MR Imaging for Early Extrapancreatic Necrosis in Acute Pancreatitis

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Rationale and Objectives: To study the MRI characteristics of early extrapancreatic necrosis and compare them with those of peripancreatic fluid collections in acute pancreatitis (AP).

Materials and Methods: This retrospective study enrolled 70 AP patients who had extrapancreatic collections visible on MRI within 1 week of onset. Extrapancreatic collections were divided into extrapancreatic necrosis and peripancreatic fluid collections based on follow-up MRI, CT, or pathology. The number and area of extrapancreatic collections, extrapancreatic inflammation on MRI (EPIM) score, MR severity index score and clinical characteristics were evaluated and compared between the two groups.

Results: Of the seventy AP patients, 32 (45.7%) had extrapancreatic necrosis, and 38 (54.3%) had peripancreatic fluid collections. The number and area of extrapancreatic collections, MR severity index score, EPIM score, and prevalence of associated hemorrhage were significantly higher in extrapancreatic necrosis patients than in those with peripancreatic fluid collections ($p < 0.001$). Among the single indicators, the accuracy of the area of extrapancreatic collections (AUC = 0.871) was comparable to that of the EPIM score for predicting extrapancreatic necrosis and was significantly higher than that of the other two indicators. The combination of all indicators showed the highest predictive accuracy (AUC = 0.949), and combinations of two or more indicators demonstrated significantly higher predictive accuracy for extrapancreatic necrosis than any single indicator ($p < 0.05$) except for the area of extrapancreatic collections ($p > 0.05$).

Conclusion: The MRI characteristics have the potential to differentiate early extrapancreatic necrosis from peripancreatic fluid collections and help indicate extrapancreatic necrosis.

Key Words: Acute pancreatitis; Extrapancreatic necrosis; Acute peripancreatic fluid collection; MRI.

INTRODUCTION

Acute pancreatitis (AP) is an inflammatory disease with various outcomes involving the pancreas and extrapancreatic tissue and has become a common acute abdominal disease in the clinic (1). There are two main morphological subtypes: interstitial edematous pancreatitis and necrotizing pancreatitis. Necrotizing pancreatitis has a more severe disease course and higher mortality (2%–39%) (2,3). In the 1992 Atlanta Classification, necrotizing pancreatitis was emphasized as necrosis of the pancreas itself, and the definition of complications was ambiguous (4). The 2012 revised Atlanta Classification proposed specifically that extrapancreatic necrosis alone was an independent subtype of necrotizing pancreatitis (2).

As is known to all that different morphological subtypes of AP have considerable differences in clinical outcome, treatment, and prognoses, and many studies have reported that the outcomes and prognoses of patients with extrapancreatic necrosis alone were better than those of patients with pancreatic parenchymal necrosis but poorer than those of patients with interstitial edematous pancreatitis (5–12). Therefore, early accurate assessment of subtype of AP and identification of potential extrapancreatic necrosis are crucial for determining disease progression, guiding clinical management, and taking timely clinical treatment (2–3). Imaging (including contrast-enhanced computed tomography [CECT], magnetic resonance imaging [MRI], and transabdominal ultrasonography) is the main method for diagnosing extrapancreatic necrosis and evaluating its complications (3). However, early extrapancreatic necrosis, especially within 3 days of AP onset, has a similar appearance to acute peripancreatic fluid collections on imaging, as both demonstrate homogeneous fluid attenuation or signal intensity, the diagnosis of early extrapancreatic necrosis is impeded by intrinsic differences among participants in image assessment (13,14). MRI, especially fat-saturated T2-weighted MR imaging, is more sensitive to the

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fluid and nonliquefied material in extrapancreatic collections than CT (3,13,15,16), and T1-weighted MR imaging can be helpful in detecting pancreatic or peripancreatic hemorrhage (17). Therefore, MRI has more advantages in diagnosing early extrapancreatic necrosis than CT. Moreover, MRI does not require radiation and can be used for repeated follow-up. The volume of extrapancreatic collections and extent of extrapancreatic inflammation were reported to be early significant predictors for the severity and outcome of AP (11,18–22). Another study also reported that extrapancreatic collections larger than 5 cm in diameter are not easily absorbed, which may lead to some degree of extrapancreatic necrosis (23), but no relevant literature has studied their association with extrapancreatic necrosis in the early stage of AP.

Therefore, the main purpose of this study is (1) to evaluate the MR imaging characteristics of early extrapancreatic necrosis; and (2) to compare these MRI characteristics of early extrapancreatic necrosis with those of peripancreatic fluid collections and determine whether these characteristics indicate early extrapancreatic necrosis.

MATERIALS AND METHODS

Patients

This study was a retrospective study approved by the Institutional Review Board and the Ethics Committee of our hospital. Informed consent was waived. All procedures involving human participants adhered to the ethical principles of the Declaration of Helsinki.

