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ORIGINAL ARTICLE

Factors Affecting Mortality in Patients with Acute Pancreatitis and Serum Calcipressin-1 (RCAN-1) Levels

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Abstract

Introduction: Acute pancreatitis (AP) is one of the most common diseases of the gastrointestinal tract. AP is a pancreatic disease with high mortality and morbidity, which can cause local and systemic complications This study aimed to determine factors that effect mortality in this patient group and whether serum RCAN-1 level can be used as a novel marker for predicting diagnosis and mortality in patients with AP and to investigate the factors affecting mortality in this patient group.

Materials and methods: This prospective clinical trial was conducted between Feb 1, 2020 and August 1, 2020 in the emergency department of a tertiary university hospital. Seventy-four patients (patient group) diagnosed with AP in the emergency department and an equal number of healthy volunteers (control group) who did not have any chronic diseases were included in the study.

Results: It have been determined that; increase in WBC, CRP, total bilirubin, and direct bilirubin values and decrease in calcium, pH, and HCO_3 values significantly increased the mortality risk in the patient group. Mean RCAN-1 level was 1002.4 ± 353.1 pg/ml in the patient group and 421.9 ± 81.1 pg/ml in the control group. Accordingly, a significant difference was found in RCAN-1 levels between the patient and control groups ($Z = -10.399$, $p < 0.001$). In addition, no correlation was found between RCAN-1 level and age, sex, Ranson and Bedside Index for Severity in Acute Pancreatitis (BISAP) scores, and etiological factors in patients with AP. When the effect of laboratory values on mortality was examined, it was seen that Furthermore, the high RCAN-1 levels detected in patients with AP did not have a significant effect on mortality.

Conclusion: In order to determine the factors that effect mortality in AP patients, we can use WBC, CRP, total bilirubin, and direct bilirubin, calcium, pH, and HCO_3 levels, but RCAN-1 levels can be used in the diagnosis but not for mortality. The most important advantages of the mortality estimation system created in the present study are that it can be used at the time of diagnosis and can be safely repeated after 24-48 hours without the need for additional data. Hence, the system can be conveniently used in the emergency department.

Keywords

Acute pancreatitis, Mortality, Calsipressin-1

Introduction

Acute pancreatitis (AP) is one of the most common diseases of the gastrointestinal tract. AP is a pancreatic disease with high mortality and morbidity, which can cause local and systemic complications. Pancreatic digestive enzymes become activated owing to an etiological factor, thereby creating widespread inflammation (systemic inflammatory response syndrome) by inflaming the pancreas and surrounding tissues [1-3].

Calcipressin-1 (RCAN-1), a product of the human DSCR1 (Adapt78) gene, plays a role in the adaptation of cells to oxidative stress and temporarily prevents apoptosis of cells against low levels of oxidative stress [4]. RCAN-1 exerts its activity by binding to the protein phosphatase subunit of calcineurin, a calcium-

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dependent serine-threonine phosphatase, and acts as an endogenous inhibitor of calcineurin [5]. In adults, the DSCR1 gene is highly expressed in the heart, brain, skeletal muscle, and pancreatic tissues [6]. Calcipressin has been shown to play an important role in diseases such as cardiac hypertrophy and atherosclerotic diseases, Down syndrome, and Alzheimer's disease, but its specific role in the pancreas is yet to be elucidated [7]. This study aimed to determine whether serum RCAN-1 level can be used as a novel marker for predicting diagnosis and mortality in patients with AP and to investigate the factors affecting mortality in this patient group.

Materials and Methods

This prospective clinical trial was conducted between Feb 1, 2020 and August 1, 2020 in the emergency department of a tertiary university hospital. The study was performed according to the World Medical Association Declaration of Helsinki for studies on human subjects. Before starting the study, ethical approval was obtained from the Scientific Research Ethics Committee of our university (02/17/2020, protocol no: INCEF-BAEK 04/11). Seventy-four patients (patient group) diagnosed with AP in the emergency department and an equal number of healthy volunteers (control group) who did not have any chronic diseases were included in the study. AP diagnosis was made based on positivity of two of the following three findings: 1) Sudden onset of upper abdominal pain. 2) Serum amylase or lipase level exceeding three times the upper normal limit. 3) Detection of AP-specific findings with ultrasonography or computed tomography [2]. Patients under the age of 18 years, pregnant women, patients with Alzhzeimer's disease/dementia, patients with Down syndrome, patients with active cancer and atherosclerosis comorbidity patients whose clinical outcome could not be detected, and patients who did not volunteer to participate in the study were excluded.

