

Full Length Research Paper

Serum markers as better predictors than Ranson, Imrie, and APACHE II systems in identifying the severity of acute pancreatitis

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The aim of this paper is to evaluate the predictability of various scoring systems and serum markers in the assessment of the severity of acute pancreatitis. All consecutive patients with acute pancreatitis were prospectively studied. Body mass index was measured at the time of admission. The demographic data, etiology, mean hospital stay, clinical, radiological, biochemical findings, morbidity, and mortality were recorded. The relations between these parameters, scoring systems (Ranson, APACHE II, Imrie, and various serum markers) and patients' outcome were determined by using appropriate tests. Ninety seven (fifty men and forty seven women) patients were incorporated in the study; mean age was 51 years. Biliary pancreatitis was the most common etiological factor, followed by idiopathic pancreatitis (60 and 29%, respectively). Seventy (72%) patients had severe pancreatitis and 27 (28%) cases had mild disease. Ranson ($P=0.2$), Glasgow ($P=0.4$), and APACHE II ($P=0.5$) appeared insignificant predictors of the severity of acute pancreatitis by multivariate analysis. More reliable serum markers were pancreatic amylase ($p \leq 0.001$), neutrophil elastase ($p \leq 0.001$), serum albumin ($p \leq 0.02$), and C-reactive protein ($p \leq 0.001$). Results turned out to be more homogenous when CT scan findings were added together. Not a single parameter achieved statistically significant predictive value when used alone. Ranson, Imrie score, and APACHE II are not accurate predictors of the severity of acute pancreatitis. Serum markers are better predictors to elucidate the severity of disease.

Key words: Acute pancreatitis, Ranson criteria, Imrie score, APACHE II, serum amylase, serum C-reactive protein.

INTRODUCTION

Refinements in the diagnostic armamentarium for acute pancreatitis (AP) have provided better understanding of the disease and many centers reported successful outcomes (Birgisson et al., 2002; Toouli et al., 2002). Although the majority of patients are successful, complications develop in 15 to 20% of the cases and cause substantial morbidity (Kaya et al., 2007). Reliable scoring systems, radiological evaluation and laboratory markers are required for the identification of high risk at an early stage in order to take prophylactic measures. Numerous scoring systems and laboratory parameters have been devised to predict the severity and mortality of

AP: Ranson, Imrie, (Glasgow), Goris and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, contrast-enhanced abdominal CT scan, C-reactive protein (CRP), serum amylase, neutrophil elastase, and serum albumin. Among these assessment tools, the Ranson and Glasgow criteria are specifically designed to predict the severity of acute pancreatitis and have been the most widely used indices in clinical practice. However, the major drawback of the Ranson or Glasgow system is that they often need at least 48 h before a reliable assessment of the severity can be established. The APACHE II was introduced for such assessment to be made within 48 h. This scoring system has been shown to have a comparable predictive accuracy to the conventional disease scoring systems in AP (Wilson et al., 1990; Venkatesan et al., 2003). These

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Table 1. Causes of acute pancreatitis encountered in the study.

No.	Cause	Number (%)
1	Biliary tract stones	58 (60)
2	Idiopathic	28 (29)
3	Hypertension	31 (33)
4	Diabetes mellitus	22 (23)
5	Hyperlipidemia	18 (19)
6	Ischemic heart disease	14 (15)

Table 2. Complications of acute pancreatitis recorded in the study.

No.	Complication	Number (%)
1	Pseudocyst	13(13.4)
2	GIT bleeding	10(10.3)
3	Shock	4(4.1)
4	Septicemia	3 (3)
5	Pleural effusion	2 (2)
6	Acute renal failure	2 (2)
7	ARDS	1 (1)

observations substantiate the fact that there is no single parameter which can reliably assess the severity, morbidity and mortality of AP.

The purpose of this study was to assess the predictive value of a variety of parameters in AP, such as Ranson, Imrie, APACHE II, and serum markers. All parameters were prospectively evaluated and statistically analyzed.

MATERIALS AND METHODS

Consecutive patients with acute pancreatitis were prospectively recruited in Ohud Hospital, Al Madina Al Munawara and King Khalid Hospital Najran, Kingdom of Saudi Arabia. Acute pancreatitis was diagnosed if serum amylase (4-fold or more) was recorded in the presence of compatible clinical features of AP (Yeung et al., 2006). Ranson, Imrie, and APACHE II scores were applied as soon as the diagnosis of AP was established. These scores were re-calculated 48 h after admission. Obesity was measured in terms of body mass index (BMI) and recorded as kg/m². Serum markers pancreatic amylase, neutrophil elastase, serum albumin, C-reactive protein, and contrast-enhanced CT scan of the abdomen were performed in all patients. Patients with suspected severe pancreatitis were admitted in Intensive Therapy Unit for close monitoring. The etiology of AP was depicted by CT scan of the abdomen and biochemical results. Systemic and local complications were outlined by the Atlanta Consensus Classification System (Bradley, 1993).

