

Liver, biliary and pancreas

Prediction of severity of acute pancreatitis: an alternative approach

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SUMMARY Admission laboratory data of 203 patients suffering from acute pancreatitis were analysed to search for a simpler method of prediction of severity than the traditional multifactor prognostic scoring system. By discriminant analysis, admission serum urea and plasma glucose were identified to be factors with independent significance in predicting severity. If the presence of either factor higher than the cutoff point (urea >7.4 mmol/l, glucose >11.0 mmol/l) was considered as an indication of severe disease, then the sensitivity of this method was 75.0%, specificity 80.3% and the accuracy 79.3%. The predictive ability of this method was comparable with the Glasgow multifactor scoring system when the latter was also used to grade severity of our patients. It has the advantage, however, of simplicity and the ability of predicting severity at the time of admission.

Acute pancreatitis is a common acute abdominal condition. It is usually self-limiting but serious complications may supervene in 25% of cases¹ with an overall mortality rate of 10%.² Many studies had been carried out to identify clinical and objective criteria which can be used to predict the outcome of the disease. These included clinical assessment by experienced clinicians,³ blood tests such as serum calcium,⁴ methaemalbumin,⁵ fibrinogen⁶ and arterial oxygen level.⁷ Unfortunately, their discriminatory ability were not satisfactory. Abdominal paracentesis⁸ is better at predicting early than late complications of the disease but is invasive and visceral puncture may occur.⁹ Nowadays multifactor prognostic scoring system adopted by Ranson *et al*¹⁰ and Imrie *et al*¹¹ are generally accepted. They are satisfactory in that the overall sensitivity is 61-100% and specificity is 85-92%.^{9,10,12} The multiple laboratory criteria has three inherent disadvantages, however: (1) too many factors and values have to be memorised, (2) assessment of severity needs 48 hours or longer to complete; by that time the patients may have already recovered or deteriorated and succumbed, (3) some of the parameters in the scoring system could be influenced by the treatment given during the 48 hours period.¹³ As it is important to

assess the severity of the disease at the time of admission, better indices based on objective criteria and readily available on admission are required. We therefore undertook a study on our patients with acute pancreatitis to determine whether a simple and reliable system could be developed.

Methods

PATIENTS

Between January 1985 and December 1987, all patients with acute pancreatitis admitted to the Department of Surgery, University of Hong Kong, Queen Mary Hospital were included. Data from these patients were collected prospectively and computerised. The diagnosis of acute pancreatitis was based on a consistent clinical presentation and a serum amylase concentration above 400 IU/l (normal range for our laboratory 25-75 IU/l). Haematological and biochemical tests were done both on admission and at 48 hours later. More blood tests were done as necessary. The patients were managed conservatively and emergency operations were done only when unrelenting biliary tract infection and/or septic complication of pancreatitis manifested. When there was persistent fever, leucocytosis or hyperamylasemia, appearance of palpable abdominal mass or organ failure, computed tomography of the abdomen would be performed. The patients were considered

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to have recovered from pancreatitis if the abdomen was not tender, intestinal function resumed and serum amylase returned to normal.

Routinely, the biliary tract was investigated by ultrasonography and endoscopic retrograde cholangiopancreatography (ERCP). Patients who had ultrasonographic evidence of biliary stones but failed cannulation during ERCP had oral cholecystography or percutaneous transhepatic cholangiography.

Local complications – for example necrotising pancreatitis, pancreatic abscess, pseudocyst, phlegmon, duodenal and biliary obstruction – and systemic complications such as respiratory failure, renal failure, cardiogenic shock, gastrointestinal bleeding, disseminated intravascular coagulation, were noted and treated accordingly. Pancreatic phlegmon was defined as pancreatic and/or peripancreatic inflammatory masses detected by computed tomography, laparotomy or postmortem examination. This condition was considered as severe pancreatitis as the clinical course was often prolonged and frequently complicated.^{14,15}

Hospital mortality was defined as death within the same hospital admission for the attack of acute pancreatitis.

Patients were considered to have severe pancreatitis if (1) patients died within the same hospital admission, (2) patients developed one or more local or systemic complications, or (3) urgent surgery was required for biliary infection or complication of pancreatitis.

