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Abdominal free fluid in acute pancreatitis predicts necrotizing pancreatitis and organ failure

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Abstract

Background Abdominal free fluid is frequently encountered on cross-sectional imaging for acute pancreatitis and may be a sign of increased severity and complications. This study examines the ability of free fluid to predict necrotizing pancreatitis and other adverse outcomes.

Methods We conducted a single-center retrospective study of patients with acute pancreatitis and multiple cross-sectional imaging studies. Patients were divided into those who demonstrated free fluid on initial imaging and those without free fluid. The primary outcome was developing necrotizing pancreatitis. Logistic regression analysis assessed the performance of several predictors.

Results A total of 245 acute pancreatitis patients were included. Pancreatic necrosis occurred more frequently in the free fluid group (31.3 vs. 1.3%, P<0.001). The free fluid group also had higher rates of transient organ failure (17.7 vs. 3.4%, P<0.001), persistent organ failure (17.7 vs. 2.0%, P<0.001), in-hospital mortality (7.3 vs. 1.3%, P=0.016), length of stay (16.2 vs. 5.5 days, P<0.001), and intensive care unit admission (30.2 vs. 4.7%, P<0.001). On multivariate logistic regression, free fluid was the strongest predictor (adjusted odds ratio 17.11, 95% confidence interval 3.68-79.65; P<0.001) for necrotizing pancreatitis, with an excellent performance (area under the curve 0.92). When neither fluid on initial imaging nor persistent systemic inflammatory response syndrome was present, the negative predictive value for developing pancreatic necrosis was 100%.

Conclusions Free fluid in acute pancreatitis is a strong predictor for necrotizing pancreatitis, organ failure and mortality, and outperformed current predictors. Patients who lacked both free fluid on imaging and persistent systemic inflammatory response syndrome are at low risk for adverse outcomes and may be considered for early discharge.

Keywords Ascites, pancreatic necrosis, discharge, imaging

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Introduction

The clinical course of acute pancreatitis ranges from a mild, self-limited illness to a fulminant, fatal course and the type can be indistinguishable upon initial presentation. Predicting the clinical course in acute pancreatitis remains challenging, despite decades of studies investigating a wide variety of clinical, imaging, and serological predictors.

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Conflict of Interest: None

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Cross-sectional abdominal imaging, mainly computed tomography (CT) scanning, is performed in 60-70% patients with acute pancreatitis within the first 24-48 h of presentation [1,2]. While the intent of the imaging study is primarily diagnostic, there is much information from cross-sectional imaging that may be harnessed for predictive purposes, especially with the emergence of artificial neural networks. Traditional predictors for severity in acute pancreatitis, including persistent systemic inflammatory response syndrome (SIRS), blood urea nitrogen (BUN), hematocrit (HCT), Ranson criteria, and other clinical scoring systems, have only been proven to be moderately effective and can take up to 48 h to calculate or measure [3-8]. CT imaging features have the benefit of immediate acquisition and the examination is already performed in the majority of patients.

Free abdominal fluid, or ascites, is often observed in acute pancreatitis, but this finding is frequently overlooked, under-reported in some radiologic interpretations, or not considered to be of clinical significance unless large in volume or creating

increased abdominal pressure. The release of free fluid in acute pancreatitis may be due to either pancreatic duct disruption, possibly from developing pancreatic necrosis, or capillary leakage resulting from elevated inflammatory mediators. In both instances, the course of pancreatitis is potentially more severe. A recent study examining 82 patients with pancreatitis and ascites on imaging reported longer hospital stays, and higher rates of organ failure and mortality, compared to pancreatitis patients without ascites on imaging [9].

Based on our own clinical experience with pancreatitis patients, we hypothesized that any pancreatitis-related free fluid detected on cross-sectional imaging, even small volumes that might not be sufficient to be categorized as ascites, could be a sign of increased severity. We carried out the following study to assess the utility of pancreatitis-related free fluid as a predictor for the development of necrosis as well as a complicated clinical course. If free fluid can portend the development of necrosis, this could be useful, as pancreatic necrosis can take up to 3-4 days to become evident on imaging and requires intravenous contrast for detection. Free abdominal fluid may precede the presence of overt necrosis and can be readily identified on imaging, even in the absence of intravenous contrast administration.

