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*Original Research Article*

# Early Risk Stratification in Peritonitis: Contemporary Predictive Markers and Clinical Assessment Tools

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***Abstract***: ***Objectives***. Early risk stratification remains a critical challenge in the management of peritonitis, as adverse outcomes are largely determined during the first 24–48 hours after disease onset. This review aims to summarize contemporary evidence on early predictive markers of complicated peritonitis and to evaluate current approaches to clinical risk assessment, with a particular focus on inflammatory, immunological, and integrated prognostic tools. ***Methods***. A narrative analytical review of the literature was conducted using PubMed, Google Scholar, Scopus, and Web of Science databases. Publications from January 2020 to January 2025 were analyzed. Studies involving adult patients with peritonitis or intra-abdominal sepsis that assessed early clinical, laboratory, inflammatory, or immunological predictors of adverse outcomes were included. Outcomes of interest comprised early postoperative complications, intensive care unit admission, multiple organ dysfunction, and in-hospital mortality. ***Results***. Contemporary studies identify several key domains of early risk prediction. Inflammatory biomarkers, particularly interleukin-6, procalcitonin, C-reactive protein, and neutrophil-to-lymphocyte ratio, demonstrate strong and reproducible associations with disease severity and poor outcomes. Immunological parameters, including reduced $CD4^+$ T-lymphocytes, natural killer cells, and low IgM levels, reflect early immune dysfunction and are linked to septic complications and mortality. Traditional severity scoring systems (APACHE II, SOFA, Mannheim Peritonitis Index) retain clinical value but show limited sensitivity when used in isolation. Combined multimodal models integrating clinical signs, biomarkers, and immune parameters provide superior prognostic accuracy. ***Conclusions***. Early risk stratification in peritonitis should be multifactorial and multimodal. Integration of clinical assessment with inflammatory and immunological biomarkers significantly improves early identification of high-risk patients and may facilitate timely therapeutic decision-making and improved outcomes.

**Keywords**: peritonitis; early risk stratification; IL-6; inflammatory biomarkers; immunological predictors; prognostic models.

## INTRODUCTION

Peritonitis is one of the most severe forms of intra-abdominal infection and is associated with a high mortality rate, in some cases reaching 20–30% (depending on the etiology and the timeliness of surgical intervention) [1,2]. Each year, methods of source control and intensive therapy continue to improve; however, despite these advances, the outcome of the disease in a substantial proportion of patients is determined by the intensity of the body's

 

response reactions, for example the systemic inflammatory response that develops during the first hours of the pathological process [3].

The first 24–48 hours are especially important for the patient; it is during this period that SIRS, sepsis, and early multiple organ dysfunction (MODS) develop, and it is also during this period that progression of the initial infectious focus or recurrence of peritonitis may occur, which, in turn, requires immediate adjustment of the treatment strategy [4]. If the diagnosis is established too late or the therapeutic approach is chosen incorrectly, the mortality rate in high-risk patients increases, and the frequency of unfavorable outcomes rises.

Traditionally accepted clinical criteria and diagnostic scoring systems widely used in practice (APACHE II, SOFA, and the Mannheim Peritonitis Index) do not account for, or only partially account for, early changes occurring in inflammatory and immune response systems. This reduces their accuracy in identifying complicated courses of peritonitis [5]. In this regard, studies of recent years demonstrate a tendency—even a clear trend—toward the search for more precise early risk markers. These include cytokines (primarily IL-6), acute-phase inflammatory indicators, cellular components of the immune response, and integrated biomarker indices [6,7]. In addition, in recent years there has been a growing trend toward the development of combined prognostic models that integrate clinical signs with laboratory parameters, including machine-learning-based algorithms [8].

The aim of this review is to summarize the findings of studies published between 2020 and 2025 that address predictors of complicated peritonitis, including early clinical, inflammatory, and immunobiochemical markers. Another objective is to evaluate contemporary approaches to risk stratification during the first 24 hours of the disease.

