Gut, 1984, **25**, 1340–1346

Alimentary tract and pancreas

Prognostic factors in acute pancreatitis

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SUMMARY Prognostic factor scoring systems provide one method of predicting severity of acute pancreatitis. This paper reports the prospective assessment of a system using nine factors available within 48 hours of admission. This assessment does not include patient data used to compile the system. Of 405 episodes of acute pancreatitis occurring in a seven year period, 72% had severity correctly predicted by the system; 31% of 131 episodes with three or more factors present were severe and 8% of 274 episodes with less than three factors were severe. Assessment of individual factors revealed only one which did not predict severity. A scoring system based on the other eight factors correctly predicted severity in 79% of episodes. Prognostic factor scoring systems (i) alert the clinician to potentially severe disease, (ii) allow comparison of severity within and between patient series and (iii) will allow rational selection of patients for trials of new treatment.

Acute pancreatitis is a disease with a wide spectrum of severity, complications, and outcome. In general in this country acute pancreatitis has been managed conservatively unless complications have required surgical intervention. Treatment options such as immediate or early operation,[1 2] endoscopic sphincterotomy[3] for gall stone associated acute pancreatitis, and peritoneal lavage[4 5] have now been proposed and require assessment. A large proportion of episodes of acute pancreatitis are mild and settle promptly, highlighting the need for accurate methods to predict outcome if unnecessary and/or potentially hazardous invasive treatment is to be avoided.

In 1974 Ranson *et al*[6 7] identified 11 objective clinical and laboratory measurements available within 48 hours of admission (Table 1) each of which had value in predicting severity and could be used as a basis for a predictive scoring system. A modification of this system was suggested by Imrie *et al*[8] (Table 1) and has been used widely in the United Kingdom[9–11] while some have preferred diagnostic peritoneal lavage for prognostic purposes.[10]

This study reappraises the discriminatory value of individual factors determined within 48 hours of admission, assesses the ability of the scoring system of Imrie *et al*[8] to define patients with severe disease, and evaluates modifications to simplify the system but improve its accuracy.

Table 1 *Basis of factor scoring systems to predict the severity of acute pancreatitis*

Ranson et al *(1974)*	*Imrie* et al *(1978)*
On admission	
age >55 years	
WBC >16 000/cu mm	
blood glucose 10 mmol/l	
LDH >700 IU%	
AST >250 Sigma Frankel Units %	
Within 48 hours	
	age >55 years
	WBC >15×10⁹/l
	blood glucose >10 mmol/l (no diabetic history)
blood urea nitrogen rise >5 mg%	serum urea >16 mmol/l (no response to iv fluids)
PaO_2 (8 kPa)	PaO_2 <60 mmHg
serum calcium 2·0 mmol/l	serum calcium <2·0 mmol/l
	serum albumin <32 g/l
	LDH >600 μ/l
	AST/ALT >100 μ/l
haematocrit fall >10%	
base deficit >4 mmol/l	
fluid sequestration >6 litres	

For either system: severe disease = three or more factors present. WBC = white blood cell count. LDH = lactic dehydrogenase. AST = aspartate aminotransferase. ALT = alanine aminotransferase. PaO_2 = arterial oxygen saturation.

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Received for publication 21 February 1984

Methods

PATIENTS

Data have been collected on patients admitted to Glasgow Royal Infirmary with acute pancreatitis since 1971. All patients in whom a final diagnosis of acute pancreatitis was sustained and who were admitted between 1 January 1974 and 31 December 1980 form the basis for this report. The diagnosis of acute pancreatitis was accepted if a compatible clinical syndrome was associated with a serum amylase greater than 1200 IU/l within 48 hours of admission. Patients with secondary acute pancreatitis have been excluded.[12] Five patients in whom the diagnosis was made at laparotomy when serum amylase had not been measured are included. Raised urinary amylase, amylase clearance or amylase creatinine clearance ratio have not been used to diagnose pancreatitis in this series.