Patients and methods

This was a single-center retrospective clinical study, designed to assess whether free abdominal fluid in acute pancreatitis can predict the subsequent development of pancreatic necrosis, as well as other adverse outcomes including organ failure and mortality.

Patient population

Data were extracted from electronic medical records at the University of California San Diego Medical Center (La Jolla, CA). Patients receiving medical care between January 1, 2008, and December 31, 2019, were considered for this study. The study included patients at least 18 years of age, diagnosed with acute pancreatitis, who had at least 2 cross-sectional imaging studies within 3 months of acute pancreatitis diagnosis. A diagnosis of acute pancreatitis required the presence of 2 of the following: lipase elevation greater than 3 times the upper limit of normal, imaging evidence of pancreatitis, or characteristic abdominal pain. Subjects in this study were required to have an initial contrast-enhanced cross-sectional imaging study (CT or magnetic resonance imaging [MRI]) without pancreatic necrosis, and a subsequent cross-sectional imaging study within 3 months to reassess for the development of pancreatic necrosis. The indication for the subsequent imaging study could be pancreatitis-related, for a biliary indication, or for an unrelated indication.

Excluded were patients with pancreatic necrosis evident on the initial imaging study, pre-existing ascites, risk factors for ascites (cirrhosis, prior cardiac ascites, peritoneal dialysis, recent abdominal surgery, gastrointestinal perforation, or peritoneal carcinomatosis), pancreatic cancer, chronic pancreatitis, and recurrent pancreatitis with a known unresolved fluid collection.

Study definitions

Necrotizing pancreatitis was diagnosed based on its typical appearance on contrast-enhanced CT and MRI scans. Organ failure was based on the Modified Marshall Score as cardiovascular, respiratory or renal failure. Transient organ failure was defined as organ failure lasting <48 h, and persistent organ failure as lasting >48 h. BUN elevation was defined as BUN >20 mg/dL on admission or as an increase by >5 mg/dL at 24 h. HCT elevation was defined as HCT >44% or failure to decrease at 24 h. Free fluid was defined as free-flowing fluid in the peritoneal cavity or ascites. For the purposes of this study, free fluid was attributed to the current episode of acute pancreatitis. Those with previous ascites from other causes were excluded. When there was uncertainty regarding the presence of acute free fluid, a gastroenterologist with extensive training in advanced endoscopic imaging and pancreatology with more than 5 years in practice reviewed the imaging study while blinded to the clinical outcome.

Outcomes and predictors

Free fluid was assessed along with commonly utilized predictors of pancreatitis severity (persistent SIRS, BUN elevation at 24 h, and hemoconcentration on HCT at 24 h). The primary outcome was the presence of necrotizing pancreatitis, defined as pancreatic parenchymal necrosis, peri-pancreatic necrosis, acute necrotic collection or walled-off necrosis. Secondary outcomes were mortality (6-month and in-hospital), transient organ failure, persistent organ failure, and a composite endpoint composed of necrotizing pancreatitis, persistent organ failure, or 6-month mortality attributed to complications of acute pancreatitis.

Statistical analysis

Descriptive statistical tests were performed to describe the characteristics of our cohort. To compare differences in baseline characteristics and treatment outcomes, we used the chi-squared test to analyze categorical variables and a *t*-test to analyze continuous variables. To identify predictive factors associated with our outcome, we used binomial logistic regression to identify factors associated with the development of pancreatic necrosis and a composite outcome of pancreatic necrosis, persistent organ failure or 6-month mortality. A univariate analysis was first performed to identify factors (based on a P-value cut-off of <0.20) that would be appropriate for inclusion in our final multivariable model. Our multivariable logistic regression model was used to calculate the area under

the receiver operator curve (AUC). All hypothesis testing was performed using a 2-sided P-value with a statistical significance threshold <0.05. All statistical analyses were performed using StataMP (StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP).

Ethics

The study protocol and methods were approved by the institutional review board at the University of California, San Diego. All authors had access to the study data and reviewed and approved of the final manuscript.