## MATERIALS AND METHODS

The aim of this review is to summarize the data on the clinical course of peritonitis or other forms of sepsis, and on early predictors indicating a deterioration in the patient's condition. A narrative analytical review of the relevant literature was performed, which was carried out in the PubMed, Google Scholar, Scopus, and Web of Science databases and covered the period from January 2020 to January 2025. The following combinations of keywords were used to select publications: "peritonitis," "intra-abdominal infection," "early predictors," "cytokines," "inflammatory markers," "immunological parameters," "risk stratification," "mortality." Additional articles were included during the examination of sources using the "snowballing" method, if they met the initial search criteria.

Studies included in this review were those involving adult patients with peritonitis or intra-abdominal sepsis, in which early clinical, biochemical, or immunological indicators associated with potentially unfavorable disease progression were assessed. The outcomes considered were complications occurring within the first two weeks, transfer to the intensive care unit, and early in-hospital mortality. Only original clinical studies were included; reviews, single-case reports, conference materials, and experimental animal studies were excluded.

The data presented were somewhat heterogeneous, which is explained by differences in study design, patient characteristics, and the sets of biomarkers investigated. This heterogeneity, unfortunately, did not allow for a full quantitative synthesis of the results. Therefore, we chose a qualitative analytical approach: from each study, information was extracted regarding the nature of the infectious process, characteristics of the patient cohort, the prognostic markers under examination, and their association with early adverse outcomes. Owing to the heterogeneity of the data, conducting a meta-analysis appeared methodologically unjustified.

## RESULTS

### 1. Clinical predictors and severity scoring systems in peritonitis

#### 1.1 Clinical predictors in the first 24–48 hours

The first two days of peritonitis development are critical for the prognosis of the disease, since they largely determine the effectiveness of further treatment tactics. According to data from a number of clinical studies, such symptoms as persistent fever, tachycardia, diffuse peritoneal signs, and paralytic ileus belong to the earliest and most reliable clinical indicators that reflect a tendency toward a malignant course of the disease [9–10].

Persistent remittent fever and pronounced tachycardia are signs of a more pronounced systemic inflammatory response and often serve as markers of bacteremia or early sepsis. These signs directly correlate with an increased probability of the development of early organ dysfunction and overall clinical deterioration of the patient's condition. In addition, the presence of symptoms of peritoneal irritation—muscular guarding, tenderness on palpation, and such a characteristic symptom as rebound tenderness—unfortunately indicates a significant volume of intra-abdominal contamination. Moreover, persistent inflammation remains, which is confirmed by the clinical picture of forming intra-abdominal abscesses that often accompany these signs. For surgeons, however, even more frightening are complications in the form of anastomotic insufficiency in the postoperative period [11,12].

Another alarming sign for the clinician is such a

 

symptom as paralytic ileus. This condition is accompanied by a decrease or even complete absence of intestinal peristalsis, abdominal distension, and impaired passage of intestinal contents. It is regarded as an early sign of toxic–septic suppression of gastrointestinal motility and subsequent microcirculatory disturbances. Its progression during the first two days often precedes clinical deterioration. Massive hypoperfusion and the development of multiple organ failure usually occur [13].

When evaluated according to modern prognostic models, the presence of two or more of the listed clinical signs within the first 24–48 hours significantly increases the probability of adverse outcomes. Such outcomes include the formation of intra-abdominal abscesses, recurrent peritonitis, anastomotic insufficiency, the need for repeated surgical intervention, or transfer of the patient to the intensive care unit. The clinical combination of predictors demonstrates high sensitivity in predicting an unfavorable course of the disease and increased in-hospital mortality [14,15].

It therefore seems appropriate to draw an intermediate conclusion that early clinical assessment allows for the timely identification of high-risk patients. This group of patients is vulnerable, as they require intensified monitoring, escalation of antimicrobial therapy—including the introduction of reserve antibiotics—and timely revision of surgical tactics. It is very important to correlate clinical predictors of deterioration with timely assessed laboratory markers (lactate, procalcitonin, C-reactive protein) and severity scoring systems. This, in turn, increases the accuracy of early risk stratification and contributes to more substantiated therapeutic decision-making.

**1.2 Severity scoring systems**

APACHE II

The APACHE II score is the most widely used tool for the integrated assessment of disease severity in critically ill patients, including those with peritonitis. It is based on the evaluation of the following parameters: age and the presence of chronic diseases. As a result, an overall characteristic of disease severity is obtained. However, despite its proven prognostic value with regard to overall mortality, its use in cases of intra-abdominal infections is limited. The APACHE II score does not take into account the features of the local inflammatory process or the degree of peritoneal contamination at all.

