Prognostic indicators in acute pancreatitis

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Several approaches have been used in an attempt to predict the severity and prognosis of attacks of acute pancreatitis. The Ranson and Glasgow criteria include a variety of simple laboratory parameters that are measured on admission and again within 48 h. They are the most widely used indices in clinical practice. The Acute Physiological and Chronic Health Evaluation II system is more complicated, but can be applied to a wide variety of conditions, especially in intensive care settings. The usefulness of this system depends on the threshold score for defining severe pancreatitis; a score of eight appears to be the most appropriate. The finding of nonperfused areas in the pancreas at contrast-enhanced computed tomography is indicative of pancreatic necrosis and portends an unfavourable prognosis. Other clinical and laboratory indices have been proposed, but the most important predictive factor of early mortality seems to be the presence and persistence of a Marshall organ failure score of two or more. This is especially true if organ dysfunction persists beyond 36 h. Radiological findings do not always correlate well with the presence of organ dysfunction, and more investigations are required.

Key Words: *Dynamics of multiple organ dysfunction syndrome; MODS*

Ever since the pioneering work by John Ranson in 1974, a variety of approaches have been used in an effort to identify, at an early stage, the minority of patients with acute pancreatitis (AP) who are at the most risk for severe complications and death. Although Ranson's original criteria applied to alcohol-related AP (1), the criteria were modified in 1979 for use in patients with gallstone-induced disease (2). Amazingly, the latter have been used by very few clinicians or investigators. The original and modified Ranson criteria are listed in Table 1. The modified Glasgow criteria, in which the original 11 Ranson criteria were reduced to eight, were shown in 1984 to be equally applicable to both of the major causes of AP (3). They are listed in Table 2.

The Acute Physiological and Chronic Health Evaluation (APACHE) II system (Table 3) (4) has been increasingly employed, especially since 1989, as a means of grading the severity of pancreatitis and of other serious medical and surgical conditions. Unfortunately, the very large multinational study of the platelet activating factor antagonist, lexipafant,

Des indicateurs pronostiques en cas de pancréatite aiguë

Diverses démarches ont été utilisées dans une tentative pour prévoir la gravité et le pronostic de crises de pancréatite aiguë. Les critères de Ranson et de Glasgow incluent divers paramètres de laboratoire simples mesurés au moment de l'hospitalisation puis 48 heures plus tard. Ce sont les indices cliniques les plus utilisés en pratique clinique. Le système *Acute Physiological and Chronic Health Evaluation II* est plus complexe, mais il peut s'appliquer à toute une gamme de pathologies, surtout aux soins intensifs. L'utilité de ce système dépend de l'indice seuil de définition d'une pancréatite grave. Un indice de huit semble le plus pertinent. L'observation d'arcs non perfusés dans le pancréas à la tomодensitométrie avec injection de contraste est indicative d'une nécrose pancréatique et présage un pronostic défavorable. D'autres indices cliniques et de laboratoire ont été proposés, mais le facteur prédictif le plus important de mortalité précoce semble être une défaillance multiorganique. C'est particulièrement vrai si la dysfonction organique persiste plus de 36 heures. Les observations radiologiques ne sont pas toujours bien corrélées en présence d'une dysfonction organique, et d'autres examens s'imposent.

used this system but included a group of 1508 patients with supposedly severe AP who had a mortality rate of only 8% (5). This study used a minimum APACHE II score of six on admission as an inclusion criterion, but most investigators now believe that a score of eight is more appropriate as a threshold for the identification of severe AP. Ranson (using the correct score for the population in question), Glasgow and APACHE II are all reasonably valuable for group analysis, but are too inaccurate for the individual at-risk patient.

Obesity, as defined by a body mass index of 30 kg/m² or greater, is associated with increased morbidity and mortality in patients with AP (6). In addition, patients who are at least 70 years of age have a mortality of 16% to 20% (1-3,7-10). The presence of chest x-ray abnormalities, especially pleural effusions at admission, predicts a poor prognosis, especially when combined with hypoxemia (arterial oxygen level less than 60 mmHg) (1-4,9-15). Therefore, a cheap but as yet untested combination of prognostic factors would be body mass index, age, chest x-ray and oxygen saturation.

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TABLE 1
Ranson criteria

Parameter	Alcohol-induced*	Gallstone-induced†
On admission		
Age (years)	>55	>70
WBC/mL	>16,000	>18,000
Glucose (mg/dL)	>200	>220
LDH (IU/L)	>350	>400
AST (IU/L)	>250	>250
Within 48 h		
Hct decreases (points)	>10	
BUN increases (mg/dL)	>5	>2
Calcium (mg/dL)	<8	<8
PaO ₂ (mmHg)	<60	
Base deficit (mEq/L)	>4	>5
Fluid (L) (I – O)	>6	>4

*From Ranson et al (1); †from Ranson et al (2). AST Aspartate transaminase; BUN Blood urea nitrogen; Hct Hematocrit; I – O Intake minus output; LDH Lactic dehydrogenase; PaO₂ Arterial partial pressure of oxygen; WBC White blood cell count

C-reactive protein is a single marker that is very useful in determining the severity of the disease (16-20). However, because it is an acute phase reactant produced in the liver, it does not peak until approximately 36 h after the onset of symptoms. This limitation is similar to that which plagues the Ranson and Glasgow criteria, which require assessment 48 h after admission. Patients with severe AP almost invariably have a C-reactive protein greater than 150 mg/L, but a skew distribution of results makes this test occasionally unreliable.

Johnson and colleagues (21) at Southampton proposed that obesity be added to the APACHE II scoring system, thus creating the APACHE-O system. Although this combination seems promising, it has not been employed in any major prospective study by another research group.

