Comparison of the Efficacy of Balthazar Score and C-Reactive Protein-Albumin Ratio for Determination of Acute Pancreatitis Severity

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ABSTRACT: Acute pancreatitis (AP) clinic has a wide spectrum ranging from asymptomatic cases to mortality. Early diagnosis and prediction are of great importance to prevent mortality in AP patients. Many prognostic scoring systems have been developed for AP to date. At the time of the initial assessment of attendance to the emergency department (ED), it is impractical to use existing prognostic scoring systems for patients with a diagnosis of AP in most patients. The prognostic performances of radiological and clinical scoring systems of 329 patients diagnosed with acute pancreatitis were compared in terms of C-reactive protein-albumin ratio (CAR) levels, mortality and severity according to Balthazar score. It was observed that the CAR value increased as the AP severity increased. For mortality estimation, the ROC curve was used for sensitivity, specificity, and cut-off values for each scoring system for CAR. When mild pancreatitis and severe pancreatitis were compared according to Balthazar score, the differences between CAR were statistically significant and positive correlations were present. The CAR value has been shown to be a useful clinical tool that can be used with its high predictive value. CAR has the advantages of being easily accessible, inexpensive, and having moderately high diagnostic power to predict AP severity.

KEYWORDS: Acute pancreatitis, Balthazar score, C-reactive protein-albumin ratio, Ranson score, mortality.

Introduction

Acute pancreatitis (AP) is a pathologic disease of the pancreas gland resulting in a systemic inflammatory response and accompanied by complications.

All patients with AP diagnosis do not follow the same clinical progression.

The AP clinic has a broad spectrum with variability from asymptomatic cases to mortality [1].

Early diagnosis and treatment of disease in severe AP has positive effect on progression and causes a reduction in mortality.

Early determination of the severity of AP has great importance in terms of long-term follow-up and treatment of AP [2].

Many prognostic scoring systems were developed to date for AP.

The use of these prognostic scoring systems, including Balthazar, has popularized over time [3].

However, most of these scoring systems are complicated, require time and comprise many parameters which cannot be obtained in the early stages of disease.

During first assessment on attendance in the emergency department (ED), it is not practical to use the prognostic scoring systems available for patients with AP diagnosis on most patients [4].

Additionally, a variety of studies showed that early imaging is inadequate to identify pancreas necrosis.

For this reason, image-based prognostic scoring systems are inadequate during emergency attendance and are mostly used for diagnostic purposes [5].

Imaging methods for patients with AP diagnosis are used to confirm diagnosis or to identify possible pancreas complications if there is no clinical amelioration within the first 48 to 72 hours.

Several studies questioned the need and use of computed tomography (CT), an inseparable part of assessment during emergency department attendance of AP patients, for those receiving clinical and laboratory diagnosis [6].

In recent periods, proinflammatory cytokines and c-reactive protein (CRP) levels were shown to be associated with AP severity.

To date, many parameters predicting the clinical progression of AP like neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and mean platelet volume (MPV) and rating systems have been used [7-9].

Just like NLR and PLR, the ratio of C-reactive protein to albumin (CAR) is a simple, rapid and easily calculated parameter based on systemic inflammation.

The aim of this study is to compare the efficacy of the Balthazar score, commonly used to predict AP severity, with the CAR value,
which can be applied at time of diagnosis and is simple, rapid, easily calculated and based on inflammation.

**Material and Methods**

**Study Design**

This study is a retrospective observational study completed in a tertiary referral center in Turkey. After receiving local ethics committee permission data from 414 patients receiving AP diagnosis from June 2018 to June 2021 were retrospectively analyzed.

Patients were screened using the International Classification of Diseases (ICD) codes for AP (K85.9 undefined, K85.0 idiopathic, K85.1 biliary K85.2 alcohol-derived K85.3 medication linked and K85.8 other).

**Patient Selection**

The clinical status of the patients, laboratory tests and radiological investigations at time of attendance at the ED were reviewed and AP diagnosis was confirmed.

Patients who were discharged of their own volition, younger than 18 years of age, with AP diagnosis as a result of trauma, with inadequate laboratory and file data were not included in the study (Figure 1).