Nevertheless, according to clinical studies, higher APACHE II values are reliably associated with an increased incidence of postoperative complications. Higher values are also associated with the need for transfer to the intensive care unit or even with higher mortality among patients [16,17].

Admittedly, in the setting of emergency surgery, calculation of the APACHE II score places an additional burden on an already extensively collected medical history. In this case, simplified physiological scoring systems, such as SAPS, may be used. According to studies, they demonstrate comparable prognostic accuracy with lower application complexity. This, in turn, makes them potentially more convenient for use in emergency clinical practice [18].

**SOFA**

The SOFA score is designed for the dynamic assessment of the degree of organ dysfunction. It plays a significant role in the context of sepsis and critical illness. Unlike APACHE II, SOFA is oriented not toward baseline severity, but rather toward the process of progression of organ dysfunction. If an increase in the SOFA score of ≥2 points is identified within the first 24 hours after diagnosis, it can be reliably stated that multiple organ dysfunction syndrome (MODS) or even septic shock has developed [19].

The prognostic accuracy of SOFA increases when it is used in combination with early laboratory markers of inflammation, for example in conjunction with measurements of CRP or procalcitonin levels [20].

**Mannheim Peritonitis Index (MPI)**

The MPI is a specialized scoring system developed specifically to assess the risk of complications in peritonitis. The MPI incorporates both clinical and intraoperative parameters, such as patient age, the presence of organ failure or malignant disease, the nature of the peritoneal exudate, the source of infection, and the degree of intra-abdominal contamination. When the MPI value exceeds 26, mortality among patients may reach or even exceed 30–40% [21,22].

In recent years, attempts have been made to modify and expand the MPI. One such modification, which appears successful, is the WSES Sepsis Severity Score (WSSS). It is aimed at a more precise stratification of the risk of complications in patients and takes into account modern concepts of sepsis development and the emergence of a systemic inflammatory response [5].

Comparative analyses frequently demonstrate that MPI outperforms APACHE II in terms of specificity for predicting mortality in patients with peritonitis. However, this scoring system remains less sensitive to rapid changes in physiological status, which limits its usefulness for dynamic monitoring [5].

Each of the presented scoring systems has both advantages and limitations. APACHE II is primarily focused on overall systemic severity, SOFA allows dynamic tracking of organ dysfunction, whereas MPI

 

is the most peritonitis-specific tool. A combined approach, integrating clinical predictors, bedside assessment, and laboratory markers, is therefore considered the most appropriate strategy for early risk stratification.

## 2. Inflammatory and metabolic biomarkers

### 2.1 Cytokines

The main link in the formation of the systemic inflammatory response in intra-abdominal infections is represented by cytokines. In recent years, it has been noted that a number of them have high prognostic significance for early risk stratification. In this context, a special place is occupied by interleukin-6 (IL-6), which is currently regarded as the most reliable marker. According to data from clinical studies, an increase in IL-6 concentration above 50–80 pg/mL within the first hours after disease onset is associated with an increased risk of sepsis and multiple organ failure, which in turn leads to patient admission to the intensive care unit [11,19]. Notably, the prognostic value of IL-6 has been demonstrated both in patients who developed postoperative intra-abdominal infections and in cases of primary peritonitis.

The cytokines IL-10 and TNF-α reflect the course of hyperinflammatory reactions and processes of compensatory immunosuppression. An increase in IL-10 levels represents a marker of the development of a compensatory anti-inflammatory response, which correlates with unfavorable outcomes, particularly in the late phases of abdominal sepsis [25]. It should be noted that, at the same time, persistently elevated TNF-α levels (which is one of the early mediators of the inflammatory cascade) are associated with progressive sepsis and the development of multiple organ dysfunction [24]. A combined assessment of these parameters (IL-6, IL-10, and TNF-α) allows characterization of the patient's cytokine profile and enables identification of a high-risk group within the first 48 hours.