Age and sex were recorded for each patient. For statistical analysis we have used the highest value recorded within 48 hours of admission for the serum concentrations of amylase, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, bilirubin, urea, lactate dehydrogenase, blood glucose, white blood cell count and the lowest concentrations of arterial oxygen saturation (PaO_2), serum albumin and calcium. Serum amylase was estimated by the Phadebas method (normal range 70—300 IU/l). Other methods have been described previously.[13]

Gall stones were diagnosed by the subsequent demonstration of calculi at surgery, necropsy or by imaging methods (oral cholecystography, intravenous cholangiography, endoscopic retrograde cholangiopancreatography, percutaneous transhepatic cholangiogram or ultrasound). Failure to show the gall bladder at oral cholecystography or intravenous cholangiography was not considered sufficient for the diagnosis of gall stones. Alcohol abuse was accepted as the aetiological factor when gall stones were excluded and there was a history from the patient of heavy alcohol intake within four days of admission or a history of prolonged alcohol abuse with further intake in the four days prior to admission, usually much greater than 80 g/day.

Pancreatitis was classified as clinically severe if the patient died, or underwent surgery during the same admission because pancreatitis did not settle, or complications became manifest. Pancreatitis was not classified as severe simply because the patient had elective surgery for gall stone associated pancreatitis during the same admission. All other episodes of pancreatitis were classified as mild.

Student's t test for unpaired data was used to determine the significance of differences of mean values for each factor between patients with severe or mild disease. Chi square analysis was used to evaluate whether defined levels of individual factors could predict disease severity. The cut points of each variable used to define the groups for χ^2 testing have been reported previously.[8]

Stepwise linear discriminant analysis was used to minimise the number of preoperative risk factors needed to produce a linear function which best separates the groups with severe and mild pancreatitis. This analysis was carried out using the BMDP computer package,[14] program P7M on an ICL 2980 computer.

Results

Within the period of study, 347 patients (149 men, 198 women) were admitted with 405 episodes of acute pancreatitis. The average age at admission was 52·3 ± SD 18·6 years; 184 episodes occurred in men and 221 in women (male:female, 1:1·2). Gall stones were identified as the only aetiological factor in 177 episodes (44%) and alcohol abuse was considered the only aetiological factor in 135 episodes (33%). Of the remaining 93 episodes (24%), two patients with pancreatic cancer each had a single episode and one patient had evidence of viral infection on sequential serology. In 56 of these episodes a single factor was not identified (these include episodes with more than one aetiological factor, patients with recurrent pancreatitis after cholecystectomy and patients who denied alcohol abuse even when this appeared clinically to be the aetiological factor), and in 34 episodes the level of investigation was not sufficient to identify an aetiological factor.

Forty three patients (10·6%) died and 21 patients (5·2%) required surgery because the pancreatitis did not settle or because complications developed during the same admission. Details of surgery on these survivors are shown in Table 2. Thus 64 patients (15·8%) were classified as having severe disease while 341 episodes were classified as mild.

Eight of the factors considered showed significant differences between the severe and mild outcome groups (Table 3). Each of these eight factors was useful in selecting patients at increased risk of severe disease using the defined cut points (Table 4). In this analysis the aminotransferase concentrations included in the original prognostic factor system by Imrie and colleagues were not useful in predicting severe pancreatitis.

The nine factor scoring system for early

Table 2 *Details of surgery in 21 patients surviving severe acute pancreatitis*

Aetiological factor	*GB*	*ECBD*	*Drainage of pseudocyst*	*Drainage of abscess*	*TV&P*	*Partial pancreat-ectomy*	*Further surgery*
Gall stones							
JS	+		+		+		
JC	+						
GH	+	+	+		+		
DJ	+	+					+
AB				+			
DW	+	+					+
JB	+	+					+
EM	+						
RW	+	+					
AA	+	+					
Alcohol							
KE	+						
JB			+				
CK	+					+	
BC			+				
MC			+				
AD				+			+
RS				+			
BS			+				
Other							
WL				+			
DQ						+	
SG			+				

GB = cholecystectomy. ECBD = exploration of common bile duct. TV&P = truncal vagotomy and pyloroplasty. Further surgery = further surgery during same admission.

