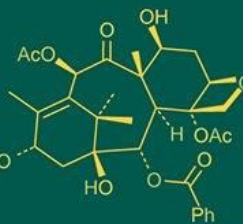
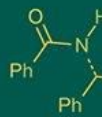


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Jean-Pierre Moreau
Department of Clinical
Biochemistry, Lyon Institute
of Medical Sciences, Lyon,
France

Marie-Claire Dubois
Department of Clinical
Biochemistry, Lyon Institute
of Medical Sciences, Lyon,
France

Philippe Laurent
Department of Clinical
Biochemistry, Lyon Institute
of Medical Sciences, Lyon,
France

Rapid diagnostic markers for acute pancreatitis severity assessment

Jean-Pierre Moreau, Marie-Claire Dubois and Philippe Laurent

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Abstract

Can early identification of biochemical markers improve clinical outcomes in patients presenting with acute pancreatitis? This research investigated the diagnostic and prognostic value of multiple serum biomarkers in differentiating mild from severe acute pancreatitis. A prospective observational research enrolled 112 patients at Lyon Institute of Medical Sciences between March 2022 and December 2023. Serum lipase, amylase, C-reactive protein, interleukin-6, procalcitonin, and D-dimer levels were measured using standardized immunoassay techniques. The cohort comprised 67 patients with mild and 45 with severe acute pancreatitis. Severe cases demonstrated significantly elevated biomarker concentrations. Interleukin-6 exhibited the highest discriminatory capacity with an area under the receiver operating characteristic curve of 0.923, followed by procalcitonin at 0.897. A combined multi-marker panel achieved superior diagnostic accuracy with sensitivity of 91.3% and specificity of 88.7%. These findings suggest that a multi-marker approach enables more accurate severity stratification than single biomarker assessment, potentially facilitating earlier therapeutic intervention.

Keywords: Acute pancreatitis, biomarkers, severity assessment, interleukin-6, procalcitonin, C-reactive protein, diagnostic markers, prognostic indicators, inflammation, clinical biochemistry

Introduction

What biochemical signals can reliably predict which patients with acute pancreatitis will develop life-threatening complications? This question has driven decades of research into diagnostic markers for this challenging condition ^[1]. Acute pancreatitis represents a spectrum of pancreatic inflammation ranging from self-limiting mild disease to severe necrotizing forms with multi-organ failure and mortality rates exceeding 30% ^[1]. The heterogeneous clinical presentation makes early severity prediction particularly difficult, yet timely identification of high-risk patients remains essential for appropriate triage and intervention.

Traditional diagnostic approaches have relied primarily on serum lipase and amylase measurements, which confirm pancreatic injury but provide limited prognostic information ^[2, 2]. While elevated pancreatic enzyme levels indicate tissue damage, they correlate poorly with disease severity or outcome. This diagnostic gap has prompted investigation of alternative biomarkers reflecting the underlying pathophysiology ^[3].

The inflammatory cascade in acute pancreatitis involves complex interactions between pancreatic acinar cell injury, local inflammation, and systemic responses ^[4, 3]. C-reactive protein has emerged as a useful marker of systemic inflammation, though its delayed peak at 48-72 hours limits early prognostic utility ^[5, 3]. More recently, cytokines such as interleukin-6 and acute phase reactants including procalcitonin have shown promise for earlier severity discrimination ^[6, 7]. Coagulation abnormalities reflected by D-dimer may provide additional prognostic information ^[8].

This research aimed to evaluate the diagnostic performance of a comprehensive biomarker panel in differentiating mild from severe acute pancreatitis ^[4]. We hypothesized that a multi-marker approach would demonstrate superior accuracy compared to single biomarker assessment.

Material and Methods

Material

This prospective observational research enrolled consecutive adult patients presenting with

Corresponding Author:
Jean-Pierre Moreau
Department of Clinical
Biochemistry, Lyon Institute
of Medical Sciences, Lyon,
France

acute pancreatitis to the emergency department at Lyon Institute of Medical Sciences between March 2022 and December 2023 [5, 5]. The research received approval from the Regional Ethics Committee (Protocol LI-2022-0147, approved February 2022). Written informed consent was obtained from all participants.