We retrospectively analyzed patients with AP admitted to our institution between September 2014 and September 2018. The diagnosis of AP conformed to two of the following three criteria according to the 2012 revised Atlanta Classification (2): (1) persistent abdominal pain; (2) a serum lipase (or amylase) level of greater than three times higher than normal; and (3) typical imaging findings of AP. The inclusion criteria in this study included the following: (1) patients hospitalized with the first diagnosis of AP; (2) patients who underwent MRI within 1 week of onset and had extrapancreatic collections; and (3) patients followed up with either MRI or CECT after the first week or with histopathological findings confirming extrapancreatic necrosis or peripancreatic fluid collections. The exclusion criteria included the following: (1) patients with pancreatic carcinoma; (2) patients with retroperitoneal neoplasia, infection, and hemorrhagic diseases; (3) patients who presented with comorbidities of chronic liver disease, hypoalbuminemia or an underlying disease that may cause peritoneal effusion; and (4) patients with a history of chronic pancreatitis. A total of 70 patients with AP were enrolled and divided into two groups: those with extrapancreatic necrosis and those with peripancreatic fluid collections.

The clinical charts of all enrolled patients were reviewed to determine age, sex, etiology, levels of serum high-sensitivity C-reactive protein (hs-CRP), and calcium within 1 week of onset, length of hospital stay, incidence of systemic inflammatory response syndrome (SIRS), incidence of organ failure, and clinical severity of AP according to the modified Marshall scoring system (2).

MRI and CT Techniques

All patients underwent MRI on a 3.0-T system (MR750, GE Medical Systems, Waukesha, WI). The sequences included the following: coronal and axial single-shot fast spin-echo T2-weighted images (T2WI); axial fast recovery fast spin-echo T2-weighted images (T2WI) with fat saturation; T1-weighted in-phase and out-of-phase images (24), which were obtained from three-dimensional liver acquisitions with volume acceleration flexible (3D LAVA-flex); single-shot fast spin-echo radial series slab MR cholangiopancreatography images and dynamic contrast-enhanced 3D LAVA-flex with fat saturation images. The parameters of the above sequences are listed in Table 1. 3D LAVA dynamic enhancement was performed with 20 mL of gadolinium (Magnevist; Schering Guangzhou, China) administered intravenously at 2–3 mL/s, followed by a 20 mL saline solution flush. Dynamic enhancement was performed at 16 seconds (early hepatic arterial phase), 30 seconds (hepatic arterial phase), 60 seconds (venous phase), and 120 seconds (delayed phase) after the injection.

Some patients underwent abdominal CECT 1 week after onset, and all CECT images were acquired by a multidetector row CT system (Somatom Definition AS+128, Siemens Healthineers). The main acquisition parameters included the

TABLE 1. The Parameters of the 3.0-T MRI Sequences.

Scanning Sequences	TR (ms)	TE (ms)	Section Thickness (mm)	Intersection Gap (mm)	Matrix	FOV (cm)
Cor SSFSE T2WI	4500–6000	90–120	5	1	384 × 256	36 × 36
Ax SSFSE T2WI	4500–6000	90–120	6	1	320 × 256	34 × 34
Ax FRFSE fs-T2WI	2500–3000	90–110	6	1	384 × 384	34 × 34
MRCP	4000–5000	900–1000	50	40–50	384 × 256	34 × 34
Ax 3D LAVA-Flex	3.6–4.4	1.7–1.9	5.2	0	224 × 192	36 × 36
Ax 3D LAVA C+*	3.6–4.4	1.7–1.9	5.2	0	224 × 192	36 × 36

FOV, field of view; FRFSE, fast recovery fast spin-echo; LAVA, liver acquisition with volume acceleration flexible; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography; SSFSE, single-shot fast spin-echo; TR, repetition time; TE, echo time.

* Dynamic enhanced imaging.

following: tube voltage, 120 kV; tube current, 200 mA; field of view, 35 × 35 cm; matrix, 512 × 512; reconstruction kernel, B30f; collimation, 128 × 0.6 mm; pitch, 1.0; and slice thickness, 5.0 mm. CECT was implemented for the arterial and portal venous phases with 25−30 seconds and 65−70 seconds delays, respectively, after intravenous administration of iodinated contrast material (Ultravist 370, Bayer Schering Pharma) at a dose of 1.5 mL/kg and an injection rate of 3.5−4 mL/s.

Definition and Imaging Evaluation

Initial MRI scans were retrospectively reviewed by 2 radiologists with 3 years of experience in abdominal imaging who were blinded to the results of follow-up imaging and the clinical data of the patients Follow-up MRI and CECT scans were evaluated by two radiology professors blinded to the clinical data of the patients. Extrapancreatic collections were divided into extrapancreatic necrosis and peripancreatic fluid collections. Extrapancreatic necrosis was defined when the extrapancreatic collections appeared as a heterogeneous signal according to the 2012 revised Atlanta Classification (12,16,25). In the early stages of AP, however, this criterion is more subjective but the diagnosis becomes easier and accurate when the disease process evolves over time. In this study, we diagnosed extrapancreatic necrosis (including extrapancreatic necrosis alone and combined necrosis) 1 week after onset, when one of the following three criteria was met: (1) the follow-up imaging findings were consistent with extrapancreatic necrosis in the 2012 revised Atlanta Classification (Fig 1) or there was a well-defined, walled-off heterogeneous extrapancreatic or pancreatic-peripancreatic collection 4 weeks after onset (Fig 2); (2) the extrapancreatic collections on follow-up imaging showed no significant decrease or even an increase compared to those on the initial MRI (8,26); and (3) there was pathological confirmation of extrapancreatic necrosis. Peripancreatic fluid collections were diagnosed when the extrapancreatic collections were mostly absorbed or there was only a small amount of exudate around the pancreas on follow-up imaging and the pancreas exhibited homogeneous enhancement (Fig 3). Hemorrhage was detected by the appearance of hyperintensity in the pancreas or extrapancreatic regions on T1WI (17).