Analysis of serum calcipressin-1 (RCAN-1) levels

Human (RCAN1) ELISA kit 201-12-6385 of Shanghai Sunred Biological Technology Co. was used for the determination of serum RCAN-1 levels. Measurements were performed in the Medical Biochemistry Department Laboratory of our university with the Biotek Instruments µQuant™ Model 218731 device via sandwich enzyme linked immunosorbent assay method.

Statistical analysis

Shapiro-Wilk test was used to check whether the data conformed to normal distribution. Student's t-test or Mann-Whitney U test were used to compare variables between two groups, and Kruskal-Wallis test was used to compare variables between more than two groups. The relationships between qualitative variables were investigated using Pearson's chi-square test and Fisher's exact test. The relationship between quantitative variables was examined using Spearman correlation analysis. Univariate logistic regression and multiple logistic regression (forward Wald method) analyses were performed to identify the risk factors and develop a mortality estimation model. Receiver operating characteristic (ROC) analysis (Youden index) was used to evaluate model performance and determine the cut-off point. The De Long test was applied to compare areas under the curve (AUC). Descriptive statistics were presented as mean and standard deviation, median, interquartile range, and minimum-maximum for quantitative variables and as frequency and percentage for qualitative variables. IBM SPSS (23.0) package program, R program pROC package, and the easy ROC program were used for all statistical analyses [8]. $P < 0.05$ was accepted as statistically significant in all analyses.

Results

The mean age of the patients diagnosed with AP was 57.1 ± 19.6 years (19-98 years), and 50.7% (n = 35) of the patients were women. No statistically significant difference was found between the patient and control groups in terms of age and sex ($p > 0.05$) (Table 1).

Etiological factors in patients diagnosed with AP were examined. It was determined that 50% (n = 37) were caused by biliary factors, 18.9% (n = 14) were caused by alcohol, and 31.1% (n = 23) were caused by other factors (hyperlipidemia, hypercalcemia, drugs, toxins, infections, trauma, autoimmune, iatrogenic, etc.) (Table 1).

Vital findings at admission and laboratory values of patients diagnosed with AP in the emergency department are shown in detail in Table 1.

Calcipressin-1 (RCAN-1) levels in patients with acute pancreatitis

Mean RCAN-1 level was 1002.4 ± 353.1 pg/ml in the patient group and 421.9 ± 81.1 pg/ml in the control group. Accordingly, a significant difference was found in RCAN-1 levels between the patient and control groups ($Z = -10.399$, $p < 0.001$). In addition, no correlation was found between RCAN-1 level and age, sex, Ranson and Bedside Index for Severity in Acute Pancreatitis (BISAP) scores, and etiological factors in patients with AP (Table 2).

Analysis of mortality

The 30-day mortality rate in patients with AP included in this study was 16.2% (n = 12).

Relationship between demographic characteristics and mortality

A significant relationship was found between the age of patients diagnosed with AP and mortality (t = -2.012,

Table 1: Descriptive statistics.

Demographic data		Study groups			
		Patients (n = 74)	**Control (n = 74)**	**Z/χ^2**	**p**
Age (year)	Mean ± SD	57.1 ± 19.6 (19-98)	52 ± 14.6 (19-86)	-1.928	0.054
	Med (IQR)	58.5 (27.5)	54.5 (15)		
Sex n (%)					
Female		35 (%50.7)	34 (%49.3)	0.027	0.869
Male		39 (%49.3)	40 (%50.7)		