Serum markers were compared using univariate analysis (Student's *t* test, Mann-Whitney). In a second step, multivariate analysis with logistic regression was applied to identify a group of markers capable of discriminating between mild and severe cases. Finally, chi-square test was applied to ascertain prediction afforded by each bivariate model; the higher the value, the better the model.

P value $p \leq 0.05$ was considered significant.

RESULTS

97 patients (50 men and 47 women) were studied during the defined period of one year 2009-2010. Their mean age was 51 years with age range of 21 to 67 years. Biliary pancreatitis was the most common etiological factor, followed by idiopathic pancreatitis (60 and 29%, respectively) as shown in Table 1. The commonest concomitant diseases were hypertension (33%), diabetes mellitus (23%), hyperlipidemia (19%), and ischemic heart disease (15%). More than 50 patients had a combination of comorbidities. Pancreatic pseudocyst was found to be the most frequent complication (Table 2). There was one death due to ARDS on the 7th day of treatment in the Intensive Therapy Unit. Seventy (72%) patients had severe pancreatitis and 27 (28%) cases had mild disease (Table 3). The median BMI in this study group was 33.5.

Ranson ($p=0.2$), Imrie ($p=0.4$), and APACHE II ($p=0.5$) appeared insignificant predictors of the severity of acute pancreatitis by multivariate analysis. More reliable serum markers were pancreatic amylase ($p \leq 0.001$), neutrophil elastase ($p \leq 0.001$), serum albumin ($p \leq 0.02$), and C-reactive protein ($p \leq 0.001$) as demonstrated in Table 4. CT scans, done within 24 h of admission, showed normal pancreas in 20 patients, edematous pancreas in 37, necrotic in 40 subjects (Figure 1). As evident from Table 3, serum amylase levels were found to be most accurate serum marker. Results turned out to be more homogenous when CT scan findings were added together. Not a single parameter achieved statistically significant predictive value when used alone.

DISCUSSION

Assessment of the severity of AP is imperative for early identification of patients who may benefit from additional supportive and specific therapeutic procedures. It is also important to standardize clinical data for comparison of results between centers. Ideal predicting criteria should therefore be simple, non invasive, accurate, and readily available. Since the concept of Ranson and Pasternack (1976), establishing a scoring system for the severity of AP, there have been several other scoring systems: Imrie (Imrie et al., 1978), APACHE II (Knaus et al., 1981), and Hong Kong (Fan et al., 1989). Several studies have recorded different results regarding the predictive value of these scoring systems (Imrie, 2003). Their complexity and limitations to evaluate the patients during any given time generated tremendous interest in the serum markers (Fan et al., 1993).

Ranson entailed 11 numerical criteria where, with the exception of patients' age, all criteria are the result of a statistical analysis of 43 parameters gathered retrospectively from 3 overlapping series totaling 450

Table 3. Average values of the serum markers at the time of admission.

Serum marker	Normal range	Mild	Severe	P value
Pancreatic amylase (μ l)	20-118	430	1800	0.01
C-reactive protein (μ l)	113-150	515	1100	0.03
Neutrophilic elastase (μ l)	25-60	240	600	0.09
Serum albumin (g/l)	35-50	33	32.2	0.04

Table 4. Imrie, Ranson, and APACHE II scores in the study.

Severity scoring system (Number)	Mild pancreatitis (27)	Severe pancreatitis (70)	Total (97)
Ranson score			
0	0	10	10
1	1	23	25
2	2	2	6
3	1	26	30
4	1	2	7
5	9	4	18
6	3	0	9
7	10	3	20
Imrie score			
0	2	8	10
1	3	7	11
2	3	11	16
3	2	31	36
4	5	18	27
5	6	1	12
APACHE II score			
Median range			
Day 0	5.3 (0-22)	8.2 (1-23)	P= 0.045
Day 1	5 (0-19)	8 (0-21)	P= 0.039
Day 2	4.8 (0-17)	7.7 (0-20)	P= 0.032
Day 3	4.6 (0-15)	7.3 (0-19)	P= 0.028
Day 4	4.2 (0-14)	7.1 (0-15)	P= 0.005
Day 5	3.9 (0-13)	6.9 (0-14)	P= 0.004

patients (Ranson and Pasternack, 1976; Ranson, 1978; Ranson et al., 1976). However, it should be noted that only 94 (21%) turned out to be suffering from AP, confirmed by surgery or postmortem examination. Despite this, the Ranson scoring system has been extensively applied since 1980s in practically all case controlled studies dealing with AP. Although the data retrieved with the APACHE II are better than Ranson's, the inconveniences attached to this multifactorial scoring system are its complexity, the need for additional data frequently not possible from outside the intensive therapy units (Kingnorth, 1989), and its questionable reproducibility (Funnell et al., 1993).

The imaging of the pancreas by contrast-enhanced CT

scan has shown contrasting results. CT scan of the pancreas was not at all predictive; as severe attacks were hardly more frequent in patients whose CT scans had shown their pancreas to be necrotic (Robert et al., 2002). In contrast, extra-pancreatic fluid collections were clearly more indicative of outcome, as severe attacks were directly related to their presence and amount. Consequently, the recourse to CT scan alone for its predictive strength deserves more research because the same information can be obtained without CT scans.

