



Early temporal dynamics of the phosphorus to calcium ratio for severity prediction in acute pancreatitis: A retrospective cohort study

Akut pankreatitte şiddet öngörüsü için fosfor/kalsiyum oranının erken zamansal dinamikleri: Retrospektif kohort çalışması

Yavuz Emre PARLAR¹, Mehmet COŞKUN¹, Bengi ÖZTÜRK²

Department of ¹Gastroenterology, Sincan Training and Research Hospital, Ankara, Turkey

Department of ²Gastroenterology, Hacettepe University School, of Medicine, Ankara, Turkey

ABSTRACT • Background and Aims: Acute pancreatitis ranges from mild disease to severe forms associated with organ failure and mortality. Early risk stratification is essential, yet current scoring systems may not fully reflect early metabolic alterations. While hypocalcemia is a recognized severity marker, the prognostic role of phosphorus remains unclear. This study evaluated whether early phosphorus-to-calcium ratio changes within 48 hours predict disease severity in acute pancreatitis. **Materials and Method:** This retrospective single-center study included adults hospitalized with acute pancreatitis between January 2023 and December 2025. Phosphorus-to-calcium ratio was calculated from routinely recorded serum phosphorus and calcium levels at admission, 24, and 48 hours. Severity was defined according to the Revised Atlanta Classification. Multivariable logistic regression and receiver operating characteristic analyses were performed. **Results:** A total of 182 patients were included [mean age 56.8 ± 15.9 years; 100 male (54.9%)]. Mild acute pancreatitis occurred in 140 patients (76.9%), moderately severe in 32 (17.6%), and severe in 10 (5.5%). Persistent organ failure occurred in 12 (6.6%), intensive care unit admission in 14 (7.7%), and in-hospital mortality in 3 patients (1.6%). Phosphorus-to-calcium ratio values increased during the first 48 hours and were higher in moderate-to-severe/severe disease. After adjustment for age, creatinine, C-reactive protein level, and clinical severity score, the 48-hour change in the phosphorus-to-calcium ratio remained independently associated with severity (Odds ratio 1.64, 95% confidence interval 1.14 - 2.36, p = 0.008). **Conclusion:** Early phosphorus-to-calcium ratio dynamics may serve as a simple adjunct biomarker to existing clinical scores for predicting severity in acute pancreatitis.

Key words: Acute pancreatitis, biomarkers, calcium, phosphorus

ÖZET • Giriş ve Amaç: Akut pankreatit, hafif seyirli hastalıktan organ yetmezliği ve mortalite ile ilişkili ağır formlara kadar değişebilen bir klinik tabloya sahiptir. Erken risk sınıflandırması önemlidir; ancak mevcut skorlama sistemleri erken metabolik değişiklikleri tam olarak yansıtmayabilir. Hipokalsemi bilinen bir şiddet belirteci olmakla birlikte, fosforun prognostik rolü net değildir. Bu çalışmada, ilk 48 saat içindeki fosfor-kalsiyum oranı değişimlerinin hastalık şiddetini öngörüp öngöremeyeceği değerlendirildi. **Gereç ve Yöntem:** Bu retrospektif tek merkezli çalışmaya Ocak 2023 ile Aralık 2025 tarihleri arasında akut pankreatit nedeniyle hastaneye yatırılan erişkin hastalar dahil edildi. Fosfor-kalsiyum oranı, başvuru anında ve 24. ile 48. saatlerde ölçülen serum fosfor ve kalsiyum düzeylerinden hesaplandı. Hastalık şiddeti Revize Atlanta Sınıflaması'na göre tanımlandı. Çok değişkenli lojistik regresyon ve alıcı çalışma özelliği eğrisi analizleri yapıldı. **Bulgular:** Toplam 182 hasta çalışmaya dahil edildi [ortalama yaş 56.8 ± 15.9 yıl; 100 erkek (%54.9)]. Hastaların 140'unda (%76.9) hafif, 32'sinde (%17.6) orta-ağır ve 10'unda (%5.5) ağır akut pankreatit saptandı. Persistan organ yetmezliği 12 hastada (%6.6), yoğun bakım ünitesi yatışı 14 hastada (%7.7) ve hastane içi mortalite 3 hastada (%1.6) görüldü. Fosfor-kalsiyum oranı ilk 48 saat içinde artış gösterdi ve orta-ağır/ağır hastalıkta daha yüksekti. Yaş, kreatinin, C-reaktif protein düzeyi ve klinik şiddet skoru için yapılan düzeltme sonrasında, 48. saatteki fosfor-kalsiyum oranı değişimi hastalık şiddeti ile bağımsız olarak ilişkili bulundu (risk oranı 1.64; %95 güven aralığı 1.14 - 2.36; p = 0.008). **Sonuç:** Erken dönem fosfor-kalsiyum oranı dinamikleri, akut pankreatitte hastalık şiddetini öngörmede mevcut klinik skorlara tamamlayıcı basit bir biyobelirteç olarak kullanılabilir.

