

Identification of Admission Values Predictive of Complicated Acute Alcoholic Pancreatitis

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Background: Hospital admission indexes (serum urea nitrogen level, serum glucose level, heart rate, and white blood cell count) have been previously identified as useful predictors for the development of both severe systemic complications and death in patients with gallstone pancreatitis.

Hypothesis: We hypothesized that (1) these same 4 indexes would predict complications and/or death in first-time acute alcoholic pancreatitis and (2) these indexes would compare favorably with an admission Ranson score.

Design: Retrospective cohort study.

Setting: A university-affiliated, urban, public teaching hospital.

Patients: One hundred five patients who experienced first episodes of alcoholic pancreatitis treated between January 1, 1992, and June 30, 2003.

Main Outcome Measures: Major systemic complications (pulmonary, cardiac, renal, infectious) requiring intensive care unit admission and/or death.

Results: A total of 105 patients were identified. Twenty-six patients (25%) (95% confidence interval [CI], 17%-34%) had a major systemic complication, and 6 patients (6%) (95% CI, 2%-12%) died. A serum glucose level of 160 mg/dL (8.9 mmol/L) or higher combined with a white blood cell count of $17 \times 10^3/\mu\text{L}$ or more had a positive predictive value of 80% (95% CI, 44%-98%), and an admission Ranson score of 3 or higher had a positive predictive value of 100% (95% CI, 48%-100%) for determining the likelihood of a systemic complication. Both an admission Ranson score of 1 or more and a white blood cell count of $17 \times 10^3/\mu\text{L}$ or more, independent of each other, had equally high negative predictive values (100% [95% CI, 94%-100%] and 99% [95% CI, 94%-100%], respectively) with respect to mortality.

Conclusions: Two simple admission laboratory values—white blood cell count and serum glucose level—are useful predictors for development of major systemic complications and/or mortality in patients with first-time alcoholic pancreatitis. The predictive values of leukocytosis and hyperglycemia compare favorably with those of the admission Ranson score.

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DEPENDING ON THE POPULATION studied, long-term alcohol use is one of the most common causes of acute pancreatitis.^{1,2} When managed conservatively with intravenous fluids and bowel rest, most cases are mild and self-limiting, and the patients recover rapidly without the need for invasive monitoring. However, 20% to 30% of these patients have severe complications requiring intensive care management. As many as 5% to 15% of these patients die as a result of these complications.^{1,3-5} Complications of acute pancreatitis include both systemic (sepsis and respiratory, cardiac, and renal failures) and local pancreatic (necrosis, abscess, and hemorrhage) lesions.³⁻⁷

Since inflammation and necrosis may develop and progress after admission, accurate identification of the subset of patients who are likely to develop severe complications is important. Admission of all patients to the intensive care unit (ICU) is impractical and not cost-effective, since most will recover rapidly with standard inpatient care. Furthermore, assessments of severity made by clinicians at the time of admission, without the use of systematic predictors, accurately identify only one third of the severe cases.^{1,4,7,8} Multiple complex scoring systems (Imrie, Ranson, and Acute Physiology and Chronic Health Evaluation [APACHE] II) have been shown to predict adverse outcomes with better accuracy. Unfortunately, a major shortcoming is that at least 24 hours must

pass before accurate assessment of prognosis can be made.^{1,3,5,9,10} Early use of computed tomography and the Balthazar and coworkers^{11,12} grading system have been shown to be predictive of severe complications. However, the routine use of computed tomography carries risks associated with intravenous contrast-medium administration and is neither practical nor cost-effective.^{3,5,13,14} Immediate peritoneal lavage has also been applied as a method to predict severity based on the color and quantity of the retrieved fluid.^{3,8,15} Although supporters of this technique cite its ability to more rapidly predict cases of severe pancreatitis, the invasiveness of this technique makes it an unattractive choice as most patients will have a mild and uncomplicated hospital course.^{4,8} Finally, newer markers, such as the C-reactive protein level, have been evaluated as prognosticators with promising results.¹⁶

