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Postoperative Complications in Generalized Peritonitis: prediction and immunoprophylaxis

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ABSTRACT

Generalized peritonitis remains a critical challenge in abdominal surgery due to its high morbidity and mortality, especially in the early postoperative period. The complexity of immune responses, intra-abdominal contamination, and systemic inflammation contributes to a high risk of postoperative complications. This review focuses on current approaches to predicting and preventing these complications, particularly the role of immunological markers and immunomodulatory interventions. The use of scoring systems, laboratory predictors, intraoperative findings, and early immune profiling is discussed as a means to stratify risk and guide therapy. Immunoprophylaxis strategies, including perioperative immunonutrition, cytokine modulation, and selective immunotherapy, are analyzed in the context of evidence-based practice. The article highlights the importance of integrated prognostic-immunological models for improving outcomes in patients undergoing surgery for generalized peritonitis.

Keywords: Generalized peritonitis, postoperative complications, immunoprophylaxis, prediction, surgical sepsis

INTRODUCTION

Generalized peritonitis remains a life-threatening surgical emergency that continues to challenge clinicians due to its complex pathophysiology, rapid systemic progression, and high postoperative complication rates. Despite advances in surgical technique, perioperative monitoring, and antimicrobial therapy, morbidity remains unacceptably high, with postoperative complications—including intra-abdominal abscesses, wound infections, organ failure, and septic relapses—occurring in up to 40-60% of cases [1, 2]. The variability in outcomes has drawn increasing attention to the host immune response as a critical determinant of prognosis and recovery.

In the context of peritonitis, the host immune system is simultaneously the first line of defense and a potential contributor to pathogenesis. The initial hyperinflammatory phase, marked by elevated proinflammatory cytokines

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such as IL-6 and TNF- α , is often followed by compensatory immunosuppression, characterized by monocyte deactivation, lymphocyte apoptosis, and cytokine imbalance [3]. This immunological rollercoaster significantly impairs the patient's ability to contain residual contamination and recover from surgical stress, particularly in elderly, malnourished, or comorbid individuals. Postoperative complications in these patients are frequently linked not only to the extent of intra-abdominal damage but also to a dysfunctional or exhausted immune system [4].

Traditional predictors of adverse outcomes—such as APACHE II and Mannheim Peritonitis Index (MPI) offer general risk stratification but fail to capture individual immune status or trajectory [5]. In recent years, a growing body of evidence has supported the use of immune biomarkers (e.g., HLA-DR expression on monocytes, neutrophil/lymphocyte ratio, serum procalcitonin, IL-10 levels) as predictive tools for postoperative outcomes [6,7]. These markers provide real-time insights into the immune competence of the host and can identify patients at high risk for sepsis recurrence, delayed wound healing, or nosocomial infection.

This recognition has prompted interest in targeted immunoprophylaxis as a means of modifying the course of postoperative recovery. Immunonutrition, selective cytokine modulation (e.g., IFN- γ , IL-7), and therapies aimed at restoring monocyte and T-cell function are increasingly being explored in clinical trials [8]. Additionally, perioperative immune support with micronutrients such as glutamine, arginine, and omega-3 fatty acids has shown potential benefits in modulating inflammatory responses and enhancing tissue repair [9].

The objective of this review is to synthesize current knowledge on the prediction and immunological prevention of postoperative complications in the surgical management of generalized peritonitis. The article examines conventional risk assessment tools, emerging immunological predictors, and the rationale for immunoprophylactic strategies. Special emphasis is placed on integrating immunomonitoring into clinical decision-making algorithms, with the goal of moving toward more personalized and preventive surgical care.

1. Immunopathophysiology of Postoperative Complications in Peritonitis

The immune response to generalized peritonitis is a dynamic, multi-phased process that involves both the innate and adaptive immune systems. While its initial activation is vital for the containment and elimination of peritoneal contamination, dysregulation at any stage of the response can predispose patients to severe postoperative complications. This dual role of the immune system—as both protector and potential source of harm forms the immunopathophysiological basis for much of the morbidity observed after surgical intervention for peritonitis [10].

