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Review

Comprehensive Review of Predictive Scoring Systems, Novel Biomarkers, and Artificial Intelligence in Acute Pancreatitis

Alina Calin Frij [1,2], Maria Comanescu [1], Cristian Velicescu [1,2], Tudor Ursuleanu [1], Andreea Luca [1], Andrei Andone[1], Roxana Covali[3*], Alin Ciubotaru[4], Radu Popa[5], Mihaela Camelia Tirnovanu [6], Cristiana Filip[7], Roxana Grigorovici [8,9], Mariana Pavel-Tanasa [10], Alexandru Grigorovici [1,2]

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1. Department of Surgery, Grigore T. Popa University of Medicine and Pharmacy, 700115 Iasi;
2. Department of Surgery I, Sf. Spiridon Hospital, 700111, Iași, Romania;
3. Department of Radiology, Biomedical Engineering Faculty, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iasi, Romania;
4. Department of Neurology, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iasi, Romania;
5. Department of Vascular Surgery, "Grigore T. Popa" University of Medicibe and Pharmacy, 700115 Iași, România;
6. Mother and Child Department, "Grigore T. Popa" University of Medicine and Pharmacy, 700115 Iasi, Romania;
7. Department of Biochemistry, Grigore T. Popa, University of Medicine and Pharmacy, 700115 Iasi, Romania;
8. Department of Gastroenterology, Sf. Spiridon Hospital, 700111, Iași, Romania;
9. Grigore T. Popa University of Medicine and Pharmacy, 700115 Iasi, Romania;
10. Department of Immunology, Grigore T. Popa University of Medicine and Pharmacy Iasi, 700115 Iasi, Romania

* Correspondence: ana.covali@umfiasi.ro

Abstract: Acute pancreatitis (AP) is a frequent gastroenterological emergency with a highly diverse clinical progression, varying from a self-resolving condition to a potentially fatal disease involving multi-organ failure. Precise early risk assessment is essential for enhancing results and efficiently distributing resources. This exhaustive review seeks to critically integrate the present status of prognostic forecasting in AP. It examines existing clinical scoring systems, new biomarkers, and the growing significance of Artificial Intelligence (AI) and Machine Learning (ML) to suggest a comprehensive framework for assessing severity. A narrative review of the scientific literature were performed. A comprehensive search of databases such as PubMed and Scopus was conducted utilizing keywords like "acute pancreatitis," "severity prediction," "biomarkers," and "machinelearning." Research offering quantitative information on predictive effectiveness (e.g., sensitivity, specificity, AUC) was prioritized for examination. Defined scores (Ranson, APACHE II, BISAP, CTSI) continue to be significant but have constraints regarding their timing and intricacy. Easily obtainable biomarkers such as C-reactive Protein (CRP), Procalcitonin (PCT), and the Neutrophil-to-Lymphocyte Ratio (NLR) offer important real-time prognostic information. New elements like visceral fat (VAI, LAP) and a lack of Vitamin D are significant, independent indicators of severity. Crucially, early research on AI and machine learning models (like Random Forest and XGBoost) demonstrates a significant enhancement in predictive accuracy, frequently surpassing traditional measures for severe AP, complications, and mortality in retrospective studies. The future of acute pancreatitis management is in a combined, multifaceted strategy. This approach ought to integrate the advantages of quick clinical assessments, real-time biomarker tracking, and AI-improved predictive analysis. Shifting from a universal model to this customized, stratified approach is essential for enhancing precision medicine and boosting patient results in acute pancreatitis.

Keywords: Acute pancreatitis, severity prediction, prognostic biomarkers, scoring systems, BISAP, Ranson; APACHE II, CT Severity Index, C-reactive protein (CRP), procalcitonin (PCT),

urinary trypsino-gen activation peptide (TAPu), trypsinogen-2, neutrophil-to-lymphocyte ratio (NLR), Aggregate Systemic Inflammation Index (AISI), machine learning, artificial intelligence, NLRP3 inflam-masome, microRNA-486-5p, vitamin D

1. Introduction

Acute pancreatitis (AP) represents a major gastrointestinal emergency, occurring globally at an estimated rate of around 34 cases per 100,000 people each year [1, 2]. Although the majority of cases have a mild and self-resolving trajectory, approximately 20-30% advance to severe illness, marked by ongoing organ failure and a mortality rate that may soar to 20-40% [2]. This stark contrast in results highlights the crucial significance of timely and precise risk assessment.

The first 24-72 hours following presentation signify a critical "therapeutic window" for detecting high-risk patients who could gain from close monitoring and intensive intervention, while simultaneously identifying low-risk patients to prevent unnecessary hospital stays and resource consumption. To address this challenge, healthcare providers utilize a mix of prognostic scoring systems and biochemical indicators.