The severity of AP was assessed using the MRSI score, by which AP was graded as mild (0−3 points), moderate (4−6 points) or severe (7−10 points) (27), and the extrapancreatic inflammation on MRI (EPIM) score, which was derived from the extrapancreatic inflammation on CT (28).

Extrapancreatic collections were assessed semiquantitatively according to the extent of the extrapancreatic spaces involved, including the following 7 locations: (1) peripancreatic space, (2) root of the mesentery, (3) transverse mesocolon, (4) gastrosplenic

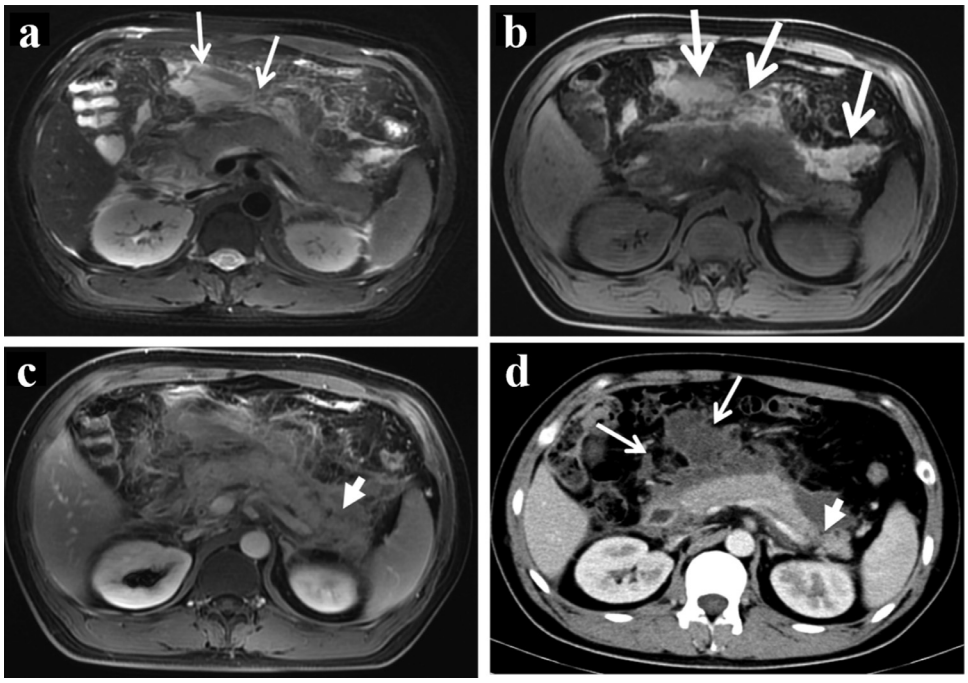

Figure 1. Combined necrosis in a 42-year-old man with extrapancreatic hemorrhage. (a−c) Axial T2-weighted MR image on the fifth day of onset show an evolving heterogeneous extrapancreatic collection around the neck, body, and tail of the pancreas involving the transverse mesocolon downward (white arrow). The extrapancreatic hyperintense signal on the axial fat-saturated T1-weighted MR image (thick white arrow) is suggestive of hemorrhage. A patchy hypointense region in the tail of the pancreas on the axial contrast-enhanced T1-weighted MR image (white arrowhead) demonstrates necrosis of the pancreatic parenchyma. (d) Axial contrast-enhanced CT imaging after 14 days shows a well-defined, heterogeneous extrapancreatic collection (white arrow), and a patchy hypoattenuating region in the tail of the pancreas (white arrowhead).