Descriptive characteristics of the patient group		
Age (years)	57.1 ± 19.6 (19-98)	58.5 (27.5)
Sex n (%)	Female 35 (50.7%)	
	Male 39 (49.3%)	
Etiological factors n (%)		
Biliary	37 (50)	
Alcohol	14 (18.9)	
Other factors	23 (31.1)	
	Mean ± SD (min-max)	Med (IQR)
Vitals		
Systolic blood pressure (mmHg)	122.7 ± 25.6 (60-198)	120 (32)
Diastolic blood pressure (mmHg)	69.1 ± 17.1 (40-130)	65 (20)
Peak heartbeat (/min)	100.1 ± 18.7 (65-155)	100 (25)
Axillary body temperature (°C)	36.9 ± 0.7 (35-39)	37 (0.8)
Respiratory rate (/min)	14.9 ± 2.9 (11-25)	14.5 (5)
Laboratory values		
WBC (10^3/uL)	12.3 ± 4.8 (2.7-28)	12 (8)
Neu (10^3/uL)	9.4 ± 4.9 (0.6-26)	8.4 (6)
Lym (10^3/uL)	2.2 ± 2.2 (0.1-13.7)	1.6 (1.5)
Neu/Lym	9.1 ± 11.7 (0.64-66)	4.5(9.3)
CRP (mg/dl)	6.9 ± 5 (0.2-19)	6 (6.1)
ALT (U/L)	142.3 ± 191.3 (9-1028)	61 (146.5)
AST (U/L)	139.6 ± 186.5 (10.7-24)	74 (122.8)
Total bilirubin (mg/dl)	2.5 ± 2.2 (0.2-9.4)	1.7 (2.9)
Direct bilirubin (mg/dl)	1.5 ± 1.7 (0.1-9)	0.8 (1.7)
Calcium (mg/dl)	8.9 ± 0.7 (7.4-10.6)	9 (1)
LDH (U/L)	428.9 ± 279.2 (140-2000)	379 (236)
pH	7.4 ± 0.1 (7.1-7.98)	7.4 (0.1)
HCO_3 (mEq/L)	21.5 ± 3.8 (8-29)	22 (4)
Amylase (U/L)	1071.7 ± 1067.9 (32-4571)	717 (1239.8)
Lipase (U/L)	2236.4 ± 2652.4 (38-12358)	1011 (2481.5)
Mortality n (%) 12 (16.2)		

SD: Standard Deviation; Med: Median; IQR: Interquartile Range other Factors Hyperlipidemia. Hypercalcemia. Drugs. Toxins. Infections

p = 0.048). The mean age of the surviving patients was 55.2 ± 18.6 years, whereas the mean age of the patients who died was 67.3 ± 22.3 years. No statistically significant difference was found in the mortality rate with respect to sex (χ^2 _ 0.042, p = 0.838) (Table 3).

In patients with AP, the mortality rate was 10% in patients without chronic diseases, 18.2% in those with one chronic disease, 26.7% in those with two chronic diseases, and 11.8% in those with three chronic diseases. No significant relationship was found between the number of chronic diseases and mortality (p = 0.572) (Table 3). When the etiological factors of AP

Table 2: RCAN-1 Levels in patients with acute pancreatitis.

RCAN-1 levels (pg/ml)					
Groups		**Mean ± SD (min-max)**	**Median (IQR)**	**z**	**p**
Control (n = 74)		421.9 ± 81.1 (218.08-549.87)	443.4 (139.1)		
Patients (n = 74)		1002.4 ± 353.1 (469.3-2100.1)	950 (393.1)	-10.399	< 0.001
Demographic characteristics					
Sex	Female	715.2 ± 381.1 (289.5-2100)	545.1 (506.6)	-0.129	0.898
	Male	709.5 ± 395.1 (218.08-2095.4)	549.9 (550.7)		
Age				0.142	0.086
Etiological factors					
Biliary		1043.8 + 410.6 (469.3 - 2100.1)	915.3 (466.4)		
Alcohol		933.2 + 200.2 (574.83 - 1158)	1007 (408)	0.268	0.875*
Other		977.8 + 328 (586.81 - 1611)	843 (638.5)		
				r	**p**
Vitals	Systolic blood pressure (mmHg)			0.078	0.511
	Diastolic blood pressure (mmHg)			-0.101	0.394
	Peak heartbeat (/min)			-0.188	0.109
	Axial body temperature (°C)			-0.184	0.116
	Respiratory rate (/min)			-0.152	0.197
Prognostic scoring systems	Ranson			-0.009	0.940
	BISAP			0.037	0.753
Laboratory values	Amylase (U/L)			0.191	0.102
	Lipase (U/L)			0.225	0.053

r: correlation coefficient; SD: Standard Deviation; Med: Median; IQR: Interquartile Range; *Chi-square test. Other factors hyperlipidemia. hypercalcemia. drugs. toxins. infections.

Table 3: Relationship between demographic characteristics and mortality.

