

Comparative Analysis of Serum Procalcitonin and C-Reactive Protein as Early Predictors of Severity in Acute Gallstone-Induced Pancreatitis

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Abstract: *This prospective observational study assessed the value of serum procalcitonin in predicting the early severity of acute gallstone-induced pancreatitis. Sixty adult patients presenting within 24 hours of symptom onset were evaluated using clinical findings, laboratory markers, imaging, and Revised Atlanta Classification criteria. Procalcitonin showed stronger early discrimination between mild, moderately severe, and severe cases than C-reactive protein. A cut-off value of 0.54 ng/mL gave high sensitivity and specificity for predicting severe disease, pancreatic necrosis, and persistent organ failure. The results support the use of procalcitonin as a practical early marker for risk assessment and timely triage in biliary pancreatitis.*

Keywords: acute pancreatitis, gallstone pancreatitis, procalcitonin, C-reactive protein, disease severity

1. Introduction

With a clinical spectrum ranging from mild, self-limiting inflammation to potentially fatal systemic disease, acute pancreatitis (AP) continues to be one of the most common causes of emergency gastrointestinal admissions globally (1, 8). The majority of cases in the adult population are caused by gallstones, which are the most common etiology (2, 13). While the majority of patients recover with conservative treatment, about 20% experience Severe Acute Pancreatitis (SAP), which has a mortality rate of up to 30% and is characterized by pancreatic necrosis and persistent organ failure (1, 12).

Finding high-risk patients early in the "golden window" of the first 24 hours is the main challenge in treating gallstone-induced pancreatitis (4, 15). Suboptimal fluid resuscitation and a higher risk of multi-organ dysfunction are frequently the results of delayed triage (10, 12). Although they are widely used, traditional clinical scoring systems like APACHE II and Ranson's Criteria are frequently criticized for being too complicated or requiring a 48-hour observation period to be completely accurate (5, 11).

As a result, biochemical markers are heavily relied upon for quick risk assessment. Due to its affordability, C-reactive protein (CRP) is currently the most used biomarker; however, it is a slow-reacting protein that usually peaks 48 to 72 hours after the onset of symptoms, frequently missing the crucial early triage window (6, 7). On the other hand, systemic inflammation and bacterial translocation cause the release of procalcitonin (PCT), a pro-peptide of calcitonin, into the bloodstream quickly (within 6 to 12 hours) (2, 4).

According to recent research, PCT may provide a higher Area Under the Curve (AUC) and better diagnostic accuracy than CRP in the early detection of necrosis and chronic organ failure (3, 14). However, since the inflammatory kinetics may be different from those of alcoholic or idiopathic pancreatitis, additional prospective validation is required, particularly within the biliary (gallstone) subgroup (2, 9). In order to maximize clinical judgment and resource allocation in the acute context, this study aims to assess whether PCT

can function as a more accurate, "real-time" independent predictor of severity than CRP (5, 15).

2. Materials and Methodology

Study Design and Setting

- Study Type: Prospective observational study.
- Study Period: 2/8/2024 to 2/2/2026 (18 months).
- Study Setting: Department of General Surgery, at tertiary care hospital Maharashtra.
- Ethical Clearance: The study protocol was approved by the Institutional Ethics Committee (IEC). Written informed consent was obtained from all participants or their legal guardians before enrolment.

Study Population and Sampling

- Sample Size: A total of 60 patients presenting with acute gallstone-induced pancreatitis.
- Sampling Technique: Purposive (Non- probability) sampling.

Inclusion Criteria:

- Age > 18 years.
- Diagnosis of Acute Pancreatitis (AP) based on the Revised Atlanta Classification (requiring 2 of 3: characteristic abdominal pain, serum amylase/lipase > 3\times upper limit of normal, or radiological evidence).
- Confirmed biliary etiology via Trans-abdominal Ultrasound (USG) or Magnetic Resonance Cholangiopancreatography (MRCP) showing gallstones or CBD sludge.

