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The relationship of biochemical parameters and radiological parameters in the evaluation of the clinical severity of acute pancreatitis in the emergency department – a retrospective analysis

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ABSTRACT

Introduction and aim. Computed tomography severity index (CTSI) and Balthazar score are among the most frequently used scorings in the determination of severe acute pancreatitis. The primary purpose of this study is evaluation of the effects of biochemical parameters, Balthazar score and CTSI on mortality in acute pancreatitis. At the same time, correlations with biochemical parameters, CTSI and Balthazar score were evaluated in patients with AP.

Material and methods. In this study, the amylase, lipase, CRP, and procalcitonin values of patients diagnosed with acute pancreatitis were retrospectively recorded. Contrast-enhanced computed tomography (CECT) images obtained at the time of presentation to the emergency department or within seven days of admission were re-evaluated by two radiologists. The CTSI scores and Balthazar scores of the patients were calculated.

Results. The study included 240 patients. The amylase level of the patients was positively correlated with the Balthazar score at a statistically significant level (R=0.189, p=0.003). In addition,, the relationship between pancreatic scoring systems and mortality, the AUC value for CTSI was 0.9 (95% CI: 0.826-0.973) and was higher than other scoring systems.

Conclusion. CTSI had better performance in the prediction of mortality in patients with acute pancreatitis.

Keywords. acute pancreatitis, amylase, computed tomography severity index, emergency department, lipase

Introduction

Acute pancreatitis (AP) is an inflammatory condition of the pancreas, most commonly caused by gallstones or excessive alcohol use. AP mostly has a mild course with rapid clinical improvement following fluid resuscitation, management of pain and nausea, and early oral feeding. However, 20-30% of AP cases are severe. The mortality rate reaches 15% in patients with severe AP.[1] Therefore, these patients should be recognized early, and their treatment should be initiated in a timely and more aggressive manner.

Many algorithms, such as the Ranson criteria, Atlanta scoring, acute physiology and chronic health evaluation (APACHE) scoring, and computed tomography severity index (CTSI), Balthazar Score have been developed for the classification of AP according to clinical severity. Balthazar evaluated the CECTs of AP patients in his study in 1985 and defined a relationship between the clinical severity of AP and the images in CECT. According to this study, images in CECT were divided into five classes from A to E according to the clinical severity of AP. Then, Balthazar included pancreatic necrosis on CECT images of AP patients in his initial scoring and defined CTSI.[2] CTSI is a scoring system based on the grading of peripancreatic inflammation, pancreatic necrosis, and phlegmon formation within a week after the onset of AP, and it helps determine the severity of the disease.[1,3] Procalcitonin and C-reactive protein (CRP) are other parameters used to determine the severity of AP in clinical follow-up[1]. CRP and procalcitonin are elevated in the presence of inflammation. However, since both biomarkers increase in many inflammatory conditions, neither is specific to AP.[4] In addition, the use of CRP in the emergency department is limited due to the late peak (48-72 hours) of this parameter. However, considering that organ failure, sepsis, and pancreatic necrosis determine the severity of AP, increased CRP and procalcitonin can be useful in the evaluation of clinical severity in patients with AP.[5-7]

One of the necessary criteria for the diagnosis of AP is a high amylase or lipase value. It has been shown that serum lipase is preferred over serum amylase due to the limited sensitivity, specificity, and positive and negative predictive values of the latter.[8] In addition, lipase rises within three to six hours after the onset of AP, has a half-life of 6-15 hours, and is reabsorbed by renal tubules; therefore, it tends to remain elevated longer than amylase in patients with AP.[9] Amylase and lipase levels can also provide an idea concerning the etiology of AP.[10]

Aim

In the literature, there are studies comparing amylase, lipase, CRP, and procalcitonin parameters separately with CTSI.[11-13] However, we found no study that evaluated all these four parameters together with CTSI. Therefore, in the current study, we aimed to evaluate the correlation of amylase, lipase, CRP, and procalcitonin parameters with CTSI in AP.