Mortality					
Demographic characteristics		**Surviving** (n = 62)	**Deceased** (n = 12)	**t/χ^2**	p
Age (years) Mean ± SD (Min-Max)		52.2 ± 18.6 (19-91)	71.3 ± 12.2 (20-98)	-2.012	0.048
Med (IQR)		57 (25.8)	65 (35)		
Sex	Female	29 (82.9)	6 (17.1)		
(n. %)	Male	33 (84.6)	6 (15.4)	0.042	0.828
Number of chronic diseases n (%)					
No of chronic diseases		18 (90.0)	2 (10.0)		
1		18 (81.8)	4 (18.2)		
2		11 (73.3)	4 (26.7)		
3		15 (88.2)	2 (11.8)	2.037*	0.572
Etiological factors n (%)					

Biliary	31 (83.8)	6 (16.2)		
Alcohol	13 (92.9)	1 (7.1)		
Other	18 (78.3)	5 (21.7)	1.230*	0.588

*: Fisher's exact test; SD: Standard Deviation; Med: Median; IQR: Interquartile Range

Table 4: Relationship of vital findings and prognostic scoring systems with mortality.

Mortality					
Vital findings		**Surviving** (n = 62)	**Deceased** (n = 12)	**t/Z**	**p**
Systolic blood pressure	Mean ± SD	127 ± 22.6	97.8 ± 26.5	-3.694	< 0.001
	(Min-Max)	(90-198)	(60-160)		
	Med (IQR)	120 (40)	90 (26.3)		
Diastolic blood pressure		71.3 ± 16.5	57.7 ± 16.5	-2.407	0.016
		(40-130)	(40-80)		
		65 (20)	56 (37.5)		
Peak heartbeat (/ min)		95.8 ± 16.1	122.8 ± 16.2	-5.150	< 0.001
		(65-136)	(100-155)		
		97.5 (25)	120 (24.5)		
Axial body temperature		36.9 ± 0.7	37.1 ± 0.8	-0.754	0.451
		(35-39)	(36-38.3)		
		37 (0.8)	37 (1.6)		
Respiratory rate (/ min)		14.5 ± 2.3	17.3 ± 4.3	-2.186	0.029
		(11-19)	(12-25)		
		14 (4)	17.5 (5)		
Prognostic scoring systems				**Z**	**p**
Ranson	Mean ± SD	2.2 ± 1.1	4 ± 1.1	-4.251	< 0.001
	(Min-Max)	(0-4)	(1-5)		
	Med (IQR)	2 (2)	4 (1)		
BISAP		3.5 ± 1.5	5.6 ± 1.3	-4.031	< 0.001
		(1-6)	(4-8)		
		3 (2.1)	5.5 (2.5)		

SD: Standard Deviation; Med: Median; IQR: Interquartile Range. BISAP: Bedside Index of Severity in Acute Pancreatitis. RCAN-1: Calcipressin-1

were examined with respect to mortality, the mortality rate was 16.2% in patients with biliary etiology, 7.1% in patients with alcohol etiology, and 21.7% in patients with other etiological factors. When the relationship between mortality and AP etiologies was examined, no statistically significant relationship was found (p = 0.588) (Table 3).

Relationship between vital findings and mortality

The relationship between vital parameters of the patients at the time of admission to the emergency department and mortality was examined. A statistically significant difference was found in all vital parameters except fever. Systolic and diastolic blood pressure values were significantly lower, whereas respiratory rate and heart rate were significantly higher in patients who died (Table 4).

Relationship between laboratory findings and mortality

When the relationship between laboratory findings and mortality was examined in patients with AP, a significant relationship was found between mortality and white blood cell (WBC) count, C reactive protein (CRP), total Bilirubin, direct bilirubin, calcium, and HCO_3 values. WBC, CRP, total bilirubin, and direct bilirubin values were significantly higher, whereas calcium and HCO_3 values were significantly lower in patients who died. In contrast, no statistically significant difference was found in amylase, lipase, and RCAN-1 levels with

Table 5: Relationship between laboratory findings and mortality.

