◆ REVISIÓN

Imaging and clinical prognostic indicators of acute pancreatitis: A comparative insight

Shagufta Wahab,[1] Rizwan Ahmad Khan,[1] Ibne Ahmad,[1] Arif Wahab [2]

[1] Deptt of Radiodiagnosis, [2] Centre of Cardiology. J. N. Medical College, AMU, Aligarh,India

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Summary

Acute pancreatitis is a disease with a broad spectrum of clinical presentation. It varies in severity from mild edematous pancreatitis with mostly uneventful recovery to severe necrotizing forms associated with significant morbidity and mortality. Various severity scoring systems are used for assessing the prognosis of acute pancreatitis. These include the clinical scoring scales as Ranson criteria, Glasgow scales, simplified acute physiology (SAP) score and acute physiology and chronic health evaluation II (APACHE II) score. The CT severity index (CTSI) derived by Balthazar grading of pancreatitis and the extent of pancreatic necrosis is now widely used in describing CT findings of acute pancreatitis and serves as the radiological scoring system. The purpose of this review is to analyze the correlation of clinical and radiological scoring scales with patient outcome and assess their role as objective prognosticators of acute pancreatitis patients.

Key words. *Pancreatitis, CT Scan, Clinical Features, Scoring*

Indicadores pronósticos por imágenes y clínicos de la pancreatitis aguda: una visión comparativa

Resumen

La pancreatitis aguda es una enfermedad con un espectro amplio de presentación clínica. Varía en severidad desde la pancreatitis edematosa leve, con recuperación completa sin mayores eventos, a las formas necrotizantes severas, asociadas a una morbimortalidad significativa. Se utilizan varios sistemas de evaluación de la severidad para determinar el pronóstico de la pancreatitis aguda. Éstos incluyen las escalas de score clínico como los criterios de Ranson, las escalas de Glasgow, el score fisiológico agudo (SAP) simplificado y el score APACHE II (acute physiology and chronic health evaluation II). El índice tomográfico de severidad (CTSI), derivado de la graduación de la pancreatitis por Balthazar y de la extensión de la necrosis pancreática se usa ampliamente en la actualidad para describir los hallazgos tomográficos de la pancreatitis aguda y sirve como sistema de score radiológico. El objetivo de esta revisión es analizar la correlación entre las escalas de score clínicas y radiológicas y la evolución de los pacientes con pacreatitis aguda, y evaluar su papel como factores pronósticos objetivos en estos pacientes.

Palabras claves. *Pancreatitis, Tomografía computada, Características clínicas, Scores.*

Acute pancreatitis is a relatively common cause of acute abdomen and the presentation may range from mild, self-limited condition to a fulminant disease with several complications leading to significant morbidity and mortality. Besides idiopathic, the other causes implicated are alcohol ingestion, cholelithiasis, drugs and upper gastrointestinal endoscopic intervention.[1] It is generally classified into mild or edematous pancreatitis and severe necrotizing pancreatitis which is associated with many local and systemic complications including infection, pseudocyst formation, pancreatic ascites, cardiovascular failure, renal failure and ARDS.[1] The need for assessing the severity of acute pancreatitis is because the management and prognosis are mainly decided by the severity of the disease. Mild pancreatitis responds well to supportive therapy while

Correspondencia: *Rizwan Ahmad Khan*
Lecturer, J. N. Medical College, AMU, Aligarh
Aligarh – 202002, India.
Tel. +91 9410210281
E-mail: drrizwanahmadkhan@yahoo.co.in

severe pancreatitis requires very intensive management and has a guarded prognosis.[2] The various clinical and radiological scoring systems[3,4] developed for severity scoring help in deciding the management protocol and in assessing the progress of the patient. An ideal severity scoring system should be able to differentiate between mild and severe pancreatitis early in the disease process, so that patients who would develop complications can be monitored intensively. It should also be accurate, reproducible and easy to use objectively.[2]