Material and methods

This study was conducted retrospectively in the emergency department of a tertiary hospital. Approximately two hundred twenty-three thousand five hundred patients apply to the emergency department of the tertiary hospital where the study was conducted per year. Patients who presented to the emergency department of our hospital from January 1, 2017, through September 1, 2022, and were diagnosed with AP (ICD diagnosis code: K85, K85.8, and K85.9) were included in the study. Data were obtained by screening the electronic patient files from the hospital information management system. Approval for the study was obtained from the local ethics committee (decision number: 22, session: 8, date: 27.10.2022). The study was performed in accordance with the tenets of the Declaration of Helsinki.

Study population

Using the hospital management system, a total of 1,029 patients were identified to have presented to the emergency department and received a diagnosis of AP during the study period. Patients aged over 18 years without any other inflammatory disease, whose data and patient files were available in the electronic system, were included in the study. Cases where >48 hours had passed from the onset of symptoms were excluded from the study. Patients with malignancies, pregnant women, and patients with immunodeficiency, known kidney or liver dysfunction, inflammatory bowel diseases, or other inflammatory conditions were also excluded from the sample. In addition, since the CTSI values were to be calculated within the scope of the study, patients that did not undergo contrast-enhanced computed tomography (CECT) at the time of presentation to the emergency department or within 48 hours of admission, as well as those with poor image quality that was not suitable for the calculation of CTSI, were also excluded. Of the patients planned to be included in the study, those with missing data and those that wanted to be discharged from the hospital during clinical follow-up were also excluded. After applying all the inclusion and exclusion criteria, 240 patients were included in the sample. The patients included in the study were divided into two groups according to their clinical outcomes as those that died and those that were discharged (Fig. 1).

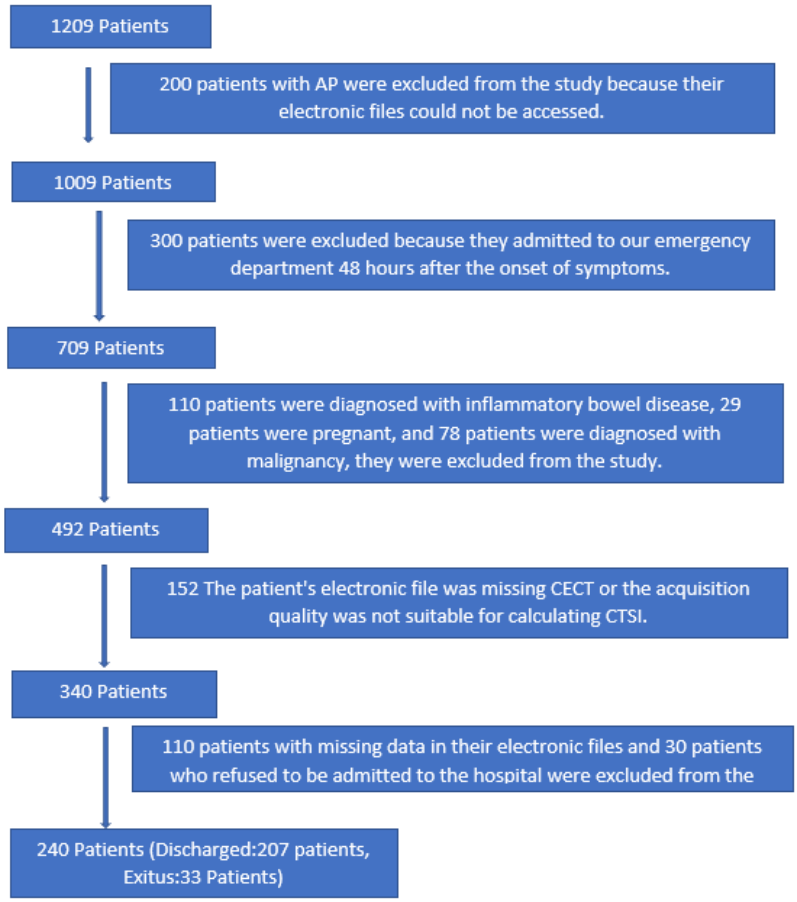

Fig. 1. Patient selection flow chart

Data collection

The patients' age, gender, laboratory results, clinical outcomes (mortality or discharge), and CECT images were obtained from the electronic files. Alkaline phosphatase (ALP), gamma glutamyl transferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, direct bilirubin, glucose, and blood urea nitrogen (BUN), creatinine, amylase, lipase, procalcitonin, CRP, white blood cell (WBC), hemoglobin, and hematocrit values measured from blood samples taken at the time of presentation to the emergency department were recorded.