		Mortality			
		Surviving (n = 62)	**Deceased** (n = 12)	**Z**	**p**
WBC (10^3/uL)	Mean ± SD (Min-Max) Med (IQR)	11.2 ± 4.1 (2.7-22) 11.5 (6)	17.6 ± 4.9 (7-28) 17.2 (4)	-4.759	< 0.001
Neu (10^3/uL)		8.9 ± 4.5 (0.6-24) 8.1 (5.1)	11.8 ± 6.2 (3.1-26) 12.5 (6.7)	-1.606	0.108
Lym (10^3/uL)		2 ± 1.8 (0.1-10) 1.6 (1.4)	3 ± 3.7 (0.5-13.7) 1.9 (3.4)	-0.440	0.660
Neu/ Lym		8.5 ± 10.7 (1.5-66) 4.5 (6.8)	12.2 ± 16.1 (0.6-52) 4.8 (14.6)	-0.073	0.942
CRP (mg/dL)		6.1 ± 4.5 (0.2-18) 6 (6.4)	11.1 ± 5.5 (3-19) 10 (8)	-2.902	0.004
ALT (u/L)		142.2 ± 203.4 (9-1028) 57 (139.8)	142.8 ± 116 (14-379) 143.5 (171.3)	-0.873	0.383
AST (u/L)		140.5 ± 200.1 (10-1221) 60 (119)	135.5 ± 93.1 (26-362) 116 (135.3)	-1.254	0.210
Total Bilirubin (mg/dL)		2.2 ± 2 (0.2-9.4) 1.4 (2.3)	4.2 ± 2.5 (0.5-8.5) 4 (3.9)	-2.678	0.007
Direct Bilirubin (mg/dL)		1.3 ± 1.6 (0.1-9) 0.7 (1.5)	2.6 ± 1.9 (0.1-6) 2.6 (2.5)	-2.447	0.014
Ca (mg/dL)		9.3 ± 0.5 (8.6-10.6) 9.2 (0.7)	8.8 ± 0.7 (7.4-10.3) 8.8 (1.3)	-2.226	0.029
LDH (u/L)		408.5 ± 225.2 (140-1495) 351.5 (253.8)	534.4 ± 470.2 (250-2000) 399 (153)	-1.093	0.274
Albumin (g/dL)		3.5 ± 0.9 (2.1-4.6) 3.5 (1)	3.5 ± 0.6 (2.4-5.6) 3.4 (1.5)	-0.06	0.953
Amylase (u/L)		1114.8 ± 1110 (50-4571) 693.5 (1457.3)	848.7 ± 818.6 (32-3000) 766.5 (912.5)	-0.352	0.725
Lipase (u/L)		2319.5 ± 2825 (38-12358) 959.5 (2578.5)	1806.7 ± 1480.7 (100-5470) 1569 (1942.5)	-0.191	0.849
pH		7.4 ± 0.1 (7.06-7.98) 7.4 (0.1)	7.3 ± 0.2 (7.01-7.44) 7.3 (0.3)	-1.671	0.095
HCO_3 (mEq/L)		22.3 ± 2.5 (14-29) 22 (3)	17.4 ± 6.1 (8-24) 20 (12.5)	4.640	< 0.001
RCAN-1 (pg/ml)		1023.3 ± 360.9 (574.8-2100.1) 966.2 (442.3)	894 ± 300.2 (469.3-1611) 805 (393.9)	-1.012	0.312

SD: Standard deviation; Med: Median; IQR: Interquartile range. RCAN-1: Calcipressin-1

respect to mortality (Table 5).

Simple regression analysis was performed to determine the factors affecting mortality risk in patients with AP. It was determined that demographic characteristics of patients, number of chronic diseases, and etiological factors had no significant effect on mortality (Table 6). When the effect of vital findings of patients with AP at the time of emergency admission on mortality was examined, all variables other than axillary body temperature were found to have a significant effect on mortality. It was found that decrease in systolic and diastolic blood pressure and increase in pulse and respiratory rate exacerbated the risk of mortality (Table 6).

When the effect of laboratory values on mortality was examined, it was seen that increase in WBC, CRP, total bilirubin, and direct bilirubin values and decrease in calcium, pH, and HCO_3 values significantly increased the mortality risk in the patient group. Furthermore, the high RCAN-1 levels detected in patients with AP did not have a significant effect on mortality.

Simple logistic regression analysis revealed factors with an effect on mortality of less than 20% margin of error ($p < 0.20$). Using these factors, multivariate logistic regression analysis was performed to create a model that could be used to predict mortality in patients with AP. Fit indices for the model were determined, which showed acceptable goodness of fit with the data (χ^2 = 2.035, p = 0.980). According to Nagelkerke result, the model explained 84.3% of the variance in mortality.

According to the results obtained from 74 patients with AP, a one-unit decrease in systolic blood pressure increased the risk of mortality by approximately 1.2 times and a one-unit increase in heart beat increased the risk of mortality by 1.25 times. Although not statistically significant, CRP and total bilirubin were included in the model owing to their contribution to the model (Table 7).

Table 6: The effect of demographic characteristics on mortality.