The Atlanta Criteria, developed in 1992, reflect the fact that major organ compromise at an early stage correlates with the presence of severe AP (22). Moreover, the prognosis is worsened in patients who develop major complications later in the course of disease, such as a pseudocyst, infection or pancreatic necrosis, but transient organ failure (less than 36 h) is not associated with high mortality and morbidity.

Many have stated that the gold standard for severe AP is evidence, at contrast-enhanced computed tomography (CT), of reduced perfusion or infarction of the pancreas (19,23-31). This criterion has been used to select patients for many trials of early antibiotic therapy. In general clinical practice, however, this test is rarely performed during the initial 24 h after admission. It is more sensible to perform this test on patients who are seriously ill 48 to 72 h later.

TABLE 3
APACHE-II system

Physiological variable	High abnormal range				Normal	Low abnormal range			
	+4	+3	+2	+1		+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 pressure (mmHg)	≥160	130-159	110-129		70-109		50-69		≤49
Heart rate	≥180	140-179	110-139		70-109		55-69	40-54	≤39
Respiratory rate	≥50	35-49		25-34	12-24	10-11	6-9		≤5

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TABLE 2
Modified Glasgow criteria

Parameter	
Age (years)	> 55
White blood cell count/mL	> 15,000
Glucose (mg/dL)	> 180
Blood urea nitrogen (mg/dL)	> 96
Arterial partial pressure of oxygen (mmHg)	< 60
Calcium (g/dL)	< 8
Albumin (g/dL)	< 3.2
Lactic dehydrogenase (IU/L)	> 600

Data from Blamey et al (3).

The most important prognostic marker of severe disease is objective evidence of significant organ dysfunction, as reflected by the multiple organ dysfunction (MODS) scoring system (32). Failure of two or more organ systems constitutes MODS. It is important to realize that organ failure can occur very early in the course of acute pancreatitis.

The author's group in Glasgow has recently shown that the dynamics of organ function are very important. Organ failure, or deterioration of organ function, that persists for more than 36 h is associated with mortality rates of 50% to 60%, whereas patients with only transient organ dysfunction rarely die from the disease (33). This concept requires validation by clinical trials. Traditional prognostic indices may be deficient, because they do not address the time-course of organ dysfunction. Employing Marshall or similar scores (32) can more clearly identify the maximal risk patients (Table 4).

Some investigators believe that there is an excellent correlation between CT evidence of pancreatic damage and clinical organ failure, but this view is not universally held, and more studies are required. The presence of MODS in the first week of illness may account for up to 50% of all deaths from AP in most prospective studies. On the other hand, most deaths that occur after the first week of illness are associated with the presence of infected necrosis of the pancreas and also MODS.

In conclusion, much work still needs to be done in establishing early prognostic factors for acute pancreatitis. Traditional indices that employ clinical findings and laboratory tests are subject to limitations. Contrast-enhanced CT scanning is also useful, but is generally not undertaken early in the course of disease and may exacerbate renal failure. Although MODS is highly predictive, it would be ideal to identify patients who require intensive therapy before the development of severe dysfunction. Exciting new work on the dynamics of organ dysfunction may offer a lead to this important clinical dilemma.

TABLE 3 (continued)
APACHE-II system

Physiological variable	+4	High abnormal range			Normal 0	Low abnormal range			+4
		+3	+2	+1		+1	+2	+3	
Oxygenation (mmHg)									
$F_iO_2 \geq 0.5$ – record (A-a) PO_2	≥ 500	350-499	200-349		< 200				
$F_iO_2 < 0.5$ – record only P_aO_2					> 70	61-70		55-60	< 55
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 sodium (mMol/L)	≥ 180	160-179	155-159	150-154	130-149		120-129	111-119	< 111
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 (mg/dL) (double score for acute failure)	≥ 3.5	2-3.4	1.5-1.9		0.6-1.4		< 0.6		
Hematocrit (%)	≥ 60		50-59.9	46-49.9	30-45.9		20-29.9		< 20
White blood count ($\times 10^3/\text{mm}^3$)	≥ 40		20-39.9	15-19.9	3-14.9		1-2.9		< 1
Glasgow Coma Scale (15–GCS)									
A. Total acute physiology score (sum of above 12 items)									
Serum HCO_3^- (venous mMol/L) (use only if ABGs not available)	≥ 52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	< 15

B. Age points

Assign points to age as follows:

Age (years)	Points
≤ 44	0
45-54	2
55-64	3
65-74	5
≥ 75	6

C. Chronic health points

Add points if the patient has evidence of severe organ system insufficiency or is immunocompromised

5 points for medical or emergency postoperative patients

2 points for elective postoperative patients

APACHE-II score = A + B + C

From Knaus et al (4). (A-a) PO_2 Alveolar-arterial oxygen gradient; ABG Arterial blood gas; F_iO_2 Fraction of inspired oxygen; HCO_3^- Bicarbonate; P_aO_2 Arterial partial pressure of oxygen

TABLE 4
Modified Marshall organ failure score (hepatic index excluded)

	0	1	Score 2	3	4
Cardiovascular system (systolic blood pressure)	> 90	< 90 , fluid responsive	< 90 , negative fluid response	< 90 , pH < 7.3	< 90 , pH < 7.2
Respiratory system (F_iO_2/PO_2)	> 400	301–400	201–300	101–200	< 101
Glasgow coma score	15	13–14	10–12	6–9	< 6
Coagulation (platelet count $\times 10^9/L$)	> 120	81–120	51–80	21–50	< 21
Renal (creatinine, $\mu\text{mol/L}$)	< 134	134–169	170–310	311–439	> 439

Data from reference 32. F_iO_2 Fraction of inspired oxygen; PO_2 Pressure of oxygen

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