Following the onset of peritonitis, the peritoneal cavity becomes a battlefield for inflammatory signaling. The innate immune system is rapidly activated, with neutrophils, macrophages, and dendritic cells responding to bacterial endotoxins and damage-associated molecular patterns (DAMPs) released from necrotic tissue. Neutrophil activation leads to respiratory bursts and release of reactive oxygen species (ROS), which contribute to microbial killing but also to local tissue injury [11].

This local inflammation rapidly spills over into systemic circulation, initiating the Systemic Inflammatory Response Syndrome (SIRS). Key cytokines such as tumor necrosis factor-alpha (TNF- α), interleukin-6 (IL-6), and interleukin-1 β (IL-1 β) are elevated in the early phase and correlate with the severity of illness [12]. In some patients, this proinflammatory surge is excessive, leading to endothelial dysfunction, capillary leak, and multi-organ failure. Notably, in the early postoperative period, patients with persistently elevated IL-6 levels are at significantly higher risk for septic shock and mortality [13].

However, the immune system does not remain in a purely activated state. Within days of the inflammatory peak, the host frequently transitions into a state of compensatory anti-inflammatory response syndrome (CARS). This phase is marked by monocyte deactivation, as evidenced by reduced HLA-DR expression, lymphopenia, and increased levels of immunosuppressive cytokines such as IL-10 and transforming growth factorbeta (TGF- β) [14]. The CARS response is particularly pronounced in patients undergoing extensive surgery or those with comorbidities such as diabetes, renal failure, or malnutrition.

This immune suppression creates a window of vulnerability for nosocomial infections, wound dehiscence, and delayed peritoneal clearance. Moreover, it contributes to the development of secondary infections, including pneumonia, intra-abdominal abscesses, or catheter-associated bacteremia. Studies have shown that patients with persistently low monocyte HLA-DR expression on postoperative days 3–7 are more likely to

experience complications and exhibit prolonged ICU stays [15].

The gut–immune axis also plays a critical role. Peritonitis is frequently associated with altered intestinal barrier function, bacterial translocation, and dysbiosis. These changes amplify systemic inflammation and further dysregulate the immune system. In turn, postoperative ileus or enteral feeding intolerance may perpetuate this imbalance, delaying recovery [16].

Therefore, understanding the immunopathophysiology of peritonitis—and the delicate balance between immune activation and suppression—is essential for developing effective predictive tools and preventive strategies. It provides the rationale for early immune profiling, enabling risk stratification and timely deployment of immunomodulatory interventions.

2. Predictive Tools and Biomarkers for Postoperative Risk Assessment

Effective risk assessment in patients undergoing surgery for generalized peritonitis is critical for reducing postoperative complications. While classical scoring systems provide general estimates of morbidity and mortality, they are often limited in individual prognostication, particularly with respect to immunological resilience. Recent advances in biomarker research and functional immune monitoring have enhanced our ability to predict complications earlier and more accurately, especially in the vulnerable postoperative window.

Traditional tools such as the Mannheim Peritonitis Index (MPI) and Acute Physiology and Chronic Health Evaluation II (APACHE II) remain widely used for preoperative and early postoperative risk estimation. The MPI incorporates intraoperative findings—such as the extent of peritoneal contamination and organ failure—to stratify patients into risk categories [17]. APACHE II, while broader in scope, is useful for identifying high-risk patients in intensive care. However, neither of these tools accounts for immune status, inflammatory dynamics, or postoperative immunosuppression.

In this context, biomarkers have emerged as promising adjuncts to improve risk prediction. Among the most validated is C-reactive protein (CRP). Elevated CRP levels (>150 mg/L) on postoperative day 3 are associated with a higher risk of intra-abdominal abscess formation and anastomotic leakage [18]. Yet, CRP is nonspecific and may reflect surgical trauma as well as infection.

More specific is procalcitonin (PCT), which correlates with bacterial infection and sepsis severity. Persistent elevation of PCT (>2 ng/mL) after 72 hours of antimicrobial therapy is a strong predictor of treatment failure and postoperative sepsis [19]. It also serves as a decision-making tool for early relaparotomy or escalation of therapy.