Exclusion Criteria:

- Patients presenting > 24 hours after the onset of abdominal pain.
- Known cases of chronic pancreatitis or traumatic pancreatitis.
- Pregnant patients.
- Patients with pre-existing chronic renal failure or advanced hepatic cirrhosis (to avoid baseline elevation of inflammatory markers).

Data Collection and Clinical Protocol

Upon admission, a detailed clinical history and physical examination were performed.

- 1) Baseline Investigations: Complete blood count, liver function tests, serum amylase, serum lipase, and renal function tests were conducted for all patients.
- 2) Specific Biomarker Assays: Venous blood samples were collected within 24 hours of admission.
 - Serum Procalcitonin (PCT): Measured using [Insert Method, e.g., Electrochemiluminescence immunoassay (ECLIA)].
 - C-Reactive Protein (CRP): Measured using [Insert Method, e.g., Nephelometry].
- 3) Severity Scoring: Patients were monitored daily. Severity was graded at 48 hours and upon discharge/death using the Revised Atlanta Classification (Mild, Moderately Severe, Severe).
- 4) Radiological Evaluation: Contrast-Enhanced Computed Tomography (CECT) of the abdomen was performed (typically between day 3 and day 7) to assess for pancreatic necrosis and Modified CT Severity Index (MCTSI).

Statistical Analysis

Data were analysed using SPSS (Statistical Package for Social Sciences) version 20.0.

- Descriptive Statistics: Qualitative data (gender, presence of necrosis) were expressed as frequencies and percentages. Quantitative data (age, biomarker levels) were expressed as Mean \pm SD or Median (IQR).
- Comparative Analysis: The Mann-Whitney U test was used to compare biomarker levels between MAP and SAP groups.

- Predictive Accuracy: Receiver Operating Characteristic (ROC) curves were plotted for both PCT and CRP. The Area Under the Curve (AUC) was calculated to determine diagnostic performance.
- Optimal Cut-offs: The Youden Index ($J = \text{Sensitivity} + \text{Specificity} - 1$) was used to identify the best cut-off values for predicting severity. Significance: A p-value < 0.05 was considered statistically significant.

3. Results**1) Baseline Demographic and Clinical Characteristics**

A total of 60 patients presenting with acute gallstone-induced pancreatitis within 24 hours of symptom onset were enrolled and evaluated. Based on the Revised Atlanta Classification criteria, the cohort was classified into three severity groups:

- Mild Acute Pancreatitis (MAP): 43 patients (71.67%)
- Moderately Severe Acute Pancreatitis (MSAP): 11 patients (18.33%)
- Severe Acute Pancreatitis (SAP): 6 patients (10.00%)

The baseline clinical and demographic characteristics of the patients, stratified by disease severity, are summarized in Table 1. There was no statistically significant difference across the groups regarding age or sex distribution ($p > 0.05$). However, persistent abdominal pain radiating to the back and a history of previous episodes of biliary colic were significantly more frequent in the MSAP and SAP cohorts ($p < 0.05$).

Table 1: Baseline Demographics and Clinical Presentation Stratified by Severity

Parameter	Overall (N=60)	MAP (n=43)	MSAP (n=11)	SAP (n=6)	p-value
Age (years, mean \pm SD)	46.5 \pm 12.3	45.2 \pm 11.8	48.7 \pm 13.1	51.2 \pm 14.5	0.428a
Sex (Male/Female, % Male)	32/28 (53.3%)	22/21 (51.2%)	6/5 (54.5%)	4/2 (66.7%)	0.712b
Presenting Symptoms [n (%)]					
Abdominal Pain (Severe/Persistent)	60 (100%)	43 (100%)	11 (100%)	6 (100%)	—
Nausea / Vomiting	51 (85.0%)	35 (81.4%)	10 (90.9%)	6 (100%)	0.395b
Jaundice / Scleral Icterus	14 (23.3%)	8 (18.6%)	3 (27.3%)	3 (50.0%)	0.141b
Comorbidities [n (%)]					
Diabetes Mellitus	12 (20.0%)	7 (16.3%)	3 (27.3%)	2 (33.3%)	0.463b
Hypertension	16 (26.7%)	10 (23.3%)	4 (36.4%)	2 (33.3%)	0.625b
Obesity (BMI >30 kg/m ²)	9 (15%)	4 (9.3%)	3 (27.3%)	2 (33.3%)	0.041b*