Anahtar kelimeler: Akut pankreatit, biyobelirteçler, fosfor, kalsiyum

INTRODUCTION

Acute pancreatitis (AP) is a common gastrointestinal emergency characterized by a broad clinical spectrum ranging from mild, self-limiting disease to severe forms associated with persistent organ failure and increased mortality (1). Early risk stratification remains a cornerstone of clinical management, as timely identification of high-risk patients allows appropriate monitoring, early intensive care support, and prevention of complications (2). Although the Revised Atlanta Classification provides standardized definitions for disease severity, predicting progression during the early phase of AP remains challenging (3).

Several clinical scoring systems, including bedside index for severity in acute pancreatitis (BISAP), Ranson, and acute physiology and chronic health evaluation II (APACHE II), have been developed to estimate disease severity and prognosis (4). Among these, the BISAP score has gained popularity due to its simplicity and early applicability; however, even simplified clinical tools may not fully capture early metabolic and biochemical alterations occurring during the initial phase of the disease (5). Consequently, there has been increasing interest in identifying easily obtainable laboratory-based biomarkers that can complement established scoring systems and enhance early prognostic assessment.

Metabolic and electrolyte disturbances are integral components of AP pathophysiology. Hypocalcemia has long been recognized as a marker of severe disease, reflecting fat necrosis, systemic inflammation, and organ dysfunction (6). In contrast, the prognostic role of serum phosphorus has received relatively limited attention, despite its association with cellular injury, metabolic stress, and inflammatory processes (7). Recent studies have highlighted the potential value of dynamic biomarkers and ratio-based indices in improving early risk

prediction, suggesting that changes over time may provide additional prognostic information beyond single measurements (8). Moreover, several recent investigations evaluating inflammatory and biochemical ratios have demonstrated that combining simple laboratory parameters with clinical scores may improve risk stratification without increasing complexity (9,10). In this context, combining metabolically linked electrolytes into a single ratio may provide a more integrated reflection of early systemic stress than isolated laboratory parameters.

The phosphorus-to-calcium ratio (PCR) may represent a simple and easily applicable marker reflecting early metabolic imbalance in AP. However, data regarding the temporal evolution of PCR during the first 48 hours and its incremental value when integrated with established clinical scores remain limited. Therefore, this study aimed to evaluate the association between early PCR dynamics and disease severity in AP and to assess whether PCR may serve as an adjunct biomarker alongside established tools such as the BISAP score.

MATERIALS and METHOD

Study Design and Setting

This retrospective, single-center observational cohort study was conducted at the Department of Gastroenterology, Sincan Training and Research Hospital (Ankara, Turkey). Adult patients hospitalized with acute pancreatitis between January 2023 and December 2025 were screened for eligibility. The study protocol was approved by the institutional ethics committee and conducted in accordance with the Declaration of Helsinki. Due to the retrospective design, informed consent was waived.

Patient Selection

The diagnosis of acute pancreatitis was established based on at least two of the following criteria: char-

acteristic abdominal pain, serum amylase and/or lipase levels greater than three times the upper limit of normal, and imaging findings consistent with acute pancreatitis. Patients younger than 18 years, those with chronic pancreatitis, end-stage renal disease or dialysis treatment, metabolic disorders affecting calcium or phosphorus metabolism, incomplete clinical records, or missing phosphorus or calcium measurements within the first 48 hours were excluded. After applying exclusion criteria, 182 patients were included in the final analysis, as illustrated in the study flow diagram.

