Efectos Multisistémicos de la Disfunción Inflamatoria Perioperatoria en Pacientes Quirúrgicos Contemporáneos

Multisystem Effects of Perioperative Inflammatory Dysregulation in Contemporary Surgical Patients

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Recibido: 30-May-2026 | **Aceptado:** 30-May-2026 | **Publicado:** 01-Jun-2026

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Cómo citar este artículo: Marrufo Sumano, E., Cobeña Guerrero, S. E., Cortez Pilco, K. O., Alvarez Morales, W. P., Vallejo Ramírez, J. E., Fernández Godínez, E., Lozano Bretón, J. D., & Portilla Galvan, M. F. (2026). Multisystem Effects of Perioperative Inflammatory Dysregulation in Contemporary Surgical Patients. México. *Revista IECCMEXICO*, 4(1, Tomo II) 376-403. Quality Consulting Instituto de Educación Capacitación y Certificación de México. https://ieccmexico.com/publishing

RESUMEN

La inflamación sistémica perioperatoria constituye una respuesta fisiológica compleja generada por el trauma quirúrgico y representa uno de los principales determinantes de los desenlaces postoperatorios en la práctica quirúrgica moderna. Esta revisión tuvo como objetivo analizar el impacto multisistémico de la inflamación perioperatoria, incluyendo sus mecanismos

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
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fisiopatológicos, biomarcadores inflamatorios, disfunción orgánica y estrategias actuales de manejo perioperatorio. Se realizó una revisión narrativa estructurada utilizando literatura científica obtenida de bases de datos internacionales como PubMed, Scopus, ScienceDirect y otras fuentes médicas revisadas por pares. La evidencia analizada demostró que la inflamación perioperatoria implica activación coordinada de citocinas, vías neuroendocrinas, disfunción endotelial, estrés oxidativo y alteraciones inmunológicas. Marcadores inflamatorios elevados como interleucina-6, proteína C reactiva y relación neutrófilo-linfocito se asociaron consistentemente con complicaciones postoperatorias incluyendo inestabilidad cardiovascular, disfunción pulmonar, lesión renal aguda, complicaciones infecciosas, retraso en la recuperación gastrointestinal y hospitalización prolongada. Estrategias perioperatorias modernas como los protocolos ERAS, cirugía mínimamente invasiva, analgesia multimodal, inmunonutrición y optimización fisiológica dirigida demostraron efectos beneficiosos en la reducción de la carga inflamatoria y mejoría de la recuperación postoperatoria. Los hallazgos enfatizan que la inflamación sistémica perioperatoria debe entenderse como un proceso multisistémico que requiere manejo perioperatorio multidisciplinario. La investigación futura enfocada en perfiles inflamatorios personalizados, monitoreo guiado por biomarcadores e inmunomodulación dirigida podría contribuir a mejores desenlaces postoperatorios y a una atención quirúrgica más individualizada.

PALABRAS CLAVE

Inflamación perioperatoria, Respuesta al estrés quirúrgico, Complicaciones postoperatorias, Interleucina-6, Proteína C reactiva, Relación neutrófilo-linfocito, Disfunción multisistémica, Protocolos ERAS, Inmunología, Medicina perioperatoria, Biomarcadores, Recuperación quirúrgica, Inflamación sistémica, Disfunción orgánica, Cirugía mínimamente invasiva

ABSTRACT

Perioperative systemic inflammation is a complex physiological response generated by surgical trauma and represents one of the principal determinants of postoperative outcomes in modern surgical practice. This review aimed to analyze the multisystem impact of perioperative inflammation, including its pathophysiological mechanisms, inflammatory biomarkers, organ dysfunction, and current perioperative management strategies. A structured narrative review was conducted using scientific literature obtained from international databases including PubMed, Scopus, ScienceDirect, and related peer-reviewed medical sources. The analyzed evidence demonstrated that perioperative inflammation involves coordinated activation of cytokines, neuroendocrine pathways, endothelial dysfunction, oxidative stress, and immune dysregulation. Elevated inflammatory markers such as interleukin-6, C-reactive protein, and neutrophil-to-lymphocyte ratio were consistently associated with postoperative complications including cardiovascular instability, pulmonary dysfunction, acute kidney injury, infectious complications, delayed gastrointestinal recovery, and prolonged hospitalization. Modern perioperative strategies such as Enhanced Recovery After Surgery protocols, minimally invasive surgery, multimodal analgesia, immunonutrition, and goal-directed physiological optimization demonstrated beneficial effects in reducing inflammatory burden and improving postoperative recovery. The findings emphasize that perioperative systemic inflammation should be understood as a multisystem process requiring multidisciplinary perioperative management. Continued research focused on personalized inflammatory profiling, biomarker-guided monitoring, and targeted immunomodulation may contribute to improved postoperative outcomes and more individualized surgical care in the future.

KEYWORDS

Perioperative inflammation, Surgical stress response, Postoperative complications, Interleukin-6, C-reactive protein, Neutrophil-to-lymphocyte ratio, Multisystem dysfunction, ERAS protocols, Immunology, Perioperative medicine, Biomarkers, Surgical recovery, Systemic inflammation, Organ dysfunction, Minimally invasive surgery

INTRODUCCIÓN

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
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Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
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Perioperative systemic inflammation has emerged as one of the most significant determinants of postoperative outcomes in modern surgical practice. Although surgery remains an essential therapeutic intervention across multiple specialties, the physiological stress generated during the perioperative period triggers a complex cascade of immunological, endocrine, metabolic, and inflammatory responses that may substantially influence recovery, morbidity, and mortality. This inflammatory response, initially intended as a protective mechanism aimed at tissue repair and host defense, may become dysregulated in susceptible individuals, leading to organ dysfunction, delayed recovery, infectious complications, thrombotic events, prolonged hospitalization, and increased healthcare costs (Ljungqvist et al., 2017; Manou-Stathopoulou et al., 2019).

The interaction between surgical trauma and the immune system represents a highly dynamic process involving activation of innate immunity, release of proinflammatory cytokines, endothelial dysfunction, neurohormonal stimulation, oxidative stress, and alterations in cellular immunity. Major surgical procedures, particularly abdominal, thoracic, vascular, oncologic, and emergency surgeries, are associated with substantial elevations of inflammatory mediators such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), C-reactive protein (CRP), and various acute-phase reactants (Rettig et al., 2016). While a moderate inflammatory response is considered physiologically necessary for wound healing and recovery, excessive or prolonged inflammation may contribute to systemic inflammatory response syndrome, immune suppression, sepsis, and multiorgan failure (Singer et al., 2016).