	Odds ratio	95% Confidence interval	p
Age	1.036	0.999-1.073	0.055
Sex			
Female	1.138	0.330-3.919	0.838
Male (ref)	-	-	-
Number of chronic diseases			
0 (ref)	-	-	-
1	2.000	0.324-12.329	0.455
2	3.273	0.512-20.934	0.210
3	1.200	0.15-9.57	0.863
Etiology			
Biliary	0.697	0.186-2.612	0.592
Alcohol	0.277	0.029-2.66	0.266
Other (ref)	-	-	-
Vital findings			
Systolic blood pressure (mmHg)	0.928	0.885-0.973	0.002
Diastolic blood pressure (mmHg)	0.939	0.893-0.988	0.015
Heartbeat (n/min)	1.112	1.048-1.18	< 0.001
Axial body temperature (°C)	1.451	0.627-3.359	0.385
Respiratory rate (/min)	1.374	1.089-1.735	0.007

ref: Reference group

Table 7 shows the performance evaluation of the model created using Ranson and BISAP criteria, which are used to determine the risk of mortality in patients diagnosed with AP in the emergency department.

ROC analysis using probability estimates on mortality revealed that the AUC for the model created by logistic regression analysis was 0.988, whereas the AUC values of the Ranson and BISAP criteria were 0.880 and 0.856, respectively. When the difference in AUC performance values was examined, it was concluded that the model was significantly better than the BISAP criterion. However, no significant difference was found with the Ranson criterion (Model-Ranson: p = 0.125, Model-BISAP: p = 0.039). Figure 1 shows the ROC curves of the

Table 7: Multiple Logistic Regression Model and ROC Analysis for Mortality.

Multiple logistic regression model				
	ß (SH)	**Odds ratio**	**95% Confidence interval**	**p**
SBP	-0.180 (0.084)	0.835	0.709-0.985	0.032
Pulse	0.225 (0.098)	1.252	1.033-1.519	0.022
CRP	0.751 (0.399)	2.118	0.969-4.632	0.060
Total bilirubin	0.943 (0.545)	2.567	0.882-7.474	0.084
Nagelkerke: 0.843. **Cox and Snell R Square:** 0.495. -2 Log likelihood: 14.980				
Hosmer and Lemeshow test: χ^2 = 2.035. df = 8. p = 0.980				

ROC analysis for mortality						
	AUC	**Cut-off**	**Sensitivity**	**Specificity**	**PPV**	**NPV**
Ranson	0.880	4	0.833	0.887	0.588	0.965
BISAP	0.856	3	0.833	0.839	0.5	0.963
Model	0.988	0.185	1	0.919	0.706	1

ß: Model coefficient; SE: Standard Error; AUC: Area under the Curve; PPV: Positive Predictive Value; NPV: Negative Predictive Value. BISAP: Bedside index of severity in acute pancreatitis