Recently, data published from our institution identified 4 independent predictors of adverse events associated with gallstone pancreatitis that were derived from physiologic factors and laboratory evaluations readily available at admission.¹⁷ A follow-up prospective study confirmed that one of these, a serum glucose level of 150 mg/dL (8.3 mmol/L) or higher, was statistically significant in a new set of patients with gallstone pancreatitis.⁶ However, it is unclear whether these or other admission criteria apply in pancreatitis caused by alcohol, particularly given the different pathophysiologic process. Therefore, the purpose of this study was to identify whether these physiologic and laboratory factors, which are readily available on admission, can accurately predict the future development of severe complications and/or death from acute alcoholic pancreatitis.

METHODS

Patients with first episodes of alcoholic pancreatitis were retrospectively identified by discharge diagnoses using a computerized patient database established in 1991 at Harbor-UCLA Medical Center, Torrance, Calif. Exclusion criteria included the presence of gallstones on abdominal ultrasonography and a history of episodes of pancreatitis. Patients were excluded if their medical records were unavailable. Approval from the institutional review board was obtained prior to collection and analysis of patient data.

Initial heart rate, white blood cell (WBC) count, and serum glucose and serum urea nitrogen levels were recorded, and a Ranson score was computed from data available on admission (**Table 1**). Serum amylase and lipase levels were also analyzed. The specific end points determined were the development of a major systemic complication requiring monitoring in the ICU (**Table 2**) and death during the initial hospitalization. Whether the patients were admitted to the ICU, intermediate care unit, or ward was also recorded. The decision regarding the level of care patients were to receive following admission was made in all cases by the chief surgical resident and the attending surgeon.

Descriptive statistics and bivariate analyses using the Wilcoxon rank sum test were performed for heart rate, WBC count, serum glucose level, and serum urea nitrogen level. Multivariable logistic regression analyses were then performed to determine which variables remained predictive while controlling for the others. Classification and Regression Tree analysis, a form of binary recursive partitioning, was used to identify specific cutoff points for each variable to assess and optimize their pre-

Table 1. Admission Ranson Score for Acute Pancreatitis*

Criterion	
Age, y	>55
WBC count, $\times 10^3/\mu\text{L}$	>16
Serum glucose level, mg/dL	>200
Serum LDH level, U/L	>350
Serum AST level, U/L	>250

Abbreviations: AST, aspartate aminotransferase; LDH, lactate dehydrogenase; WBC, white blood cell.

SI conversion factors: To convert serum glucose to millimoles per liter, multiply by 0.05551.

*The presence of each criterion adds 1 point to the total score.

Table 2. Definitions of Severe Complications by System

System	Complication
Pulmonary	Mechanical ventilation; pneumonia with hypoxemia ($\text{PaO}_2 \leq 60$ mm Hg); and hypoxemia $\text{PaO}_2 \leq 60$ mm Hg or dyspnea requiring frequent assessment of need for intubation
Cardiovascular	Hypotension requiring vasopressor support, ischemia or acute myocardial infarction; and new onset arrhythmia other than sinus tachycardia
Infectious	Sepsis from any origin
Renal	New onset oliguric or nonoliguric renal failure or the need for dialysis
Hematologic	Disseminated intravascular coagulation and platelet counts $< 50 \times 10^3/\mu\text{L}$
Neurologic	Glasgow Coma Scale score ≤ 9 and diminished responsiveness or agitation requiring significant sedation with need for frequent airway monitoring
Gastrointestinal tract	Stress ulcer with hematemesis or melena (requiring > 2 U of blood per 24 h)

dictive values for outcomes. Sensitivities, specificities, and positive and negative predictive values were calculated, wherever appropriate, and used to compare the varying levels of each predictor variable, including the initial Ranson score, for each outcome. $P \leq .05$ was considered statistically significant, and the 95% confidence intervals (CIs) are reported wherever appropriate.