In recent years, increasing attention has been directed toward understanding the mechanisms through which perioperative inflammation affects multisystem outcomes in surgical patients. Contemporary evidence suggests that systemic inflammation does not act in isolation but rather influences multiple organ systems simultaneously, including the cardiovascular, pulmonary, renal, neurological, gastrointestinal, hematological, and endocrine systems (Verdonk et al., 2021). Consequently, perioperative inflammation has become a major focus within general surgery, internal medicine, anesthesiology, critical care, and immunology, particularly because of its implications for postoperative complications and long-term patient prognosis.

From a cardiovascular perspective, inflammatory activation has been associated with endothelial injury, coagulation abnormalities, myocardial stress, and increased risk of postoperative cardiovascular events. Elevated inflammatory markers during the perioperative period have been linked to atrial fibrillation, myocardial injury after non-cardiac surgery, thromboembolic events, and impaired tissue perfusion (Becher et al., 2012). Similarly, pulmonary complications remain among the leading causes of postoperative morbidity, with systemic inflammation contributing to increased vascular permeability, pulmonary edema, impaired gas exchange, and acute respiratory distress syndrome in vulnerable populations (Cusack & Buggy, 2020).

Renal complications also represent an important concern in surgical patients. Acute kidney injury has been increasingly associated with inflammatory dysregulation, oxidative stress, microvascular dysfunction, and cytokine-mediated tissue damage. Evidence from colorectal and major abdominal surgery demonstrates that exaggerated postoperative inflammatory responses correlate with higher rates of renal impairment and prolonged recovery (Mannion et al., 2024). Furthermore, gastrointestinal dysfunction, postoperative ileus, metabolic instability, and alterations in gut barrier integrity have also been linked to inflammatory activation and surgical stress responses (Carli, 2015).

Another relevant aspect involves the immunological paradox observed in surgical patients. Although the immediate postoperative phase is characterized by hyperinflammation, many patients subsequently develop a state of immune suppression that increases susceptibility to secondary infections, poor wound healing, and sepsis. This dual phenomenon highlights the complexity of perioperative immune regulation and underscores the importance of balancing inflammatory control without compromising protective immune mechanisms (Verdonk et al., 2021).

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Revista IECCMEXICO

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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The growing incidence of complex surgical procedures worldwide, combined with population aging and increasing prevalence of chronic diseases such as obesity, diabetes mellitus, cardiovascular disease, and cancer, has amplified the clinical relevance of perioperative inflammation. Patients with preexisting comorbidities often exhibit baseline inflammatory dysregulation, making them more vulnerable to exaggerated postoperative responses and adverse outcomes (Scott et al., 2015). Likewise, emergency surgery and oncologic surgery frequently involve heightened inflammatory activation due to tissue injury, infection risk, malnutrition, or tumor-associated immune alterations.

Current perioperative medicine increasingly recognizes that modulation of the surgical stress response may improve clinical outcomes. Enhanced Recovery After Surgery (ERAS) protocols, minimally invasive surgical approaches, multimodal analgesia, optimized fluid therapy, early mobilization, and perioperative nutritional support have demonstrated beneficial effects in reducing inflammatory burden and accelerating postoperative recovery (Fearon et al., 2005; Ljungqvist et al., 2017). Similarly, immunonutrition strategies and targeted perioperative interventions have gained attention as potential tools for reducing infectious complications and modulating systemic inflammation in surgical populations (Buzquurz et al., 2020).

Despite these advances, significant gaps remain regarding the precise mechanisms through which perioperative systemic inflammation contributes to multisystem complications. Moreover, substantial variability exists among patients in terms of inflammatory responses, biomarker profiles, and postoperative trajectories. This variability suggests that perioperative inflammation is influenced not only by surgical factors but also by patient-specific immunological, metabolic, and genetic characteristics (Ivascu et al., 2024). Therefore, a deeper understanding of perioperative inflammatory pathways is necessary to improve risk stratification, personalize perioperative care, and identify potential therapeutic targets.

Recent investigations have explored the prognostic value of inflammatory biomarkers such as CRP, IL-6, neutrophil-to-lymphocyte ratio (NLR), procalcitonin, and cytokine panels in predicting postoperative complications and mortality (Adamina et al., 2015; Perry et al., 2022). Elevated postoperative CRP levels, for example, have been consistently associated with infectious complications following major abdominal surgery, demonstrating their potential utility in early clinical decision-making (Gans et al., 2015). Similarly, perioperative NLR has emerged as an accessible marker associated with systemic inflammatory burden and adverse cardiovascular outcomes in surgical patients (Perry et al., 2022).

Beyond immediate postoperative complications, chronic postoperative inflammation has also been associated with delayed rehabilitation, persistent pain syndromes, impaired quality of life, and worse oncological outcomes. Persistent immune dysregulation may contribute to tumor progression, impaired antitumor immunity, and reduced survival in patients undergoing cancer surgery, particularly in gastrointestinal and hepatobiliary malignancies (Crippa et al., 2018). Consequently, perioperative inflammatory modulation may have implications not only for short-term recovery but also for long-term patient outcomes.

The present review article aims to analyze perioperative systemic inflammation from a multisystem perspective in surgical patients, integrating current evidence from general surgery, internal medicine, anesthesiology, immunology, and perioperative medicine. The review focuses on the pathophysiological mechanisms underlying the inflammatory response to surgery, the relationship between systemic inflammation and postoperative complications, the role of inflammatory biomarkers, and contemporary perioperative strategies aimed at reducing inflammatory burden and improving clinical outcomes.

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
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This review was developed through an extensive analysis of recent scientific literature indexed in international databases including PubMed, Scopus, and related peer-reviewed medical sources. Relevant studies, systematic reviews, clinical trials, consensus statements, and narrative reviews focusing on perioperative inflammation, surgical stress response, immunological alterations, and postoperative outcomes were examined. The methodological design of this review aligns with the central objective of synthesizing contemporary evidence regarding the multisystem impact of perioperative inflammation while identifying current challenges and future perspectives in perioperative management.

Understanding perioperative systemic inflammation is essential for the development of more individualized, evidence-based, and multidisciplinary surgical care models. As surgical populations continue to become increasingly complex, optimization of perioperative inflammatory responses may represent a fundamental strategy for reducing postoperative complications, improving patient recovery, and enhancing overall healthcare outcomes worldwide.

DESARROLLO

Perioperative systemic inflammation represents a multidimensional physiological response generated by surgical trauma, tissue injury, anesthesia exposure, ischemia-reperfusion phenomena, and neuroendocrine activation. Although inflammatory activation is essential for tissue repair and protection against microbial invasion, excessive or prolonged inflammatory responses may become pathological, contributing to significant postoperative morbidity and mortality across multiple surgical populations (Manou-Stathopoulou et al., 2019).