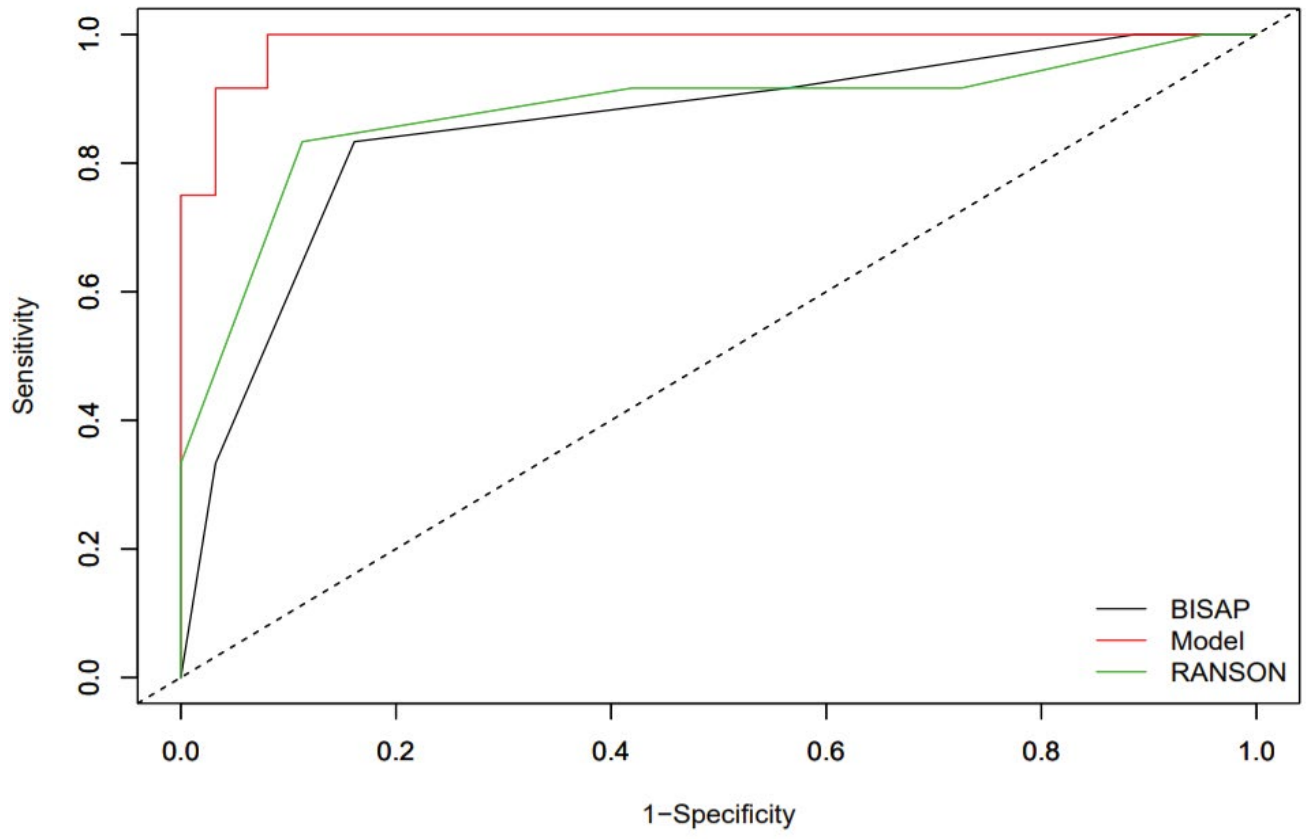

Figure 1: ROC Curves of logistic regression model and BISAP and Ranson Criteria.

logistic regression model and Ranson and BISAP criteria.

With a cut-off value of 0.185, the sensitivity, specificity, positive predictive value, and negative predictive value of the model were calculated to be 1, 0.919, 0.706, and 1, respectively. With a cut-off value of 4 for Ranson criterion and 3 for BISAP criterion, sensitivity was 0.833 for both criteria, specificity was 0.887 and 0.839, respectively, positive predictive value was 0.588 and 0.5, respectively, and the negative predictive value was 0.965 and 0.963, respectively.

Discussion

Of late, the mortality rate of AP has been decreasing. According to literature, the mortality rate has decreased from 10% to 2%-7% in recent years. In a study involving 129 patients with AP in Turkey, only 6 patients died [1]. In another study, 60 patients were screened and

the mortality rate was found to be 3% [3]. In a study conducted by Tamer, et al. [2], the overall mortality rate was 5%, with no mortality in mild AP cases and 19% in severe cases. In their study, Sharma, et al. [9] reported a mortality rate of 7.6%. In the present study, the mortality rate in the first 30 days after emergency admission was 16.2%. The mortality rate observed in the present study is higher than that reported in other studies in the literature. This discrepancy may be attributed to the fact that our hospital is a tertiary center and, therefore, a high number of patients with comorbidities are referred to our hospital for follow-up and treatment.

It is known that sex does not have any effect on the severity and mortality of AP [1-3]. In the present study, 17.1% of women and 15.4% of men died. Consistent with the literature, no significant difference was found in the mortality rate between the two sexes.

Advanced age is associated with an increase in mortality in many diseases, and it is closely associated with mortality in AP too. Carvalho, et al. [10] found a significant correlation between advanced age and mortality. In a meta-analysis of 1.203 patients in 18 centers, it was reported that advanced age and accompanying comorbid diseases had an important role in predicting AP severity and prognosis [11]. Weitz, et al. [12] showed that age and comorbid diseases were important factors for predicting pancreatitis severity and mortality.

Other studies have also been performed to examine the relationship between etiological factors and mortality in patients with AP. In China, Zhu, et al. [13] reported that although biliary causes were at the forefront in patients with AP, idiopathic factors (15.9%) were the most common cause of mortality, while biliary factors accounted for 5.6% of the mortality. In the United Kingdom, 283 patients with AP were evaluated and no significant difference was found between the groups in terms of etiological factors [14]. In a retrospective study conducted by Chen, et al. [15] with 497 patients in China, no significant correlation was found between etiological factors and disease severity. Consistent with the literature, no statistically significant difference was found in mortality with respect to etiological factors in the present study too.