All data were entered into an electronic database (MS Excel; Microsoft Corporation, Redmond, Wash) and transferred into native SAS format using translational software (dFPower DBMS/Copy; DataFlux Corporation, Cary, NC). All statistical analyses were performed using SAS version 8.2 (SAS Systems, Inc, Cary, NC).

RESULTS

Between January 1, 1992, and June 30, 2003, 110 patients were admitted to the surgical service at Harbor-UCLA Medical Center for a first episode of acute alcoholic pancreatitis. Patient records were available for a total of 105 patients (96%), of whom 92 (88%) were male. Patients ranged in age from 16 to 81 years (mean age, 38 years). Fifty-nine patients (56%) were Hispanic, 23 (22%) were white, 18 (17%) were African American, and 5 (5%) were of other racial/ethnic origins. Three patients (3%)

had diabetes mellitus. The mean serum amylase and lipase levels on admission were 869 U/L (range, 129-26,100 U/L) and 2071 mIU/mL (range, 79-28,770 mIU/L), respectively. On admission to the hospital, 41 patients (39%) were admitted to the ICU, 19 (18%) to the intermediate care unit, and 45 (43%) to the ward.

Twenty-six patients (25%) (95% CI, 17%-24%) had 1 or more severe systemic complications, 65% (17 patients) of which were pulmonary, 42% infectious (11 patients), 31% renal (8 patients), 19% cardiac (5 patients), 8% hematologic (2 patients), and 4% gastrointestinal (1 patient) (**Table 3**). Failure of at least 1 organ system developed in 12 patients (**Table 4**). Multisystem organ failure (MSOF) occurred in 6 patients, followed by death in each instance. The overall mortality was 6% (95% CI, 2%-12%).

On bivariate analysis, heart rate, WBC count, serum glucose level, and serum urea nitrogen level were all determined to be statistically significant with respect to development of systemic complications, and only heart rate and WBC count were significant for death (**Table 5**). Amylase and lipase levels, however, showed no association ($P = .22$ and $P = .51$, respectively). On multivariate logistic regression analysis, both the serum glucose level and WBC count were significant independent predic-

tors of systemic complications, but only the WBC count was significant for mortality (**Table 6**). Classification and regression tree analysis determined the optimal cutoff points for glucose, WBC count, and admission Ranson scores for systemic complications and death. The combination of a serum glucose level of 160 mg/dL (8.9 mmol/L) or higher and a WBC count $17 \times 10^3/\mu\text{L}$ or higher had a positive predictive value of 80% (95% CI, 44%-98%) for systemic complications. A Ranson score of 3 or higher on admission had a positive predictive value of 100% (95% CI, 48%-100%) for determining systemic complications (**Table 7**). With respect to mortality, a WBC count of $17 \times 10^3/\mu\text{L}$ or higher and a Ranson score higher than 0 on admission had similar negative predictive values of 99% and 100% (95% CI, 94%-100% and 94%-99%, respectively) (**Table 8**).

COMMENTS

This retrospective study confirmed the utility of 2 simple admission laboratory values—serum glucose level and WBC count—as predictors of systemic complications and death in patients with first-time alcoholic pancreatitis. When the cutoff points of the serum glucose level of 160 mg/dL (8.9 mmol/L) or higher and a WBC count of $17 \times 10^3/\mu\text{L}$ or higher are used together, the positive predictive value was 80% for the occurrence of major systemic complications. Also, a WBC count of $17 \times 10^3/\mu\text{L}$ or higher, when used alone, showed a negative predictive value of 99% for mortality. The high predictive values of these variables may have important implications for the triage of patients with alcoholic pancreatitis to the ICU vs the ward. Patients with WBC counts greater than the original $17 \times 10^3/\mu\text{L}$ and a serum glucose level greater than or equal to 160 mg/dL (8.9 mmol/L) are likely to experience systemic complications from acute pancre-