Table 3 *Relationship between mean values of individual parameters and severity of acute pancreatitis*

Factor	*Severity*	*No*	*Mean*	*SD*	*t test*	*p*
Calcium	severe	52	2·01	0·20		
(mmol/l)	mild	311	2·17	0·18	5·26	p<0·001
Urea	severe	61	9·46	6·8		
(mmol/l)	mild	337	5·83	2·7	4·08	p<0·001
LDH	severe	33	1076	876		
(U/l)	mild	202	497	257	3·77	p<0·001
PaO_2	severe	57	62·1	12·1		
(mm^2Hg)	mild	319	68·9	13·7	3·87	p<0·001
WBC	severe	58	16·6	7·8		
($\times 10^9/l$)	mild	309	12·8	4·9	3·62	p<0·001
Albumin	severe	56	36·4	6·0		
(g/l)	mild	316	39·1	5·0	3·18	p<0·01
Glucose	severe	41	12·25	14·53		
(mmol/l)	mild	169	7·07	2·85	2·27	p<0·05
Age	severe	64	56·6	17·4		
(yr)	mild	341	51·5	18·7	2·14	p<0·05
ALT	severe	58	122	191		
(U/l)	mild	321	180	376	1·77	NS
Alk phos	severe	59	386	285		
(U/l)	mild	320	433	362	1·11	NS
Bilirubin	severe	59	36·6	30·5		
(μmol/l)	mild	318	33·4	29·8	0·73	NS
Amylase	severe	60	5158	3568		
(IU/l)	mild	340	4827	3387	0·67	NS
AST	severe	58	142	200		
(U/l)	mild	322	162	343	0·63	NS

LDH = lactic dehydrogenase. PaO_2 = arterial oxygen saturation. WBC = white blood cell count. ALT = alanine aminotransferase. Alk phos = alkaline phosphatase. AST = aspartate aminotransferase.

Table 4 *Significant factors in predicting severity of acute pancreatitis*

Factor	*Value*	*No*	*Mild (%)*	*Severe (%)*	χ^2	*p*
Calcium	<2·00	58	62	38		
(mmol/l)	>2·00	305	91	9	31·34	p<0·0001
Urea	>16	13	31	69		
(mmol/l)	<16	385	86	14	30·09	p<0·0001
LDH	>600	70	67	33		
(U/l)	<600	165	94	6	29·24	p<0·0001
Glucose	>10	29	48	52		
(mmol/l)	<10	181	74	26	22·20	p<0·0001
PaO_2	<60	114	75	25		
(mmHg)	>60	262	89	11	13·44	p<0·001
WBC	>15	130	73	27		
(×10/l)	<15	237	90	10	11·53	p<0·001
Albumin	<32	28	64	36		
(g/l)	>32	344	87	13	10·11	p<0·01
Age	>55	198	80	20		
(yr)	<55	207	88	12	5·64	p<0·05

LDH = lactic dehydrogenase. PaO_2 = arterial oxygen saturation. WBC = white blood cell count.

prediction of outcome in acute pancreatitis was first assessed with the assumption that unrecorded factors (see Table 3) were negative; 31·3% of 131 episodes with three or more factors positive had a severe outcome and 8·4% of 274 episodes with less than three factors positive had a severe outcome. Overall, the prediction of severity based on this scoring system proved correct in 72·1% of the 405 episodes (Table 5). The removal of the aminotransferase concentrations as a predictive factor improved the accuracy of the scoring system; 39% of 92 episodes with three of more factors positive had a severe outcome and 9% of 313 episodes with less than three factors positive had severe disease. Overall, 79·3% of the 405 episodes had an appropriate prediction of severity with this modification (Table 6).