STATISTICAL ANALYSIS

Mann-Whitney test was used for comparison of the admission laboratory values between patients with mild and severe disease. Discriminant analysis was used to determine which of the factors were having independent significance in predicting the outcome. χ^2 analysis (with Yates' correction for small cell numbers) was used to establish the significance of comparison.

Results

Two hundred and three patients were seen during the study period. The patients' age ranged from 16 to 95 years with a median of 59. There were 94 men and 109 women.

Biliary stones account for 55.7% (113 patients) of cases of acute pancreatitis. Alcohol abuse was the cause in 34 (16.7%) patients only. One patient was found to have hepatocellular carcinoma; the exact aetiology of pancreatitis in this patient was not certain but could be the result of transient obstruction of the pancreatic duct as a result of tumour fragment

Table 1 Complications* and direct causes of hospital mortality

Local	
necrotising pancreatitis	6 (6)
pancreatic pseudocyst	4
pancreatic abscess	4 (1)
pancreatic phlegmon	18
duodenal obstruction	1
biliary obstruction	1
Systemic	
gastrointestinal bleeding	8 (1)
renal failure	5
respiratory failure	9 (1)
disseminated intravascular coagulopathy	3
cardiogenic shock	2
Others	
cholangitis	2 (2)
cholangitic liver abscess	1 (1)
myocardial infarction	2 (1)
dissecting aneurysm	1 (1)
Urgent operations	
exploration of bile duct	5
perforated duodenal ulcer	1

Figure in parenthesis indicates the number of patients who died of the complication. *40 patients had one or more complications.

passing through the ampulla. The other causes included ascaris in pancreatic duct (two patients), clonorchis in bile duct (one patient), hyperlipidaemia (one patient), carcinoma of pancreas (one patient) and steroid (one patient). In 49 patients the aetiology of acute pancreatitis could not be defined.

Forty patients (19.7%) developed one or more local or systemic complications of acute pancreatitis (Table 1). Ten of 18 patients with phlegmon had concomitant systemic or delayed local complications. The other eight patients without concomitant complications had prolonged hospital stay of over two weeks because of unresolved fever, pain,

Table 2 Necropsy findings in the deceased patients

Patient	Age	Findings
1	40	Necrotising pancreatitis, retroperitoneal phlegmon, fatty liver
2	60	Necrotising pancreatitis
3	68	Necrotising pancreatitis
4	86	Necrotising pancreatitis, stone impacted at ampulla
5	74	Necrotising pancreatitis, myocardial infarction
6	77	Necrotising pancreatitis, dissecting aortic aneurysm
7	62	Necrotising pancreatitis, myocardial infarction
8	80	Oedematous pancreatitis, centrilobular necrosis of liver
9	82	Oedematous pancreatitis, gangrenous acute cholecystitis, impacted stone at ampulla
10	93	Necrotising pancreatitis, ascaris in pancreatic duct
11	43	Not done
12	53	Not done
13	90	Not done
14	87	Not done

Table 3 Comparison of admission data between patients with mild disease* and severe disease† by Mann-Whitney test