CECT images obtained at the time of presentation to the emergency department or within seven days of admission, were re-evaluated by two radiologists with five to 10 years of professional experience. The CTSI scores of the patients were calculated using the Balthazar score and pancreatic necrosis degree. The Balthazar score was evaluated from A, B, C, D, and E according to the severity of pancreatitis, and the corresponding score was calculated as 0, 1, 2, 3, and 4, respectively. The presence of pancreatic necrosis was calculated by assigning a score of 0 for no necrosis, 2 for <30% necrosis, 4 for <30-50% necrosis, and 6 for >50% necrosis. The overall CTSI score was grouped as mild (0-3), moderate (4-6), and severe (7-10)[2] (Table 1).

Table 1. Balthazar Sore and CTSI[1]

Grade	CT Finding
A	Normal pancreas
B	Pancreatic enlargement
C	Pancreatic inflammation and/or peripancreatic fat
D	Single peripancreatic fluid collection
E	Two or more fluid collections and/or retroperitoneal air

CTSI [1]		Necrosis		
CT Grade	**Points**	**Percentage**	**Additional points**	**Severity index***
A	0	0	0	0
B	1	0	0	1
C	2	<30	2	4
D	3	30-50	4	7
E	4	>50	6	10

* CT grade points are added to points assigned for percentage of necrosis

Statistical analysis

Statistical analyses were performed using IBM SPSS v. 23.0 software package (IBM, Armonk, NY, USA). Categorical data were presented as frequency and percentages, and numerical data as mean and standard deviation if normally distributed and median and interquartile range (IQR) values otherwise. The Kolmogorov-Smirnov test was used to check the normality of data distribution. For the comparison of two groups in terms of non-normally distributed data, the Mann-Whitney U test was used. The Spearman correlation test was conducted for the correlation analysis of the data that did not show a normal distribution. The receiver operating characteristic (ROC) analysis was performed to explore the relationship of the Balthazar score, pancreatic necrosis grade, and CTSI with patient outcome. Multivariate logistic regression

analysis was performed to determine risk factors on death. Enter model was used in multivariate logistic regression analysis. Statistical significance was taken as $p<0.05$.

Results

The study included 240 patients, of whom 67.5% (n=162) were female, and the median age was 59 (47-74) years. When the distribution of the patients according to the groups was examined, it was determined that the median age of the mortality group (n=33) was 56 (44.5–72) years, and that of discharged group (n=207) was 60.0 (48–74) years, indicating no statistically significant difference (p=0.272). The GGT, AST, and ALT values were determined to be 83.5 (36.3–200.8), 56.0 (24.5–243.5), and 34.5 (17.3–125) respectively in the mortality group and 180.0 (42.5–388.5), 141.5 (50.3–295.5), and 122.5 (31.3–263), respectively in the discharged group. All three laboratory findings statistically significantly differed between the two groups ($p<0.05$). Table 2 presents the demographic characteristics and laboratory findings of the patients according to the groups.

Table 2. Demographic characteristics and laboratory findings of the patients according to the groups

Variable, median (IQ)	**Mortality (n = 33)**	**Discharged (n = 207)**	**p**
Age, years	56.0 (44.5–72)	60.0 (48–74)	0.272
Gander, n (%)			
Male	12 (5%)	66 (27.5%)	0.611
Female	21 (8.75%)	141 (58.75%)	
Alkaline phosphatase (U/L)	108.0 (68.5–172)	127.0 (91–208.3)	0.114
Gama glutamyl transferase (U/L)	83.5 (36.3–200.8)	180.0 (42.5–388.5)	0.015
Aspartate aminotransferase (U/L)	56.0 (24.5–243.5)	141.5 (50.3–295.5)	0.014
Alanine aminotransferase (U/L)	34.5 (17.3–125)	122.5 (31.3–263)	0.008
Total bilirubin (mg/dL)	0.88 (0.55–1.92)	1.07 (0.6–2.)	0.295
Direct bilirubin (mg/dL)	0.25 (0.12–0.82)	0.41 (0.18–1.09)	0.119
Glucose (mg/dL)	129.0 (107.5–151)	130.0 (108–161.5)	0.779