The inflammatory response to surgery begins immediately after tissue disruption. Damage-associated molecular patterns released from injured cells activate macrophages, neutrophils, dendritic cells, endothelial cells, and circulating cytokine networks. This activation stimulates the release of proinflammatory mediators including interleukin-1 (IL-1), IL-6, tumor necrosis factor-alpha (TNF-α), interferon-gamma, prostaglandins, and chemokines, all of which coordinate the systemic response to surgical stress (Verdonk et al., 2021). Simultaneously, activation of the hypothalamic-pituitary-adrenal axis and sympathetic nervous system induces cortisol release, catecholamine secretion, hyperglycemia, insulin resistance, and metabolic alterations aimed at maintaining physiological homeostasis during acute stress conditions.

One of the principal concerns associated with perioperative inflammation is the development of endothelial dysfunction. Inflammatory cytokines increase vascular permeability, impair microcirculatory regulation, and promote leukocyte adhesion, potentially leading to tissue hypoperfusion and organ dysfunction. In major surgical procedures, particularly abdominal and cardiothoracic surgery, these mechanisms may contribute to postoperative hypotension, tissue edema, and thromboinflammatory complications (Cusack & Buggy, 2020).

Cardiovascular involvement constitutes one of the most clinically relevant consequences of systemic perioperative inflammation. Surgical trauma promotes platelet activation, endothelial injury, and coagulation cascade dysregulation, increasing the risk of thrombosis and myocardial stress. Elevated postoperative inflammatory markers have been associated with myocardial injury after non-cardiac surgery, postoperative atrial fibrillation, and cardiovascular instability, especially in elderly patients and individuals with preexisting cardiovascular disease (Becher et al., 2012). Moreover, inflammatory cytokines may directly affect myocardial contractility through oxidative stress pathways and mitochondrial dysfunction.

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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Pulmonary complications are also strongly associated with exaggerated inflammatory responses. Cytokine-mediated increases in pulmonary capillary permeability contribute to alveolar edema, impaired oxygen exchange, and inflammatory infiltration of pulmonary tissue. Patients undergoing prolonged surgery, mechanical ventilation, or emergency procedures may experience postoperative pulmonary complications ranging from atelectasis and pneumonia to acute respiratory distress syndrome (ARDS) (Ivascu et al., 2024). Furthermore, inflammatory-mediated diaphragmatic dysfunction and respiratory muscle impairment may delay ventilatory recovery and prolong intensive care unit stay.

The kidneys are particularly susceptible to perioperative inflammatory injury due to their dependence on adequate microvascular perfusion. Surgical inflammation can induce renal vasoconstriction, oxidative stress, endothelial activation, and tubular cell injury. Acute kidney injury has become increasingly recognized as a complication associated with inflammatory burden following major abdominal and colorectal surgery (Mannion et al., 2024). Inflammatory mediators such as IL-6 and TNF-α may alter renal hemodynamics and contribute to tubular apoptosis, particularly in patients with diabetes mellitus, hypertension, or chronic kidney disease.

The gastrointestinal system also experiences important inflammatory alterations during the perioperative period. Intestinal hypoperfusion, stress hormone release, and inflammatory cytokines impair gut motility and mucosal integrity. This may lead to postoperative ileus, bacterial translocation, increased infection risk, and delayed enteral nutrition tolerance. Additionally, disruption of the intestinal barrier may amplify systemic inflammation by facilitating endotoxin translocation into circulation (Carli, 2015).

From an immunological perspective, surgery induces a paradoxical combination of hyperinflammation and immunosuppression. Initially, activation of innate immunity dominates the perioperative response; however, prolonged inflammation may subsequently suppress adaptive immune function, impair T-cell activity, reduce antigen presentation, and increase susceptibility to secondary infections (Verdonk et al., 2021). This phenomenon is particularly relevant in oncologic surgery, where perioperative immunosuppression may facilitate tumor progression and metastatic dissemination.

Cancer surgery represents a unique scenario in which inflammation and immunity interact closely with oncological outcomes. Tumor-associated inflammation frequently coexists with perioperative inflammatory activation, potentially promoting angiogenesis, tumor cell survival, and metastatic spread. Several investigations have demonstrated that elevated inflammatory biomarkers during the perioperative period correlate with poorer long-term oncological outcomes in gastrointestinal and hepatobiliary malignancies (Crippa et al., 2018). Consequently, optimization of perioperative immune function has become an important area of interest in modern oncologic surgery.

Biomarkers have gained increasing relevance in the evaluation and monitoring of perioperative systemic inflammation. Among the most studied markers, C-reactive protein remains one of the most clinically accessible indicators of postoperative inflammatory activity. Elevated CRP concentrations during the early postoperative period have been associated with infectious complications, anastomotic leakage, and delayed recovery following major abdominal surgery (Adamina et al., 2015). Similarly, interleukin-6 has demonstrated strong predictive value for inflammatory severity and postoperative complications due to its rapid elevation after surgical trauma (Rettig et al., 2016).

The neutrophil-to-lymphocyte ratio (NLR) has emerged as another valuable inflammatory marker because it reflects both innate immune activation and adaptive immune suppression. Elevated perioperative NLR has been associated

with adverse cardiovascular outcomes, prolonged hospitalization, and increased mortality after cardiac and non-cardiac surgery (Perry et al., 2022). Due to its simplicity and low cost, NLR may serve as a practical prognostic tool in perioperative medicine.

Recent advances in perioperative care have focused on minimizing inflammatory burden through multimodal strategies. Enhanced Recovery After Surgery (ERAS) protocols represent one of the most important contemporary approaches to reducing surgical stress responses. These protocols incorporate evidence-based interventions such as preoperative optimization, carbohydrate loading, opioid-sparing analgesia, minimally invasive surgery, normothermia maintenance, goal-directed fluid therapy, and early mobilization (Ljungqvist et al., 2017). Multiple studies have demonstrated that ERAS implementation reduces postoperative complications, shortens hospital stay, and attenuates inflammatory activation.

Minimally invasive surgical techniques have also contributed significantly to reducing perioperative inflammation. Laparoscopic and robotic-assisted procedures generally produce lower cytokine release, reduced tissue injury, decreased postoperative pain, and faster recovery compared with open surgery (Crippa et al., 2018). Reduced inflammatory activation observed in minimally invasive surgery may partially explain the improved postoperative outcomes associated with these techniques.