Multi-factor scores that have been established serve as the foundation for forecasting. The Ranson criteria are commonly employed but necessitate 48 hours for complete evaluation, possibly postponing vital decisions [3]. The APACHE II score is thorough yet intricate, restricting its practicality at the bedside [4, 5]. The BISAP (Bedside Index of Severity in Acute Pancreatitis) score provides a more straightforward, 24-hour option with a significant negative predictive value regarding mortality [5, 6]. Radiologically, the CT Severity Index (CTSI) is crucial but is most accurately conducted 48-72 hours after symptoms begin to permit complications such as necrosis to manifest [3].

Simultaneously, biochemical indicators provide a hopeful avenue for swift evaluation. C-reactive Protein (CRP) is the most commonly utilized marker, yet its levels reach their maximum 48-72 hours after onset, restricting its usefulness in the early stage [7, 11]. Procalcitonin (PCT) has been identified as a more effective early marker for organ dysfunction and infected necrosis [7,13]. Additionally, pathophysiologically direct indicators such as Urinary Trypsinogen-2 and its activation peptide (TAP) demonstrate high specificity, with quick dipstick tests currently accessible for point-of-care applications [8, 9].Nevertheless, the relative precision and best use of these different instruments—spanning from intricate scoring systems to individual biomarkers—continue to be a topic of active investigation. Inconsistent results from research by authors such as Mounzer, Yeung, and Papachristou underscore the necessity for more precise clinical direction [6, 9, 10]. This review aims to compile existing evidence regarding the predictive effectiveness of significant scoring systems (Ranson, APACHE II, BISAP) and important biomarkers (CRP, PCT, Urinary Trypsinogen-2) for early prediction of severity in acute pancreatitis [15, 16, 17, 18].

Table 1 presents a comparison of the most established clinical scoring systems, focusing on their specific parameters, timing, and clinical usefulness. The Ranson criteria, despite being very sensitive, necessitate a complete 48 hours for computation, potentially hindering urgent management decisions [3]. Conversely, the APACHE II score serves as an effective predictor of mortality; however, its complexity frequently restricts its application for quick bedside triage [4, 5]. The BISAP score achieves a beneficial equilibrium, providing an uncomplicated, 24-hour evaluation with great specificity for detecting necrosis and organ failure, rendering it especially valuable for initial risk stratification [6]. Ultimately, CTSI continues to be the imaging gold standard for evaluating local complications, but its best predictive value is achieved only after 48-72 hours, allowing pancreatic necrosis to fully delineate [3].

Table 1: Comparison of Established Prognostic Scoring Systems in Acute Pancreatitis

Scoring System	Basis & Key Parameters	Optimal Timing	Key Strengths	Key Limitations
Ranson's Criteria	11 clinical & laboratory parameters (e.g., age, WBC, glucose, LDH, Hct drop, BUN rise)	At admission & 48 hours	High sensitivity for organ failure; Well-validated over decades; Excellent predictor of severe AP (AUC 0.97) [33].	Requires 48 hours for full score; Delays early intervention; Less practical for immediate decision-making.
APACHE II	12 physiological variables, age, chronic health status	At admission; can be serially updated	Most reliable single predictor of overall mortality in first 24h [27, 33]; Allows for dynamic reassessment.	Complex calculation with 12 variables; Not user-friendly for rapid triage in busy emergency settings.
BISAP Score	5 clinical elements: **B**UN >25 mg/dL, **I**mpaired mental status, **S**IRS, **A**ge >60, **P**leural effusion	Within 24 hours of admission	Simple, fast, and highly specific for necrosis/organ failure [6, 22]; Excellent for early triage and risk stratification.	May have lower sensitivity than more complex scores; Relies on accurate identification of SIRS and mental status.
CTSI / mCTSI	CT imaging findings (pancreatic inflammation, necrosis, extrapancreatic complications)	48-72 hours after symptom onset	Gold standard for visualizing local complications (necrosis, collections); Essential for guiding invasive interventions [3].	Poor sensitivity in the first 48 hours; Involves radiation exposure; Not a tool for very early prediction.

Scope of the study

- This comprehensive review aims to deliver a critical and synthesized evaluation of the present state of prognostic prediction in acute pancreatitis.
- Consistently evaluate the accuracy of predictions, usefulness in clinical settings, and constraints of existing multi-factor scoring models.
- Assess the predictive significance of traditional and new biological markers.
- Investigate the influence of particular pathophysiological factors, including visceral fat and micronutrient levels, on the severity of diseases.
- Explore the groundbreaking capacity of artificial intelligence and machine learning algorithms in reshaping risk stratification.
- Suggest a cohesive, practical structure for predictive evaluation that merges the finest aspects of current instruments with cutting-edge technologies.