Most attacks of AP (80%) are mild and self limiting, subsiding spontaneously within 3 to 5 days (Uhl et al., 2002). This finding is not consistent with our study (27 mild and 70 severe AP). The mortality rate is less than

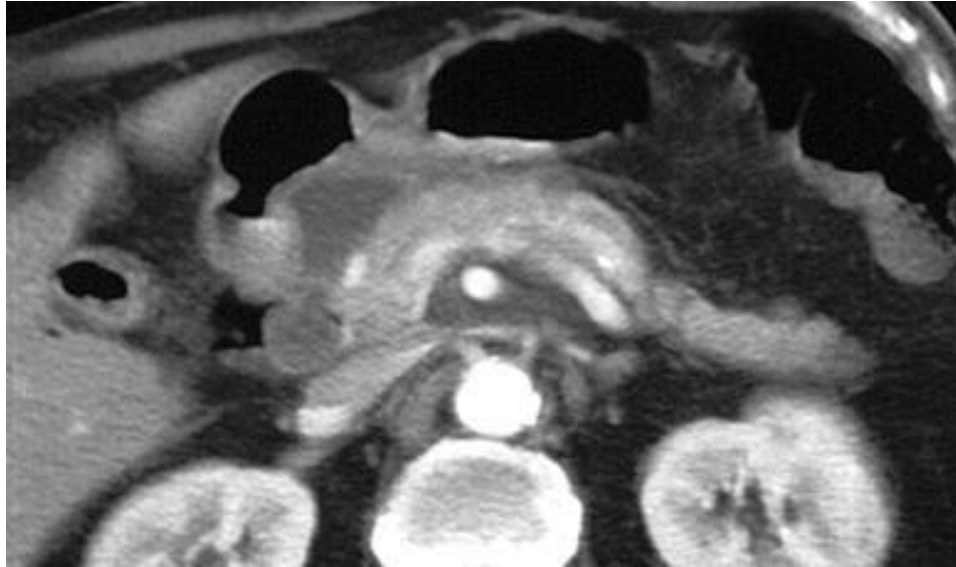


Figure 1. Severe form of acute pancreatitis seen in contrast enhanced CT of the abdomen.

1% and these patients normally do not need intensive care treatment and pancreatic surgery (Buchler et al., 2000). Our study had one mortality, matching the published data. In 10 to 20% of the cases, however, severe disease develops and parts of the pancreas and surrounding tissue become necrotic. This process raises a number of serum markers including serum amylase, pancreatic lipase, CRP, neutrophilic elastase, and decreases serum albumin levels (Lankisch et al., 2000). We applied serum amylase, CRP, neutrophilic elastase, and serum albumin to predict the severity of AP. Although several studies have reported that increased serum amylase and lipase do not correlate with the severity of AP, our study has shown that parameter has potential to serve an important tool to indicate the severity of AP ($p=0.01$). Similar statistically significant results were reported regarding other serum markers. The Ranson, Imrie, and APACHE II scores did not correlate with the severity of AP.

Infection of the necrotic pancreatic tissue develops in the second phase of the disease and has been reported in as many as 40 to 70% of patients with necrotizing pancreatitis (Berger et al., 1986). The risk of infection increases with the extent of intra- and extra-pancreatic necrosis. Even with the use of prophylactic antibiotic therapy, infection of necrotic pancreatic tissue remains a major risk in severe pancreatitis. Sepsis-related multiple organ failure is the main life-threatening complication with mortality rate of 20 to 50% (Ho and Frey, 1997). This finding substantiates the need for prophylactic antibiotic as suggested by the IAP Guidelines for the management of acute pancreatitis (Uhl et al., 2002). Once pancreatic necrosis has developed, the differentiation between sterile and infected necrosis becomes essential for the

management of AP. Fine Needle Aspiration Cytology (FNAC) of pancreas and peri-pancreatic fluid has been established as an accurate, safe, and reliable technique for the identification of infected necrosis (Banks et al., 1995). The complication rate of this procedure is low (Hiatt et al., 1987). It is important that only those patients who develop clinical signs of sepsis should undergo FNAC, since the procedure bears the potential risk of secondary infection (Rau et al., 1998). The issue of FNAC was not addressed as this procedure does not predict the severity and prognosis of AP.

Significant association between obesity and the development of AP have been reported though the exact pathogenesis is still not clear (Martinez et al., 2004). In our study, the mean BMI was found to be 33.5 which did not confirm the relation of morbid obesity with severe form of pancreatitis ($p=0.71$). To our knowledge, there is only one study which reported the prognostic significance of obesity in AP in Asian population (Tsai, 1998). Tsai (1998) showed that obese subjects did not confer an increases risk of organ failure or mortality in patients with AP. Therefore, further clinical studies are required to delineate the prognostic role of obesity in AP.

To conclude, the multifactorial scoring systems like Ranson, Imrie, and APACHE II are not reliable predictors of the severity of AP. Our study suggested that the serum markers amylase, neutrophilic elastase, CRP, and albumin are better predictors of the severity of AP.

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