Clinical features and diagnosis

The clinical features of acute pancreatitis are not specific and may mimic other causes of acute abdomen. The most common presentation of acute pancreatitis is the sudden onset of severe abdominal pain in epigastric region usually with nausea and vomiting. Patients usually feel some relief on bending forward. Physical examination findings include tachycardia, hypotension, severe abdominal tenderness, guarding, respiratory distress and shock. Flank ecchymosis (Grey-Turner sign) or periumbilical ecchymosis (Cullen sign) are more specific though they are rarely seen and appear later.[5] The diagnosis of acute pancreatitis is thus difficult to establish by clinical examination alone and requires laboratory evaluation and imaging studies.

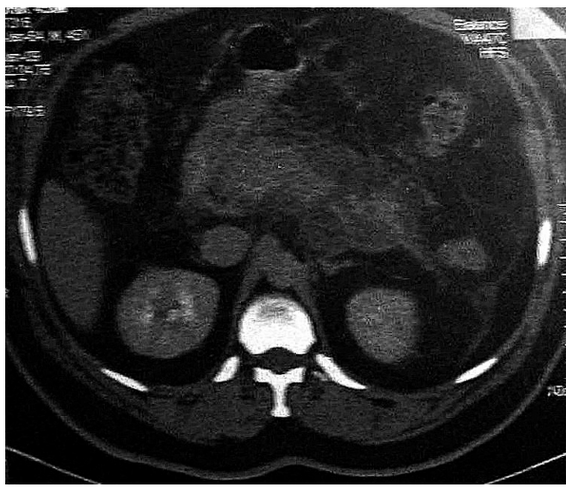
Biochemical evaluation includes serum amylase and lipase levels. Serum amylase rises within 6-12 hours of an acute attack; and remains elevated for 3-5 days. Elevated levels of serum lipase are also noted, though these enzymes are not specific for acute pancreatitis, serum lipase being more sensitive and specific than amylase.[6] The serum trypsinogen level may be a more specific marker than both amylase and lipase. Also, measurement of serum lipase and amylase has no role in assessing the disease severity.[7] Recent research has shown promising role of urinary trypsinogen activation peptide and other pancreatic proteases.[6] Markers of immune system activation like C-reactive protein is used to assess the prognostic indication of severity. However, it can only be used as indicator of severity after 2-3 days of onset.[7] The plasma concentration of polymorphonuclear cell elastase appears to be a very good indicator of severe pancreatitis.[8] The assay for this enzyme has been reported to have a positive predictive value of over 90% in severe pancreatitis.[8] TNF, IL-6 and phospholipase A2 can also be assessed for disease severity. However, many of the assays are cumbersome and difficult to perform.

Imaging, particularly contrast-enhanced CT, has thus become an essential part of the investigation protocol of acute pancreatitis. Abdominal radiography in acute pancreatitis may occasionally show sentinel loop (localized ileus in small bowel) or colon cut-off sign (spasm of splenic flexure of colon), though its main role is to rule out bowel obstruction or perforation as a cause of acute abdomen. Chest X-ray may reveal infiltrates, elevated hemidiaphragm or pleural effusion, left sided effusion being more specific. Ultrasound has limited applications only because of impaired visualization of pancreas due to overlying bowel gas. Pancreas appears diffusely enlarged and hypoechoic with fluid collections in lesser sac, peripancreatic, anterior pararenal space and pelvis in severe disease. Abdominal ultrasonography is excellent for evaluation of biliary tree and the detection of gallstones and biliary tree obstruction. Abnormal US findings are seen in 33% to 90% of patients with acute pancreatitis.[9] However, according to Ricke et al, contrast enhanced sonography renders excellent results in staging of acute pancreatitis comparable to CT. Hence, it can be recommended as the imaging procedure of choice especially when iodinated contrast media are contraindicated.[10] CT scan has become the most important aid for establishing the diagnosis of acute pancreatitis, grading its severity and detecting local complications. Patients should be scanned after 48 hrs, with oral and intravenous contrast to allow an estimation of extent of pancreatic parenchymal necrosis and differentiation between mild and severe pancreatitis.[11] The CT severity index developed by Balthazar et al in 1994 is especially invaluable in differentiating mild, moderate and severe forms of acute pancreatitis and it also shows good correlation with patient outcome. It grades pancreatitis based on the extent of pancreatic necrosis, pancreatic and peripancreatic inflammation on contrast enhanced CT.[12] (Figure 1).