Factors	n	Median	(range)	p value
Age (y)	163*	57.0	(14-96)	
	40†	65.0	(38-93)	0.4181
Haemoglobin (g/dl)	156*	13.7	(7.8-17.6)	
	39†	13.8	(8.3-19.2)	0.8852
White cell count (× 10 ⁹ /l)	156*	13.0	(3.7-61.0)	
	39†	13.9	(3.1-34.5)	0.2797
Platelet concentration (× 10 ⁹ /l)	149*	212.0	(64.0-781)	
	39†	220.0	(70.0-575)	0.6061
Serum amylase (IU/l)	163*	912.0	(422-2980)	
	40†	1190.0	(405-7700)	0.0689
Serum alanine aminotransferase (IU/l)	156*	124.5	(9-2013)	
	36†	98.0	(4-1370)	0.4111
Serum aspartate aminotransferase (IU/l)	154*	125.5	(2-876)	
	36†	67.0	(3-913)	0.0544
Serum γ-glutamyl transpeptidase (IU/l)	153*	218.0	(5-1913)	
	36†	158.0	(13-1406)	0.3972
Serum Alk. phosphatase (IU/l)	153*	133.0	(40-1490)	
	36†	116.0	(38-999)	0.0815
Serum bilirubin (μmol/l)	153*	36.0	(5-282)	
	39†	27.0	(5-204)	0.4003
Serum lactate dehydrogenase (IU/l)	112*	278.0	(43-1924)	
	30†	346.0	(129-1653)	0.1043
Serum urea (mmol/l)	158*	5.5	(2.3-21.5)	
	40†	7.3	(2.5-27.5)	0.0006
Serum creatinine (mmol/l)	156*	0.08	(0.04-0.55)	
	39†	0.091	(0.047-0.48)	0.0252
Plasma glucose (mmol/l)	121*	7.0	(3.7-25.6)	
	28†	8.6	(4.4-40.0)	0.0008
Serum calcium (mmol/l)	160*	2.185	(1.47-3.24)	
	40†	2.145	(1.11-2.57)	0.1409
Serum albumin (g/l)	157*	43.0	(23.0-57.0)	
	39†	39.0	(26.0-60.0)	0.1730
PaO ₂ (kPa)	144*	9.7	(4.6-13.8)	
	40†	8.5	(3.2-12.5)	0.0038

leucocytosis, and abdominal masses. Gastrointestinal bleeding occurred in eight patients in the subsequent clinical course. None had gastrointestinal bleeding at time of presentation. Hospital mortality occurred in 14 patients (6.9%). The postmortem findings and the age of the deceased were listed in Table 2. There was no evidence of previous renal and pancreatic damage. One patient died of uncontrolled

bleeding gastric erosions which occurred in the later phase. Thus 40 patients were classified as having severe disease while 163 patients were classified as mild. The median values of the laboratory measurements on admission between patients with mild and severe disease were compared by Mann-Whitney test (Table 3). Of the 17 parameters tested, four factors (urea, creatinine, glucose and PaO₂) were

Table 4 Prediction of actual outcome of 145 patients with complete urea and glucose values by various approaches

Actual outcome	Predicted outcome by							
	Urea >7.4		Glucose >11.0		Urea >7.4 and/or glucose >11.0		Glasgow system ²	
	Mild	Severe	Mild	Severe	Mild	Severe	Mild	Severe
Mild	96	21	111	6	94	23	90	27
Severe	13	15	18	10	7	21	7	21
Sensitivity	15/28 = 53.6%		10/28 = 35.7%		21/28 = 75.0%		21/28 = 75.0%	
Specificity	96/117 = 82.1%		111/117 = 94.9%		94/117 = 80.3%		90/117 = 76.9%	
Predictive value of positive	15/36 = 41.7%		10/16 = 62.5%		21/44 = 47.7%		21/48 = 43.8%	
Predictive value of negative	96/109 = 88.1%		111/129 = 86.0%		94/101 = 93.1%		90/97 = 92.8%	
Accuracy	111/145 = 76.6%		121/145 = 83.4%		115/145 = 79.3%		111/145 = 76.6%	

found to be statistically significant and one factor (aspartate aminotransferase) was marginally significant.

One hundred and thirty five patients had all these five significant values complete. Discriminant analysis of the data of these 135 patients showed that the factors with independent significance in determining severity were serum urea and venous plasma glucose.

One hundred and forty five patients had complete data of serum urea and plasma glucose concentration at admission. Further analysis showed that serum urea level of 7.4 mmol/l ($\chi^2=15.4$, $p<0.001$) and plasma glucose level of 11 mmol/l ($\chi^2=18.5$, $p<0.001$) were the cutoff points that could maximally separate the 28 patients with severe disease from the other 117 patients with mild disease. Based on either factor alone, however, the indices had a low sensitivity in predicting severity (Table 4). We then combined the results of the two indices and regarded the presence of either factor higher than the cutoff point as an indication of severe disease. By such an approach, the sensitivity markedly increased. The specificity was not lowered and the overall accuracy of prediction approached 80% (Table 4). Moreover, all the 10 deaths in this group of 145 patients were correctly predicted. The seven patients with severe disease not correctly predicted by this approach were identified to have phlegmon as the only complication.