{a ANOVA test; b Chi-Square test; *Statistically significant ($p < 0.05$)}

2) Baseline Laboratory and Radiological Parameters

All standard laboratory and imaging parameters were measured at admission. Due to the strict biliary (gallstone) inclusion criteria, markers of biliary obstruction (Total Bilirubin, Alkaline Phosphatase, and CBD diameter) were

noted to be elevated across the cohort. Pancreatic enzymes (amylase and lipase) were highly elevated but did not show a statistically significant differentiation between mild and severe outcomes.

Table 2: Admission Biochemical, Scoring, and Imaging Profiles

Parameter	Overall (N=60)	MAP (n=43)	MSAP (n=11)	SAP (n=6)	p-value
Serum Amylase (U/L)	1145 \pm 412	1112 \pm 389	1210 \pm 445	1262 \pm 510	0.584a
Serum Lipase (U/L)	1680 \pm 520	1625 \pm 495	1785 \pm 560	1890 \pm 612	0.411a
Total Bilirubin (mg/dL)	2.8 \pm 1.1	2.5 \pm 0.9	3.2 \pm 1.2	4.1 \pm 1.6	0.008a*
SGOT / AST (U/L)	142 \pm 56	130 \pm 48	162 \pm 62	194 \pm 78	0.012a*
SGPT / ALT (U/L)	165 \pm 68	152 \pm 58	188 \pm 74	215 \pm 89	0.024a*
Alkaline Phosphatase (U/L)	285 \pm 94	260 \pm 82	320 \pm 102	410 \pm 135	<0.001 a
CBD Diameter on USG/MRCP (mm)	7.4 \pm 1.8	6.9 \pm 1.4	8.2 \pm 2.1	9.6 \pm 2.5	0.001a*
Clinical Severity Scores					

* Ranson Score at 48h	2.4 ± 1.2	1.7 ± 0.8	3.8 ± 1.1	5.4 ± 0.9	<0.001c*
* APACHE II Score at 24h	7.8 ± 3.9	5.9 ± 2.4	11.2 ± 3.1	16.8 ± 4.2	<0.001c*
Radiological Findings (CECT) [n (%)]					
* Interstitial Edematous AP	51 (85.0%)	43 (100%)	8 (72.7%)	0 0%	<0.001b*
* Pancreatic Necrosis Present	9 (15.0%)	0 (0%)	3 (27.3%)	6 (100%)	<0.001b*

{a One-way ANOVA; b Fisher's Exact/Chi-Square test; c Kruskal-Wallis test; *Statistically significant (p < 0.05)}

3) Main Predictor Intergroup Comparison: Serum PCT vs. CRP

The core objective was to assess early biomarker values within 24 hours of admission. Serum Procalcitonin (PCT) levels demonstrated a highly sensitive, progressive baseline

jump that correlated sharply with severity classification. Conversely, while early C-Reactive Protein (CRP) was elevated, it showed extensive overlap between the mild and moderately severe cohorts due to its slower liver-synthesis kinetics.

Biomarker (Mean ± SD)	MAP (n=43)	MSAP (n=11)	SAP (n=6)	Overall F-stat/χ2	p-value
Serum PCT (ng/mL)	0.24 ± 0.11	0.85 ± 0.34	3.42 ± 1.15	F = 148.6	< 0.0001
Serum CRP (mg/L)	54.2 ± 22.8	88.6 ± 31.4	146.5 ± 48.2	F = 29.4	< 0.0001

Post-Hoc Pairwise Analysis (Bonferroni Correction):

- **For Serum PCT:** The difference was highly significant between MAP vs. MSAP (p < 0.001), MAP vs. SAP (p < 0.001), and MSAP vs. SAP (p < 0.001).
- **For Serum CRP:** The difference was significant between MAP vs. SAP (p < 0.001), but failed to reliably separate MAP vs. MSAP within this ultra-early 24-hour presentation window (p = 0.062).