The Balthazar and Ranson scores were used to assess AP severity.

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**Statistical Analysis**

After excluding cases, data from 329 patients were recorded in the Microsoft Excel program by a single clinician.

Results were transferred to SPSS for Windows (20.0, SPSS, Chicago, United States of America) for statistical analysis.

Demographic features, laboratory values, degree of severity, comorbidities, mortality rates, NLR, PLR, CAR, Balthazar and Ranson scores were noted.

Descriptive properties of the study groups were expressed as mean-standard deviation (SD) for quantitative data or percentage (%) and counts for qualitative data.

The student’s-t independent test was used to compare two groups with a normal distribution data.

The prognostic performance of all radiological and clinical scoring systems, NLR, PLR and CAR levels were compared in terms of mortality and severity according to Balthazar and Ranson criteria using student’s-t independent test.

Additionally, for prediction of mortality the receiver operating curve (ROC) analysis was used for sensitivity, specificity and cut-off values for each points system for NLR, PLR and CAR.

Significance was set at p<0.05 and the results are given within a 95% confidence interval.

**Results**

The study included a total of 329 patients with AP diagnosis.
The most common etiologic causes among patients were biliary (76.9%), hyperlipidemia (8.8%) and alcohol (5.2%).

The 3 most common comorbid diseases were hypertension (20.1%), diabetes mellitus (10.9%) and coronary artery disease and/or congestive heart failure (7.6%) (Table 1).

Table 1. Gender, comorbid diseases, complaints and etiological causes of study population.

| Variables                              | N  | %   |
|----------------------------------------|----|-----|
| Female                                 | 173| 52.6|
| Male                                   | 156| 47.4|
| None                                   | 160| 48.6|
| Hypertension                           | 66 | 20.1|
| Diabetes mellitus                      | 36 | 10.9|
| Coronary artery disease / Congestive heart failure | 25 | 7.6|
| Chronic obstructive pulmonary disease / Asthma | 22 | 6.7|
| Chronic kidney disease                 | 4  | 1.2 |
| Others                                 | 16 | 4.9 |
| Upper abdominal pain                   | 280| 85.1|
| Nausea and/or vomiting                 | 39 | 11.9|
| Jaundice                               | 6  | 1.8 |
| None                                   | 4  | 1.2 |
| Biliary                                | 253| 76.9|
| Hyperlipidemia                         | 29 | 8.8 |
| Alcohol                                | 17 | 5.2 |
| Others                                 | 30 | 9.1 |

When the distribution of AP according to gender is examined, the number of women was 173 (52.6%) and the number of men were 156 (47.4%).

The mean age of male patients was 50.3±15.7 years, with youngest patient 20 and oldest 89.

The mean age of female patients was 54.3±17.4 years, with youngest patient 18 and oldest patient 95.

The age distribution in our study was 25 patients under 30 years (7.6%), 48 patients from 30-39 years (14.6%), 85 patients from 40-49 years (25.8%), 67 patients from 50-59 years (20.4%), 38 patients from 60-69 years (11.5%), 46 patients from 70-29 years (14%) and 20 patients from 80-95 years (6.1%).

The maximum number of patients were 85 from 40-49 years of age.

When the complaints of patients during AP diagnosis are examined, 280 patients had abdominal pain (85.1%), 39 patients had nausea-vomiting (11.9%), 6 patients had jaundice (1.8%), while 4 patients had no active complaints (1.2%).

Reflecting clinically mild pancreatitis, 18.5% of patients were in Balthazar A group (61 patients), 42.9% were Balthazar B group (141 patients) and 10.9% were Balthazar C group (36 patients).

Representing severe acute pancreatitis, 23.1% of patients were in Balthazar D group (76 patients) and 4.6% were in Balthazar E group (15 patients).

The CAR mean values for Balthazar A, B, C, D and E AP patients were 1.8±1.3, 1.9±1.3, 4.1±2.4, 6.6±2.2, and 7±1.3, respectively.