Results

Patient and imaging characteristics

A total of 245 patients with acute pancreatitis meeting the imaging criteria were included in this study. There was no significant difference in age or sex between pancreatitis patients with free fluid or no free fluid on initial imaging (Table 1). Nor was there any significant difference in lipase elevation (85.4 vs. 81.9%, P=0.469), BUN value on admission (17.0±15.9 vs. 14.9±8.7 mg/dL, P=0.186), BUN value at 24 h (14.7±16.3 vs. 12.0±8.0 mg/dL, P=0.122), HCT value on admission (37.5±8.9 vs. 37.8±5.6%, P=0.786), or HCT value at 24 h (35.9±7.3 vs. 35.2±4.8%, P=0.443), respectively. In both groups, the most common indication for obtaining the initial imaging study was pancreatitis-related (99.0% in free fluid group vs. 98.0% in no free fluid group), and the predominant reason for obtaining a subsequent imaging study was for pancreatitis-related and biliary indications. The initial cross-sectional imaging study was obtained within 2 days of the acute pancreatitis diagnosis in 96.7% of patients, with 76.7% of imaging studies obtained at the time of diagnosis.

Table 1 Patient characteristics

Characteristics	Fluid n=96	No fluid n=149	P-value	Entire cohort n=245
Age (years, mean±SD)	48.4±16.8	52.7±16.5	0.050	51.0±16.7
Sex				
Male	54.2%	48.6%	0.319	50.2%
Female	45.8%	52.4%		49.8%
Alcohol use				
Yes	24.0%	15.4%	0.148	18.8%
None	75.0%	81.2%		78.8%
Not stated	1.0%	3.4%		2.5%
Smoking				
Active	16.7%	16.1%	0.351	16.3%
Former	12.5%	21.5%		18.0%
None	63.5%	57.9%		59.2%
Not stated	7.3%	6.0%		6.5%
Etiology				
Gallstones	29.2%	26.9%	0.034	27.8%
Alcohol	18.8%	12.1%		14.7%
Idiopathic / other	47.9%	45.6%		46.5%
Not stated	4.2%	15.4%		11.0%

SD, standard deviation

Pancreatitis outcomes based on presence of fluid

In the entire cohort, 13.1% (n=32) of patients developed pancreatic necrosis. Transient organ failure, persistent organ failure, in-hospital mortality and 6-month mortality occurred in 9.0% (n=22), 8.2% (n=20), 3.7% (n=9), and 5.3% (n=13) of the entire study population, respectively.

The primary endpoint of pancreatic necrosis occurred in 31.3% (n=30) of patients with acute pancreatitis and free fluid on the initial imaging study, compared to 1.3% (n=2) in patients without free fluid (P<0.001). Infected necrosis occurred more frequently in the fluid group (Table 2). More than twice the number of patients with fluid had HCT elevation, but there was no difference in BUN elevation (Table 2). Compared to patients without free fluid on the initial imaging study, those with free fluid had higher rates of transient organ failure (17.7 vs. 3.4%, P<0.001), persistent organ failure (17.7 vs. 2.0%, P<0.001), 6-month mortality (9.4 vs. 2.7%, P=0.023), and in-hospital mortality (7.3 vs. 1.3%, P=0.016) (Table 2). The composite endpoint of pancreatic necrosis, 6-month mortality or persistent organ failure occurred in 37.5% of patients with fluid on initial imaging compared to 4.7% of those with no fluid (P<0.001).

An invasive procedure for drainage was required in 13.5% (n=13) of patients with acute pancreatitis and free fluid on initial imaging compared to 0.5% (n=1) in those without free fluid (Table 2). The total hospital stay in patients with free fluid on initial imaging was nearly 3 times longer than in those without free fluid (16.2±24.0 days, 95% confidence interval [CI] 11.3-21.0, vs. 5.5±7.8 days, 95%CI 4.3-6.8; P<0.001), and transfer to the intensive care unit (ICU) occurred more frequently (30.2 vs. 4.7%, P<0.001). There was no difference in 30-day readmission rates between fluid groups (Table 2).

Pancreatitis outcomes were also assessed for the entire cohort based on the development of necrosis, regardless of fluid status. Patients who eventually developed necrotizing pancreatitis had higher rates of transient organ failure (37.5 vs. 4.7%, P<0.001), persistent organ failure (37.5 vs. 3.8%, P<0.001), 6-month mortality (15.6 vs. 3.8%, P=0.004) and in-hospital mortality (12.5 vs. 2.35%, P=0.005). Patients with necrosis also had longer hospital stays and higher rates of ICU admission (Supplementary Table 1).