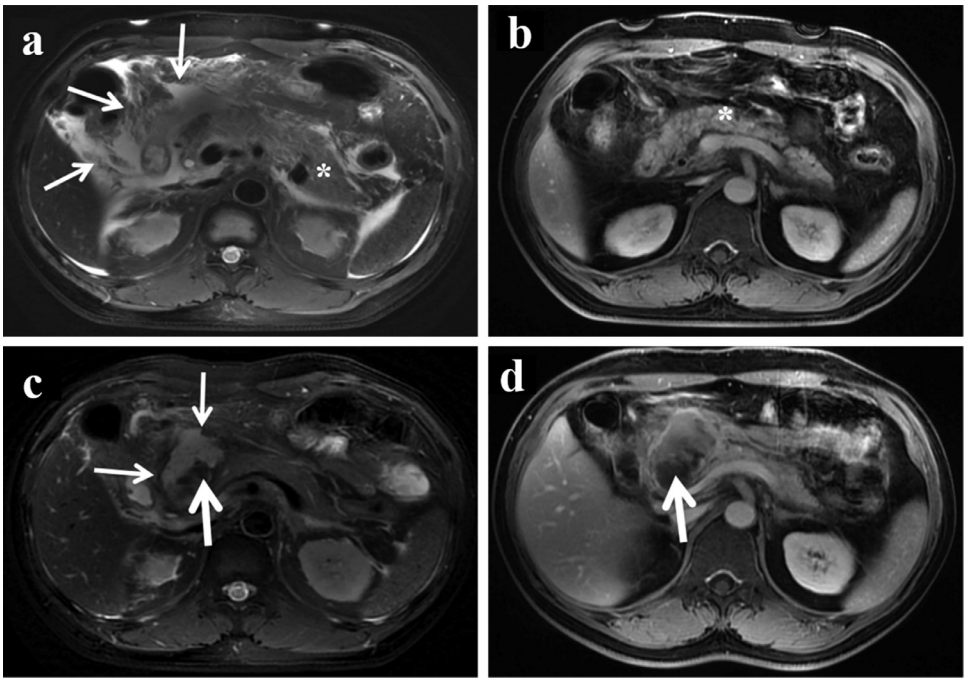

Figure 2. Combined necrosis in a 46-year-old man. (a–b) Axial fat-saturated T2-weighted MR images on the second day of onset show an irregular, homogeneous collection around the head of the pancreas and hepatoduodenal ligament (white arrow) and a normal-appearing pancreatic parenchyma (*). (c–d) Axial fat-saturated T2-weighted MR images obtained 2+ months after discharge reveal the evolution of the homogeneous extrapancreatic collection into well-defined walled-off heterogeneous pancreatic-peripancreatic collections involving the head and neck of the pancreas, with a fluid component that appears hyperintense (white arrow) and necrotic nonliquefied material that appears hypointense (thick white arrows). Axial contrast-enhanced T1-weighted imaging shows no enhancement in the necrotic tissue (thick white arrows), with an enhanced wall surrounding the walled-off necrosis (WON) (white arrowhead).

ligament, (5) hepatoduodenal or gastrohepatic ligament, (6) right anterior or posterior pararenal space, and (7) left anterior or posterior pararenal space (10). We recorded the number of extrapancreatic collections involving these locations in each patient. To measure the area of extrapancreatic collections, we selected the slice with the largest amount of collections on the initial fat-saturated T2WI and then measured the cross-sectional area of the collections in all involved locations (29). The area of extrapancreatic collections was manually drawn along the margin of the collections (Fig 4). Extrapancreatic collections included fat infiltration, collections of fluid, or collections of nonliquid components. Any disagreements between two radiology professors and betweentwo2 radiologists were discussed until consensus was reached. The area of extrapancreatic collections and the MRSI and EPIM scores determined from the initial MRI were averaged between the two readers.

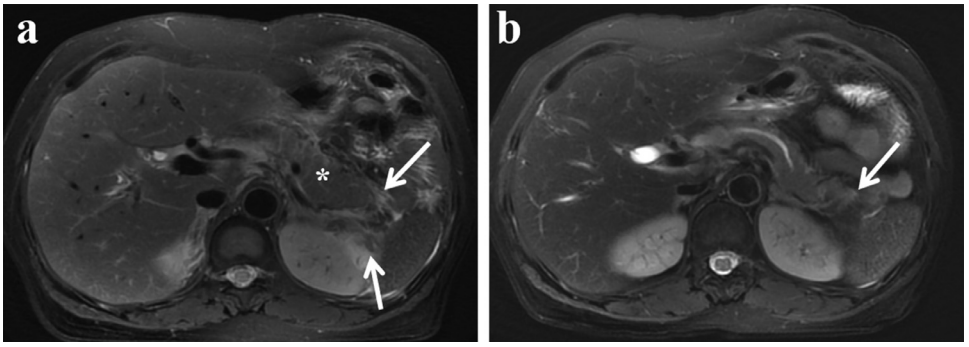

Figure 3. Interstitial edematous pancreatitis with APFC in a 53-year-old woman. (a) Axial fat-saturated T2-weighted MR image on the first day of onset reveals extrapancreatic fluid and stranding around the tail of the pancreas and the left anterior pararenal space (white arrows), with a normal-appearing pancreatic parenchyma (*). (b) Axial fat-saturated T2-weighted MR imaging 10 days later shows that the extrapancreatic collections were basically absorbed.

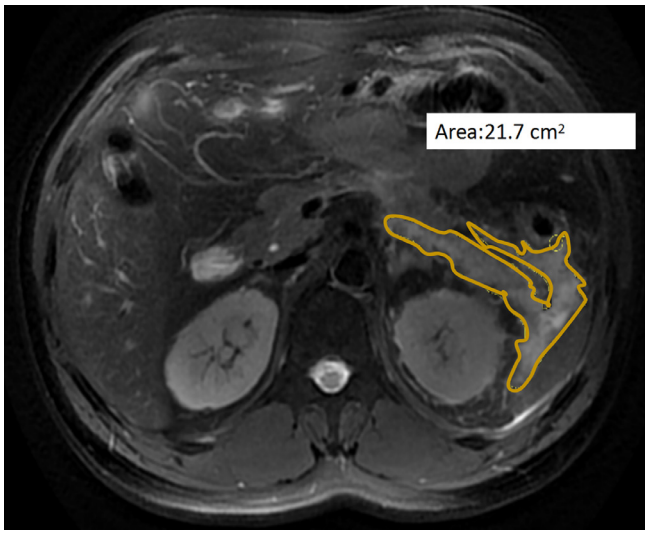

Figure 4. Interstitial edematous pancreatitis with APFC in a 44-year-old man. On axial fat-saturated T2-weighted MR images, the area of extrapancreatic collections (AEPC) was manually drawn along the margin of collection, and the value of this area (21.7 cm^2) was automatically derived by software.