### 2.2 Acute-phase markers and integrated inflammatory indices

C-reactive protein (CRP) and procalcitonin (PCT) are the most well-known traditional biomarkers of the inflammatory response that are widely used in clinical practice. They are applied to assess the severity of inflammation and bacterial burden in peritonitis. If, within the first 48 hours after disease onset, an increase in CRP with a plateau or further rise is observed, this indicates ongoing peritoneal inflammation and leads to an increased risk of intra-abdominal abscess formation. In most cases, this reflects insufficient control of the infectious source [25]. If the concentration of PCT exceeds 2 ng/mL, this is regarded as a reliable sign of a severe bacterial process and early clinical deterioration [26].

Indicators such as integrated cellular indices, including the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR), have gained increasing importance in recent years. For example, elevated NLR values demonstrate a stable association with the risk of developing multiple organ failure, which reflects the need for repeated surgical intervention and, unfortunately, an increase in mortality [27]. PLR reflects the degree of systemic inflammatory response and is often considered an independent predictor of unfavorable clinical outcomes [28]. Of particular interest in the context of this review are combined indices integrating CRP, PCT, and NLR, which demonstrate higher sensitivity in predicting treatment failure and septic complications. This, in turn, is consistent with contemporary concepts of the immunometabolic mechanisms of surgical sepsis [29].

### 2.3 Metabolic markers

For the assessment of metabolic indicators of tissue hypoperfusion and the severity of microcirculatory disturbances, plasma lactate remains one of the most important markers. When a lactate level exceeding 2 mmol/L is detected in the early period of the disease, it can be stated with confidence that this represents an independent predictor of early mortality and a high risk of developing septic shock [30]. The absence of a decrease in lactate concentration after the initiation of therapy is often an equally significant prognostic factor. This condition is consistently correlated with the development of multiple organ failure and the ineffectiveness of therapeutic interventions [31].

Assessment of lactate dynamics should be performed in combination with inflammatory markers, such as cytokine levels and PCT concentrations. With timely and appropriate interpretation, this approach allows for an integrated assessment of the state of the microcirculatory bed, the adequacy of surgical source control, and the effectiveness of ongoing intensive care therapy [32].

Overall, analysis of the available data indicates that a key role in the early prediction of a complicated course of peritonitis belongs to IL-6, dynamic changes in CRP and PCT levels, integrated cellular indices (NLR, PLR), and fluctuations in lactate levels. Integrating these parameters into multimodal prognostic algorithms significantly improves the accuracy of early risk stratification compared with the use of clinical severity scoring systems alone [33,34].

## 3. Immunologic Predictors

### 3.1 Cellular immunity markers

In recent years, increasing attention has been paid to the role of disturbances in the cellular immune response in the development of a complicated course of peritonitis. It has been noted that an early decrease in T-lymphocyte subpopulations and natural killer cells reflects the development of pronounced immune

 

dysfunction. These processes are directly associated with unfavorable clinical outcomes. In particular, in clinical cases, a reduction in the proportion of **$CD4^+$ lymphocytes below 30%** and **NK cells below 10%** within the first day of disease represents a strong independent predictor of sepsis, multiple organ dysfunction, and mortality [35]. These data have been repeatedly reproduced in a number of studies and are comparable with the results presented in several reviews and clinical investigations of recent years [36].

Disturbance of the **$CD4^+/CD8^+$ ratio** also has significant prognostic value. A decrease in this parameter reflects an imbalance between the regulatory and cytotoxic components of the immune response, which in turn is associated with insufficient elimination of infection and a high risk of secondary infectious complications [37]. These changes underlie the concept of **"immune paralysis,"** in which, after an initial phase of active inflammation, a state of functional immunosuppression develops, characterized by a reduced ability of the organism to control the infectious process.

### 3.2 Humoral immunity markers

Changes in humoral immunity, in addition to cellular immunity, also play an important prognostic role. At present, the most studied and clinically significant marker is a decrease in the level of **immunoglobulin M (IgM)**, which reflects exhaustion of the primary immune response. A number of studies have shown that low IgM concentrations in the early stages of peritonitis are associated with a higher frequency of septic complications and unfavorable outcomes [38].