It can be seen from Tables 3 and 4 that complete information was not available on all factors in each episode of acute pancreatitis. Complete information on all significant risk factors was available for 145 episodes and the modified (eight factor) system maintained its accuracy in predicting severity; in 40% of 47 episodes with three or more factors positive the patients had severe disease and in 6% of 98 episodes with less than three factors positive the patients had severe disease. Overall, 76·6% of the 145 episodes with complete information on prognostic factors had the predicted severity borne out by the clinical course of the disease (Table 6).

Linear discriminant analysis showed that the factors with independent significance in determining severity were lactate dehydrogenase and calcium. Information on lactate dehydrogenase and calcium was complete for 228 episodes. The discriminant function (R) generated by this method is

$R = -8{\cdot}96 + 4{\cdot}51 \log_{10}(\text{LDH}) - 9{\cdot}70 \log_{10}(\text{calcium})$.

The mean value for R for episodes of mild pancreatitis is −0·22 and that for severe pancreatitis is 1·37. Increasing values of R define groups of patients with an increasing proportion of patients who prove to have severe acute pancreatitis. For example, if R>0 (100 episodes) 26% were severe, while if R<0 (128 episodes) 5% were severe and if R>1 (33 episodes) 58% were severe, while if R<1 (185 episodes) 7% were severe. The distribution of values of R for patients with severe and mild acute pancreatitis are shown in the Figure.

Discussion

The early identification of potentially severe acute pancreatitis enables the selection of patients who may require more intensive and invasive methods

Table 5 *Predictive value of the original scoring system of Imrie* et al (1978) *in acute pancreatitis*

Factors	*No*	*Mild*	*Severe*	*Severe (%)*
0	63	59	4	6
1	107	99	8	8
2	104	93	11	11
3	66	55	11	17
4	37	25	12	32
5	20	6	14	70
6	5	3	2	40
7	2	1	1	50
8	1	0	1	100
9	0	0	0	—

Table 6 *Predictive value of modified scoring system in acute pancreatitis*

	All patients		*Patients with complete data on each factor*	
Factors	*No*	*Severe (%)*	*No*	*Severe (%)*
0	101	7	32	3
1	125	6	37	8
2	87	16	29	7
3	49	20	20	15
4	28	61	15	53
5	11	55	8	63
6	2	100	2	100
7	1	0	1	0
8	1	100	1	100

of management than are appropriate in mild pancreatitis. Prognostic factor analysis provides an objective and reproducible system for the comparison of results, both within and between series of patients under study. Ranson and colleagues[4 6 7] found that 11 of 43 clinical, biochemical, and haematological factors determined within 48 hours of admission had prognostic significance in their group of patients with acute pancreatitis. When used prospectively a scoring system based on these 11 factors (Table 1) identified 162 patients who had less than three factors present of whom only one proved to have severe disease, while 24 of 38 patients with three or more factors present had major complications or died. Imrie *et al*[8] used concentrations similar to those suggested by Ranson to define positivity of individual factors but discarded three factors (fluid sequestration >6 litres, base deficit >4 mmol/l and haematocrit decrease of >10% within the first 48 hours of admission) and introduced serum albumin <32 g/l to provide nine factors for analysis. In addition the criterion SGOT (AST) values greater than 250 Sigma Frankel units% was replaced by the criterion that either aspartate aminotransferase or alanine aminotransferase concentrations exceeded 100 U/l. The overall accuracy of Imrie's system appeared high in that in their original report[8] all patients who died had been predicted as having severe disease by the scoring criteria.

An objective and widely applicable definition of clinically severe disease is difficult to attain. Criteria such as the period of admission to hospital, admission to an intensive care area or the delay before resuming normal oral intake are influenced by availability of facilities and the management policy of individual clinicians. Criteria such as respiratory or renal failure, which depend in part for their definition on factors also used in predicting outcome may not be appropriate. In view of these difficulties, we have used death and need for emergency surgery as indicators of severe disease but accept that these strict criteria may exclude some patients who may be considered as suffering from severe disease.