Blood urea nitrogen (mg/dL)	15.0 (10.3–18.7)	14.55 (11.68–18.57)	0.968
Creatinine (mg/dL)	0.69 (0.59–0.89)	0.75 (0.6–0.97)	0.297
Amylase (U/L)	1043 (465–1780)	1342 (689–2616)	0.118
Lipase (U/L)	2400 (1111.3–2985.9)	2657 (1500–4230)	0.084
C-reactive protein (mg/dl)	40.5 (10.2–48.2)	40.5 (19.8–56)	0.407
Procalcitonin (ng/mL)	0.19 (0.07–1.04)	0.14 (0.07–0.89)	0.877
White blood cell (10^3/μL)	12.3 (9.7–16.8)	10.9 (8.6–13.5)	0.071
Hematocrit (%)	42.2 (38.3–45.2)	42.8 (39.2–45.7)	0.312
Hemoglobin (g/dL)	14 (12.4–15.1)	14.2 (13.0–15.4)	0.442

The comparison of the Balthazar score, pancreatic necrosis grade, and CTSI between the groups is given in Table 3. Accordingly, these three parameters were found to be statistically significantly affect mortality ($p<0.001$).

Table 3. Comparison of the Balthazar score, pancreatic necrosis grade, and CTSI between the groups

Variable, n (%)	**Mortality (n=33)**	**Discharged (n=207)**	**p**
Balthazar score			
Normal pancreas	2 (6.1%)	58 (28%)	<0.001
Pancreatic enlargement	1 (3%)	17 (8.2%)	
Pancreatic inflammation and/or peripancreatic	3 (9.1%)	86 (41.5%)	
Single peripancreatic fluid collection	1 (3%)	34 (16.4%)	
Two or more fluid collections and/or retroperitoneal air	26 (78.8%)	12 (5.8%)	

Percentage of pancreatic necrosis			
0	23 (69.7%)	205 (99%)	
<30	4 (12.1%)	2 (1%)	<0.001
30-50	4 (12.1%)	–	
>50	2 (6.1%)	–	
Computed tomography severity index			
Low degree	5 (15.2%)	195 (94.2%)	<0.001
Middle degree	23 (69.7%)	12 (5.8%)	
High degree	5 (15.2%)	–	

Table 4 shows the correlation of the patients' amylase, lipase, CRP, and procalcitonin values with the Balthazar score, pancreatic necrosis grade, and CTSI. Accordingly, the amylase level was positively correlated with the Balthazar score at a statistically significant level (R=0.189, p=0.003). However, the remaining parameters did not have a statistically significant correlation with the Balthazar score, pancreatic necrosis grade, and CTSI (p>0.05).

Table 4. Correlation of amylase, lipase, C-reactive protein, and procalcitonin values with the Balthazar score, pancreatic necrosis grade, and CTSI*

Variables		**Balthazar score**	**Percentage of pancreatic necrosis**	**CTSI**
Amylase	R	0.189	0.022	0.071
	p	0.003	0.738	0.274
Lipase	R	0.135	0.019	0.042
	p	0.05	0.656	0.548
C-reactive protein	R	0.012	-0.051	-0.034
	p	0.850	0.432	0.595

Procalcitonin	R	-0.109	-0.037	-0.067
	p	0.09	0.576	0.317

* CTSI – computed tomography severity index

The relationship of the Balthazar score, pancreatic necrosis grade, and CTSI with patient outcome is shown in Figure 2 and Table 5. The area under the ROC curve value was determined as 0.861 [95% confidence interval (CI): 0.776–0.947] for the Balthazar score, 0.648 (95% CI: 0.531–0.764) for pancreatic necrosis degree, and 0.900 (95% CI: 0.826–0.973) for CTSI, and all these values were statistically significant ($p<0.05$).