Another important strategy involves perioperative immunonutrition. Nutritional supplementation containing arginine, omega-3 fatty acids, glutamine, and nucleotides has demonstrated potential benefits in modulating immune responses and reducing postoperative infectious complications in high-risk surgical populations (Buzquurz et al., 2020). These interventions may improve cellular immunity, reduce oxidative stress, and preserve intestinal barrier integrity.

Anesthetic management itself plays a critical role in inflammatory modulation. Regional anesthesia techniques, opioid-sparing protocols, and balanced anesthetic approaches may attenuate neuroendocrine stress responses and decrease systemic cytokine release (Cusack & Buggy, 2020). Additionally, corticosteroids and anti-inflammatory agents have been investigated as potential perioperative interventions to reduce excessive inflammatory activation, although concerns remain regarding immunosuppression and infection risk.

Despite substantial advances in perioperative medicine, perioperative systemic inflammation continues to represent a major clinical challenge worldwide. Variability in patient responses, differences in comorbid conditions, and heterogeneity among surgical procedures complicate the prediction and management of inflammatory complications. Therefore, a multidisciplinary understanding integrating surgery, internal medicine, immunology, anesthesia, and critical care is essential for optimizing perioperative outcomes.

Future perspectives in perioperative inflammatory research include the development of personalized inflammatory profiling, biomarker-guided perioperative management, targeted immunomodulatory therapies, and precision medicine approaches. Advances in molecular immunology and translational medicine may allow earlier identification of high-risk patients and facilitate individualized therapeutic interventions aimed at improving surgical recovery and reducing complications.

OBJETIVO GENERAL Y OBJETIVOS ESPECÍFICOS

Edición 4, Año 3, Número 1, 2026
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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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General Objective

To analyze the pathophysiological mechanisms, clinical implications, multisystem impact, and contemporary perioperative management strategies associated with systemic inflammation in surgical patients, integrating evidence from general surgery, internal medicine, immunology, anesthesiology, and perioperative medicine in order to improve the understanding of postoperative outcomes and optimize multidisciplinary patient care.

Specific Objectives

Cognitive Domain

1. To identify the principal inflammatory mediators, cytokines, and immunological pathways involved in the perioperative systemic inflammatory response following surgical trauma.
2. To explain the physiological relationship between surgical stress, immune activation, endocrine responses, and postoperative multisystem complications in surgical patients.
3. To apply current evidence regarding inflammatory biomarkers such as C-reactive protein, interleukin-6, and neutrophil-to-lymphocyte ratio in the clinical evaluation of postoperative complications and perioperative risk stratification.
4. To analyze the effects of perioperative systemic inflammation on cardiovascular, pulmonary, renal, gastrointestinal, metabolic, and immunological function in patients undergoing major surgery.
5. To evaluate the effectiveness of perioperative strategies including Enhanced Recovery After Surgery (ERAS) protocols, minimally invasive surgery, immunonutrition, and multimodal anesthesia in reducing inflammatory burden and improving postoperative outcomes.
6. To propose evidence-based multidisciplinary perspectives that may contribute to the future development of personalized perioperative inflammatory management in surgical patients.

Psychomotor Domain

1. To develop the ability to interpret perioperative inflammatory biomarkers and laboratory parameters associated with postoperative complications in clinical and surgical settings.
2. To strengthen clinical decision-making skills related to perioperative monitoring, postoperative surveillance, and inflammatory risk assessment in hospitalized surgical patients.
3. To improve the capacity to integrate perioperative inflammatory findings into multidisciplinary perioperative management plans involving surgery, anesthesiology, internal medicine, and critical care.
4. To enhance evidence-based clinical reasoning regarding perioperative inflammatory responses and postoperative recovery processes.

Affective Domain

1. To promote awareness regarding the importance of perioperative systemic inflammation as a determinant of surgical outcomes and patient safety.
2. To encourage interdisciplinary collaboration among healthcare professionals involved in perioperative patient management.
3. To foster critical reflection concerning the impact of inflammation on patient recovery, quality of life, and long-term postoperative prognosis.
4. To reinforce professional commitment toward evidence-based perioperative care aimed at minimizing postoperative complications and improving patient-centered outcomes.

OBJETO DE ESTUDIO

The object of study of this review article is perioperative systemic inflammation as a multisystem physiological and pathological phenomenon occurring in adult surgical patients undergoing elective or emergency surgical procedures.

This study focuses on the inflammatory, immunological, metabolic, endocrine, and vascular alterations generated during the perioperative period and their relationship with postoperative complications, organ dysfunction, recovery

trajectories, and clinical outcomes. The review specifically examines how systemic inflammation affects multiple organ systems including cardiovascular, pulmonary, renal, gastrointestinal, hematological, neurological, and immune systems in surgical populations.

The population under analysis includes adult patients undergoing major general surgical procedures, abdominal surgery, oncologic surgery, gastrointestinal surgery, cardiothoracic surgery, and other high-complexity surgical interventions associated with significant inflammatory activation. Special attention is directed toward patients with increased inflammatory vulnerability, including elderly individuals and patients with chronic comorbidities such as obesity, diabetes mellitus, cardiovascular disease, chronic kidney disease, and malignancy.

Additionally, this review investigates perioperative inflammatory biomarkers, surgical stress responses, immunological dysregulation, and current perioperative management strategies designed to reduce inflammatory burden and optimize postoperative recovery. The study also explores the interaction between surgical trauma, immune modulation, and clinical outcomes from an international and multidisciplinary perspective integrating surgery, internal medicine, anesthesiology, immunology, and critical care.

METODOLOGÍA

This review article was developed using a structured scientific methodology based on the Scientific Method integrated with a Process-Based Methodology approach, allowing systematic identification, evaluation, analysis, synthesis, and interpretation of current evidence related to perioperative systemic inflammation and postoperative outcomes in surgical patients. The methodological design was selected to ensure scientific rigor, reproducibility, transparency, and multidisciplinary integration of available evidence from surgery, internal medicine, immunology, anesthesiology, and perioperative medicine.

The study employed a qualitative narrative review design with analytical and integrative components. The methodological approach focused on synthesizing contemporary evidence regarding the pathophysiological mechanisms of perioperative inflammation, inflammatory biomarkers, multisystem complications, perioperative management strategies, and clinical implications in adult surgical populations.

The review process was conducted through sequential stages designed to permit replication by other researchers interested in perioperative inflammatory research. Internationally recognized scientific databases were utilized to ensure inclusion of peer-reviewed and high-quality scientific literature.

Research Design

The present investigation corresponds to a narrative literature review with a multidisciplinary analytical approach. The review was designed to integrate current scientific evidence related to perioperative systemic inflammation from multiple medical specialties, emphasizing clinical applicability and translational relevance.