The aetiology of acute pancreatitis was further analysed in those with severe diseases. Eighteen patients (15.9%) with biliary pancreatitis, two (5.9%) with alcoholic pancreatitis and 17 (34.7%) with idiopathic pancreatitis developed complications. The sensitivity of our scoring system was about the same for each group: alcohol 50%, idiopathic 60.0%, biliary 76.9%.

Of those surviving, at time of discharge, eight patients had raised serum urea over 7.4 mmol/l and only two patients had blood glucose over 11 mmol/l.

Multifactor prognostic scoring system was also used to grade the severity of the pancreatitis of these 145 patients. The modified Glasgow system¹² was used as it had been shown to more accurately predict the outcome of patients with biliary pancreatitis and there is a high incidence of biliary pancreatitis in Hong Kong.¹⁶ It was found that the predictive ability of our new approach was comparable with Glasgow multifactor scoring system (Table 4).

Discussion

Prediction of severity of acute pancreatitis is important because those with severe disease could be selected for, and may be benefited by prompt intensive treatment; those with mild disease could be

spared from costly and invasive protocol.² A multiple laboratory factor scoring system is the yardstick of early assessment but previous studies have reported a varying degree of accuracy. The difference between series probably results from differences in the definition of severe pancreatitis. Criteria such as the period of admission in the intensive care unit¹⁰ and the period of hospital stay^{3,17} depend as much on the availability of service and individual management policy as the severity of the disease. A more logical definition of severe disease would be to base the criteria on the development of fatal or non-fatal systemic and local complications of acute pancreatitis.^{9,18}

A major deficiency of the multifactor prognostic scoring system is the large number of factors that are involved. Complete data of each patient are often not available.^{9,18} To assume unmeasured factors as negative would seriously affect the validity of the scoring system. Efforts had been made to reduce the number of significant factors by multivariate analysis. In 1974 Romero *et al*¹⁹ identified seven significant variables on admission in predicting severity. Unfortunately five of the seven variables (abdominal distension, ascites, mass and chest roentgenogram findings) were subjective and difficult to quantify. Multivariate analysis on the nine factors of the Glasgow multifactor scoring system have recently been performed and the number of factors with independent significance were reduced to two in Blameys' report¹⁸ and four in Leese's report.¹⁷ As the data base in their studies needs 48 hours to complete, however, they were of less value in the initial assessment. By our stringent criteria of severity of acute pancreatitis, we were able to identify by multivariate analysis two objective parameters that can predict patients with fatal or non-fatal complications with a high degree of accuracy. The only group of patients that could not be predicted by this approach were those with phlegmon as the only complication. In our previous study on this condition, however, we have already shown that the development of phlegmon could not be readily predicted by the multifactor scoring system.¹⁵

A possible drawback of our new approach is that the serum urea and plasma glucose concentration at the time of admission can be influenced by non-pancreatic factors such as renal dysfunction, gastrointestinal bleeding, and the rising incidence of glucose intolerance with age. The higher the serum urea concentration could well be a reflection of poor physiologic reserve of major organs and patients are susceptible to complications when stressed by an attack of acute pancreatitis. The higher serum urea and plasma glucose concentrations may also be a reflection of severity of damage to the body tissue and

islet cells by the pancreatitis.⁹ Resorption of blood from the bowel was not contributory to high serum urea level in our series as none presented with gastrointestinal bleeding at the time of admission.

Our new approach may overdiagnose severity as it has a low predictive value of positive result. A similar feature was also seen in a recent report on the accuracy of multifactor scoring system.⁹ For the clinicians, however, this defect is not serious as we do not want to miss 'occult severe' patients who may be improved therapeutically or prophylactically.²⁰ Thus from a practical point of view, sensitivity is more important than predictive value of positive.

In conclusion, we have developed a simple method of predicting severity of acute pancreatitis. It is as good as the traditional multifactor scoring system but is superior in that only two factors are needed and prediction can be readily made on admission. The validity of this approach needs to be confirmed in a prospective study.

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