A novel and functionally relevant marker is monocyte HLA-DR expression, a measure of antigen-presenting capacity and overall immune competence. HLA-DR downregulation is consistently associated with postoperative immunosuppression and poor outcomes. Patients with low HLA-DR expression on days 3–5 after surgery are more likely to develop nosocomial infections and experience delayed wound healing [20].

Other emerging biomarkers include:

Neutrophil-to-lymphocyte ratio (NLR): Elevated values (>7) predict systemic inflammation and are associated with increased risk of postoperative complications.

IL-6 and IL-10 serum levels: A high IL-6/IL-10 ratio indicates immune dysregulation and predicts poor outcomes in peritonitis-related sepsis.

Soluble CD14-subtype (sCD14-ST or presepsin): An early marker of endotoxin exposure, useful for stratifying risk in septic peritonitis [21].

In addition to biomarkers, functional immune assays—such as ex vivo cytokine release tests (e.g., LPSstimulated TNF- α production)—can assess innate immune capacity. These tests may be particularly helpful in patients with borderline clinical status, providing early insight into the potential for immunological collapse or recovery [22].

Risk assessment tools are most powerful when combined. Recent studies advocate for multimodal risk models that integrate clinical scores, biomarkers, and immune function parameters into dynamic prediction algorithms. These models offer a more individualized approach, allowing for real-time adjustment of postoperative monitoring intensity, antibiotic duration, and decisions regarding early immunomodulation.

In summary, the integration of biomarkers and immune-based parameters into postoperative risk stratification represents a paradigm shift in the management of generalized peritonitis. Such tools enhance the precision of clinical judgment, enable earlier intervention, and ultimately reduce the burden of postoperative complications.

3. Immunoprophylaxis Strategies in the Surgical Treatment of Peritonitis

While surgical source control and antimicrobial therapy remain foundational in the management of generalized peritonitis, the growing recognition of immune dysfunction as a driver of postoperative complications has led to the emergence of immunoprophylaxis as a complementary therapeutic strategy. Immunoprophylaxis in this context refers to targeted interventions aimed at supporting, modulating, or restoring immune function in the perioperative period to reduce infectious and systemic complications.

One of the most studied modalities is perioperative immunonutrition, which seeks to optimize immune competence through targeted nutritional supplementation. Formulas enriched with arginine, glutamine, omega-3 fatty acids, nucleotides, and selenium have demonstrated the ability to modulate the inflammatory response, enhance T-cell proliferation, and support epithelial barrier integrity [23]. Meta-analyses have shown that immunonutrition reduces postoperative infection rates, particularly in gastrointestinal and septic surgery populations [24]. For patients with generalized peritonitis who often present with malnutrition, catabolism, and gut barrier compromise—early enteral immunonutrition may improve immune resilience and accelerate recovery.

Another avenue of immunoprophylaxis involves cytokine modulation. Agents such as recombinant interferon-gamma (IFN- γ) have been explored to reverse monocyte deactivation and restore antigen-presenting capacity in postoperative sepsis. In small trials, IFN- γ administration improved monocyte HLA-DR expression and reduced secondary infections in high-risk surgical patients [25]. Other agents, such as interleukin-7 (IL-7) and granulocyte-macrophage colony-stimulating factor (GM-CSF), have shown potential in reversing lymphopenia and enhancing innate immunity, although data remain limited to experimental settings [26].

Selective immunoglobulin therapy, particularly IgMenriched preparations, has been proposed for patients with evidence of endotoxemia or low immunoglobulin levels after peritonitis surgery. Some randomized trials have demonstrated reduced mortality and shorter ICU stays with early immunoglobulin administration, though larger studies are required to confirm routine use [27].

In addition to pharmacological agents, prehabilitation and metabolic optimization constitute non-pharmacological forms of immunoprophylaxis. Correction of anemia, protein-energy malnutrition, and vitamin D deficiency prior to surgery has been associated with improved immune responsiveness and reduced complication rates. Furthermore, maintaining tight glycemic control (blood glucose 6–10 mmol/L) postoperatively is crucial, as hyperglycemia impairs neutrophil function and increases susceptibility to infection [28].