Statistical Analysis

Continuous variables are expressed as means or medians. The area and number of extrapancreatic collections, MRSI score, EPIM score, follow-up interval, length of hospital stay, and hs-CRP and calcium levels of patients in the two groups were compared using independent *t* tests or Mann-Whitney *U* tests according to the distributions of the data. Categorical and rank variables are presented as percentages. The percentage of heterogeneity in extrapancreatic collections, and the incidences of hemorrhage, SIRS, and organ failure were compared using chi-squared or Fisher's exact tests. The receiver operating characteristic (ROC) curves were generated, and the area under the curve (AUC) of one or more of the indicators (area and number of extrapancreatic collections, EPIM score, and MRSI score) were calculated to predict extrapancreatic necrosis. The AUCs were compared using the DeLong test.

Two radiologists simultaneously delineated the area of the extrapancreatic collections in all patients on the initial fat-saturated T2WI and followed the same procedure to delineate the area again 1 week later. Intraobserver and interobserver agreement on the area of extrapancreatic collections was evaluated by the intraclass correlation coefficient.

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) for Windows (Version 13.0, Chicago, IL). A p value of < 0.05 was considered statistically significant.

RESULTS

Demographics and Clinical Characteristics of the Patients

Of the 70 patients with AP, 28 were male (51.7 ± 16.8 years) and 42 were female (51.2 ± 10.9 years); 38 patients (54.3%) were diagnosed with peripancreatic fluid collections, and 32 patients (45.7%) had extrapancreatic necrosis (including extrapancreatic necrosis alone and combined necrosis), of which 20/32 (62.5%) had only extrapancreatic necrosis (Fig 5). The baseline demographics and clinical outcomes of the patients are shown in Table 2. The average time to initial MRI from onset was 3.34 ± 1.727 days. Follow-up imaging was performed in all patients, and two patients had pathological biopsies. The median interval from initial MRI to follow-up examination in patients with peripancreatic fluid collections was 10 (range: 4−127) days, and that in patients with

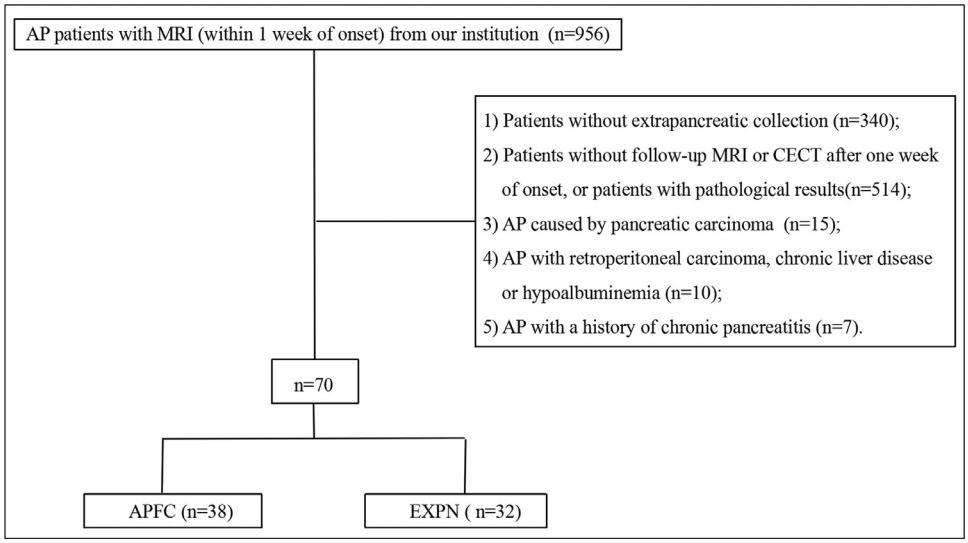

Figure 5. Patient selection flowchart for final diagnosis. AP, acute pancreatitis; APFC, acute peripancreatic fluid collection; EXPN, extrapancreatic necrosis.

TABLE 2. Baseline Demographics, Clinical Characteristics, and MRI Characteristics of Patients with EXPN/APFC.