Amylase levels measured in patients with AP have no predictive value regarding the severity of the disease, morbidity, or mortality. However, an elevation of more than three times the normal level is highly specific for the diagnosis of pancreatitis. Amylase levels higher than three times the normal level in patients with abdominal pain have high specificity for the diagnosis of pancreatitis, but they have no predictive value for disease severity, morbidity, or mortality. Although there was no correlation between the lipase level measured in these patients and AP severity and mortality, studies on some pediatric patients with AP have shown that high lipase level may be predictive of severity in AP [16]. In the present study, when the relationship between amylase and lipase levels and mortality was examined in patients with AP, no significant correlation with mortality was found for either of the parameters.

Popa, et al. [17] reported a positive correlation between hyperglycemia and high WBC levels and mortality in patients with AP. In a study involving 214 patients, Liu, et al. [18] found a significant difference in laboratory findings such as WBC, creatine, blood urea nitrogen, lactate dehydrogenase, CRP, Ca, partial pressure of oxygen (PaO_2), and base deficiency in the group that developed severe and persistent organ failure compared with the other group. Their linear regression analysis revealed that BE, PaO_2, and Ca were independent predictors. In the literature, studies evaluating the relationship between CRP and AP severity showed that CRP value was generally higher in patients having severe AP when compared with those having mild AP. In the study conducted by Zrnic, et al. [19], it was shown that CRP level was correlated with disease severity in patients with AP and that it was a useful factor in predicting possible complications. In the study conducted by Dambrauskas, et al. [20], it was determined that CRP and leukocyte values were important distinctive parameters in the development of infected necrotizing pancreatitis. In the study by Schütte, et al. [21], erythrocyte sedimentation rate and CRP were successful in determining AP severity in the first 24 hours. Given that hypocalcemia usually develops because of fat necrosis or sepsis, low serum calcium levels have been shown to be a marker of poor prognosis [22]. Furthermore, Castineira, et al. showed that peripheral venous blood gas is associated with decreased serum HCO_3 levels and AP severity and can be used for predicting mortality [23]. When the relationship between laboratory test parameters and mortality rate was examined in the present study, a significant relationship was found between mortality and WBC, CRP, total bilirubin, direct bilirubin, calcium, and HCO_3 values. WBC and CRP were higher in deceased patients than in surviving patients. It was found that both total and direct bilirubin values were significantly higher in deceased patients compared with surviving patients. Finally, mean HCO_3 level was 17.4 ± 6.1 mEq/L in deceased patients and 22.3 ± 2.5 mEq/L in surviving patients. HCO_3 levels were significantly lower in deceased patients than in surviving patients. In the present study, laboratory findings associated with mortality were generally consistent with the literature.

Simple logistic regression analysis was performed to determine the factors affecting mortality risk in patients with AP. In this analysis, it was found that demographic characteristics of the patient, number

of chronic diseases, etiological factors, and RCAN-1 levels had no significant effect on mortality. Decrease in systolic and diastolic blood pressure and increase in pulse and respiratory rate increased the mortality risk at a significance level of 5%. It was concluded that amylase and lipase levels did not have a significant effect on mortality. In addition, WBC, CRP, total bilirubin, direct bilirubin, calcium, pH, and HCO_3 values of the patients were found to be significant. Increase in WBC, CRP, total bilirubin, and direct bilirubin values and decrease in calcium value significantly increased the mortality risk. It was also observed that decrease in pH and HCO_3 values led to an increased risk of mortality in patients with AP.

Simple logistic regression analysis revealed the factors with an effect on mortality of less than 20% margin of error ($p < 0.20$). Using these factors, multivariate logistic regression analysis was performed to create a model that could be used to predict mortality in patients with AP.

There are a few limitations in this study. The present study was conducted in only one center. Multicenter studies should be conducted to validate the usefulness of the model obtained in the present study in determining mortality in AP.

In conclusion, in the present study, RCAN-1 levels were significantly higher in patients with AP compared with healthy controls. However, increased RCAN-1 level was not sufficient on its own to assess mortality risk and severity of AP. The most important advantages of the mortality estimation system created in the present study are that it can be used at the time of diagnosis and can be safely repeated after 24-48 hours without the need for additional data. Hence, the system can be conveniently used in the emergency department.

Conflict of Interest

There is no conflict of interest between the authors.

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