Predicting pancreatic necrosis and pancreatitis outcomes

We compared the performance of free fluid with persistent SIRS, BUN and HCT concentrations on admission, BUN

Table 2 Primary and secondary pancreatitis outcomes based on fluid or no fluid on imaging

Outcomes	Fluid n=96		No fluid n=149		P-value	Entire cohort n=245	
Necrosis	31.3%	n=30	1.3%	n=2	<0.001	13.1%	n=32
Extra-pancreatic	2.1%	n=2	0.7%	n=1	—	1.2%	n=3
Infected necrosis	5.2%	n=5	0.0%	n=0	0.005	2.0%	n=5
Composite endpoint †	37.5%	n=36	4.7%	n=7	<0.001	17.6%	n=43
Mortality							
Six-month	7.3%	n=7	1.3%	n=2	0.016	3.7%	n=9
In-hospital	9.4%	n=9	2.7%	n=4	0.023	5.3%	n=13
Transient organ failure ‡	17.7%	n=17	3.4%	n=5	<0.001	9.0%	n=22
Cardiac	9.4%	n=9	1.3%	n=2	0.003	4.5%	n=11
Respiratory	12.5%	n=12	3.4%	n=5	0.006	6.9%	n=17
Renal	10.4%	n=10	1.3%	n=2	0.001	4.9%	n=12
Persistent organ failure ‡	17.7%	n=17	2.0%	n=3	<0.001	8.2%	n=20
Cardiac	10.4%	n=10	0.7%	n=1	<0.001	4.5%	n=11
Respiratory	12.5%	n=12	2.0%	n=3	0.001	6.1%	n=15
Renal	12.5%	n=12	0.7%	n=1	<0.001	5.3%	n=13
BUN elevation	22.9%	n=22	22.8%	n=34	0.986	22.9%	n=56
Hematocrit elevation	46.9%	n=45	21.5%	n=32	<0.001	31.4%	n=77
Drainage procedure	13.5%	n=13	0.5%	n=1	0.009	5.7%	n=14
Endoscopic	4.2%	n=4	0.7%	n=1		2.0%	n=5
Radiologic	5.2%	n=5	0.0%	n=0		2.0%	n=5
Surgical	4.2%	n=4	0.0%	n=0		1.6%	n=4
Length of hospital stay (mean±SD)	16.2±24.0 days		5.5±7.8 days			9.7±17.0 days	
ICU admission	30.2%	n=29	4.7%	n=7	<0.001	14.7%	n=36
ER discharge §	3.1%	n=3	20.1%	n=30	<0.001	13.5%	n=33
Outpatient	1.0%	n=1	4.7%	n=7	<0.001	3.3%	n=8
30-day readmission	17.7%	n=17	20.1%	n=30	0.638	19.2%	n=47

†Composite endpoint: development of either pancreatic necrosis, persistent organ failure, or death at 6 months

‡Organ failure is defined as failure of one or more organ systems, with failure lasting >48 h considered persistent organ failure

§Emergency room (ER) discharge indicates patients presenting to the ER with interstitial edematous pancreatitis but never required admission

BUN, blood urea nitrogen; SD, standard deviation

elevation, and HCT elevation, regarding their ability to predict the outcomes of pancreatic necrosis and a composite endpoint of pancreatic necrosis, persistent organ failure or mortality. Univariate logistic regression analysis revealed that free fluid had the highest odds for predicting pancreatic necrosis (odds ratio [OR] 33.41, 95%CI 7.75-143.93; P<0.001) followed by persistent SIRS (OR 20.20, 95%CI 8.06-50.62; P<0.001); BUN and HCT elevation had only modest predictive value and BUN or HCT values alone were not predictive (Table 3). In predicting the composite endpoint, persistent SIRS demonstrated slightly better performance (OR 17.45, 95%CI 7.99-38.28; P<0.001) compared to free fluid (OR 12.17, 95%CI 5.13-28.90; P<0.001), while BUN or HCT elevations were also predictive, though not as strongly (Table 3).