Objectives

- This review outlines the subsequent specific objectives to achieve its aim:
- To outline the operational features, ideal usage periods, and relative efficacy of the Ranson, APACHE II, BISAP, and CTSI scores in forecasting severe AP, local complications, and mortality.
- To evaluate the predictive value of inflammatory biomarkers (CRP, PCT), pancreatic-specific urine markers (TAP, Trypsinogen-2), and accessible hematological indices (NLR, LAR, AISI, RPR) in early risk assessment.
- To examine the link between etiopathogenetic elementssuch as visceral obesity (assessed by VAI, LAP), vitamin D deficiency, and coagulation profiles specific to etiology—and clinical consequences in AP.
- To examine the evidence indicating the higher predictive accuracy of AI/ML models compared to conventional scoring systems and to address the route for their clinical incorporation.
- To combine the gathered evidence into a stratified, context-sensitive method for prognostic assessment in AP, customized for various clinical environments and resource capacities.

Innovation of the study

This review sets itself apart by advancing beyond a standard comparison of scoring systems to incorporate innovative research areas that are transforming the prognostic framework in AP. Its originality is in:

Highlighting the Visceral Adiposity Paradigm: It presents strong evidence that anthropometric indicators of visceral fat distribution (e.g., Visceral Adiposity Index - VAI, Lipid Accumulation Product - LAP) are more effective predictors of severity compared to general adiposity metrics such as BMI, establishing a metabolic connection to disease severity [19].

Integrating Molecular and Genetic Perspectives: It examines biomarkers like serum microRNA-486-5p and NLRP3 not solely as passive prognostic factors but as key players in the inflammatory and autophagic pathways that propel disease development .

Predicting the Transformation through AI and ML in AP Management : It offers an in-depth examination of how AI and ML algorithms (such as XGBoost, Random Forest) are reaching unparalleled predictive effectiveness, enabling a transition from reactive to proactive, customized patient management .

Pathophysiological rationale and clinical significance of study

The pathophysiology of AP includes the early activation of pancreatic digestive enzymes within the acinar cells, resulting in autodigestion of the gland and an ensuing systemic inflammatory response syndrome (SIRS). This sequence can lead to capillary leak, hypovolemic shock, and remote organ failure. The clinical significance of AP arises from its unpredictability and the likelihood of swift clinical decline. Severe AP impacts approximately 20% of patients and has a mortality rate ranging from 20% to 40%, representing most deaths associated with AP. The significant illness, extended hospital admissions, frequent requirements for intensive treatment, and elevated expenses tied to handling complications (e.g., infected necrosis) impose a heavy strain on healthcare systems. Consequently, any progress in early, precise forecasting that allows for preemptive treatment and effective resource distribution has significant consequences for both individual patient longevity and overall healthcare efficiency [11].

Practical Relevance of the Research

This thorough review combines evidence directly applicable to clinical practice, providing a guide to improve the prognostic assessment of AP in various healthcare environments. The results support a layered, multifaceted strategy that can be adjusted according to local resources and knowledge.

In environments rich in resources, the combination of traditional scoring systems with new biomarkers and Artificial Intelligence represents the most promising direction ahead. Healthcare professionals can employ the Bedside Index for Severity in Acute Pancreatitis for quick, initial assessment within 24 hours, subsequently complemented by ongoing surveillance with dynamic biomarkers such as the Neutrophil-to-Lymphocyte Ratio and Procalcitonin. For conclusive morphological evaluation, the CT Severity Index is essential after 48-72 hours. The analysis emphasizes that the forthcoming standard of care in these environments will probably incorporate AI-driven clinical decision support systems merged with Electronic Health Records. These systems are capable of handling multimodal data instantaneously, offering enhanced predictive precision for serious AP, complications, and mortality, thus allowing preemptive measures and improved resource distribution in intensive care units.

For settings with limited resources, the research highlights the important benefits of affordable and accessible tools. The BISAP score is notable for its ease of use and excellent specificity. Additionally, easily accessible hematological metrics like the Neutrophil-to-Lymphocyte Ratio, Lactate Dehydrogenase-to-Albumin Ratio, and Aggregate Systemic Inflammation Index provide valuable, affordable prognostic data that

can be monitored over time to assess a patient's course. This lessens exclusive dependence on more complicated or slower scoring methods such as APACHE II or Ranson's criteria.

The assessment offers practical recommendations for personalized patient care. It promotes going beyond Body Mass Index by including evaluations of visceral fat (Visceral Adiposity Index - VAI) and checking for Vitamin D deficiency, since these are significant, changeable risk factors.