Additional prognostic value is provided by an integrated parameter such as the **IgA×IgM/IgG index**. Assessment of this index makes it possible to evaluate the balance between early and mature humoral immune responses. A decrease in this index indicates impaired immune adaptation and correlates with severe disease course, development of secondary infections, and increased mortality [39]. Inclusion of humoral immunity parameters in a comprehensive assessment of patient condition allows for more accurate identification of patients at high risk of a complicated course of peritonitis.

## 4. Predictive models and emerging approaches

### 4.1 Probabilistic predictive models

Probabilistic models combining key clinical features—such as body temperature, the presence of paralytic ileus, and the severity of peritoneal signs—have been repeatedly proposed. Their value lies in early identification of high-risk patients within the first hours after disease onset. Implementation of probabilistic models into routine clinical practice reduces the number of false-negative predictions and improves early identification of patients at high risk of failure of standard therapy [40]. This approach is particularly valuable because it does not require substantial resource investment, which is especially relevant in settings with limited access to advanced laboratory or immunological testing, and is therefore more economically feasible.

### 4.2 Composite inflammatory indices

Composite inflammatory indices that combine multiple biomarkers represent another promising direction. In particular, indices incorporating **NLR**, **CRP**, and **PCT** have demonstrated high prognostic accuracy, especially when compared with the isolated use of individual markers. According to data reported, such combined models reliably predicted the development of complications and were sensitive to early treatment failure in peritonitis [41]. Notably, these indices reflect both cellular and humoral components of the inflammatory response and represent a convenient tool for clinical practice.

### 4.3 Machine learning–based models

With the popularization of artificial intelligence technologies and the global trend toward investment and development in this field, applications of machine learning algorithms for outcome prediction in peritonitis and intra-abdominal infections have begun to emerge. **AI-based risk classifiers** demonstrate high predictive accuracy for adverse outcomes, as they are capable of rapidly evaluating combinations of clinical data, laboratory parameters, and intensive care variables. However, their widespread implementation in clinical practice is currently limited, primarily due to the lack of multicenter validation, difficulties in result interpretation, and the need for standardization of input data [35]. Once these barriers are addressed, a new surge in the development of prognostic scoring systems and risk stratification for adverse and fatal outcomes can be expected.

Thus, integration of **immunological markers**, clinical signs, and laboratory parameters into **combined prognostic models**, including probabilistic and AI-oriented approaches, represents a promising direction for early risk stratification in peritonitis. These multimodal strategies have substantial potential and may significantly improve prognostic accuracy and optimize patient management as early as the first day of disease.

## DISCUSSION

Thus, a complicated course of peritonitis develops already at the early stages of the disease. In one way or another, it is not possible to identify a single dominant mechanism underlying its progression; rather, a variable interaction of inflammatory reaction cascades takes place. In a subset of patients, these processes even reach a markedly pronounced level of cascading inflammatory or overtly

 

hyperinflammatory responses, followed by the development of immune dysfunction. The evident progress achieved in surgical source control does not guarantee a favorable outcome of the disease, just as advances in intensive care and resuscitation do not. In a substantial proportion of patients, the outcome continues to be determined by the systemic host response, which forms early—within the first hours to days from the onset of the condition. It is precisely during this short time interval that the key determinants of the subsequent clinical course are established [16–19].

Within this context, interleukin-6 (IL-6) represents the most significant early biomarker of a complicated course of peritonitis. Among the biomarkers studied and presented, it remains the most reproducible and clinically informative [11,19]. We did not observe contradictions in the available data; on the contrary, the authors are remarkably consistent in their conclusions. In one way or another, an increase in IL-6 concentration during the first hours of the disease is associated with the development of sepsis, multiple organ dysfunction, and the urgent need for intensive care. These associations are observed both in primary and postoperative peritonitis.

Severity scoring systems based on clinical symptoms remain the cornerstone of treatment strategy in resource-limited settings. However, time does not stand still, and there is a clear need for predictors that can be assessed within the first hours of disease development. For this reason, we place particular emphasis on the fact that IL-6 fundamentally differs from traditional severity scores. This parameter reflects inflammatory activity at a stage when clinical signs of organ dysfunction are not yet evident. IL-6 captures not an already established severity of illness, but early pathophysiological processes that unfold during the first hours of disease progression. It is precisely this feature that confers particular value to IL-6 in early risk stratification.