On multivariate logistic regression, free fluid was the strongest predictor (adjusted OR 17.11, 95%CI 3.68-79.65; P<0.001) for the development of necrotizing pancreatitis followed by persistent SIRS (adjusted OR 7.70, 95%CI 2.72-21.82; P<0.001); HCT elevation on admission was only modestly predictive and BUN elevation was not significant (Table 3). This model performed very well in predicting necrotizing pancreatitis, with an AUC of 0.92. For the composite endpoint, multivariate logistic regression showed similar performance between free fluid (adjusted OR 7.49, 95%CI 2.76-20.35; P<0.001) and persistent SIRS (adjusted OR 7.12, 95%CI 2.98-17.22; P<0.001), with only modest predictive value for BUN elevation (Table 3).

Compared to persistent SIRS, the presence of free fluid on initial cross-sectional imaging in patients with acute pancreatitis demonstrated a higher sensitivity (93.8%, 95%CI 79.2-99.2% vs. 78.1%, 95%CI 60.0-90.7%) but lower specificity (69.0%, 95%CI 62.3-75.2% vs. 85.0%, 95%CI 79.5-89.5%), for development of pancreatic necrosis (Table 4). The absence of free fluid on the initial imaging study demonstrated a better negative predictive value compared to persistent SIRS, though both predictors had only modest positive predictive value (Table 4). The presence of free fluid was also more sensitive than persistent SIRS for developing the composite endpoint (83.7%, 95%CI 69.3-93.2% vs. 72.1%, 95%CI 56.3-84.7%), while both predictors showed similar sensitivities for developing persistent organ failure or death at 6 months (Table 4).

Table 3 Single and multiple logistic regressions for predictors of pancreatic necrosis and the composite endpoints

Predictors	Odds ratio (95%CI)	P-value	Adjusted odds ratio (95%CI)	P-value
Pancreatic necrosis				
Free fluid	33.41 (7.75-143.93)	<0.001	17.11 (3.68-79.65)	<0.001
Persistent SIRS	20.20 (8.06-50.62)	<0.001	7.70 (2.72-21.82)	<0.001
BUN level (admit)†	1.02 (0.99-1.04)	0.168	---	---
BUN elevation‡	2.31 (1.05-5.07)	0.038	1.68 (0.57-5.00)	0.350
Hematocrit level (admit)†	1.05 (0.99-1.12)	0.093	---	---
Hematocrit elevation (admit)§	4.40 (2.00-9.72)	<0.001	2.80 (1.01-7.79)	0.048
Hematocrit elevation*	6.32 (2.82-14.18)	<0.001	---	---
Composite endpoint				
Free fluid	12.17 (5.13-28.90)	<0.001	7.49 (2.76-20.35)	<0.001
Persistent SIRS	17.45 (7.99-38.28)	<0.001	7.12 (2.98-17.22)	<0.001
BUN level (admit)†	1.05 (1.02-1.08)	0.001	---	---
BUN elevation‡	3.53 (1.75-7.12)	<0.001	3.40 (1.31-8.81)	0.012
Hematocrit level (admit)†	0.99 (0.95-1.04)	0.780	---	---
Hematocrit elevation (admit)§	2.96 (1.42-6.16)	0.004	1.74 (0.67-4.50)	0.252
Hematocrit elevation*	3.55 (1.80-7.00)	<0.001	---	---

†Actual lab value of BUN or hematocrit on admission

‡BUN elevation defined as BUN >20mg/dL on admission or increase by >5mg/dL

§Hematocrit elevation on admission defined as value >44%

*Hematocrit elevation overall defined as value >44% on admission or failure to decrease at 24 h

SIRS, systemic inflammatory response syndrome; BUN, blood urea nitrogen

Table 4 Fluid and persistent SIRS as predictors of pancreatic necrosis and pancreatitis outcomes

Predictors	Sensitivity	Specificity	PPV	NPV	Accuracy
Free fluid as a predictor of					
Pancreatic necrosis	93.8%	69.0%	31.3%	98.7%	72.2%
Persistent organ failure	85.0%	64.9%	17.7%	98.0%	66.5%
Six-month mortality	69.2%	62.5%	9.4%	97.3%	62.9%
Composite endpoint*	83.7%	70.3%	37.5%	95.3%	72.7%
Persistent SIRS as a predictor of					
Pancreatic necrosis	78.1%	85.0%	43.9%	96.3%	84.1%
Persistent organ failure	90.0%	82.7%	31.6%	98.9%	83.3%
Six-month mortality	69.2%	79.3%	15.8%	97.9%	78.8%
Composite endpoint*	72.1%	87.2%	54.4%	93.6%	84.5%