Materials and Method

This research was carried out as a narrative review and meta-synthesis of the current scientific literature regarding prognostic instruments in acute pancreatitis (AP). To provide a thorough and up-to-date summary, the literature review concentrated on publications released from January 2000 to July 2024.

A comprehensive search approach was utilized across three primary electronic databases: PubMed, Scopus, and Web of Science. The search employed a blend of keywords and Medical Subject Headings (MeSH) terms pertinent to the essential subjects of the review, such as: "acute pancreatitis," "prediction of severity," "prognostic assessment," "Ranson score," "APACHE II," "BISAP score," "CT Severity Index," "biomarkers," "C-reactive protein," "procalcitonin," "neutrophil-lymphocyte ratio," "machine learning," and "artificial intelligence."

Criteria for inclusion were established to choose the most pertinent studies. We incorporated primary research studies, meta-analyses, and systematic reviews that:

- Engaged human participants suffering from acute pancreatitis
- Supplied numerical information regarding the forecasting efficacy of a scoring system, biomarker, or AI model (e.g., sensitivity, specificity, Area Under the Curve [AUC], positive/negative predictive values).

Exclusion criteria were implemented to ensure focus and quality. We left out:

- Case studies, opinion pieces, and conference summaries
- Research not released in the English language
- Studies concentrated solely on chronic pancreatitis, pediatric pancreatitis, or animal models.

The process of selecting studies consisted of two stages. At first, a single reviewer screened all identified records using their titles and abstracts to eliminate obvious irrelevancies. To increase rigor and reduce selection bias, a second independent reviewer evaluated a random 20% sample of the titles and abstracts, showing a significant level of agreement. The remaining records were evaluated for eligibility by two independent reviewers through full-text articles based on the established inclusion and exclusion criteria. Any conflicts that arose during the full-text screening were settled through dialogue and agreement between the two reviewers.

Out of an initial set of 1,250 identified records, the systematic screening and selection approach led to the inclusion of 98 articles for the final data extraction and synthesis. The synthesis procedure encompassed a thorough evaluation of the chosen literature to glean essential findings, contrast predictive accuracies, pinpoint agreements and disputes, and compile a cohesive overview of the existing situation regarding prognostic prediction in AP.

2. Results

Traditional scoring systems

Ranson's Criteria: Established in 1974, this scoring system continues to be commonly utilized. It includes 11 parameters evaluated at admission and after 48 hours. A score greater than 3 signifies severe AP. Although it shows significant sensitivity for ongoing organ failure and was recognized in one study as the most reliable predictor of severe AP (AUC 0.97)(33), its primary drawback is the required 48-hour observation window, which may postpone urgent treatments [4; 12].

APACHE II (Acute Physiology and Chronic Health Evaluation II): one of the most dependable indicators of overall mortality in AP, with reported AUCs around 0.72-0.89 for this specific outcome, underscoring its strength in predicting patient survival [27; 33]. Nonetheless, its computation is complex, needing several variables, which restricts its usefulness for quick, bedside assessment [5]. BISAP (Bedside Index for Severity in Acute Pancreatitis): Created for ease of use and prompt application, the BISAP score employs five factors accessible within 24 hours of admission. It demonstrates remarkable specificity (100%) for forecasting pancreatic necrosis and ongoing organ failure, rendering it an effective "rule-in" instrument [6; 12]. Research directly contrasting it with Ranson's criteria has shown that BISAP exhibits similar or better predictive accuracy, along with enhanced practicality and efficiency [13]. CT Severity Index (CTSI) and modified CTSI: Serving as the imaging benchmark, the (m)CTSI offers a direct morphological evaluation of both inflammation and necrosis. It shows remarkable sensitivity (96.9%) in identifying pancreatic necrosis [12]. Nonetheless, its usefulness is restricted in the hyper-acute stage, with guidelines suggesting performance at 48-72 hours after admission. The mCTSI is a strong indicator of localized complications [13].

Even though these clinical scores establish an important basis for risk assessment, they are enhanced by dynamic biological markers that give immediate insight into the underlying inflammatory and necrotic mechanisms.

Biomarkers (conventional vs. emerging)

The prognostic value of biomarkers differs according to their pathophysiology and kinetics, providing additional insights alongside clinical scores. A direct examination of their profiles is crucial for clinical use (refer to Table 2 for a summary).

C-Reactive Protein (CRP) is the most commonly utilized biomarker because of its availability. Nonetheless, its effectiveness is restricted by a lagging peak at 48-72 hours after onset, with a value exceeding 150 mg/L at 48 hours indicating severe AP (Sens 80%, Spec 75%) [2, 7, 11].