Data Collection and Definitions

Clinical and laboratory data were retrospectively obtained from electronic hospital records. Routinely recorded serum phosphorus and calcium levels obtained at admission, 24 hours, and 48 hours were used to calculate the phosphorus-to-calcium ratio (PCR). For PCR calculation, total serum calcium values obtained from routine laboratory measurements were used; corrected calcium values were not applied. Temporal changes in PCR were evaluated by comparing measurements across the first 48 hours. The change in PCR was defined as the difference between PCR at 48 hours (Δ PCR48) and baseline PCR. Disease severity was classified according to the Revised Atlanta Classification. The BISAP score was calculated using data obtained within the first 24 hours.

Outcomes

Primary outcome was moderately severe/severe acute pancreatitis according to the Revised Atlanta Classification. Moderately severe and severe acute pancreatitis were analyzed together as a composite outcome due to the relatively limited number of severe cases, which could reduce statistical power if analyzed separately. Secondary outcomes included persistent organ failure, intensive care unit admission, and in-hospital mortality.

Statistical Analysis

Continuous variables were expressed as mean \pm standard deviation or median values depending on distribution characteristics. Between-group comparisons were performed using independent samples t-test or Mann–Whitney U test for continuous variables and chi-square or Fisher's exact test for categorical variables. Temporal changes in PCR values were evaluated across predefined time points. Multivariable logistic regression analysis was used to identify independent predictors of moderately severe/severe acute pancreatitis, including age, creatinine, C-reactive protein (CRP), BISAP score, and Δ PCR48. Variables included in the multivariable model were selected based on clinical relevance and variables showing $p < 0.10$ in univariate analysis. Predictive performance was evaluated using receiver operating characteristic (ROC) curve analysis comparing BISAP, PCR48, Δ PCR48, and the combined BISAP + PCR48 model. Optimal cut-off values were determined using Youden's index. Statistical analyses were performed using IBM SPSS Statistics and R software, with a two-sided p -value < 0.05 considered statistically significant.

Ethics Approval

This study was approved by the Ethics Committee of Sincan Training and Research Hospital, University of Health Sciences (Approval No: SEAH-BAEK-2026-174; Date: February 17, 2026). Since this was a retrospective study, informed consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

A total of 182 patients were included in the analysis. The mean age was 56.8 ± 15.9 years, and 100 patients (54.9%) were male. According to the Re-

vised Atlanta Classification, 140 patients (76.9%) had mild acute pancreatitis, 32 (17.6%) had moderately severe disease, and 10 (5.5%) had severe disease. Baseline demographic, clinical, and laboratory characteristics according to disease severity are summarized in Table 1.

Temporal evaluation of PCR values demonstrated progressive increases during the first 48 hours, with consistently higher levels observed in patients with moderate-to-severe/severe disease compared with mild cases (Table 2). The separation between severity groups became more evident at later time points, as illustrated by the PCR trajectory over 0, 24, and 48 hours (Figure 1).

Clinical outcomes stratified by disease severity are presented in Table 3. Persistent organ failure occurred in 12 patients (6.6%), intensive care unit (ICU) admission was required in 14 (7.7%), and in-hospital mortality was observed in 3 patients (1.6%). Increasing disease severity was associated with higher rates of adverse outcomes.

In multivariable logistic regression analysis including age, creatinine, CRP, BISAP score, and Δ PCR48, BISAP score remained the strongest independent predictor of moderately severe/severe acute pancreatitis, while Δ PCR48 also demonstrated an independent association (OR 1.64, 95% CI 1.14 - 2.36, $p = 0.008$) (Table 4).