Prophylactic strategies must also include avoidance of iatrogenic immunosuppression. Excessive surgical trauma, uncontrolled fluid shifts, and inappropriate antimicrobial overuse can impair the immune system and predispose to nosocomial infections or fungal overgrowth. Tailored surgical techniques that minimize peritoneal insult and limit operative duration are integral to immune preservation.

Finally, the future of immunoprophylaxis lies in personalized immune support algorithms, which utilize baseline immune profiling to select candidates for intervention. For example, patients with low monocyte HLA-DR expression, elevated IL-10, or reduced ex vivo cytokine production may be candidates for early immune adjuvants. Conversely, patients with signs of immune overactivation may benefit more from anti-inflammatory or supportive strategies.

In conclusion, immunoprophylaxis represents a promising adjunct in the multimodal management of generalized peritonitis. Its success hinges on timing, patient selection, and integration with surgical and antimicrobial protocols. As more data emerge, it is likely to become a central element in the prevention of postoperative complications in this high-risk cohort.

4. Integrated Prognostic Models and Clinical Implementation

As the complexity of managing generalized peritonitis becomes increasingly apparent, the integration of multidimensional prognostic models into routine clinical workflows has emerged as a strategic priority. Traditional surgical decision-making, based primarily on intraoperative findings and empirical assessment, is being supplanted by structured, data-driven approaches that incorporate clinical scores, immune markers, metabolic parameters, and surgical factors into comprehensive risk prediction systems.

Several clinical frameworks have already been proposed to facilitate such integration. One example is the PIRO model(Predisposition, Infection, Response, Organ dysfunction), which offers a sepsis-specific staging system adaptable to surgical populations. Within the context of generalized peritonitis, the PIRO approach

allows for classification of patients based on immune predisposition (e.g., diabetes, malnutrition), infection source and burden (e.g., fecal vs. serous peritonitis), host response (e.g., IL-6, PCT levels), and extent of organ dysfunction [29]. Such stratification supports more personalized perioperative planning.

An increasingly accepted practice is the incorporation of immune status variables into daily ICU scoring rounds. For example, combining monocyte HLA-DR expression or neutrophil/lymphocyte ratio (NLR) trends with SOFA scores has been shown to enhance prediction of deterioration or secondary infections. This model has been referred to as "immunologically extended" scoring, and its use in patients with peritonitis has correlated with lower rates of delayed diagnosis of complications [30].

To facilitate widespread clinical adoption, several institutions have developed electronic clinical decision support systems (CDSS) that incorporate immune monitoring into postoperative dashboards. These systems flag deviations from expected biomarker trends and suggest escalation or de-escalation of treatment. For instance, rising CRP with persistent immunosuppression markers may prompt earlier reimaging or consideration of second-look surgery, even in the absence of overt clinical deterioration [31].

At the bedside, implementation of integrated models requires standardized sampling protocols, early immune profiling (e.g., within 24–48 hours of surgery), and trained personnel capable of interpreting immunological data. Surgeons, intensivists, infectious disease specialists, and clinical immunologists must work in coordination to define thresholds for intervention. Multidisciplinary case reviews have been shown to reduce variability in management and improve adherence to immune-based protocols [32].

Moreover, education and protocol development are essential for bridging the gap between research and practice. Guidelines that outline how to act on specific immune findings—e.g., when to initiate immunonutrition, consider cytokine therapy, or intensify monitoring—are urgently needed. Several international working groups are currently developing such recommendations, aiming to standardize immunological stratification and response in septic surgical care.

Looking forward, integration will likely expand through mobile health platforms, wearable immune biosensors, and machine learning algorithms capable of real-time decision support. These innovations promise to move risk assessment from reactive to anticipatory, allowing for preemptive intervention before the onset of overt deterioration.

In conclusion, the clinical implementation of integrated prognostic-immunological models represents a pivotal evolution in the management of generalized peritonitis. By combining predictive accuracy with operational feasibility, such systems empower clinicians to intervene earlier, tailor care more effectively, and reduce the burden of postoperative complications.

CONCLUSION

Generalized peritonitis continues to present significant postoperative risks despite surgical and antimicrobial advances. A growing body of evidence suggests that outcomes are determined not only by technical factors and microbial control but also by the host's immunological trajectory. The transition from an early hyperinflammatory state to postoperative immunosuppression creates a window of vulnerability, during which many complications—including sepsis recurrence, wound failure, and secondary infections—develop.