Conversely, Procalcitonin (PCT) acts as a more responsive early indicator, especially for systemic issues. It shows significant sensitivity (up to 100%) for organ failure and serves as a strong negative predictor for infected necrosis, thus proving useful for directing antibiotic treatment [13, 143].

The most directly pathophysiological markers are the urinary biomarkers, Trypsinogen-2 and its activation peptide (TAP). Directly released from the inflamed pancreas, they provide high specificity for the severity of the disease and the distinctive benefit of quick detection through a point-of-care dipstick test, enabling very early evaluation [11, 15, 16].

Conventional serum biomarkers provide accessible but temporally distinct information. C-Reactive Protein (CRP) is the most widely utilized due to its low cost and availability; however, its clinical utility is constrained by a delayed peak at 48-72 hours, with a level >150 mg/L thereafter indicating severe AP [7, 11]. In contrast, Procalcitonin (PCT) rises earlier and shows superior sensitivity for systemic complications, particularly for predicting organ failure and excluding infected pancreatic necrosis, making it a valuable tool for guiding intensive care and antimicrobial therapy [13, 143].

Pancreatic-specific urinary biomarkers offer a more direct window into disease activity. Urinary Trypsinogen-2 and Trypsinogen Activation Peptide (TAP) are released directly during pancreatic inflammation. Their key advantage is the potential for very early detection at the point-of-care via a rapid dipstick test, providing high specificity for severe disease [11, 15, 16].

Beyond specialized laboratory tests, routine complete blood count (CBC) parameters can be leveraged to create powerful and accessible prognostic indices.

Available Hematologic and Inflammatory Measures

Neutrophil-to-Lymphocyte Ratio (NLR): This easily accessible inflammatory measure is flexible and inexpensive. The NLR at 24 hours effectively predicts severe AP, whereas the NLR at 48 hours is more indicative of mortality and organ failure [17]. It

demonstrates a robust positive correlation with the CT Severity Index [35]. Lactate Dehydrogenase-to-Albumin Ratio (LAR): The LAR measured at 48 hours has shown a strong correlation with mortality, organ failure, and duration of hospitalization, acting as a composite indicator of cellular damage and nutritional condition[18].

Aggregate Systemic Inflammation Index (AISI): This new index, based on complete blood count parameters, has shown strong correlations with recognized severity scores and clinical results. It demonstrated 94.4% sensitivity and 91.0% specificity in forecasting hospitalizations longer than 10 days, emphasizing its robust predictive ability. Red Blood Cell Distribution Width-to-Platelet Ratio (RPR): The RPR upon admission can distinguish between mild and moderate-to-severe acute pancreatitis (AP) and is associated with mortality, providing an easy prognostic overview at the time of presentation, Table 2 [19;20].

In addition to composite scoring systems, various biomarkers provide an alternative method for swift prognostic assessment. These are condensed in Table 2, which outlines their rationale and clinical effectiveness. Among standard serum markers, CRP is still commonly utilized because of its availability, even though it peaks late at 48-72 hours [7, 11]. PCT acts as a more sensitive early marker for systemic issues, especially organ failure and infected necrosis [13]. Pathophysiologically, direct markers such as urinary Trypsinogen-2 and its activation peptide (TAP) offer significant specificity, along with the benefit of swift point-of-care testing [11, 15, 16].

Additionally, recent studies have underscored the predictive significance of easily accessible hematological indicators. The NLR and the LDH/Albumin Ratio are active indicators of systemic inflammation and damage that reliably forecast severe illness, organ dysfunction, and mortality. More intricate composite indices, like the AISI, demonstrate remarkable potential in forecasting extended hospital admissions [28]

Table 2: Emerging and Accessible Biomarkers in Acute Pancreatitis Biomarker Category	Specific Marker	Key Characteristic / Rationale	Prognostic Utility & Performance
Conventional Serum	C-Reactive Protein (CRP)	Acute-phase reactant; peaks at 48-72h post-onset.	Level >150 mg/L at 48h predicts severe AP (Sens 80%, Spec 75%) [7, 11].
Conventional Serum	Procalcitonin (PCT)	Precursor of calcitonin; early marker of severe infection and sepsis.	High sensitivity for organ failure (100%) and severe AP (86.4%) [13]. Strong negative predictor of infected necrosis.
Pancreatic-Specific (Urinary)	Trypsinogen-2 / TAP	Released early from inflamed pancreas; rapid dipstick test available.	Strong correlation with severity; high sensitivity (up to 100%) and specificity (85%) reported [11, 15, 16].
Hematological Indices	Neutrophil-Lymphocyte Ratio (NLR)	Dynamic, readily available measure of systemic inflammatory response.	**24h NLR:** Predicts severe AP. **48h NLR:** Predicts mortality & organ failure [26, 35].
Hematological Indices	LDH/Albumin Ratio (LAR)	Combines marker of cellular injury (LDH) and systemic nutritional/inflammatory status (Albumin).	**48h LAR:** Significantly correlates with mortality, organ failure, and increased length of stay [26].
Hematological Indices	Systemic Inflammation Index (SII) & Aggregate Index of Systemic Inflammation (AISI)	Novel composite indices derived from platelet, neutrophil, and lymphocyte counts (SII: Platelets × Neutrophils/Lymphocytes; AISI: (Neutrophils × Monocytes × Platelets)/Lymphocytes).	**AISI:** High accuracy in predicting prolonged hospitalization (>10 days) with 94.4% Sensitivity and 91.0% Specificity [28]. SII is also a significant predictor of severity.
Hematological Indices	Red cell Distribution Width-to-Platelet Ratio (RPR)	Simple snapshot of inflammation (RDW) and potential consumption (Platelets).	Elevated RPR at admission is an independent predictor of persistent organ failure and severe AP [29, 30].