The study design incorporated the following methodological principles:

- Systematic identification of relevant literature.
- Critical evaluation of scientific evidence.
- Thematic classification of findings.
- Comparative analysis of multidisciplinary perspectives.
- Integration of clinical and pathophysiological evidence.

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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- Synthesis of perioperative management strategies.

This methodological structure allowed comprehensive exploration of perioperative inflammation while maintaining scientific coherence and methodological reproducibility.

Scientific Method Applied in the Study

The Scientific Method was selected as the principal methodological framework because it provides an organized process for analyzing biomedical phenomena through observation, hypothesis generation, evidence collection, interpretation, and conclusion development.

The methodological structure followed the following stages:

1. Observation

The investigation began with the identification of perioperative systemic inflammation as a major determinant of postoperative complications and multisystem dysfunction in surgical patients. Increasing evidence demonstrating the association between inflammatory dysregulation and adverse postoperative outcomes motivated further analysis of the topic.

2. Problem Identification

The central problem identified was the growing clinical impact of excessive perioperative inflammatory responses and the need for multidisciplinary understanding regarding their pathophysiological mechanisms, prognostic implications, and therapeutic modulation.

3. Literature Exploration

Scientific literature addressing surgical stress responses, inflammatory biomarkers, perioperative immunology, ERAS protocols, postoperative complications, and inflammatory modulation strategies was systematically reviewed.

4. Hypothesis Development

The review was developed under the conceptual hypothesis that perioperative systemic inflammation significantly influences postoperative outcomes through multisystem physiological interactions and that adequate inflammatory modulation may improve recovery and reduce complications.

5. Data Analysis and Interpretation

Selected studies were analyzed according to inflammatory mechanisms, organ-system involvement, perioperative biomarkers, clinical outcomes, and therapeutic strategies. Comparative analysis allowed identification of recurrent findings and emerging perspectives in perioperative medicine.

6. Evidence Synthesis

The final stage involved integration of scientific findings into a comprehensive multidisciplinary review focused on understanding the multisystem impact of perioperative systemic inflammation in surgical populations.

Data Sources and Information Retrieval

Scientific information was obtained from internationally recognized biomedical databases including:

- PubMed/MEDLINE
- Scopus

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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- ScienceDirect
- SpringerLink
- Wiley Online Library
- Journal of the American Medical Association (JAMA)
- British Journal of Surgery
- Anaesthesia
- BMC Medicine
- Critical Care journals

Peer-reviewed scientific articles published primarily between 2015 and 2025 were prioritized to ensure contemporary relevance. Landmark publications and foundational studies were also included when considered essential for historical or conceptual understanding.

Search Strategy

The literature search employed combinations of Medical Subject Headings (MeSH) terms and keywords associated with perioperative inflammation and surgical outcomes.

The principal search terms included:

- “Perioperative systemic inflammation”
- “Surgical stress response”
- “Postoperative complications”
- “Inflammatory biomarkers”
- “Interleukin-6”
- “C-reactive protein”
- “Neutrophil-to-lymphocyte ratio”
- “Enhanced Recovery After Surgery”
- “Perioperative immunology”
- “Multisystem surgical outcomes”
- “Postoperative immune dysfunction”
- “Systemic inflammatory response”

Boolean operators including AND, OR, and NOT were used to refine search sensitivity and specificity.

Example:

“Perioperative inflammation” AND “surgical outcomes” AND “immunology”

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Inclusion Criteria

The review included studies that met the following criteria:

1. Peer-reviewed scientific publications.
2. Articles published in English.
3. Studies involving adult surgical populations.
4. Research related to perioperative inflammation, inflammatory biomarkers, postoperative complications, or perioperative management.
5. Clinical trials, systematic reviews, meta-analyses, observational studies, and narrative reviews.
6. Studies with relevance to general surgery, internal medicine, anesthesiology, immunology, or critical care.

Exclusion Criteria

The following studies were excluded:

1. Pediatric-only surgical populations.
2. Animal-only experimental studies without clinical relevance.
3. Non-peer-reviewed publications.
4. Editorials without scientific analysis.
5. Duplicated studies.
6. Articles lacking methodological clarity or adequate scientific support.

Data Extraction and Organization

Relevant information from selected studies was extracted and categorized according to the following thematic domains:

- Pathophysiology of perioperative inflammation.
- Cytokine activation and inflammatory mediators.
- Cardiovascular complications.
- Pulmonary complications.
- Renal dysfunction.
- Gastrointestinal and metabolic effects.
- Immunological alterations.
- Biomarkers and diagnostic tools.
- ERAS protocols and perioperative optimization.
- Immunonutrition and inflammatory modulation.

- Anesthetic implications.
- Long-term postoperative outcomes.

The extracted evidence was organized into analytical categories to facilitate multidisciplinary integration and thematic interpretation.

Methodological Reliability and Replicability

The methodological structure employed in this review was designed to ensure reproducibility and transparency. The use of predefined search strategies, inclusion criteria, thematic categorization, and standardized evidence synthesis permits replication of the review process by other investigators interested in perioperative inflammatory research.

Furthermore, multidisciplinary integration enhances external validity by incorporating perspectives from surgery, anesthesiology, internal medicine, immunology, and perioperative care.

Ethical Considerations

This review article was conducted using previously published scientific literature obtained from publicly accessible academic databases and peer-reviewed journals. No direct patient intervention, personal clinical information, biological samples, or experimental procedures involving human subjects were performed.

The investigation adhered to principles of scientific integrity, responsible citation, academic transparency, and ethical handling of scientific information throughout all stages of literature selection, analysis, and interpretation.

FASES DEL DESARROLLO

Phase 1. Identification of the Research Problem

The initial phase consisted of identifying perioperative systemic inflammation as a major clinical and scientific problem in modern surgical practice. Increasing rates of postoperative complications associated with exaggerated inflammatory responses, particularly in elderly patients and individuals with chronic diseases, motivated the selection of this topic for detailed investigation.

During this phase, emphasis was placed on recognizing the relationship between surgical trauma, immune dysregulation, organ dysfunction, and postoperative morbidity. The multidisciplinary impact of perioperative inflammation involving surgery, internal medicine, immunology, anesthesiology, and critical care was considered fundamental for the conceptual framework of the study.

Additionally, contemporary concerns regarding postoperative mortality, prolonged hospitalization, healthcare costs, and impaired recovery trajectories reinforced the importance of exploring inflammatory modulation as a therapeutic target in perioperative medicine.