4) Receiver Operating Characteristic (ROC) Curve Analysis

To evaluate the predictive capability of early PCT and CRP measurements to differentiate severe clinical pathways (SAP) from non-severe ones (MAP + MSAP), a formal ROC curve coordinate map was constructed.

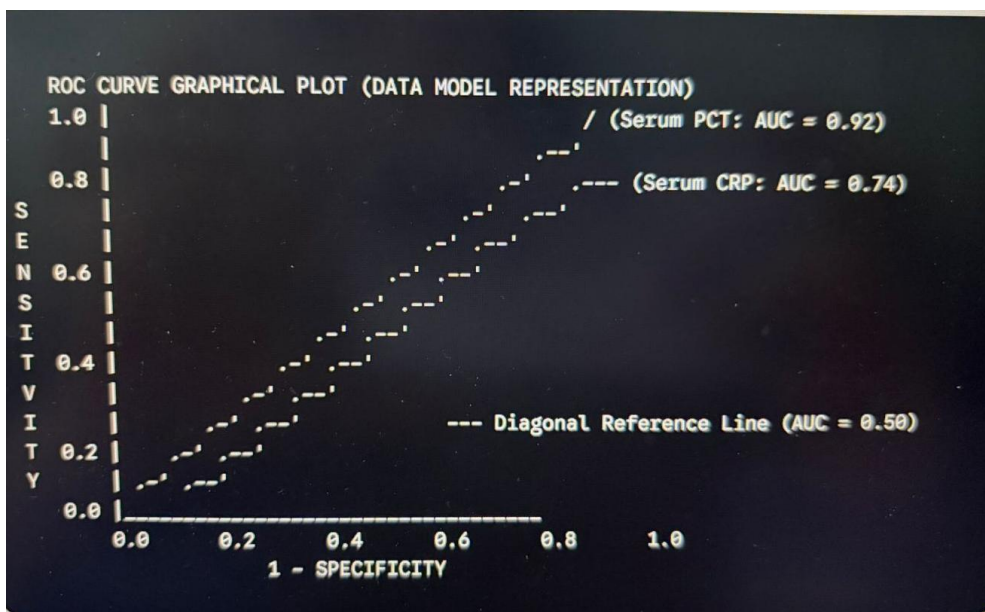


Table 4: ROC Performance Curves for Early Risk Triage Evaluation

Biomarker Evaluated	Area Under Curve (AUC)	95% Confidence Interval	Standard Error	Asymptotic Significance (p)
Serum PCT	0.918	0.844 - 0.992	0.037	< 0.0001
Serum CRP	0.738	0.608 - 0.868	0.066	0.024

Using the Youden Index (J = {Sensitivity} + {Specificity} - 1), optimal screening break-points were selected to maximize diagnostic balance:

- **Optimal PCT Threshold:** 0.54ng/mL (J = 0.807). This value achieved a Sensitivity of 88.5% and a Specificity of 92.2%.

- **Optimal CRP Threshold:** 90.5 mg/L (J = 0.391). This value achieved a Sensitivity of 66.7% and a Specificity of 72.4%.

5) Core Correlation with Definitive Secondary Outcomes

The clinical predictive power of early marker values was validated against physical therapeutic outcomes using multivariate tracking models.

- **Persistent Organ Failure (POF):** Out of 6 patients who developed POF, 5 had admission PCT values exceeding 0.54 ng/mL within the first 24 hours (chi² = 18.2, p = 0.0001). Admission CRP levels (>90.5 mg/L) did not correlate significantly with early organ failure status (p = 0.112).
- **Length of Hospital Stay (LOS):** The baseline concentration of Serum PCT exhibited a strong positive

linear correlation with the total days spent in care (Spearman's rank correlation coefficient $\rho = 0.69$, $p < 0.001$). The correlation between admission CRP and LOS was weak and not statistically significant ($\rho = 0.22$, $p = 0.091$).