Characteristic	All Patients (n = 70)	APFC (n = 38)	EXPN (n = 32)	p
Age* (y)	51.50 ± 14.35	51.7 ± 16.8	51.3 ± 10.9	0.891
Male sex (%)	28 (40)	15 (39.5)	13 (40.6)	0.992
Etiology (%)				0.885
Biliary	43 (61.4)	24 (63.2)	19 (40.6)	
Hyperlipidemia	13 (18.6)	6 (15.8)	7 (21.8)	
Alcohol abuse	6 (8.6)	3 (7.9)	3 (9.3)	
Idiopathic	8 (11.4)	5 (13.1)	3 (9.3)	
Follow-up Interval†	12 (4-127)	10 (4-127)	13.5 (6-83)	0.555
Positive SIRS (%)	18 (25.7)	4 (10.5)	14 (43.8)	0.040
OF (%)	10 (5.7)	5 (13.2)	5 (15.6)	0.769
POF (%)	3 (4.3)	0 (0)	3 (9.3)	0.091‡
AP severity (%)				0.091‡
Moderate-severe AP	67 (95.7)	38 (100)	29 (90.6)	
Severe AP	3 (4.3)	0 (0)	3 (9.4)	
Hospital stay* (d)	18.3±7.1	15.7±5.6	21.4±7.5	0.010
Hs-CRP† (mg/L)	77.07 (0.56-535.50)	64.64(0.56-176.83)	92.50 (42.94-535.50)	0.000
Ca* (mmol/L)	2.19±0.23	2.27±0.16	2.08±0.26	0.001
MRSI (%)				0.000‡
Mild	6 (8.6)	6 (15.8)	0 (0)	
Moderate	61 (87.1)	32 (84.2)	29 (90.6)	
Severe	3 (4.3)	0	2 (9.4)	
MRSI score†	4 (3-10)	4 (3-4)	4 (4-10)	0.000
EPIM score†	7 (2-7)	5 (2-7)	7 (3-7)	0.000
NEPC†	3 (1-7)	2 (1-7)	4 (1-7)	0.000
AEPC† (cm^2)	13.23 (1.07-109.82)	7.53 (1.07-44.65)	27.95 (4.31-109.82)	0.000
Hemorrhage (%)	15 (21.4)	0 (0)	14 (46.9)	0.000‡

AP, acute pancreatitis; AEPC, area of extrapancreatic collections; APFC, acute peripancreatic fluid collection; EPIM, extrapancreatic inflammation on magnetic resonance imaging; EXPN, extrapancreatic necrosis; hs-CRP, high-sensitivity C-reactive protein; IP, interstitial edematous pancreatitis; MRSI, magnetic resonance severity index; NEPC, number of extrapancreatic collections; OF, organ failure; POF, persistent organ failure; SIRS, systemic inflammatory response syndrome.

* Data are the means ± standard deviations.

† Data are the medians (ranges).

‡ Fisher's exact test.

extrapancreatic necrosis was 13.5 (range: 6−83) days. There was no statistically significant difference in the interval (z = 0.593, p = 0.555) between the two groups. The length of hospital stay, level of hs-CRP and frequency of SIRS in patients with extrapancreatic necrosis were significantly higher (p = 0.01, 0.000, and 0.04, respectively), and the calcium level of patients with extrapancreatic necrosis was significantly lower than those of patients with peripancreatic fluid collections (p = 0.001). The prevalence of organ failure between the two groups was not significantly different (p = 0.769). All patients with peripancreatic fluid collections had moderate-severe AP according to the revised Marshall scoring system; among patients with extrapancreatic necrosis, 29/32 (90.6%) had moderate-severe AP and 3/32 (9.4%) had severe AP. No statistically significant difference was noted between the two groups (p = 0.091).

Initial MRI Characteristics of the Patients

The initial MRI characteristics of patients with extrapancreatic necrosis and peripancreatic fluid collections are shown in Table 2. On the initial MRI, a total of 35/70 (50%) AP patients were diagnosed with extrapancreatic necrosis according to the 2012 revised Atlanta Classification, which was not significantly different from the extrapancreatic necrosis diagnosed by follow-up (p = 0.607) (Table 3). According to the MRSI score, of the 32 patients with extrapancreatic necrosis, the percentages of patients with mild, moderate and severe AP were 0% (0/32), 90.6% (29/32), and 9.4% (3/32),

TABLE 3. The number of patients diagnosed with EXPN according to the revised Atlanta Classification.

	APFC†	EXPN†		Sensitivity	Specificity	p
APFC*	29	6	35	0.813	0.763	0.607
EXPN*	9	26	35			
	38	32	70			

APFC, acute peripancreatic fluid collection; EXPN, extrapancreatic necrosis.

* Diagnosed by the 2012 revised Atlanta Classification in the early stage of AP.

† Diagnosed in this study.