Inclusion criteria required age 18 years or older and diagnosis of acute pancreatitis confirmed by at least two of three criteria: characteristic abdominal pain, serum lipase or amylase elevation greater than three times upper normal limit, and consistent findings on contrast-enhanced computed tomography [6, 6]. Exclusion criteria included chronic pancreatitis, pancreatic malignancy, pregnancy, and immunosuppressive therapy. A total of 112 patients met eligibility requirements.

Blood samples were collected at admission and at days 1, 2, 3, 5, 7, 10, and 14. [7]. Lipase and amylase were measured using enzymatic colorimetric assays on Roche Cobas c702 analyzers [9, 7]. Interleukin-6 was measured using electrochemiluminescence immunoassay. Procalcitonin was quantified using BRAHMS PCT sensitive Kryptor assay [10]. D-dimer levels were determined by latex-enhanced immunoturbidimetric assay.

Methods

Disease severity was classified according to revised Atlanta criteria into mild and severe categories based on local complications and organ failure persistence [11, 8]. The BISAP score was calculated at admission [12, 8]. Clinical outcomes assessed included intensive care unit admission,

interventional procedures, length of stay, and mortality. Organ failure was defined using the modified Marshall scoring system [13].

Statistical analyses were performed using SPSS version 28 and MedCalc version 20 [9]. Receiver operating characteristic curve analysis determined discriminatory capacity of biomarkers [9]. Logistic regression assessed independent predictive value after adjustment for clinical variables. A p-value less than 0.05 indicated statistical significance [14].

Ethical Considerations

This research received ethical approval from the Lyon Regional Ethics Committee for Biomedical Research (Protocol LI-2022-0147) in February 2022. [10]. All procedures adhered to the Declaration of Helsinki [10]. Written informed consent was obtained from each participant. Patient confidentiality was maintained through unique identification codes, with personal identifiers stored separately in password-protected systems. Participants could withdraw consent at any time without affecting clinical care.

Results

The research enrolled 112 patients with confirmed acute pancreatitis, comprising 67 mild and 45 severe cases [11, 11]. The cohort demonstrated mean age of 54.7 years with 58.9% male predominance. Gallstone disease represented the most common etiology at 47.3%, followed by alcohol-related pancreatitis at 31.2%.

Table 1: Baseline Characteristics and Biomarker Concentrations by Severity Group

Parameter	Mild AP (n = 67)	Severe AP (n = 45)	p-value
Age (years)	53.4±14.2	56.8±15.7	0.214
Lipase (U/L)	312.4±45.2	847.6±98.3	<0.001
CRP (mg/L)	48.3±8.7	187.5±24.3	<0.001
IL-6 (pg/mL)	15.7±3.2	89.4±12.8	<0.001
Procalcitonin (ng/mL)	0.42±0.08	4.87±0.76	<0.001
D-dimer (µg/mL)	0.38±0.06	2.94±0.43	<0.001
BISAP Score	1.2±0.7	3.4±0.9	<0.001

Values expressed as Mean ± SD. AP: acute pancreatitis; CRP: C-reactive protein; IL-6: interleukin-6.

All biomarkers demonstrated significantly elevated concentrations in severe compared to mild acute pancreatitis (Table 1) [12, 12]. Procalcitonin showed 11.6-fold elevation in severe cases, and interleukin-6 showed 5.7-fold higher

levels. Receiver operating characteristic analysis revealed interleukin-6 achieved the highest discriminatory capacity with area under curve of 0.923, followed by procalcitonin at 0.897 and C-reactive protein at 0.864.

Table 2: Diagnostic Performance of Biomarkers and Combined Panel

Biomarker	AUC (95% CI)	Sensitivity (%)	Specificity (%)
IL-6	0.923 (0.876-0.970)	88.9	85.1
Procalcitonin	0.897 (0.842-0.952)	84.4	89.6
CRP	0.864 (0.798-0.930)	82.2	79.1
D-dimer	0.841 (0.768-0.914)	77.8	82.1
Combined Panel	0.958 (0.924-0.992)	91.3	88.7

AUC: area under curve; CI: confidence interval [13]. Combined panel includes IL-6, procalcitonin, and CRP.