Based on the groundwork of inflammatory and hematological indicators, recent studies have discovered new patient-specific risk elements and initiated a new phase of predictive modeling using artificial intelligence.

New pathophysiological predictors (visceral fat, vitamin D, coagulation)

Visceral Obesity: A change in perspective is occurring, transitioning from overall fatness (BMI) to targeted assessments of problematic visceral fat as indicators of AP severity. The Visceral Adiposity Index (VAI) and Lipid Accumulation Product (LAP) are derived from basic clinical information: waist circumference, BMI, triglyceride levels, and HDL cholesterol. In contrast to BMI, which solely assesses size, VAI and LAP indicate the metabolic function of visceral fat—a crucial factor in systemic inflammation and insulin resistance that worsens AP severity. Consequently, they consistently surpass BMI, as VAI demonstrates an AUC of 0.737 for predicting severe AP [19].

Clinical Application: Although there are no universal standards yet, these indices can be easily computed at admission using standard data. An elevated VAI or LAP score should trigger immediate concern for an increased risk of severe pancreatitis, necessitating closer observation regardless of the patient's BMI. Incorporating them into initial assessment protocols is a viable move toward enhanced personalized risk stratification

Coagulation profiles specific to etiology: Individuals with hyperlipidemic AP have greater coagulation abnormalities than those with biliary AP, with fibrinogen and coagulation factor VIII recognized as potential indicators of severity in this group [22].

Artificial intelligence and ML

Artificial intelligence and machine learning: AI/ML models demonstrate significant promise for predictive precision in early research. Algorithms like XGBoost and Random Forest have shown excellent results in research, reaching AUCs of 0.93 for severe AP, 0.891 for complications, and 0.975 for mortality (31, 34). Algorithms like XGBoost and Random Forest have shown a notable boost in performance, reaching AUCs of 0.93 for severe AP, 0.891 for complications, and 0.975 for mortality. These figures indicate a significant enhancement compared to the AUCs of approximately 0.70-0.80 usually documented for standard scores such as BISAP and APACHE II in comparable assignments.

It is important to recognize that numerous promising outcomes arise from retrospective, single-center research or simulations employing fabricated data, and their applicability relies on external validation in varied, prospective clinical environments. AI systems have demonstrated competence in using clinical guidelines (e.g., ACG 2024) with significant accuracy, although not without errors [23].

3. Discussion

Integrated framework

This synthesis highlights a core principle: no single predictive instrument is universally the best for all forecasting endpoints in AP. Navigating the clinical landscape effectively requires insight into the unique role of each tool. BISAP provides an ideal combination of speed and precision for preliminary assessment. APACHE II is still a strong, albeit intricate, predictor of death. Ranson's criteria, although outdated, remains useful for pinpointing high-risk patients, while the CTSI is essential for morphological staging.

The emergence of straightforward, inexpensive biomarkers (NLR, LAR, AISI) signifies a significant progress for areas with limited resources and for delivering continuous, dynamic evaluations of the inflammatory response. Additionally, the investigation of pathogenic mediators such as miR-486-5p and NLRP3 creates new opportunities for both prognosis and the creation of targeted treatments.

Still, one of the most encouraging developments is the rise of AI and ML. Their ability to integrate large, multimodal datasets enables an extensive patient assessment that has, in numerous studies, outperformed traditional scoring systems. For example, models like Random Forest (AUC: 0.89) have demonstrated benefits over metrics like BISAP (AUC: ~0.70) in these studies [34].

These findings, however, need to be viewed carefully. The 'established benefits' are frequently shown on the identical datasets utilized for training the models, and their actual reliability in real-world scenarios needs verification through external assessment. Concerns regarding model generalizability, algorithmic bias, and incorporation into clinical workflows continue to pose major obstacles before an upcoming transformation' can occur.