MRI does not offer any special advantage over CT except for preventing radiation exposure and being useful in patients allergic to iodine based contrast agents. MRCP is a newer, noninvasive technique that provides an excellent evaluation of the pancreatobiliary ductal system. It is helpful in patients when ERCP is not possible, though unlike ERCP, MRCP does not have interventional capability.[13] ERCP is helpful in evaluating cases of pancreatitis

where other modes have been unsuccessful in establishing the etiology and offers the advantage of intervention at the same time.[14] In patients with severe gallstone pancreatitis, morbidity and mortality are reduced with the use of ERCP.[13] Another new diagnostic tool is endoscopic ultrasonography, which is highly accurate in documenting small calculi and tumors.[15]

Figure 1. *CT Scan.*



Prognostic indexes and their correlation with patient outcome

A few decades ago, the disease severity evaluation was done subjectively, on the basis of clinical parameters like fever, peritonitis, oliguria, shock and the presence of other complications.[16] Flank ecchymoses (Grey Turner Sign) and periumbilical eccymoses (Cullen Sign) were used as specific markers of severity.[7] Later on, a number of disease-specific scoring systems were developed. These include Ranson criteria (Table 1), original and modified Glasgow criteria (Table 2), simplified acute physiology (SAP) score, Imrie scales and, recently developed, the acute physiology and chronic health evaluation II (APACHE II) *score*.[14-17] The two most popular scoring systems are the Ranson and Glasgow scales. Ranson criteria are based on 11 objective signs: five of them are determined at the presentation while others must be estimated 48 hours. The higher is the score, the greater is the associated morbidity and mortality. Pancreatitis is mild when there are two or fewer grave signs, whereas pancreatitis is severe with more than six grave signs. In patients with fewer than three signs, there is no mortality, while in patients with six or more signs the mortality rate is above 50%.[18] The system is an objective indicator of disease severity though it requires a total of 48 hours after onset of symptoms for proper scoring assessment.

Table 1. *Ranson criteria.*

0 hours		48 hours	
Age	> 55 years	Hematocrit	Fall by 10%
Blood Glucose	>200 mg/dl	Serum Calcium	< 8mg/dl
WBC	>16,000/ cu.mm	Blood urea nitrogen	Increase by 5 mg/dL (1.8 mmol/L) despite fluids
LDH	>350 U/L	Base deficit	> 4 MEq/L
		PaO_2	< 60 mmHg
		Fluid sequestration	> 6 L

Adapted from Ranson JHC, Rifkind KM, Roses DF, et al. Surg Gynecol Obstet 1974;139:69.

Table 2. *Glasgow scoring system .*

White blood cell count	>15,000/µL
Serum glucose concentration	>180 g/dL (10 mmol/L) with no history of diabetes
Blood urea nitrogen	>45 mg/dL (16 mmol/L) with no response to fluids
PaO_2	<60 mmHg
Lactate dehydrogenase	>600 U/L
Aspartate aminotransferase (AST)	>200 U/L
Serum albumin concentration	<3.2 g/dL (32 g/L)
Serum calcium concentration	<8 mg/dL (2 mmol/L)

The presence of three or more of these criteria within the first 48 hours is indicative of severe pancreatitis. Adapted from Corfield AP, Williamson RCN, McMahon MJ et al. Lancet 1985;24: 403.