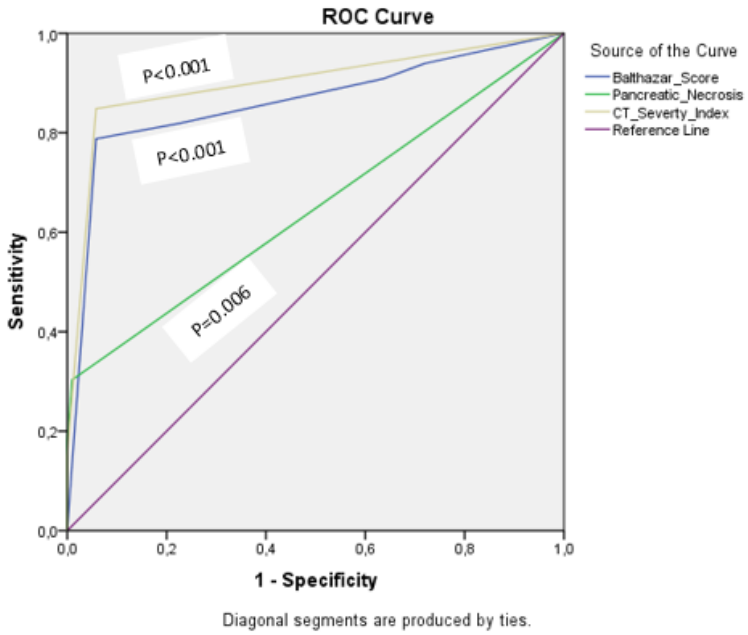

Fig. 2. Relationship between pancreatic scoring systems and mortality

Table 5. Receiver operating characteristic curve for the predictors of cases with acute pancreatitis*

Parameter	Cut off	AUC	% 95 CI	p	Sensitivity (%)	Specificity (%)	PPD	NPD
Balthazar score	3.5	0.861	0.776–0.947	<0.001	0.818	0.778	68%	97%

Percentage of pancreatic necrosis	1	0.648	0.531–0.764	0.006	0.303	0.99	83%	90%
Computed tomography severity index	1.5	0.9	0.826–0.973	<0.001	0.848	0.942	70%	98%

* CI – confidence interval; AUC – area under curve; PPD – positive predictive value; NPD – negative predictive value

Multivariate logistic regression was performed using the Enter model. As a result of logistic regression analysis, it was determined that mortality and CTSI were statistically significant (p <0.001) (Table 6). A 1-degree increase in CTSI increases a person's risk of dying 270 times. No statistical significance was found in other variables (p>0.05).

Table 6. Multivariate logistic regression analysis results for acute pancreatitis

Variables	**B**	**SE**	**OR**	**95% Cl for OR**	**p**
Age	0.028	0.021	1.029	0.988–1.072	0.174
Gender	0.437	0.315	1.548	0.834–2.872	0.315
Alanine aminotransferase	0.002	0.002	0.998	0.994–1.002	0.338
Balthazar score	-0.404	0.395	0.668	0.308–1.448	0.306
Percentage of pancreatic necrosis	0.237	0.432	1.267	0.543–2.954	0.584

Discussion

In this study, the correlation of the amylase, lipase, CRP, and procalcitonin values with the Balthazar score, pancreatic necrosis grade, and CTSI was investigated in patients with AP. Among these parameters, a weak positive correlation was found between the amylase value and the Balthazar score. In addition, the Balthazar score, pancreatic necrosis grade, and CTSI had a strong correlation with patient outcome. When the

relationship between mortality and the Balthazar score, pancreatic necrosis grade, and CTSI was examined, it was determined that mortality had the strongest correlation with CTSI (area under the ROC curve: 0.9, $p<0.01$). This finding is consistent with previous studies in the literature.[1] In light of these results, we consider that the use of amylase and lipase values in the emergency department would not be appropriate to determine mortality, but CTSI can be used as a mortality indicator.