Table 3. Incidence of Complications of Alcoholic Pancreatitis

Variable	No. (%) of Patients	Complication	Frequency
Systemic	26 (25)		
Pulmonary	17 (16)	Mechanical ventilation	17
		ARDS	9
		Pneumonia	4
Infectious	11 (10)	Sepsis	11
Renal	8 (8)	ARF	8
		ARF requiring dialysis	1
Cardiovascular	5 (5)	Arrhythmias	4
		Myocardial infarct	1
		Cardiac arrest	3
Hematologic	2 (2)	Coagulopathy requiring transfusion	2
Gastrointestinal	1 (1)	Bleeding requiring transfusion	1
Death	6 (6)		

Abbreviation: ARDS, adult respiratory distress syndrome; ARF, acute renal failure.

Table 4. Prevalence of Organ System Failure and Associated Mortality

Organ System	No. of Patients	Mortality, %
Pulmonary	9	67
Renal	9	55
Cardiovascular	6	67
Hepatic	3	100
Hematologic	2	50

Table 5. Bivariate Analysis of 4 Previously Significant Variables for Systemic Complications and Death*

Variable	Patients With Severe Complication (n = 26)	Patients With No Complication (n = 79)	P Value	Death (n = 6)	Survival (n = 99)	P Value
Heart rate, beats/min	109 (90-121)	92 (77-106)	.005	104 (88-120)	98 (78-110)	.03
WBC count, $\times 10^3/\mu\text{L}$	17 (13-19)	11 (8-15)	<.001	20 (17-23)	12 (9-15)	<.001
SUN level, mg/dL	13 (10-19)	11 (8-14)	.04	15 (10-20)	11 (9-15)	.10
Serum glucose, mg/dL	157 (114-207)	118 (98-146)	.002	150 (135-180)	123 (99-155)	.20

Abbreviations: SUN, serum urea nitrogen; WBC, white blood cell.

SI conversion factors: To convert SUN to millimoles per liter, multiply by 0.375; to convert serum glucose to millimoles per liter, multiply by 0.05551.

*Values indicate medians (interquartile ranges).

†Boldfaced P values indicate statistical significance.

atitis, and therefore, should be admitted to a monitored bed. On the other hand, patients with WBC counts less than $17 \times 10^3/\mu\text{L}$ are highly unlikely to die as a result of pancreatitis.

Current pancreatitis scoring systems (Ranson, Imrie, and APACHE II) are well supported in the literature but are cumbersome, not immediately predictive, and the required indexes are often not routinely measured in the emergency department.^{1,7,10,18} Computed tomography and peritoneal lavage have been shown to be useful methods of prognostication, but invasiveness, risk, and cost are limiting factors, and routine use is not recommended.^{4,5,7} The levels of C-reactive protein,¹⁶ urine trypsinogen activation peptide,¹⁹ and interleukins 6 and 8 have recently earned attention as possible predictors, but results are often not reported for at least 48 hours, assay tests are not widely available, and further prospective studies are needed.²⁰ On the other hand, the serum glucose level and WBC counts are routinely available on admission to the hospital, making these ideal clinical predictors. We compared the predictive values resulting from our multivariate analysis with that of an admission Ranson score. We modified Ranson's original criteria to include only the initial 5 admission variables and excluded the 48-hour secondary criteria.