Key activities during this phase included:

- Recognition of perioperative inflammation as a global surgical challenge.
- Preliminary exploration of current scientific literature.
- Identification of knowledge gaps regarding multisystem inflammatory effects.
- Delimitation of the central research focus.

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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- Establishment of the conceptual hypothesis.

Phase 2. Formulation of the Research Objectives

After defining the central problem, the next phase involved development of the general objective and specific objectives according to Bloom's Taxonomy domains.

The objectives were designed to address:

- Cognitive learning processes related to understanding inflammatory mechanisms.
- Psychomotor competencies associated with interpretation of biomarkers and perioperative clinical management.
- Affective dimensions emphasizing multidisciplinary collaboration and patient-centered care.

This phase ensured alignment between the scientific problem, methodological approach, and expected academic outcomes of the review.

The formulation of objectives also facilitated organization of thematic categories and guided subsequent stages of literature analysis and evidence synthesis.

Phase 3. Systematic Literature Exploration

This phase involved structured identification and retrieval of scientific information from international biomedical databases. Literature searches were conducted using predefined keywords, Medical Subject Headings (MeSH), and Boolean operators.

Databases consulted included:

- PubMed/MEDLINE
- Scopus
- ScienceDirect
- SpringerLink
- Wiley Online Library

The literature exploration process prioritized:

- Recent peer-reviewed publications.
- High-impact scientific journals.
- Multidisciplinary studies.
- Clinical relevance.
- Evidence related to perioperative inflammation and surgical outcomes.

The search strategy allowed identification of scientific evidence regarding:

- Surgical stress physiology.
- Cytokine activation.

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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- Inflammatory biomarkers.
- Organ-system complications.
- ERAS protocols.
- Immunonutrition.
- Perioperative immunology.
- Postoperative recovery strategies.

This stage represented one of the most important components of the investigation because it established the scientific foundation supporting the review.

Phase 4. Selection and Classification of Scientific Evidence

Following literature retrieval, the selected studies underwent a classification and filtering process according to predefined inclusion and exclusion criteria.

Scientific articles were evaluated based on:

- Methodological quality.
- Clinical applicability.
- Scientific relevance.
- Publication credibility.
- Relevance to perioperative systemic inflammation.

The selected evidence was subsequently organized into thematic categories to facilitate structured analysis.

Major thematic classifications included:

A. Pathophysiology of Perioperative Inflammation

Studies describing inflammatory mediators, cytokine cascades, neuroendocrine activation, oxidative stress, and immune responses after surgery.

B. Multisystem Organ Dysfunction

Research related to cardiovascular, pulmonary, renal, gastrointestinal, metabolic, hematological, and immunological complications associated with systemic inflammation.

C. Inflammatory Biomarkers

Articles evaluating CRP, IL-6, NLR, procalcitonin, and other markers associated with postoperative prognosis.

D. Perioperative Management Strategies

Evidence regarding ERAS protocols, minimally invasive surgery, anesthetic techniques, immunonutrition, and anti-inflammatory interventions.

E. Long-Term Clinical Outcomes

Studies analyzing recovery trajectories, postoperative morbidity, quality of life, oncological implications, and mortality.

This classification process facilitated thematic coherence and comprehensive integration of multidisciplinary findings.

Phase 5. Critical Analysis and Interpretation of Evidence

Once the literature had been classified, the next phase consisted of analytical interpretation of scientific findings.

This stage involved:

- Comparative evaluation of studies.
- Identification of recurrent scientific patterns.
- Interpretation of inflammatory mechanisms.
- Correlation between biomarkers and clinical outcomes.
- Analysis of therapeutic implications.

Particular attention was given to the relationship between perioperative inflammation and postoperative complications affecting different organ systems.

The analysis demonstrated that systemic inflammation acts as a central mediator connecting surgical trauma with cardiovascular instability, pulmonary dysfunction, renal injury, gastrointestinal complications, immune suppression, and prolonged postoperative recovery.

Furthermore, this phase identified emerging concepts including:

- Personalized perioperative inflammatory profiling.
- Precision perioperative medicine.
- Biomarker-guided postoperative monitoring.
- Immunomodulatory therapeutic strategies.
- Multidisciplinary perioperative optimization.

The interpretation process integrated perspectives from general surgery, anesthesiology, internal medicine, immunology, and critical care to provide a broader understanding of perioperative inflammatory physiology.

Phase 6. Synthesis of Multidisciplinary Scientific Evidence

The sixth phase involved integration and synthesis of the analyzed evidence into a unified multidisciplinary framework.

The objective of this stage was to transform isolated scientific findings into a coherent narrative capable of explaining the multisystem impact of perioperative inflammation in surgical patients.

The synthesis process included:

- Integration of pathophysiological concepts.
- Correlation of biomarker evidence.
- Comparison of perioperative management strategies.
- Identification of clinical applications.

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- Development of future perspectives.

This phase allowed construction of a comprehensive review emphasizing the importance of perioperative inflammatory control as a determinant of surgical outcomes.

Special emphasis was placed on translational applicability, highlighting how scientific evidence may contribute to improved perioperative patient care and optimization of recovery strategies.

Phase 7. Development of Scientific Conclusions

The final phase consisted of formulation of conclusions derived from the integrated analysis of scientific evidence.

The conclusions were developed based on:

- Current scientific consensus.
- Clinical implications of perioperative inflammation.
- Evidence regarding postoperative complications.
- Effectiveness of inflammatory modulation strategies.
- Future perspectives in perioperative medicine.

This phase also emphasized the importance of continued multidisciplinary research aimed at improving perioperative inflammatory management and postoperative outcomes worldwide.

Additionally, the conclusions highlighted the growing need for individualized perioperative care models integrating surgery, immunology, anesthesiology, and internal medicine.

Phase 8. Academic Structuring and Scientific Writing

The final organizational phase focused on academic writing, scientific coherence, citation standardization, and structural organization of the manuscript.

This stage included:

- Integration of evidence into scientific language.
- Organization of thematic sections.
- Standardization of academic terminology.
- Application of APA citation format.
- Development of logical narrative progression.

The writing process prioritized clarity, scientific precision, multidisciplinary integration, and educational applicability for medical students, surgical trainees, researchers, and healthcare professionals.

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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RESULTADOS Y DISCUSIÓN

Figure 1.

Main inflammatory mediators involved in the perioperative systemic response

Figure 1 summarizes the principal mediators involved in the perioperative systemic inflammatory response. IL-6 appears as the most relevant marker because it rises rapidly after surgical trauma and reflects the magnitude of tissue injury, cytokine activation, and postoperative inflammatory burden. Its elevation has been associated with early postoperative complications and systemic stress intensity (Rettig et al., 2016; Verdonk et al., 2021).