Table 1 Baseline characteristics

Variable	Mild AP (n = 140)	Mod/Severe AP (n = 42)	p value
Age (years)	56.5 ± 15.5	58.0 ± 16.0	0.99
Male sex, n (%)	74 (52.9)	26 (61.9)	0.28
BMI (kg/m ²)	27.6 ± 4.3	28.1 ± 4.5	0.46
Biliary etiology, n (%)	82 (58.6)	23 (54.8)	0.66
Alcohol etiology, n (%)	21 (15.0)	7 (16.7)	0.79
BISAP score	1.3 ± 0.9	2.0 ± 1.0	< 0.001
CRP (mg/L), median (IQR)	65 (40 - 110)	95 (60 - 160)	0.07
Creatinine (mg/dL)	0.95 ± 0.35	1.10 ± 0.45	0.88
Calcium (mg/dL)	8.4 ± 0.7	8.0 ± 0.8	0.006
Phosphorus (mg/dL)	3.5 ± 0.9	3.8 ± 1.0	0.11
Baseline PCR (median, IQR)	0.38 (0.31 - 0.45)	0.46 (0.38 - 0.58)	0.006

AP: Acute pancreatitis; BMI: Body-mass index; BISAP: Bedside index for severity in acute pancreatitis; CRP: C-reactive protein; IQR: Interquartile range; PCR: Phosphorus-to-calcium ratio.

Table 2 PCR temporal changes

Parameter	Mild AP	Mod/Severe AP	p
PCR at admission	0.38 ± 0.09	0.46 ± 0.12	0.006
PCR at 24h	0.39 ± 0.10	0.51 ± 0.13	0.002
PCR at 48h	0.41 ± 0.11	0.55 ± 0.14	< 0.001
Δ PCR48	0.04 ± 0.07	0.09 ± 0.09	0.003

AP: Acute pancreatitis; PCR: Phosphorus-to-calcium ratio; Δ PCR48: Change in PCR during first 48 hours.

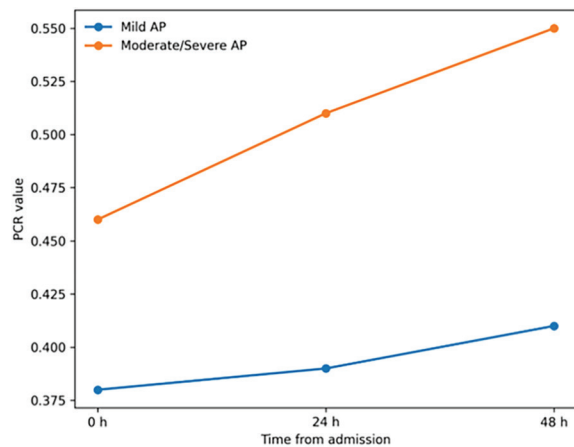


Figure 1 PCR trajectory first 48 hours in acute pancreatitis. Temporal trajectory of PCR during the first 48 hours after admission. PCR values increased over time, with higher levels observed in patients with moderately severe/severe acute pancreatitis compared with mild disease. The dynamic change in PCR (Δ PCR48) reflects evolving metabolic alterations associated with disease progression.

AP: Acute pancreatitis; PCR: Phosphorus-to-calcium ratio.

Receiver operating characteristic (ROC) analysis demonstrated acceptable discrimination for severity prediction (Figure 2). BISAP showed the highest performance [Area under the curve (AUC) 0.76], followed by PCR48 (AUC 0.71) and Δ PCR48 (AUC 0.66). The combined BISAP + PCR48 model yielded a modest improvement in predictive performance (AUC 0.77).

Optimal cut-off values for PCR48 and Δ PCR48 were determined using ROC curve analysis for major clinical outcomes, including mortality, persistent organ failure, and ICU admission (Table 5). PCR48 demonstrated acceptable discriminatory ability across outcomes, with AUC values ranging from 0.71 to 0.74. The optimal PCR48 threshold for predicting persistent organ failure was identified as 0.52, yielding 75% sensitivity and 70% specificity. For mortality prediction, a slightly higher cut-off of 0.58 showed balanced performance (sensitivity 67%, specificity 82%).

Table 3 Clinical outcomes

Outcome	Mild AP	Mod/Severe AP	p
Persistent organ failure	2 (1.4%)	10 (23.8%)	< 0.001
ICU admission	5 (3.6%)	9 (21.4%)	< 0.001
Mortality	0 (0%)	3 (7.1%)	0.003
LOS (days)	6 (4 - 9)	11 (7 - 16)	< 0.001

AP: Acute pancreatitis; ICU: Intensive care unit; LOS: Length of hospital stay.