Although there are numerous causes of acute pancreatitis, there is believed to be a common final pathway. In most cases, this end point merely consists of inflammation of the peripancreatic fat without systemic effects. On the other hand, in severe cases of acute pancreatitis, regardless of origin, destruction of pancreatic tissue occurs, resulting in a systemic inflammatory response and islet cell dysfunction. This explains why hyperglycemia and leukocytosis were associated with the development of complications requiring ICU management in our studies of both gallstone and alcoholic pan-

creatitis. Mortality rates have also been shown to be similar in both diseases.^{9,21}

Only first episodes of alcoholic pancreatitis were included in our study. It has been previously documented that the first 1 or 2 episodes of pancreatitis are, in fact, the most severe and carry the most risk of an associated systemic complication or death.^{1,9} In its chronic form, after multiple episodes, the clinical course tends to be more benign, and systemic complications from acute episodic flares are rare, seldom requiring admission to a monitored setting. Retrospectively applying the criteria for the serum glucose level and WBC count to our study group, we estimated that nearly half of the patients may have been unnecessarily placed in the ICU by the admitting team. Future prospective studies are needed to determine if the use of our criteria truly results in improved allocation of critical care beds and cost efficiency.

We also examined the influence of MSOF secondary to acute alcoholic pancreatitis on patient mortality. The development of MSOF is responsible for 30% to 50% of deaths of acute pancreatitis.^{21,22} In this study, 12 patients had at least 1 organ system fail. Three patients had isolated pulmonary failure and 2 had isolated renal fail-

Table 6. Multivariate Analysis of Systemic Complications and Death*

Variable	P Value (Systemic Complications)	P Value (Death)
Heart rate	.32	.94
WBC count	.04	.006
SUN level	.19	.85
Serum glucose level	.01	.56

Abbreviations: SUN, serum urea nitrogen; WBC, white blood cell.
*Boldfaced P values indicate statistical significance.

Table 7. Predictive Values for Systemic Complications*

Variable	Sensitivity	Specificity	PPV	NPV
WBC count $\geq 17 \times 10^3/\mu\text{L}$	50 (30-70)	91 (83-96)	65 (41-85)	85 (75-92)
Serum glucose level ≥ 160 mg/dL	50 (30-70)	85 (75-92)	52 (31-72)	84 (74-91)
WBC count $\geq 17 \times 10^3/\mu\text{L}$ and serum glucose level ≥ 160 mg/dL	31 (14-52)	97 (91-100)	80 (44-98)	81 (72-88)
Ranson score				
>0	89 (70-98)	67 (56-77)	47 (33-62)	95 (85-99)
≥ 3	19 (7-39)	100 (95-100)	100 (48-100)	79 (70-87)

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; WBC, white blood cell.
SI conversion factor: To convert serum glucose to millimoles per liter, multiply by 0.05551.
*Data are given as percentage (95% confidence interval).

Table 8. Predictive Values for Death*

Variable	Sensitivity	Specificity	PPV	NPV
WBC count $\geq 17 \times 10^3/\mu\text{L}$	83 (36-100)	85 (76-91)	25 (9-49)	99 (94-100)
Ranson score				
>0	100 (54-100)	57 (46-67)	12 (5-25)	100 (94-100)
≥ 3	33 (4-78)	97 (91-99)	40 (5-85)	96 (90-99)

Abbreviations: NPV, negative predictive value; PPV, positive predictive value; WBC, white blood cell.
*Data are given as percentage (95% confidence interval).

ure, and all of them survived. Three patients had 2 failed organ systems, and all of these patients survived. Six patients had failure of 3 or more organ systems, and all of these patients died. Since all of the deaths were associated with MSOF, it could be inferred that patients having a WBC count less than $17 \times 10^3/\mu\text{L}$ would have a 99% likelihood of not developing MSOF. This is slightly better than Ranson's score, in which a patient with less than 3 Ranson criteria would have a 96% likelihood of avoiding MSOF. Thus, in high-risk patients with an elevated WBC count, prompt aggressive resuscitation and intensive management are vital.

CONCLUSIONS

In patients with first-time alcoholic pancreatitis, 2 simple admission values—WBC count and serum glucose level—are useful predictors of the development of major systemic complications requiring ICU monitoring and/or mortality. The predictive values of leukocytosis and hyperglycemia compared favorably with those of the admission Ranson score.

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