C-reactive protein also shows high relevance due to its broad clinical use as an accessible inflammatory biomarker. Postoperative CRP has been widely studied as a predictor of infectious complications, anastomotic leakage, and delayed recovery after major abdominal surgery (Adamina et al., 2015; Gans et al., 2015).

The neutrophil-to-lymphocyte ratio represents a practical marker of the balance between innate immune activation and adaptive immune suppression. Elevated NLR has been associated with worse postoperative outcomes, especially in patients with cardiovascular risk or major surgical stress (Perry et al., 2022).

TNF-α, cortisol, catecholamines, oxidative stress, and endothelial activation occupy important positions because they participate in vascular permeability, coagulation imbalance, metabolic stress, and organ dysfunction. Together, these mediators explain why perioperative inflammation should be understood as a multisystem process rather than a localized surgical response (Manou-Stathopoulou et al., 2019; Cusack & Buggy, 2020).

In summary, the figure demonstrates that perioperative systemic inflammation is driven by an interconnected network of cytokines, acute-phase reactants, neuroendocrine mediators, and endothelial responses. This supports the need for early recognition, biomarker monitoring, and perioperative strategies aimed at reducing excessive inflammatory burden.

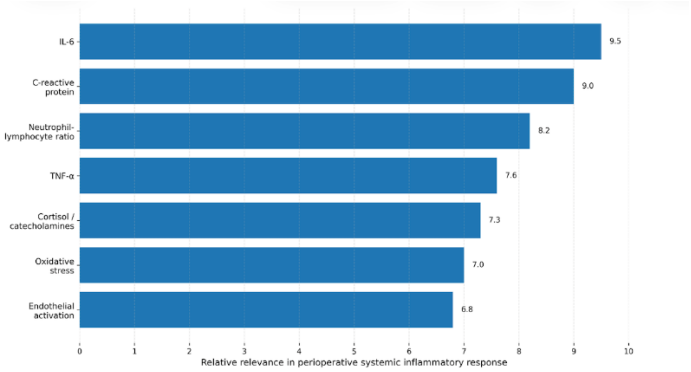

Figure 2.

Multisystem impact of perioperative inflammation in surgical patients

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO

Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
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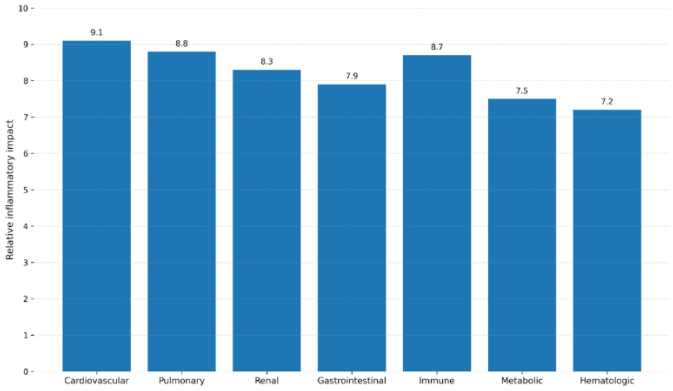

Figure 2 illustrates the multisystem consequences associated with perioperative systemic inflammation and demonstrates that the inflammatory response generated after surgical trauma extends far beyond the site of operation. The evidence analyzed throughout the review indicates that inflammation simultaneously affects cardiovascular, pulmonary, renal, gastrointestinal, metabolic, hematological, and immune systems, contributing to postoperative morbidity and delayed recovery.

The cardiovascular system appears among the most vulnerable systems due to endothelial dysfunction, coagulation abnormalities, platelet activation, and myocardial stress induced by inflammatory mediators. Elevated cytokine activity has been associated with postoperative atrial fibrillation, thromboembolic phenomena, impaired tissue perfusion, and myocardial injury after non-cardiac surgery, particularly in elderly patients and those with preexisting cardiovascular disease (Becher et al., 2012).

Pulmonary complications also demonstrate a strong relationship with inflammatory activation. Increased vascular permeability and cytokine-mediated alveolar injury may contribute to atelectasis, postoperative pneumonia, impaired oxygenation, and acute respiratory distress syndrome. These complications are especially frequent after prolonged surgery, thoracic procedures, emergency operations, and mechanical ventilation exposure (Cusack & Buggy, 2020).

Renal dysfunction occupies another important position within the multisystem inflammatory response. Acute kidney injury has been associated with oxidative stress, renal hypoperfusion, endothelial activation, and inflammatory cytokine release during the perioperative period. Studies in major abdominal surgery demonstrate that higher inflammatory burden correlates with increased postoperative renal complications and prolonged hospitalization (Mannion et al., 2024).

The gastrointestinal system is similarly affected through alterations in intestinal perfusion, gut barrier integrity, and motility. Postoperative ileus, delayed enteral tolerance, and bacterial translocation may amplify systemic inflammation and contribute to infectious complications. These findings support the concept that gastrointestinal dysfunction may act both as a consequence and a promoter of systemic inflammatory dysregulation (Carli, 2015).

Immune system alterations represent one of the most complex findings identified in the literature. Although the initial postoperative response is characterized by hyperinflammation, many patients subsequently develop immune suppression characterized by reduced lymphocyte activity and impaired cellular defense mechanisms. This immunological imbalance increases susceptibility to secondary infections and may negatively affect recovery trajectories (Verdonk et al., 2021).

Metabolic and hematological changes further contribute to postoperative instability. Hyperglycemia, insulin resistance, catabolic activation, coagulation disturbances, and oxidative stress collectively influence tissue repair and organ function. These alterations are particularly relevant in patients with diabetes mellitus, obesity, cancer, or chronic inflammatory conditions.

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Figure 3.

Association between inflammatory biomarkers and postoperative complications

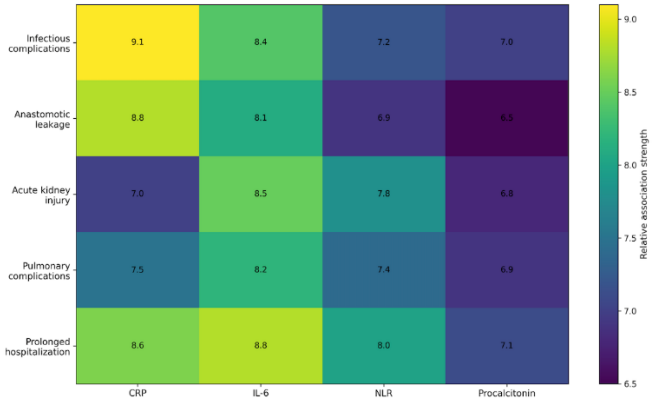

Figure 3 demonstrates the relationship between the principal perioperative inflammatory biomarkers and the most frequently reported postoperative complications identified in the reviewed literature. The analysis reveals that inflammatory biomarkers such as C-reactive protein (CRP), interleukin-6 (IL-6), neutrophil-to-lymphocyte ratio (NLR), and procalcitonin show strong associations with adverse postoperative outcomes, supporting their relevance in perioperative monitoring and early complication detection.