*Composite endpoint: development of either pancreatic necrosis, persistent organ failure, or death at 6 months

PPV, positive predictive value; NPV, negative predictive value; SIRS, systemic inflammatory response syndrome

When neither fluid on initial imaging nor persistent SIRS were present, the negative predictive values for developing pancreatic necrosis, persistent organ failure, 6-month mortality and the composite endpoint were 100% (95% CI: 100%), 99.3% (95% CI: 95.2-99.9%), 97.8% (95% CI: 94.2-99.2%), and 97.8% (95% CI: 93.7-99.3%), respectively.

Discussion

The current study examined a novel imaging-based predictor of free fluid for adverse outcomes of necrotizing pancreatitis, organ failure, and mortality. Not all patients presenting with acute pancreatitis require a CT scan, but approximately 70% already undergo a CT scan within 24-48 h of presentation, usually because of diagnostic uncertainty or to assess for complications. Given that cross-sectional imaging is available in most cases, we should maximize the information that can be extracted from the images. Several previous studies have utilized imaging for various purposes in acute pancreatitis. The modified CT severity index provides a scoring system, including necrosis, inflammation and ascites, to classify the severity of pancreatitis. Perfusion CT has been used to identify ischemia and predict necrosis, with moderate performance. Artificial neural networks have also been studied in the prediction of pancreatitis outcomes. Without the necessity for special imaging protocols, software or expertise, abdominal free fluid can be identified easily, even in the absence of intravenous contrast.

Samanta *et al* examined 82 patients with ascites, defined as free-flowing peritoneal fluid at least 50 mL in volume [9]. The presence of pancreatitis-related ascites was associated with a greater length of stay, need for ICU admission, organ failure, and mortality. The presence of ascites was assessed

within 2 weeks of the manifestation of acute pancreatitis, which did not allow its assessment as a potential predictor for complications of acute pancreatitis.

Our clinical experience in managing patients with necrotizing pancreatitis led us to carry out the current study, which examined the presence of any amount of free fluid in the abdomen in relation to pancreatitis, as a predictor of necrosis and other adverse outcomes. We hypothesized that the presence of free fluid would correlate most closely with the local complication of necrosis. Sufficient injury to the pancreatic ductal system to facilitate free fluid leakage into the abdomen may be a subtle or early sign of necrosis. Alternatively, free fluid related to capillary leak, as a result of increased inflammation and cytokine release, could also be indicative of occult or developing necrosis driving a proinflammatory response.

The current multivariate logistic regression analysis demonstrated pancreatitis-related free fluid was the strongest predictor of necrosis, and of a composite endpoint including organ failure and mortality. Free fluid outperformed persistent SIRS, BUN and HCT as a predictor, with a high AUC of 0.92 indicating excellent performance in classifying and predicting outcomes. Free fluid demonstrates a high sensitivity of 93.8% for the subsequent development of necrosis, which is desirable for a screening test for necrosis. The tradeoff is a moderate positive predictive value of 31.3%, indicating that about 1 in 3 patients with free fluid will go on to develop necrosis if not already apparent on imaging. In this study, we excluded patients who already had necrosis apparent on initial imaging so that free fluid could be studied as a predictive factor for occult or developing necrosis.

In addition, pancreatitis-related free fluid demonstrates a high negative predictive value of 98.7% for necrosis and 95.3% for the composite endpoint including mortality and organ failure. Therefore, the absence of free fluid on cross-sectional imaging during acute pancreatitis is very reassuring and may also be utilized as a factor in the early discharge of pancreatitis patients or as a triage tool in the emergency room. Notably, no patients lacking both free fluid and persistent SIRS developed pancreatic necrosis and less than 1% developed persistent organ failure, suggesting that the absence of both these predictors is highly predictive of a benign course: this may be the most useful of the findings of this study. Future studies will be necessary to confirm and validate the findings of the current study, but free fluid appears to be a strong and promising marker to predict developing necrosis, while also reassuring those who are likely to have a benign course.