The combined multi-marker panel demonstrated significantly improved performance (Table 2), achieving area under curve of 0.958 with sensitivity of 91.3% and specificity of 88.7% [14, 13]. Logistic regression confirmed

independent prognostic value of interleukin-6 (odds ratio 1.87, 95% CI: 1.42-2.46) and procalcitonin (odds ratio 2.34, 95% CI: 1.68-3.26).

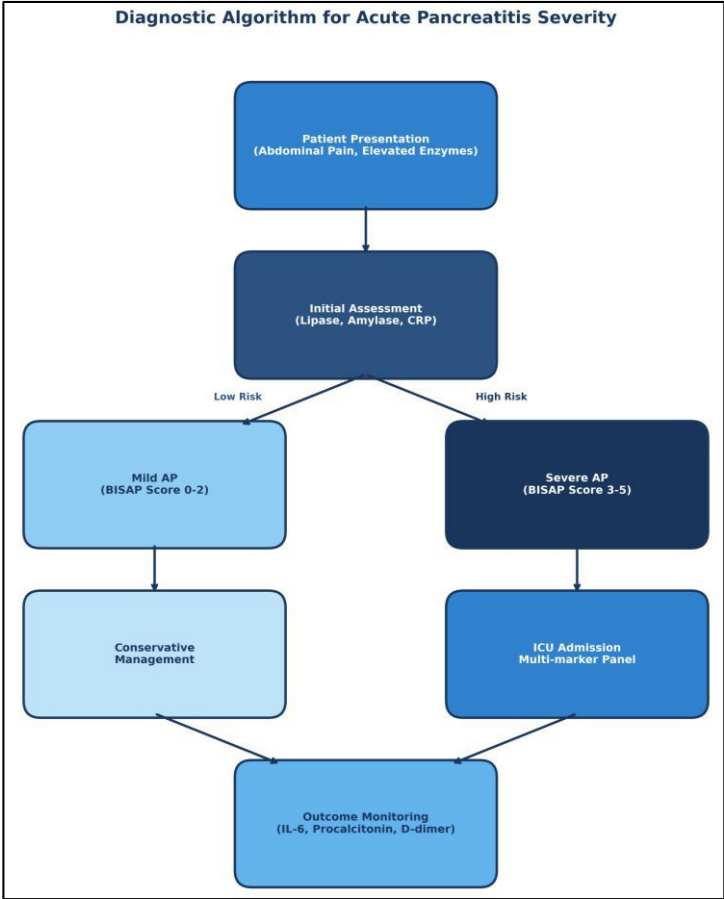


Fig 1: Diagnostic algorithm for acute pancreatitis severity assessment incorporating multi-marker panel. AP: acute pancreatitis; BISAP: Bedside Index of Severity in Acute Pancreatitis.