It should be noted that pancreatitis in Ranson's series was predominantly because of alcohol abuse (69% of 300 patients) and occurred more commonly in men (78%). In the United Kingdom, biliary disease is the most common aetiological factor and acute pancreatitis occurs more commonly in women than in men.[8 11 15 17] In view of these differences the predictive value of individual factors must be verified within each clinical setting. The relationship already shown between aetiology and both age and aminotransferase concentrations in our own series of patients[17] underlines the need to confirm the individual predictive value of the factors in the system. Furthermore, Osborne *et al*[18] found that in the subgroup of patients with gall stone associated pancreatitis, the factor (age >55 years) was not of individual prognostic significance and suggested modification of Imrie's original system to use only eight factors.

Analysis of 405 episodes of acute pancreatitis in the present report has confirmed the predictive value of eight of the nine factors originally adopted by Imrie *et al*.[8] Only the aminotransferase concentrations originally suggested had no significance in

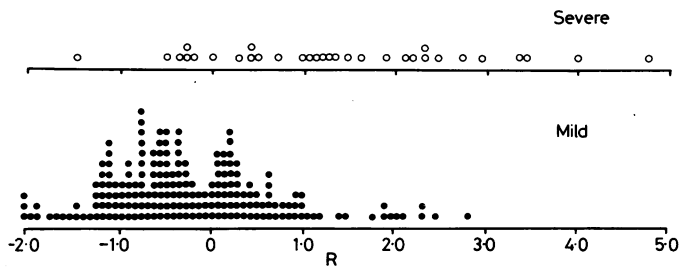

Figure *Values of the discriminant function (R) for 228 episodes of mild and severe pancreatitis. $R = -8{\cdot}96 + 4{\cdot}51 \log_{10}(LDH) - 9{\cdot}70 \log_{10}(calcium)$.*

predicting the severity of acute pancreatitis. Analysis of the original scoring system, however, confirms its predictive value; 31% of patients with three or more factors positive were subsequently found to have severe disease whereas the pancreatitis was severe in only 8% of patients with less than three factors positive. Exclusion of the aminotransferases from the original system, leaving eight individually significant risk factors, increased overall predictive value in that 79% of episodes were correctly predicted as either severe or mild as opposed to 72% in the nine factor system. The assumption that unmeasured prognostic factors are considered negative introduces a further possible source of error in the assessment of any scoring system. When only patients with complete information on all eight factors are considered, 40% of patients with three or more factors positive had severe disease whereas pancreatitis was severe in only 6% with less than three factors; in 77% of episodes the clinical course of the disease had been predicted correctly by the scoring system. In view of these findings, we recommend the use of the eight factor system.

Multivariate analysis of risk factors had been used by Ranson and Pasternack[19] for accurate prediction of severity of acute pancreatitis. Whereas they used as many as nine of the variables, our own multivariate analysis has sought to minimise the number of variables used by using only those factors with independent significance. This may provide an alternative method for identifying high risk patients, but must await prospective verification.

Any system designed to predict the severity of an episode of acute pancreatitis has limited value unless the prediction can be used to influence treatment and outcome. The ability to identify a group of patients at high risk of major complications and mortality, coupled with the ability to identify which patients have a high probability of pancreatitis because of gall stones or alcohol[17] may have important benefits. The power of any study of a potential method of treatment is increased if patients liable to run an uncomplicated course can be excluded with confidence. This problem is highlighted in the recent controversy regarding the timing of biliary tract surgery in gall stone associated pancreatitis.[1 2 20 21] Studies of early biliary tract surgery and/or endoscopic methods of stone disimpaction seem most likely to answer the question of whether these methods are of benefit if confined to high risk patients. Similarly, peritoneal lavage may have a role to play in alcohol associated pancreatitis[5] but is clearly not required in the large group of patients who settle quickly on current methods of conservative treatment.

Satisfactory trials of treatment of acute pancreatitis require reliable methods of identifying patients at risk of severe disease early in the course of the illness and prognostic factor analysis provides one such method.

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