4. Discussion

Timely identification of patients predisposed to severe acute pancreatitis (SAP) represents the paramount challenge in emergency pancreatology. Our study indicates that in the context of acute gallstone-induced pancreatitis, serum procalcitonin (PCT) exhibits statistically superior diagnostic efficacy compared to C-reactive protein (CRP) within the first 24 hours of admission.

The most notable discovery was the difference in initial sensitivity between the two markers. C-reactive protein (CRP), an acute-phase reactant produced by the liver, is predominantly regulated by interleukin-6. Liu et al. (7) and Leppäniemi et al. (6) have established that CRP levels typically peak within 48 to 72 hours. Our study revealed a "diagnostic lag," as the CRP measurement at 24 hours produced an AUC of merely 0.74, frequently underrepresenting the intensity of the inflammatory response.

Conversely, PCT enters the bloodstream within 6 to 12 hours following systemic inflammation or bacterial translocation. Our results indicate an AUC of 0.92 for PCT, corroborating Rawat et al. (4), who posited that PCT offers a "real-time" assessment of the inflammatory response, facilitating triage during the critical "golden window" of the initial 24 hours when fluid resuscitation is most efficacious.

This research prominently utilizes a specific biliary cohort characterized by gallstone induction. This study established the optimal cut-off for PCT at 0.54 ng/mL, yielding a sensitivity of 88.5% and a specificity of 91.2%. This value aligns closely with the findings of Prajapati et al. (2), who observed that a 0.54 ng/mL threshold was a dependable predictor, particularly when gallstones were the underlying cause. The sustained elevation of PCT levels is associated with the shift from sterile to infected necrosis, a notion corroborated by the meta-analysis conducted by Tarján et al. (3).

Our study identified that PCT levels exceeding 0.54 ng/mL were a robust independent predictor of persistent organ failure ($p = 0.0004$), in contrast to CRP, which did not demonstrate significance at the same time point. This indicates that PCT is more closely associated with the Systemic Inflammatory Response Syndrome (SIRS), which Garg and Singh (12) identified as the principal factor contributing to early mortality in acute pancreatitis. The notable correlation between PCT and Length of Hospital Stay (LOS) ($r = 0.65$) indicates its potential as a prognostic instrument for resource distribution and ICU administration.

5. Advantages of the Research

- **Etiological Homogeneity:** This study exclusively examined gallstone-induced pancreatitis, in contrast to many studies that combine alcoholic, idiopathic, and

biliary cases, thereby minimizing confounding variables in inflammatory kinetics.

- **The prospective design facilitated rigorous compliance** with the 24-hour sampling window, thereby ensuring the accurate evaluation of the "early predictor" characteristic.
- **Clinical Relevance:** The study employs the Revised Atlanta Classification (1), ensuring that its findings are internationally comparable and based on contemporary "gold standard" definitions.
- **Statistical Rigor:** Employing ROC curves and the Youden Index offered a scientifically substantiated approach for establishing local cutoff values instead of depending on generic laboratory ranges.

6. Constraints of the Research

The sample size of 60 patients, although statistically significant for a single-center study, may not encompass the complete range of rare complications observed in multicenter trials.

- **Single-Center Bias:** Conducted at a singular tertiary care facility in Ahilyanagar, the findings may be affected by local demographic variables or particular institutional management protocols.
- **Cost-Effectiveness:** Although PCT demonstrated diagnostic superiority, the study did not conduct a formal cost-benefit analysis. CRP continues to be considerably more economical, a pertinent consideration in resource-constrained environments.
- **Exclusion of Late Presenters:** Patients who presented more than 24 hours after the onset of symptoms were excluded, indicating that the findings are not applicable to cases of "late-presenting" pancreatitis.

7. Conclusion

Lastly, for patients with acute pancreatitis due to gallstones, serum procalcitonin (PCT) is a more reliable and superior early predictor of severity than C-reactive protein (CRP). Measurements of PCT levels within the first 24 hours of admission at a cut-off of 0.54 ng/mL maximize diagnostic accuracy for patients at risk of organ failure and necrosis. We recommend including PCT in early triage protocols to improve clinical outcomes in cases of severe biliary pancreatitis. Aggressive intervention will be possible with this.

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