In this context, the exceptional role of immunological markers should also be emphasized. It is important to consider parameters of cellular and humoral immunity in combination, particularly in the form of integrated indices. In a number of studies [23,24], the authors conclude that fluctuations in IgM demonstrate the highest prognostic accuracy compared with classical severity scores when the latter are applied in isolation. Sensitivity has also been reported for reductions in the proportion of $CD4^+$ lymphocytes and natural killer (NK) cells, as well as disturbances in the $CD4^+/CD8^+$ ratio, which reflect the development of functional immunosuppression [35,36]. This phenomenon corresponds to the well-established concept of immune paralysis.

The clinical consequences of such a shift are well known. Impairment of the immune response leads to inadequate pathogen elimination, an increased frequency of secondary complications, and, consequently, poorer outcomes. The situation becomes increasingly unfavorable as the signs of immunosuppression intensify in combination with persistent hyperinflammatory activity.

Nevertheless, we note that no single biomarker or prognostic scoring system provides sufficient sensitivity and specificity for reliable prediction of the course of peritonitis. No individual parameter or score can be used in isolation—only combined approaches are appropriate. These approaches integrate clinical signs identified during the first 48 hours, laboratory markers of inflammation (CRP, PCT), integrated cellular indices (NLR, PLR), metabolic parameters—primarily plasma lactate levels—as well as immunological markers. Such multimodal models reduce the risk of incorrect clinical assessment and allow confident identification of high-risk patients at an early stage of the disease [25,28,24,31,37,41].

With the development of technological solutions in the field of artificial intelligence and the growth of investments in this area, it is not surprising that probabilistic and AI-oriented prognostic models in medicine have attracted particular interest. This interest is well founded, as their high accuracy is largely explained by the simultaneous analysis of numerous heterogeneous and sometimes non-obvious parameters. Unfortunately, their widespread implementation in routine clinical practice remains limited. The main obstacles include the lack of multicenter validation, heterogeneity of source data, absence of unified standards for data input and output, and difficulties in the clinical interpretation of the obtained results [35, 38–41].

We cannot overlook the limitations of the existing evidence base. Substantial variability in study design, relatively small sample sizes, heterogeneity of outcome measures, and the absence of standardized threshold values for a number of immunological markers are still present in the original studies and reviews we analyzed. These factors underscore the need for large prospective multicenter studies with external cross-validation of proposed prognostic models. Overall, the results obtained confirm that early risk stratification in peritonitis must be multifactorial and should involve integration of clinical assessment with inflammatory biomarkers, immunological parameters, and modern analytical approaches.

## CONCLUSION

After analyzing the literature and a number of independent, reliable studies, we arrive at the

 

following conclusions.

First, effective early risk stratification in peritonitis must be multifactorial in nature and should go beyond isolated clinical assessment. The use of individual prognostic scoring systems should also be avoided. The course of the disease is largely determined by the characteristics of the systemic inflammatory and immune response that form during the first hours to days from the onset of the pathological process.

Second, among the studied parameters, the most significant predictors of a complicated course of peritonitis are interleukin-6 (IL-6). Integrated cellular indices (NLR), markers of bacterial inflammation (PCT), as well as parameters of cellular and humoral immunity, such as IgM levels and the proportions of $CD4^+$ lymphocytes and NK cells, are encountered less frequently due to the absence of routine practice for their monitoring. Nevertheless, they are highly sensitive and require integration into everyday clinical practice. These markers allow identification of high-risk patients even before organ dysfunction and clinical deterioration become manifest.

Third, traditional prognostic severity scoring systems, such as APACHE II, SOFA, and MPI, retain their practical value and remain useful tools for clinical assessment. However, their isolated prognostic accuracy is clearly inferior to combined approaches based on the integration of clinical signs and laboratory and immunological biomarkers.

Thus, we arrive at the final summarizing conclusion: at present, the most promising direction is the development of unified prognostic platforms that integrate clinical data with inflammatory and immunological markers and are fundamentally based on the use of machine-learning capabilities. These multimodal models have the potential to significantly improve the accuracy of early prediction, optimize patient management strategies, and ultimately improve treatment outcomes in peritonitis.

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