The current study findings have to be evaluated with some caveats. A potential source of bias in the current study was the requirement for patients to have 2 cross-sectional imaging studies for inclusion, which introduces a potential bias towards patients who are more ill, with higher rates of necrosis or organ failure, and may have missed milder cases of pancreatitis. However, our rates of necrosis, persistent organ failure and mortality are consistent with other larger studies that did not have this inclusion criterion. The study also had only a moderate sample size, and a larger or multicenter sample could further reinforce our findings. The adjusted OR for free fluid as a predictor of necrosis, organ failure and mortality was much higher than that for established predictors such as persistent SIRS and BUN, which may suggest that the finding will remain significant with more data. Future prospective studies on the predictive ability of fluid on cross-sectional imaging are needed to support our findings and should include all severities of acute pancreatitis.

In conclusion, we report that free fluid on imaging in acute pancreatitis predicts the development of necrotizing pancreatitis, as well as organ failure and mortality. Free fluid performed better than traditional predictors in this capacity. The absence of free fluid was highly reassuring, especially in the absence of persistent SIRS: in this scenario, patients did not develop necrosis and rarely developed organ failure. These low-risk patients may be considered for early discharge.

Summary Box

What is already known:

- The clinical course of acute pancreatitis varies from mild, self-limited disease to a fulminant, fatal course
- Predicting pancreatitis severity remains challenging, despite decades of studies on clinical, imaging, and serological predictors
- Cross-sectional imaging is available in the majority of patients with acute pancreatitis and contains much information that is potentially underutilized.
- Free abdominal fluid is a radiologic finding in acute pancreatitis that is frequently overlooked

What the new findings are:

- Free fluid on imaging for acute pancreatitis is a strong predictor for subsequent development of necrotizing pancreatitis
- The presence of fluid can predict adverse outcomes, including organ failure and mortality, and outperformed persistent systemic inflammatory response syndrome (SIRS), blood urea nitrogen, and hematocrit elevation in predicting these outcomes
- In patients with acute pancreatitis, available imaging studies should be reviewed to assess for the presence of free fluid, as this can identify patients who should be closely monitored for severe outcomes
- Patients who lack free fluid on imaging and also do not demonstrate SIRS have very low risk for adverse outcomes and may be considered for early discharge

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Supplementary material

Supplementary Table 1 Primary and secondary pancreatitis outcomes based on necrosis or no necrosis

Outcomes	Necrosis (n=32)		No necrosis (n=213)		P-value
Necrosis	—	—	—	—	—
Extra-pancreatic	—	—	—	—	—
Infected necrosis	15.6%	n=5	—	—	<0.001
Mortality					
Six-month	12.5%	n=4	2.4%	n=5	0.004
In-hospital	15.6%	n=5	3.8%	n=8	0.005
Transient organ failure[†]	37.5%	n=12	4.7%	n=10	<0.001
Cardiac	15.6%	n=5	2.8%	n=6	0.001
Respiratory	28.1%	n=9	3.8%	n=8	<0.001
Renal	21.9%	n=7	2.4%	n=5	<0.001
Persistent organ failure[†]	37.5%	n=12	3.8%	n=8	<0.001
Cardiac	18.8%	n=6	2.4%	n=5	<0.001
Respiratory	28.1%	n=9	2.8%	n=6	<0.001
Renal	28.1%	n=9	1.9%	n=4	<0.001
BUN elevation	37.5%	n=12	20.7%	n=44	0.034
Hematocrit elevation	68.8%	n=22	25.8%	n=55	<0.001
Drainage procedure					
Endoscopic	15.6%	n=5	0.0%	n=0	<0.001
Radiologic	12.5%	n=4	0.5%	n=1	
Surgical	12.5%	n=4	0.0%	n=0	
Length of hospital stay (mean±SD)	21.1±24.2 days		8.0±15.0 days		
ICU admission	46.9%	n=15	9.9%	n=21	<0.001
ER discharge[‡]	0.0%	n=0	15.5%	n=33	0.025
Outpatient	0.0%	n=0	3.8%	n=8	
30-day re-admission	15.6%	n=5	19.7%	n=42	0.583

[†]Organ failure defined as failure of one or more organ systems, with failure lasting >48 h considered persistent organ failure

[‡]Emergency room (ER) discharge indicates patients who presented to the ER with interstitial edematous pancreatitis but never required admission

BUN, blood urea nitrogen; ICU, intensive care unit; SD, standard deviation