As the acute pancreatitis Balthazar severity score progressed, the CAR value was observed to increase in direct proportion.

This situation changed in direct proportion to the increase in the inflammation process.

For this reason, the lowest CAR value was observed in Balthazar A group and the highest CAR value was observed in Balthazar E group.

The difference in CAR values between Balthazar A and Balthazar B group was not statistically significant (p=0.997).

The difference between Balthazar D and E was not statistically significant (p=0.905).

The difference between Balthazar D and Balthazar C appeared to be statistically significant (p<0.001).

The mean CAR value for Balthazar A, B and C groups representing mild acute pancreatitis was 2.2±1.7, while the mean CAR value for Balthazar D and E groups representing severe acute pancreatitis was 6.6±2.

In other words, the mean CAR values were higher in severe AP compared to mild AP.

The difference in mean CAR values between mild AP and severe AP according to the Balthazar scoring was statistically significant (p<0.001).

In the severe AP group according to Balthazar score, C-reactive protein (CRP) (p<0.001), albumin (p=0.026), white blood cell
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(WBC) (p<0.001), neutrophil (p<0.001), lymphocyte (p<0.001), NLR (p<0.001), PLR (p<0.001) and CAR (p<0.001) values were higher compared to mild AP and the differences were statistically significant (Table 2).

Table 2. Comparison of laboratory values of mild and severe AP groups according to Balthazar score.

| Balthazar Severity score | Mean  | SD    | P      |
|--------------------------|-------|-------|--------|
| Crp (mg/dL)              |       |       |        |
| Mild AP                  | 7.9   | ±1.9  | <0.001*|
| Severe AP                | 21.9  | ±5    |        |
| Amylase (U/L)            |       |       |        |
| Mild AP                  | 1671.6| ±1078.8| <0.001*|
| Severe AP                | 2300.8| ±987.8|        |
| Lipase (U/L)             |       |       |        |
| Mild AP                  | 3864.9| ±1820.7| 0.002* |
| Severe AP                | 4570.9| ±1769 |        |
| AST (U/L)                |       |       |        |
| Mild AP                  | 152.1 | ±99.7 | <0.001*|
| Severe AP                | 441.8 | ±123.1|        |
| ALT (U/L)                |       |       |        |
| Mild AP                  | 132.9 | ±128.4| <0.001*|
| Severe AP                | 247.5 | ±165.1|        |
| Albumin (gr/dL)          |       |       |        |
| Mild AP                  | 4.3   | ±0.4  | 0.026* |
| Severe AP                | 3.4   | ±0.4  |        |
| LDH (U/L)                |       |       |        |
| Mild AP                  | 353.8 | ±150.7| <0.001*|
| Severe AP                | 421.9 | ±278.8|        |
| WBC (µL)                 |       |       |        |
| Mild AP                  | 12.9  | ±3.2  | <0.001*|
| Severe AP                | 20.5  | ±3.8  |        |
| Neutrophil (µL)          |       |       |        |
| Mild AP                  | 9.7   | ±3    | <0.001*|
| Severe AP                | 17.9  | ±3.3  |        |
| Lymphocyte (µL)          |       |       |        |
| Mild AP                  | 2.2   | ±0.9  | <0.001*|
| Severe AP                | 1.4   | ±0.6  |        |
| NLR                      |       |       |        |
| Mild AP                  | 7.6   | ±5.2  | <0.001*|
| Severe AP                | 16.8  | ±8    |        |
| PLR                      |       |       |        |
| Mild AP                  | 178.6 | ±66.9 | <0.001*|
| Severe AP                | 398.4 | ±140.7|        |
| CAR                      |       |       |        |
| Mild AP                  | 2.2   | ±1.7  | <0.001*|
| Severe AP                | 6.6   | ±2    |        |

*p<0.05 (Student’s t test), AST: aspartate aminotransferase, ALT: alanine aminotransferase, LDH: lactate dehydrogenase, CRP: C-reactive protein, WBC: white blood cell, PLR: platelet to lymphocyte ratio, NLR: neutrophil to lymphocyte ratio, CAR: C-reactive protein to albumin ratio.