Traditional prognostic systems offer broad stratification but lack precision in identifying patients at risk for immune-related deterioration. The emergence of biomarkers such as CRP, PCT, HLA-DR expression, and cytokine ratios, as well as immune-functional assays, has enabled more refined prediction of outcomes. These tools, combined with individualized immunoprophylaxis strategies—such as immunonutrition, cytokine modulation, and immune surveillance—represent a new frontier in the prevention of postoperative complications.

Integrated models that combine clinical scores, biomarker trends, and immune function data offer the potential for real-time, adaptive decision-making. Implementation of such models through electronic platforms, multidisciplinary teams, and standardized protocols will be essential for translating immunological insight into clinical impact.

In conclusion, the future of postoperative care in generalized peritonitis lies in personalized, immune-informed strategies. By predicting risk and intervening prophylactically at the immunological level, clinicians can reduce complications, shorten recovery time, and improve long-term outcomes in one of the most critically ill surgical populations.

Conflict of Interest

The author declares no conflict of interest related to the publication of this article.

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TARQALGAN PERITONITDA JARROHLIKDAN KEYINGI ASORATLARNI PROGNOZ QILISH VA IMMUNOPROFILAKTIKA

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ANNOTATSIYA

Tarqalgan peritonit abdominall jarrohlikda yuqori oʻlim va kasallik darajasi bilan kechuvchi jiddiy muammo bo'lib qolmoqda. Operatsiyadan keyingi davrda immun javoblarning murakkabligi, qorin bo'shlig'i infeksiyasi va tizimli yalligʻlanish yuqori xavfli asoratlar bilan bogʻliq. Ushbu maqolada asosan immunologik belgilar va immunomodulyatsion yondashuvlar asosida jarrohlikdan keyingi asoratlarni prognoz qilish va oldini olish usullari koʻrib chiqiladi. Ball tizimlari, laborator prediktorlar, intraoperatsion topilmalar va erta immun monitoring immunologik yondashuvni aniqlashda muhokama qilinadi. Immunoprofilaktikaning asosiy yoʻnalishlari immunitetsizlanishga qarshi ozuqaviy qoʻllab-quvvatlash, sitokinlarni modulyatsiya qilish va selektiv immunoterapiya - daliliy tibbiyot nuqtai nazaridan baholanadi. Maqola prognozlash va immunologik boshqaruvga asoslangan kompleks yondashuvlar orqali natijalarni yaxshilash zarurligini ta'kidlaydi.

Kalit soʻzlar: Tarqalgan peritonit, jarrohlikdan keyingi asoratlar, immunoprofilaktika, prognozlash, jarrohlik sepsisi

ПРОГНОЗИРОВАНИЕ И ИММУНОПРОФИЛАКТИКА ПОСЛЕОПЕРАЦИОННЫХ ОСЛОЖНЕНИЙ ПРИ РАСПРОСТРАНЁННОМ ПЕРИТОНИТЕ

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АННОТАЦИЯ

Распространённый перитонит остаётся серьёзной проблемой абдоминальной хирургии с высокой летальностью и частотой осложнений в послеоперационном периоде. Сложность иммунного ответа, внутрибрюшное инфицирование и системное воспаление способствуют высокому риску послеоперационных осложнений. Настоящий обзор посвящён современным подходам к прогнозированию и профилактике осложнений с особым акцентом на иммунологические маркеры и иммуномодулирующие вмешательства. Рассматриваются балльные системы, лабораторные индикаторы, интраоперационные данные и ранняя иммунодиагностика как инструменты стратификации риска. Иммунопрофилактика включая иммунопитание, модуляцию цитокинов и селективную иммунотерапию — анализируется в контексте доказательной практики. Отмечается необходимость интеграции иммунопрогностических моделей для улучшения результатов хирургического лечения пациентов с перитонитом.

Ключевые слова: Распространённый перитонит, послеоперационные осложнения, иммунопрофилактика, прогнозирование, хирургический сепсис