Table 4 Multivariable logistic regression for prediction of moderately severe/severe AP

Variable	Adjusted OR	95% CI	p value
Age (per year)	1.01	0.99 - 1.03	0.21
Creatinine	1.24	0.87 - 1.76	0.24
CRP	1.005	0.999 - 1.011	0.09
BISAP score	2.68	1.72 - 4.18	< 0.001
Δ PCR48	1.64	1.14 - 2.36	0.008

BISAP: Bedside index for severity in acute pancreatitis; CRP: C-reactive protein; OR: Odds ratio; Δ PCR48: Change in PCR during first 48 hours.

Table 5 Optimal cut-off values of PCR48 and Δ PCR48 for adverse clinical outcomes

Outcome	Marker	Cut-Off Value	Sensitivity	Specificity	AUC (95% CI)
Mortality	PCR48	0.58	67%	82%	0.72 (0.61 - 0.83)
	Δ PCR48	0.11	67%	75%	0.68 (0.57 - 0.79)
Persistent organ failure	PCR48	0.52	75%	70%	0.74 (0.65 - 0.82)
	Δ PCR48	0.08	72%	65%	0.69 (0.60 - 0.78)
ICU hospitalization	PCR48	0.50	71%	63%	0.71 (0.62 - 0.79)
	Δ PCR48	0.07	68%	60%	0.66 (0.57 - 0.75)

AUC: Area under curve; ICU: Intensive care unit; Δ PCR48: Change in PCR during first 48 hours; PCR: Phosphorus-to-calcium ratio.

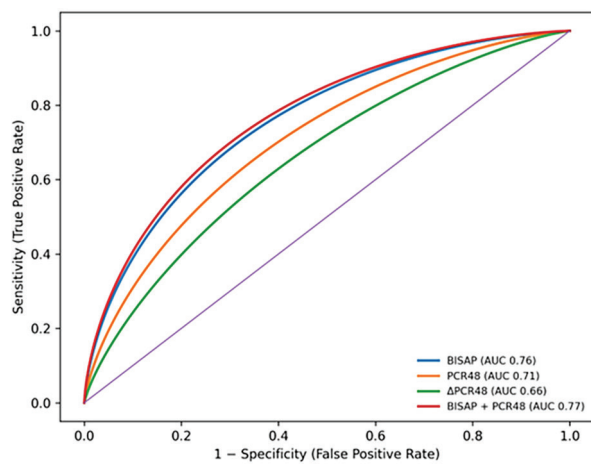


Figure 2 ROC curve for prediction of moderately severe/severe AP. Receiver operating characteristic curve analysis comparing the discriminatory performance of BISAP score, PCR48, and Δ PCR48 for predicting moderately severe/severe acute pancreatitis. The BISAP score demonstrated the highest discriminative ability (AUC 0.76), followed by PCR48 (AUC 0.71) and Δ PCR48 (AUC 0.66). The combined BISAP+PCR48 model showed modest incremental improvement (AUC 0.77), suggesting potential additive prognostic value when metabolic parameters are integrated with established clinical scores.

ROC: Receiver operating characteristic; AP: Acute pancreatitis; BISAP: Bedside index for severity in acute pancreatitis; AUC: Area under curve; Δ PCR48: Change in PCR during first 48 hours.

DISCUSSION

In this retrospective cohort study, we demonstrated that the PCR calculated in the early phase of acute pancreatitis, particularly Δ PCR48, was associated with disease severity. Both PCR48 and Δ PCR48

showed significant associations with moderately severe/severe disease, and Δ PCR48 remained independently associated with severity after adjustment for age, creatinine, CRP, and BISAP score in multivariable analysis. However, PCR-based parameters did not outperform established clinical scoring systems, with BISAP demonstrating the highest discriminatory performance. Nevertheless, the combined evaluation of PCR48 with BISAP provided a modest but statistically significant incremental prognostic benefit.

Early risk stratification is a cornerstone of clinical management in acute pancreatitis. Several clinical scoring systems, including APACHE II, Ranson, and BISAP, have been extensively validated for predicting mortality and severe disease (1,11,12). Among these, BISAP has gained prominence due to its simplicity and early applicability in clinical practice (12). In our cohort, the higher AUC observed for BISAP compared with PCR is consistent with existing literature and reinforces the continued importance of structured clinical scoring systems. These findings suggest that PCR should be positioned not as an independent scoring tool but rather as a complementary metabolic parameter.