The stated benefits of models like Random Forest (AUC: 0.89) compared to traditional scores such as BISAP (AUC: ~0.70) indicate a significant enhancement in forecasting capability. In clinical language, a rise in AUC of this scale could improve the precision of pinpointing high-risk patients, possibly signaling a forthcoming change in clinical decision-making [34]. The current challenge is to move these effective algorithms from research settings into verified, user-friendly clinical decision support systems that are incorporated within electronic health records.

The classification of AP severity is essential for treatment choices and predicting outcomes. Conventional scoring systems, although historically important, demonstrate significant drawbacks in timing, complexity, and differences between observers. The Ranson and APACHE II scores are reliable for predicting mortality but do not provide timely results. In contrast, BISAP offers a convenient but similarly precise bedside option [24].

The introduction of biochemical markers has transformed early evaluation by providing a dynamic indication of systemic inflammation and pancreatic damage. CRP, PCT, and urinary enzyme indicators improve the accuracy of current scoring systems, while blood ratios (NLR, LAR, AISI) offer affordable options suitable for various healthcare environments.

New molecular and genetic biomarkersNLRP3 inflammasome activity and miR-486-5p expression—go beyond prognostic measurement by highlighting pathogenic pathways that connect inflammation, autophagy dysregulation, and cell death [21; 25]. This combined diagnostic and mechanistic function marks a significant progress in the field of biomarker science.

Artificial intelligence and machine learning signify the upcoming frontier in acute pancreatitis management. Their ability to integrate multimodal data, perform real-time computations, and learn adaptively allows for unmatched predictive accuracy. Despite progress, issues persist regarding the generalizability of models, ethical execution, and their integration into clinical workflows [23; 31; 32; 33 26; 27].

In the end, a multimodal, layered approach that integrates quick bedside assessment (BISAP), real-time biochemical monitoring (CRP, PCT, NLR), and computational modeling stands out as the best framework for early risk assessment and individualized treatment targeting, Table 3.

This multi-center research by Yasuda et al. (2019) confirmed the effectiveness of urinary biomarkers for acute pancreatitis (AP). The quick trypsinogen-2 dipstick test showed moderate diagnostic precision (sensitivity 73.1%, specificity 62.5%) [34; 35].

In quantitative terms, the concentrations of urinary trypsinogen-2 and Trypsinogen Activation Peptide (TAP) demonstrated enhanced prognostic capabilities, achieving the highest Area Under the Curve (AUC) values for forecasting severity in relation to both clinical prognostic factors (AUC 0.704) and CT Grade (AUC 0.701 and 0.692, respectively). Importantly, both markers showed a significant correlation with the degree of extra-pancreatic inflammation. The research validates the diagnostic usefulness of the dipstick and identifies quantitative urinary trypsinogen-2 and TAP as important, non-invasive prognostic indicators for evaluating AP severity [36].

The proven advantages of models such as Random Forest (AUC: 0.89) compared to conventional scores (BISAP AUC: ~0.70) indicate an impending transformation in clinical decision-making [34].

The effectiveness and asserted superiority of these AI models fundamentally rely on the quality, quantity, and diversity of their training data. Numerous high-performing models mentioned in the literature have not been subjected to thorough external validation in various real-world clinical environments.

The absence of validation, along with the mainly retrospective characteristics of the current evidence, indicates that extensive clinical implementation remains untimely. Addressing issues tied to model generalization, algorithmic prejudice, and smooth incorporation into clinical processes is an essential subsequent step. The current challenge is to move these effective algorithms from research settings into verified, user-friendly clinical decision support systems.

Table 3: Novel Risk Factors and Advanced Predictive Tools

Category	Specific Factor / Tool	Key Finding / Application	Clinical Implication
Patient-Specific Factors	**Visceral Obesity (VAI, LAP)**	Superior predictors of severity compared to BMI; VAI AUC=0.737(19)	Fat distribution is more important than total weight. Integrate anthropometric measures.
Patient-Specific Factors	**Vitamin D Deficiency**	Strong inverse correlation with severity; deficiency linked to longer stay, more ICU admissions[24]	A potentially modifiable risk factor; screening may be beneficial.
Etiology-Specific Factors	**Coagulation Profile (HLAP)**	Hyperlipidemic AP shows more pronounced abnormalities (Fibrinogen AUC=0.721, Factor VIII AUC=0.700)[25]	Tailor coagulation monitoring and assessment based on etiology.
Molecular Biomarkers	**Serum microRNA-486-5p**	Powerful predictor of severe AP (AUC=0.916); mediates inflammation & cell death via ATG7/p38 MAPK[32]	Links prognostication to active disease pathogenesis; future therapeutic target.
Molecular Biomarkers	**Serum NLRP3**	Inflammasome component; correlates with severity and predicts post-AP delirium[21]	A dual-function biomarker for severity and a specific clinical complication.
Artificial Intelligence	**Machine Learning (e.g., Random Forest, XGBoost)**	Significantly outperforms traditional scores (e.g., Random Forest AUC: 0.89 vs. BISAP AUC: ~0.70)[31]	