There were statistically significant and positive correlations present between CAR values, Ranson score, Balthazar score and 1-year mortality accepted for correlation analyses.

When mild severity pancreatitis and severe pancreatitis according to Balthazar score are compared, the differences between NLR (p<0.001), PLR (p<0.001) and CAR (p<0.001) were statistically significant and there were positive correlations.

The mean CAR value for mild pancreatitis according to Ranson criteria during emergency attendance was 2.4±1.9, while it was 5.5±2.6 for severe pancreatitis and the difference was statistically significant (p<0.001).

In our study, the CAR values for acute pancreatitis cases with mortal progression was 6.5±1.2, while it was 3.3±2.6 for cases without mortal progression and the difference between these two groups was statistically significant (p<0.001) (Table 3).

Table 3. NLR, PLR and CAR values according to Balthazar score, Ranson score and mortality.

| Ranson score | Balthazar score | Mortality |
|--------------|-----------------|-----------|
|               | Mild AP | Severe AP | P   | Mild AP | Severe AP | P   | Mortality - | Mortality + | P       |
| NLR           | 8.2±6.5 | 14.1±7.2 | <0.001* | 7.6±5.2 | 16.8±7.9 | <0.001* | 9.8±7.2 | 17.2±6.2 | <0.001* |
| PLR           | 190.7±87 | 340.2±160 | <0.001* | 178.5±66.9 | 398.4±140 | <0.001* | 235.7±135 | 314.8±128.8 | 0.027* |
| CAR           | 2.4±1.9 | 5.5±2.6 | <0.001* | 2.2±1.7 | 6.6±2 | <0.001* | 3.3±2.6 | 6.5±1.2 | <0.001* |

*p<0.05 (Student’s t test), NLR: neutrophil to lymphocyte ratio, PLR: platelet to lymphocyte ratio, CAR: C-reactive protein to albumin ratio.
ROC curve analysis was performed to determine the CAR, NLR and PLR cut-off values in the emergency department for use to differentiate AP patients progressing with and without mortality (Figure 2).

CAR value was found to have higher sensitivity and specificity than NLR and PLR values in predicting mortality in AP patients. The area under curve (AUC) for CAR value was 0.856. For prediction of mortality in AP patients, a CAR value of 5.34 had 93.3% sensitivity and 80.6% specificity and it was found to be an important marker to predict mortality (p<0.001) (Table 4).

**Table 4. Regression analysis in terms of mortality for NLR, PLR and CAR.**

|   | AUC(95%)         | Cut off | p       | Sensitivity (%) | Specificity (%) |
|---|------------------|---------|---------|-----------------|-----------------|
| NLR | 0.839 (0.774-0.905) | 12.72  | <0.001* | 80              | 79.9            |
| PLR | 0.681 (0.532-0.830) | 262.4  | 0.018*  | 73              | 70              |
| CAR | 0.856 (0.811-0.902) | 5.34   | <0.001* | 93.3            | 80.6            |

* p<0.05 (Student’s t test), AUC: area under curve, CAR: C-reactive protein to albumin ratio, PLR: platelet to lymphocyte ratio, NLR: neutrophil to lymphocyte ratio.

**Discussion**

Acute pancreatitis is a significant clinical picture related to tissue injury caused by oxidative stress and cytokine release with severe inflammation and linked development of organ failure and complications which may be life-threatening [10,11].

The first and most important stage of acute pancreatitis management is to determine the severity of disease and to plan treatment approaches accordingly. Nearly 10-15% of cases are encountered as severe and complicated AP cases with progression to organ failure [12].

Currently, the incidence of AP disease diagnosed in emergency departments is increasing in recent years. However, the most significant disadvantage for determining the severity of AP cases is that most prognostic scoring systems cannot be applied at time of attendance.

Scoring systems which can calculate the severity of disease from blood tests taken at time of attendance in the emergency department will positively contribute to management of AP patients [13]. When compared with traditional prognostic scoring systems, CAR is simple, cheap, can be immediately obtained at time of attendance and is a parameter which can be calculated independent of cross-sectional imaging methods [14]. In our study, when patients with AP diagnosis are assessed according to the Ranson score, patients with diagnosis of severe AP had
higher CAR values compared to patients diagnosed with mild-moderate severity AP.

