				2					B point	
	Unable to operate or after emergency surgery				5						
	None of the above				0						
Glasgow coma score (GCS)	6	5	4	3	2					1	
1. eye opening reponse			spontaneous	to speech	to pain					none	
2. language reponse		oriented	confused	inappropriate words	unintelligible sounds					none	
3. motor response	obey commands	localize	with drawal	decorticate flexion	decerebrate extension					no response	
GCS score=1+2+3	C point= 15 minus actual GCS										
D= Acute Physiology Score (APS)	score										D point
	+4	+3	+2	+1	0	+1	+2	+3	+4		
Temperature rectal (°C)	≥41	39-40.9		38.5-38.9	36-38.4	34-35.9	32-33.9	30-31.9	≤29.9		
Mean arterial perssure (mmHg)	≥160	130-159	110-129		70-109		50-69		≤49		
heart rate ventricular response	≥180	140-179	110-139		70-109		55-69	40-54	≤39		
Respiratory frequency	≥50	35-49		25-34	12-24	10-11	6-9		≤5		
PaO ₂ (mmHg) (FiO ₂ <50%)					70	61-70		55-60	<55		
A-aDO ₂ (FiO ₂ >50%)	≥500	350-499	200-349		200						
Arterial PH	≥7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	<7.15		
Serum HCO ₃ (vernous-mmol/L) (Not preferred, use if no ABGs)	≥52	41-51.9		32-40.9	23-31.9		18-21.9	15-17.9	<15		
Serum Sodium (mmol/L)	≥180	160-179	155-159	150-154	130-149		120-129	111-119	≤110		
Serum Potassium (mmol/L)	≥7	6-6.9		5.5-5.9	3.5-5.4	3-3.4	2.5-2.9		<2.5		
Serum creatinine (ummol/L)	≥305	170-304	130-169		54-129		<54				
Hematocrit (%)	≥60		50-59.9	46-49.9	30-45.9		20-29.9		<20		
White blood score (total/mm ³) (in 1,000s)	≥40		20-39.9	15-19.9	3-14.9		1-2.9		<1		
APACHE II toltal point =A+B+C+D											

Chronic Health Points

If the patient has a history of severe organ system insufficiency or is immuno-compromised assign points as follows: (i) for nonoperative or emergency postoperative patients, 5 points or (II) for elective postoperative patients, 2 points. Definitions: Organ Insufficiency or immuno-compromised state must have been evident prior to this hospital admission and conform to the following criteria: LIVER: Biopsy proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic lailurelencephalopathy/coma. CARDIOVASCULAR: New York Heart Association Class IV. RESPIRATORY: Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction, i.e., unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40 mmHg), or respirator dependency. RENAL: Receiving chronic dialysis. IMMUNO-COMPROMISED: The patient has received therapy that suppresses resistance to infection, e.g., immuno-suppression, chemotherapy, radiation, long term or recent high dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection, e.g., leukemia, lymphoma, AIDS.

Definitions

Organ Insufficiency or immuno-compromised state must have been evident prior to this hospital admission and conform to the following criteria:

Liver: Biopsy proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic lailurelencephalopathy/coma.

Cardiovascular: New York Heart Association Class IV.

Respiratory: Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction, i.e. , unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (> 40mmHg), or respirator dependency.

Renal: Receiving chronic dialysis.

Immuno-compromised: The patient has received therapy that suppresses resistance to infection, e.g.. immuno-suppression, chemotherapy, radiation, long term or recent high dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection, e.g. leukemia, lymphoma, AIDS.

Table S4 An overview of CT scan models and their important parameters

CT scanning model	Tube current (mA)	Tube voltage (kVp)	Reconstructed kernel function	collimator (mm)	Pitch	layer thickness (mm)
Siemens Definition AS+ 128	200	120	B30f	128×0.6	1.0	5.0
GE LightSpeed VCT	200	120	B30f	64×0.6	0.9	5.0
Brilliance 64	200	120	B30f	64×0.6	0.8	1.5
SOMATOM Definition Flash	200/155	140/80	B30f	2×128×0.6	0.9	5.0
Toshiba Aquilion ONE 320	250	120	B30f	64×0.6	0.5	5.0

Table S5 Modified CT severity index, MCTSI score (3)

Grade score	Definition
0	Normal pancreas
2	pancreas and / or peripancreatic inflammation
4	Single or more ill-defined collections or pancreatic/peripancreatic gas
Necrosis score	
0	Uniform pancreatic enhancement
2	Non-enhancement of lower 30% of the gland
4	Non-enhancement of over 30% of the gland
Extrapancreatic complications	
2	One or more of pleural effusion, ascites, vascular complications, parenchymal complications, or gastrointestinal tract involvement.

Mild (0–2 points), moderate (4–6 points), or severe (8–10 points).

References

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2. Knaus WA, Zimmerman JE, Wagner DP, Draper EA, Lawrence DE. APACHE-acute physiology and chronic health evaluation: a physiologically based classification system. *CRIT CARE MED* 1981;9:591-597.
3. Bollen TL, Singh VK, Maurer R, Repas K, van Es HW, Banks PA, et al. Comparative evaluation of the modified CT severity index and CT severity index in assessing severity of acute pancreatitis. *AJR Am J Roentgenol* 2011;197:386-392.