In recent years, the prognostic role of inflammatory and ratio-based biomarkers has been increasingly investigated. Zahorec introduced the concept of the neutrophil-lymphocyte stress factor, demonstrating that simple ratios derived from routine

laboratory parameters may reflect the severity of systemic inflammatory responses (13). Similarly, Azab and colleagues reported that the neutrophil-to-lymphocyte ratio (NLR) was superior to total leukocyte count in predicting intensive care requirement and hospital length of stay in acute pancreatitis (14). The lactate dehydrogenase/albumin ratio has also been proposed as a marker associated with adverse outcomes in inflammatory conditions (15). A common feature of these studies is the integration of biologically meaningful laboratory parameters into composite ratios that may better capture the overall inflammatory burden. Consistent with these findings, studies from Turkey have also reported that the neutrophil-to-lymphocyte ratio may predict clinically important outcomes in acute pancreatitis, including acute kidney injury, intensive care requirement, prolonged hospitalization, and mortality (16,17). PCR represents a similar approach; however, data evaluating this ratio in acute pancreatitis, particularly with respect to temporal changes, remain limited.

Electrolyte disturbances constitute an integral component of the pathophysiology of acute pancreatitis. Hypocalcemia has long been recognized as a marker of severe disease and has been associated with fat necrosis and systemic inflammatory processes (18,19). In contrast, the prognostic role of phosphorus metabolism has been less extensively explored. Some studies have suggested that hypophosphatemia may be associated with severe disease, while others indicate that phosphate alterations may reflect systemic stress responses and organ dysfunction (20,21). Importantly, most prior investigations have relied on single time-point measurements. The novelty of our study lies in evaluating the dynamic interaction between phosphorus and calcium through ratio-based analysis and assessing its early temporal trajectory. The observed increase in PCR during the first 48 hours among patients with more severe disease supports

the hypothesis that temporal metabolic trends may better reflect ongoing inflammatory progression.

The independent association between Δ PCR48 and disease severity observed in our analysis suggests that dynamic changes may provide more clinically relevant information than isolated measurements. This finding aligns with experimental and clinical evidence indicating that inflammation and metabolic stress evolve over time rather than presenting as static processes (22). Nonetheless, the moderate discriminatory performance indicates that PCR reflects only one component of the complex pathophysiological cascade underlying acute pancreatitis.

In combined model analyses, integrating PCR48 with BISAP resulted in a modest yet statistically significant improvement in predictive performance. Similar findings have been reported for other biomarkers such as NLR, where combined models outperform single parameters but typically yield only incremental gains (14,23). Accordingly, our results support the interpretation of PCR as a complementary biomarker reflecting early metabolic imbalance rather than a replacement for established clinical scoring systems.

Strengths of this study include standardized evaluation of laboratory parameters at predefined early time points, the use of the Revised Atlanta Classification for severity assessment, and comprehensive comparison with both clinical scores and relevant clinical outcomes. However, several limitations should be acknowledged. The retrospective single-center design may limit generalizability, and the relatively low number of severe cases may reduce statistical power for certain analyses and may increase the risk of model overfitting and instability of coefficient estimates in multivariable logistic regression analysis. Additionally, phosphorus levels may be influenced by renal function and overall metabolic status, and residual confounding cannot be fully excluded.

In conclusion, PCR48 and particularly Δ PCR48 are associated with disease severity in acute pancreatitis and may reflect early metabolic alterations accompanying disease progression. Rather than replacing established clinical scoring systems, PCR may serve as a practical adjunct biomarker that enhances early risk stratification when interpreted alongside validated tools such as BISAP. Because PCR is derived from routinely measured laboratory parameters, it may be easily incorporated into early clinical assessment without adding complexity to existing risk stratification tools.

Ethics: *This study was approved by the Ethics Committee of Sincan Training and Research Hospital, University of Health Sciences (Approval No: SEAH-BAEK-2026-174; Date: February 17, 2026). Since this was a retrospective study, informed consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki.*

Conflict of Interest: *There is no conflict of interest with any institution or person.*

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