Amylase and lipase are the most commonly used biomarkers in the diagnosis of AP.[14] The amylase level may also be elevated in gastrointestinal pathologies other than AP and diseases of the salivary glands. Therefore, although amylase is also widely increased in AP, it is less sensitive and specific than lipase.[15] Amylase and lipase values in patients with AP are important not only for diagnosis but also in elucidating the etiology of the disease. The lipase/amylase ratio has been proposed as a possible new index that can differentiate AP attacks with or without alcohol use.[16] In line with all these data, amylase and lipase values are measured in emergency departments to diagnose AP. Some studies have also evaluated the use of amylase and lipase levels in determining the clinical severity of AP, but these parameters were not found useful for this purpose.[17,18] In the literature, there are also studies in which CECT tests and scoring systems have been used in combination with amylase or lipase or both parameters to determine the severity of AP. In a study by Hamer et al., the lipase value was found to be positively correlated with modified CTSI.[19] In contrast, Thakur et al. observed no correlation between the serum lipase value and CTSI.[20] In the current study, there was no correlation between the lipase value and CTSI, Balthazar score, and pancreatic necrosis grade. In another study, the severity of AP was determined using CECT, and the correlation between the amylase level and AP severity was evaluated. No correlation was reported between the severity of AP determined by CECT and the amylase level.[13] Contrary to that study, we found a weak positive correlation between amylase and CTSI.

CRP and procalcitonin, which are other biomarkers associated with clinical severity and mortality in AP, are more valuable than amylase and lipase in evaluating the severity of the disease.[21] However, since these parameters are non-specific, they are not sufficient to determine clinical severity. In a previous study, a weak correlation was found between the CRP value and CTSI in patients diagnosed with AP. In the same study, a weak negative correlation was reported between CRP and the Balthazar score.[22] In our study, however, the CRP value had no correlation with the Balthazar score, pancreatic necrosis grade, and CTSI, which is also supported by the study of Ganesh et al.[23] In addition, we detected no correlation between the procalcitonin value and the Balthazar score, pancreatic necrosis grade, and CTSI.

Predicting the severity of AP and administering adequate treatment can reduce mortality rates. Therefore, APACHE II, the bedside index for severity in AP, and the Ranson score are widely used to estimate the severity of AP in clinical practice. However, these scoring systems are complex and difficult to apply in the emergency department. For this reason, CECT is used as a reference standard for both the diagnosis of AP and the assessment of its severity.[24] In CECT, the Balthazar score is defined primarily. Later, CTSI was

defined by adding pancreatic necrosis to this score.[2,25] CTSI was found to be more effective than the Balthazar score in predicting mortality.[2] In the current study, consistent with the literature, the success of CTSI in predicting mortality was higher than that of pancreatic necrosis grade or the Balthazar score alone.

Study limitations

This study had a single-center and retrospective design, resulting in a small number of participants. In addition, the etiology of AP was not available in many cases included in the sample. Therefore, we were not able to classify the cases according to their etiology.

Another limitation is that the CECTs evaluated in our study were performed in the early period. In the emergency department where the study was conducted, CECT is performed in the evaluation of patients with a diagnosis of AP to rule out complications or intra-abdominal conditions that require urgent treatment.

Conclusion

In this study, no correlation was found between the procalcitonin and CRP values, which are the most common parameters in predicting the clinical severity of AP, and the amylase and lipase values, which are valuable in diagnosing AP. There was also no correlation between the radiological methods used to predict the clinical severity of AP (the Balthazar score, pancreatic necrosis grade, and CTSI) and the lipase, procalcitonin, and CRP values. However, a weak positive correlation was observed between the amylase value and CTSI. Therefore, we consider that the use of amylase or lipase level alone is not appropriate in predicting the clinical severity of AP. In addition, as a result of our study, it can be concluded that CTSI, which includes both the pancreatic necrosis level and the Balthazar score, is more successful than either parameter alone in the prediction of mortality in patients with AP who have undergone CECT.

Declarations

Funding

None declared by the authors.

Author contributions

Conceptualization, F.T. and E.T.; Methodology, F.T.; Software, E.T. and F.A.; Validation, E.T., F.A. and E.Ö.; Formal Analysis, F.T.; Investigation, E.Ö.; Resources, E.Ö. and K.T.; Data Curation, E.Ö.; Writing – Original Draft Preparation, F.T.; Writing – Review & Editing, F.T and E.T.; Visualization, F.A. and K.T.; Supervision, E.Ö.; Project Administration, F.T.; Funding Acquisition, E.T.

Conflicts of interest

None declared by the authors.

Data availability

All data used in the study are available.

Ethics approval

Approval for the study was obtained from the local ethics committee (decision number: 22, session: 8, date: 27.10.2022).

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