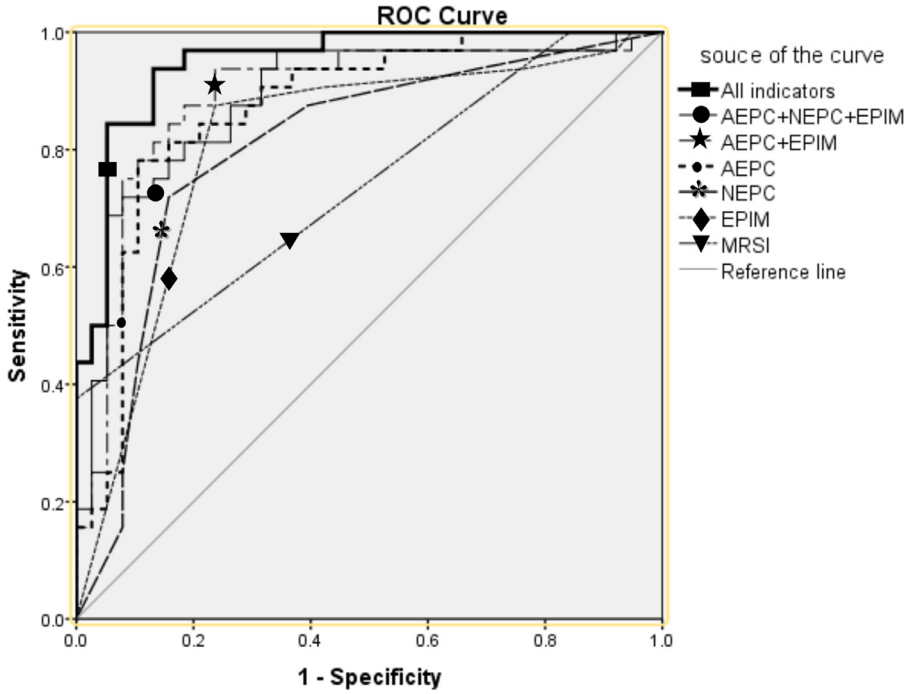

Figure 6. ROC curves of MRI and clinical characteristics for predicting EXPN. AEPC, area of extrapancreatic collections; EPIM, extrapancreatic inflammation on magnetic resonance imaging; EXPN, extrapancreatic necrosis; MRSI, magnetic resonance severity index; NEPC, number of extrapancreatic collections involving the indicated locations.

respectively; of the 38 patients with peripancreatic fluid collections, the percentages of patients with mild, moderate, and severe AP were 15.8% (6/38), 84.2% (32/38), and 0% (0/38), respectively ($p < 0.001$). The MRSI and EPIM scores of patients with extrapancreatic necrosis were significantly higher than those of patients with peripancreatic fluid collections ($p < 0.001$). Only patients with extrapancreatic necrosis had hemorrhage in or surrounding the pancreas (14/32, 43.8%), and no patients with peripancreatic fluid collections presented hemorrhage (43.8% vs 0%; $p = 0.000$).

All patients had peripancreatic collections. In addition, the left anterior pararenal space was the most common location for extrapancreatic collections, accounting for 54.3% (38/70), followed by the gastrosplenic ligament (45.7%), hepatoduodenal or gastrohepatic ligament (42.9%), right anterior pararenal spaces (38.6%), mesenteric root (27.1%), and transverse mesocolon (24.3%). The frequencies of extrapancreatic collections involving each location in patients with extrapancreatic necrosis were significantly higher than those in patients with peripancreatic fluid collections ($p < 0.05$). The number of extrapancreatic collections in patients with extrapancreatic necrosis (4 [range: 1−7] locations) was significantly higher than that in patients with peripancreatic fluid collections (2 [range: 1−7] locations, [$z = -4.402$, $p < 0.001$)]. The area of extrapancreatic collections in patients with extrapancreatic necrosis (27.95 [range: 4.31-109.82] cm^2) was also significantly larger than that in patients with peripancreatic fluid collections (7.53 [range: 1.07-44.65] cm^2, $p < 0.001$]. Intraobserver agreement for the area of extrapancreatic collections was 0.91, and interobserver agreement was 0.86.

ROC Analyses of MRIs for Predicting Extrapancreatic Necrosis

The ROC curves for one or more of the indicators (the area and number of extrapancreatic collections, EPIM score, and MRSI score) for predicting extrapancreatic necrosis are shown in Figure 6. The performance statistics of all indicators are shown in Table 4. Among the single indicators, the accuracy of the area of extrapancreatic collections (AUC = 0.871) was comparable to that of the EPIM score for predicting extrapancreatic necrosis ($p = 0.275$) and significantly higher than that of the other two indicators (area vs number, $p = 0.024$; area vs MRSI, $p = 0.027$). The combination of all indicators showed the highest predictive accuracy (AUC = 0.949), and the combination of two or more indicators demonstrated significantly higher predictive accuracy for extrapancreatic necrosis than any single indicator ($p < 0.05$) except for the area of extrapancreatic collections ($p > 0.05$). There were no statistical differences between each pair of combined indicators for predicting extrapancreatic necrosis ($p = 0.060$, 0.092, and 0.909, respectively).

DISCUSSION

In this study, we found that the characteristics of extrapancreatic collections on MRI could indicate early extrapancreatic

TABLE 4. Performance Statistics of the Indicators for Predicting EXPN.