A study by Kaplan et al. including 192 AP patients identified the CAR value showed positive correlation with significant prognostic indicators like the Ranson score [15].

In our study including 329 patients, just like NLR and PLR values, the CAR value had positive correlation with the Ranson score for determination of AP severity, which is consistent with the literature.

In this study, when patients with AP diagnosis are assessed according to Balthazar scoring, Balthazar E patients had higher CAR values compared to Balthazar D patients, while they had higher CAR value compared to Balthazar C patients.

In studies about determining AP severity, Petrescu et al. compared NLR values with Balthazar score and reported that as the severity of Balthazar score increased, there was an increase in the NLR values, similar to the increase in CAR value in our study [16].

In a study about predicting the severity and prognosis of AP disease in the early period, Zhou et al. stated that there were statistically significant associations observed between NLR, PLR, and RDW with 28-day mortality [17].

In our study, the association between CAR value of patients diagnosed with AP and 1-year mortality was assessed and increased CAR levels were found to have statistically significant correlation in terms of 1-year mortality of patients.

This finding leads to consideration that CAR score is a reliable parameter to predict mortality.

CRP is one of the most important acute phase reactants synthesized in the liver in response to inflammation.

A study by Cifci et al. researched the correlation between CRP levels obtained on first attendance in the emergency department due to AP with one-year mortality and observed a significant correlation, with mortality rates increasing as CRP increased [18].

A study including 700 patients by Hong et al. associated the acute negative phase reactant of albumin alone in AP patients with permanent organ failure [19].

Similar findings for CRP and albumin for prediction of AP prognosis are consistent with findings in our study, with the albumin and CRP levels of AP cases confirmed to have a determinant role in terms of mortality and morbidity.

Low albumin and elevated CRP were significantly different in severe AP according to the Balthazar score and in cases with mortal progression compared to cases with mild progression and no mortality, respectively, which is compatible with the literature [20,21].

Additionally, we analyzed the ratio of CRP to albumin in addition to albumin and CRP values.

In addition to the albumin and CRP values at time of first attendance for patients receiving AP diagnosis, we assessed the difference in CAR level for mild and severe AP using the Balthazar score.

In severe AP patients according to the Balthazar score, low albumin (p=0.026), elevated CRP (p<0.001) and elevated CAR (p<0.001) were positively correlated and statistically significant.

According to our results, mean CAR was correlated with the Balthazar score.

When the CAR values are compared in the mild AP group and severe AP group according to Balthazar score, it was higher in the severe AP group and this situation makes CAR a beneficial parameter to predict prognosis at time of AP diagnosis.

In severe AP, the mean CAR values were higher compared to the mild AP group.

The mean CAR value showed variability according to the Balthazar score and the CAR value was observed to increase as AP severity progressed.

Additionally, high CAR value at time of diagnosis in cases with mortal progression makes it an appropriate tool to determine prognosis in patients.

In similar studies, attempts were made to calculate cut-off values for different prognostic markers.

In our study, cut-off values were calculated using the ROC curve.

According to our results, the cut-off value calculated for CAR was >5.34; this value is an indicator for higher risk in complicated cases at time of diagnosis.

In conclusion, the CAR value is considered to be an easy, simple, cheap and easily accessible marker of severity for AP.

The main advantage of our study is that in addition to analyzing the predictive value of the CAR value for AP severity, it is the first study in the literature to analyze the correlation between the Balthazar score for determining AP severity with CAR.

Limitation of the study is that it is a single-center retrospective study.
Conclusion

The CAR value was shown to be a beneficial clinical tool that can be used with high prediction value.

Early detection and prediction are of great importance to prevent mortality in AP patients.

CAR has the advantages of being easily accessible, cheap and having moderately high diagnostic power to predict AP severity.

More comprehensive studies involving more patients in multi-center prospective studies may be beneficial to validate the value of our results.

Conflict of interests

None to declare.

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