Limitations of study

For novel biomarkers: Calls for large-scale, multi-center studies to validate and standardize them. For AI models: Emphasizes the need for external validation and addressing algorithmic bias. Overall Integration: suggests the next logical step is to study how to implement these tools in real-world clinics and measure their actual impact on patient care.Prospective Research Avenues

This narrative review is inherently susceptible to selection bias, as it lacks a systematic method for identifying and incorporating literature. The gathered evidence originates from studies with various designs, differing patient populations, and distinct endpoint definitions, which may impede direct comparison. Many findings concerning new biomarkers and AI technologies arise from limited or initial studies; their wider relevance and clinical validity require validation. To overcome these constraints and advance the discipline, upcoming studies must focus on several crucial aspects.

AI/ML Validation and Development: It is essential to conduct prospective, multicenter external validation of current AI/ML models to guarantee their applicability across varied populations. Additionally, studies ought to investigate multimodal AI that combines clinical information, blood-based biomarkers, and quantitative imaging characteristics (from CT or MRI) into cohesive predictive systems.

Standardization and Translation: Creating uniform data pipelines and reporting protocols is crucial for ensuring the reproducibility of biomarker studies and AI mod-

els. The subsequent step is to carry out implementation studies to explore how to effectively utilize these tools in actual clinics and assess their effects on patient outcomes and healthcare expenses.

Investigating New Mechanisms: In addition to the biomarkers mentioned, upcoming research should examine genomic, proteomic, and metabolomic profiles to reveal new prognostic indicators and clarify the underlying mechanisms of the disease, facilitating the development of targeted treatments.

4. Conclusions

The prediction of acute pancreatitis is experiencing a significant change, transitioning from dependence on postponed, single-component assessments to a fluid, multifaceted approach. Recognized clinical scores (BISAP, APACHE II, CTSI) are essential for targeted functions but should be used judiciously, considering their ideal timing and intended use. Easily obtainable biomarkers such as NLR, LAR, and PCT offer vital, real-time information about the inflammatory condition, whereas new risk factors like visceral adiposity (VAI, LAP) and vitamin D deficiency contribute important individualized aspects to risk evaluation.

The greatest transformative potential is found in the combination of Artificial Intelligence and Machine Learning (AI/ML). To transition this from research to tangible outcomes, upcoming initiatives should focus on three key areas:

Clinical Feasibility and Implementation: The subsequent essential phase is to move verified AI/ML models from research environments into accessible Clinical Decision Support Systems (CDSS) incorporated within Electronic Health Records. This will transform advanced, real-time risk evaluation into an actionable resource for healthcare providers during patient interaction.

Pathways for Implementation Specific to Resources:

- In high-resource environments, the aim should be the complete incorporation of AI/ML-based CDSS with real-time biomarker tracking and imaging for precise management.
- In resource-limited environments, the primary emphasis should be on enhancing the application of efficient and affordable tools, specifically the BISAP score along with ongoing assessment of hematological markers (NLR, LAR).

Key Research Areas: Future investigations need to go further than model creation to tackle:

- Future and Multi-Center Confirmation of AI/ML algorithms to guarantee general applicability.
- Clinical Impact Studies that assess how these integrated tools genuinely enhance patient outcomes, optimize resource distribution, and lower expenses.
- Normalizing the assessment and clinical use of new biomarkers and risk indices such as VAI and LAP.

In the end, the management of acute pancreatitis will be shaped by a collaborative relationship between clinical knowledge, swift biomarker-based monitoring, and smart, AI-augmented forecasting. Adopting this layered, evidence-driven strategy is crucial for enhancing precision medicine and greatly boosting patient results worldwide.

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Conceptualization, A.C.F. and A.G.; methodology, M.C.; software, C.V.; validation, T.U., A.L. and R.C.; formal analysis, A.C.; investigation, R.P.; resources, M.C.T.; data curation, C.F.; writing—original draft preparation, A.C.F.; writing—review and editing, R.G.; visualization, M.P.T.; supervision, A.G.; project administration, A.G.; funding acquisition, R.C. All authors have read and agreed to the published version of the manuscript." Please turn to the CRediT taxonomy for the term explanation. Authorship must be limited to those who have contributed substantially to the work reported.

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