Nowadays, the APACHE II scoring system is more widely used.[19] The system requires measurement of 12 physiologic and clinical parameters, the higher the score, the higher the morbidity and mortality. An APACHE II score of greater than 8 indicates severe pancreatitis.[18] The major advantage of the APACHE II scoring system, as compared with the other systems, is that it can be used in monitoring the patient's response to therapy[18] while Ranson and Glasgow scales are mainly meant for assessment at the presentation.

However, all these scoring systems are difficult and complex to perform, considering that they depend on various clinical and laboratory parameters. Besides, these systems are more indicative of

systemic effects of acute pancreatitis. Grading of pancreatic necrosis, pancreatic and peripancreatic inflammation and local complications are better done by scoring system based on imaging. As already mentioned above an ideal severity scoring system should be able to grade the severity of acute pancreatitis early in the disease process, so that patients who would develop complications can be monitored intensively. It should be accurate, reproducible and easy to use objectively.[2] In 1985, Balthazar et al.[16] developed a system for assessing the severity of acute pancreatitis based on pancreatic and peripancreatic findings. Based on the criteria described in 1985 and the pancreatic necrosis assessment on contrast enhanced CT, Balthazar and colleagues developed the CT severity index.[4] On a 10-point severity scale, points are awarded for peripancreatic inflammation, the presence or absence of fluid collections, in combination with an assessment of the presence and degree of pancreatic necrosis (Table 3, a and b).

Table 3 a. *Balthazar grading of acute pancreatitis.*

A	Normal pancreas	0
B	Focal or diffuse enlargement of the pancreas	1
C	Peripancreatic inflammation with intrinsic pancreatic abnormalities	2
D	Intrapancreatic or extrapancreatic fluid collections	3
E	Two or more large collections of gas in the pancreas or retroperitoneum	4

Table 3 b. *Necrosis score.*

No necrosis	0
<30%	2
30-50%	4
>50%	6

CT severity index = Balthazar Grading + Necrosis score. Maximum score -10, Mild disease 0-3, moderate disease 4-6, severe disease 7-10. Adapted from Balthazar EJ, Robinson DL, Megibow, AJ, Ranson JH. Radiology 1990;174:331.

Contrast-enhanced CT is now the modality of choice in acute pancreatitis as it helps in staging the severity and in depicting the local complications. It has been shown to have a sensitivity of 90% for pancreatic necrosis. The CT severity index has shown an excellent correlation with the morbidity, mortality and the development of local complications in acute pancreatitis. In 2005, Gurleyik et al [17,20] showed that a CTSI higher than 3 was found to have a superior sensitivity, specificity, negative and positive predictive values for severe pancreatitis than either serum C-reactive protein or APACHE II scoring.[17,20] They concluded that the CTSI was more sensitive and correlated better with the patient outcome [17,20] than the APACHE II score. However, De Sanctis et al [21] had earlier in 1997 prospectively evaluated 35 consecutive patients with acute pancreatitis and found that CTSI was a good predictor of local complications (P = 0.0048) but compared unfavorably with APACHE II scoring for assessing the need for ICU admission (P = 0.022). They showed that CTSI was a better indicator of local complications and APACHE II scoring was more useful for predicting systemic organ failure. They also found that the prognostic results were not better when the scores were combined.[21] Although the CT severity scoring system has been used successfully to predict the morbidity and mortality in acute pancreatitis, it is not without its limitations. First, the score does not significantly correlate with the development of organ failure and secondly, despite being fairly objective marker, the assessment of pancreatic inflammation and necrosis by different radiologists may vary slightly in grading.[2]

To conclude, significant evidence suggests that Balthazar CT severity scoring system is the best scoring system available for predicting severity and local complications of acute pancreatitis while for predicting organ failure and systemic complications, clinical scores are superior.[17] Thus, the search for a single best prognosticator that combines both advantages continues.

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