Indicator	AUC (95% CI)	Cutoff	Sensitivity	Specificity
All indicators	0.949 (0.900−0.998)	/	0.938	0.868
AEPC + EPIM + NEPC	0.887 (0.805−0.968)	/	0.719	0.921
AEPC + EPIM	0.888 (0.803−0.973)	/	0.875	0.816
AEPC (cm^2)	0.871 (0.785−0.957)	≥18.56	0.781	0.895
NEPC	0.803 (0.694−0.912)	≥4	0.719	0.842
EPIM	0.812 (0.704−0.920)	≥6	0.875	0.763
MRSI	0.737 (0.620−0.854)	≥5	0.375	1.000

AEPC, area of extrapancreatic collections; EXPN, extrapancreatic necrosis; EPIM, extrapancreatic inflammation on magnetic resonance imaging; MRSI, magnetic resonance severity index; NEPC, number of extrapancreatic collections.

necrosis; the greater the extent of extrapancreatic collections, the greater the amount of extrapancreatic collections, and the broader the extent of extrapancreatic inflammation, which is associated with hemorrhage in AP on MRI, the higher was the probability of extrapancreatic necrosis. Our results indicate some additional factors to indicate extrapancreatic necrosis in the early phase of AP beyond those in the 2012 revised Atlanta Classification, which may provide a method to diagnose early extrapancreatic necrosis and differentiate it from peripancreatic fluid collections more comprehensively and accurately. This advancement is clinically important to allow timely, appropriate management.

Previous studies reported that the prevalence of extrapancreatic necrosis alone varied from 15% to 50% (2,3,6−9,30) in necrotizing pancreatitis. In our study, the prevalence of extrapancreatic necrosis (including combined necrosis) in all AP patients was 45.7%, and the prevalence of extrapancreatic necrosis alone was 62.5% in patients with necrotizing pancreatitis, which was higher than that in the 2012 Atlanta Classification and previous studies. Some possible reasons for this discrepancy include the following: (1) the inclusion criteria are different: all enrolled patients underwent MRI within 1 week of onset, had extrapancreatic collections, and were followed up with MRI or CECT, which resulted in the exclusion of a large number of patients with mild AP and patients with severe AP with combined necrosis; and (2) patients in the previous studies were evaluated based on CT, which has lower sensitivity than MRI for differentiating heterogeneous extrapancreatic fat from liquefied components (3,13,15,16) and could lead to an understatement of the prevalence of extrapancreatic necrosis.

Extrapancreatic necrosis can be diagnosed according to the 2012 revised Atlanta Classification (2,5−12). However, in this study, we found that early extrapancreatic necrosis was still not completely distinguishable from peripancreatic fluid collections according to the 2012 revised Atlanta Classification, because in early stages, extrapancreatic necrosis has a similar appearance to peripancreatic fluid collections—both demonstrate a homogeneous fluid signal caused by toxic edema of extrapancreatic adipocytes, a small amount of nonliquefied necrotic material and extrapancreatic stranding (13,16). We found that in addition to the heterogeneous MR signal, other features on MRI, including the extent of extrapancreatic collections and extrapancreatic inflammation, were helpful for indicating extrapancreatic necrosis. The combination of the area and number of extrapancreatic collections, EPIM score, and MRSI score showed the highest predictive accuracy, and the combination of two or more indicators demonstrated significantly higher predictive accuracy for extrapancreatic necrosis than any individual indicator except for the area of extrapancreatic collections. These findings revealed that the greater the extent and amount of extrapancreatic collections and the broader the extent of extrapancreatic inflammation, the higher was the possibility of extrapancreatic necrosis, and the area of extrapancreatic collections was an especially good discriminator. Our results are consistent with Kloppel G's results (23) that extrapancreatic collections larger than 5 cm in diameter are not easily absorbed in the early stage of AP, which may lead to some degree of extrapancreatic necrosis. The possible reasons for this finding are that pathophysiologically, AP is related to activation of the inflammatory cascade (3,31), which causes inflammation of the pancreas and extrapancreatic fat/tissues, edema in acinar cells and extrapancreatic adipocytes, and even liquefaction and necrosis (11,31). Therefore, the more severe the inflammation is, the more collections there are, and the more significant the necrosis of extrapancreatic adipocytes is.

The MRSI score was strongly correlated with clinical severity according to the MRSI guideline (27,32). Serum calcium, hs-CRP, and SIRS are all known, simple clinical markers for assessing the severity of AP (12,21,33). In this study, our results showed that the proportion of moderate and severe AP according to the MRSI score in patients with extrapancreatic necrosis was higher than that in patients with peripancreatic fluid collections; the length of hospital stay, hs-CRP level, and incidence of SIRS were significantly higher and the calcium level was significantly lower in patients with extrapancreatic necrosis than in patients with peripancreatic fluid collections, consistent with the conclusion of previous studies on the severity of extrapancreatic necrosis. However, there was no significant difference in the incidence of organ failure between the two groups, possibly due to the small sample size and the small number of patients with organ failure in this study.

There were some limitations in this study. First, this study is a retrospective analysis, although after strict exclusion, there was no significant difference in the interval between initial MR and follow-up examination in patients with peripancreatic fluid collections and extrapancreatic necrosis. Some patients had longer intervals between examinations, which may have some impact on our results. Second, the inclusion and exclusion criteria are explicit, therefore, the patient sample size is small, with an especially small number of patients with peripancreatic fluid collections; the number of patients with severe AP enrolled in our study was also small, which caused some clinical indicators to be nonsignificantly different between the groups. Therefore, a study with a larger sample size and more objective indicators for early extrapancreatic necrosis should be performed in the future.

In conclusion, the MRI characteristics of extrapancreatic collections, especially the extent and amount of extrapancreatic collections, could differentiate early extrapancreatic necrosis from peripancreatic fluid collections and indicate extrapancreatic necrosis.

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