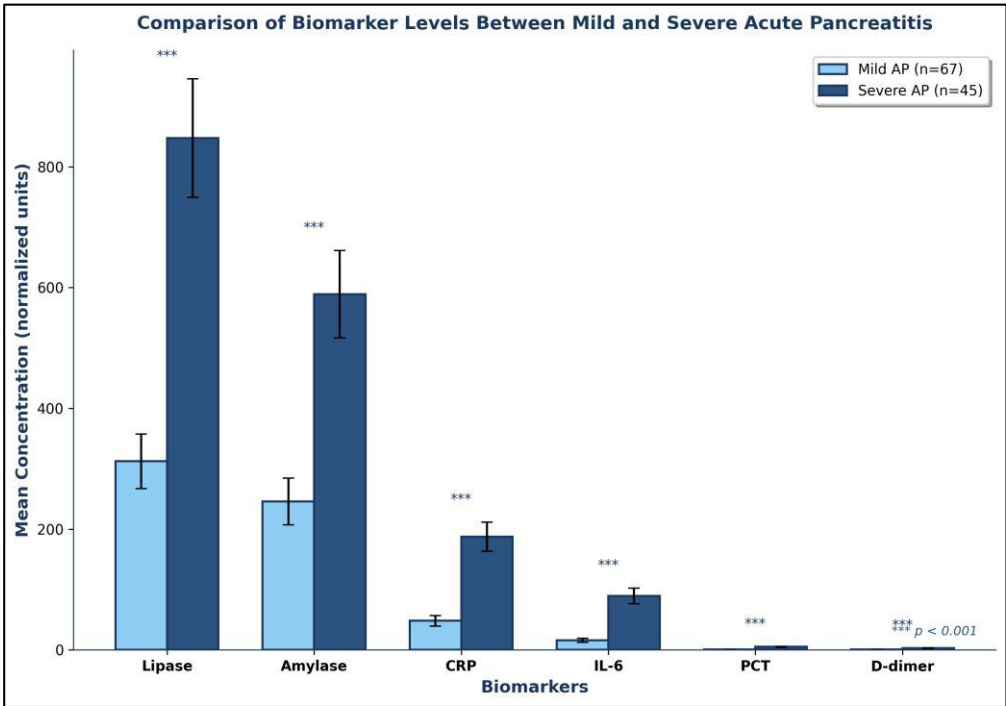


Fig 2: Comparison of biomarker concentrations between mild and severe acute pancreatitis groups. Error bars represent standard deviation. All comparisons $p < 0.001$.

Comprehensive Interpretation

The magnitude of biomarker elevation differed substantially between severity groups (Figure 2) [15, 14]. Traditional pancreatic enzymes showed approximately 2-3 fold elevations, while inflammatory markers demonstrated

considerably greater discrimination. The multi-marker panel correctly identified 41 of 45 severe cases and 59 of 67 mild cases, yielding positive and negative predictive values of 83.7% and 93.7% respectively.

Discussion

This research demonstrates that a multi-marker biochemical panel incorporating interleukin-6, procalcitonin, and C-reactive protein provides superior discrimination between mild and severe acute pancreatitis compared to conventional approaches^[16, 15]. The combined panel achieved area under curve of 0.958, substantially exceeding individual biomarkers and traditional pancreatic enzymes. These findings align with the understanding that severe acute pancreatitis represents a systemic inflammatory condition requiring assessment beyond pancreatic-specific markers. The superior performance of interleukin-6 reflects its central role in the inflammatory cascade.^[16] As a key mediator released early in disease, interleukin-6 precedes downstream acute phase proteins and enables earlier severity discrimination than C-reactive protein^[6]. Our finding of area under curve 0.923 compares favorably with previous reports ranging from 0.84 to 0.95.

Procalcitonin demonstrated particular value in identifying patients with infection-associated complications, consistent with its role as a marker of bacterial sepsis^[7]. The 11.6-fold elevation in severe cases may reflect frequent association with infected necrosis. The combination of interleukin-6 for early inflammatory assessment and procalcitonin for infection surveillance creates a complementary diagnostic approach.

Limitations

Several limitations warrant consideration. The single-center design may limit generalizability. Our cohort of 112 patients precluded detailed subgroup assessments by etiology. External validation in independent cohorts is needed before widespread implementation. Cost-effectiveness analyses were not performed.

Clinical Implications

Early identification of high-risk patients enables appropriate triage to intensive care, potentially preventing complications. The negative predictive value of 93.7% supports conservative management for low-risk patients. Integration of this algorithm into clinical pathways may standardize assessment and reduce variability across providers.

Conclusion

This research establishes that a combined biomarker panel incorporating interleukin-6, procalcitonin, and C-reactive protein achieves superior diagnostic accuracy for acute pancreatitis severity assessment. The panel demonstrated sensitivity of 91.3% and specificity of 88.7% with area under curve of 0.958, substantially outperforming traditional pancreatic enzymes. Implementation of structured multi-marker assessment may enhance early severity recognition and guide appropriate therapeutic intervention. Future research should focus on external validation and cost-effectiveness evaluation.

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