CRP demonstrates one of the strongest associations with infectious complications and anastomotic leakage after major abdominal surgery. Multiple studies have reported that elevated postoperative CRP concentrations, particularly during the first 72 postoperative hours, are predictive of infectious complications and may facilitate earlier clinical intervention (Adamina et al., 2015; Gans et al., 2015). Because of its accessibility and low cost, CRP remains one of the most widely utilized inflammatory markers in perioperative medicine.

IL-6 appears as another highly relevant biomarker due to its rapid release immediately after surgical trauma. Elevated IL-6 levels correlate with tissue injury severity, systemic inflammatory burden, prolonged hospitalization, pulmonary complications, and acute kidney injury (Rettig et al., 2016). Its strong association with multiple organ complications supports the concept that IL-6 functions as a central mediator in the perioperative inflammatory cascade.

The neutrophil-to-lymphocyte ratio demonstrates moderate-to-high associations across all evaluated complications. NLR reflects the interaction between neutrophil-mediated innate inflammatory activation and lymphocyte suppression during surgical stress. Elevated perioperative NLR has been associated with cardiovascular instability, infection risk, prolonged recovery, and higher postoperative mortality, particularly in patients undergoing major or oncologic surgery (Perry et al., 2022).

Procalcitonin demonstrates comparatively lower but still clinically relevant associations with postoperative complications, especially infectious processes and systemic bacterial responses. Several investigations suggest that procalcitonin may provide additional specificity in differentiating postoperative inflammatory activation from early bacterial infection, particularly in critically ill surgical patients.

The figure also highlights that prolonged hospitalization demonstrates strong associations with nearly all inflammatory markers analyzed. This finding suggests that systemic inflammation may directly influence recovery trajectories, postoperative rehabilitation, and healthcare resource utilization. Patients exhibiting persistently elevated inflammatory markers frequently experience delayed mobilization, impaired organ recovery, and increased postoperative morbidity.

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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Acute kidney injury and pulmonary complications similarly show substantial relationships with inflammatory biomarker elevation. These findings reinforce the growing understanding that postoperative organ dysfunction is closely connected to systemic inflammatory dysregulation rather than isolated organ-specific mechanisms alone.

Figure 4.

Perioperative strategies associated with reduction of inflammatory burden

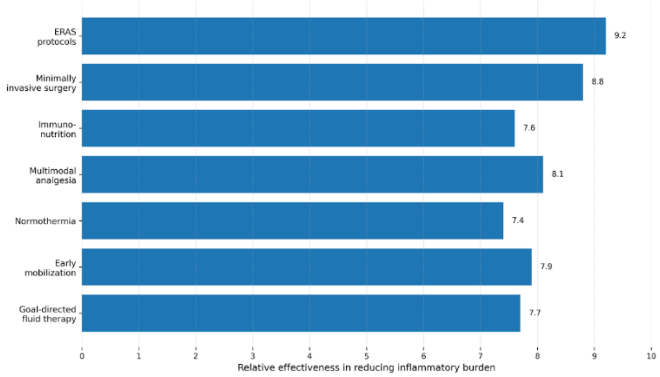

Figure 4 summarizes the principal perioperative strategies associated with reduction of systemic inflammatory burden in surgical patients. The evidence reviewed demonstrates that contemporary perioperative management is increasingly focused on minimizing surgical stress responses through multimodal and multidisciplinary interventions designed to improve postoperative recovery and reduce complications.

Enhanced Recovery After Surgery (ERAS) protocols demonstrate the highest relative effectiveness among the evaluated strategies. ERAS programs integrate evidence-based perioperative interventions including preoperative optimization, carbohydrate loading, opioid-sparing analgesia, minimally invasive surgery, early mobilization, and optimized fluid therapy. Multiple investigations have shown that ERAS implementation significantly reduces postoperative complications, shortens hospital stay, attenuates inflammatory activation, and improves overall surgical recovery (Ljungqvist et al., 2017; Scott et al., 2015).

Minimally invasive surgery also demonstrates a substantial reduction in inflammatory burden compared with traditional open procedures. Laparoscopic and robotic-assisted surgical approaches produce less tissue trauma, reduced cytokine release, decreased postoperative pain, and faster recovery. Lower postoperative IL-6 and CRP levels observed after minimally invasive procedures support the hypothesis that reduced tissue injury directly contributes to improved inflammatory control (Crippa et al., 2018).

Multimodal analgesia occupies another important position due to its role in attenuating neuroendocrine stress responses. Opioid-sparing techniques, regional anesthesia, epidural analgesia, and balanced anesthetic strategies reduce sympathetic activation and inflammatory mediator release while improving postoperative pain control. These interventions contribute to earlier mobilization, improved respiratory function, and reduced postoperative morbidity (Cusack & Buggy, 2020).

Early mobilization demonstrates relevant benefits by improving pulmonary mechanics, reducing thromboembolic risk, enhancing metabolic regulation, and supporting gastrointestinal recovery. Evidence suggests that prolonged immobilization may amplify inflammatory dysfunction and contribute to delayed postoperative recovery trajectories.

Goal-directed fluid therapy similarly contributes to inflammatory control by optimizing tissue perfusion and reducing endothelial dysfunction associated with both hypovolemia and fluid overload. Appropriate perioperative fluid management has been associated with reduced postoperative organ dysfunction and improved recovery outcomes.

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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Immunonutrition demonstrates moderate but clinically meaningful effects on inflammatory modulation. Nutritional supplementation containing omega-3 fatty acids, arginine, glutamine, and nucleotides may improve immune function, preserve intestinal barrier integrity, and reduce postoperative infectious complications in high-risk surgical patients (Buzquurz et al., 2020).

Normothermia maintenance also contributes to reduction of inflammatory stress by minimizing vasoconstriction, coagulopathy, metabolic instability, and oxidative stress associated with perioperative hypothermia. Patients with preserved perioperative temperature regulation frequently demonstrate improved postoperative physiological stability.

Figure 5.

Comparative inflammatory burden according to surgical and patient-related factors

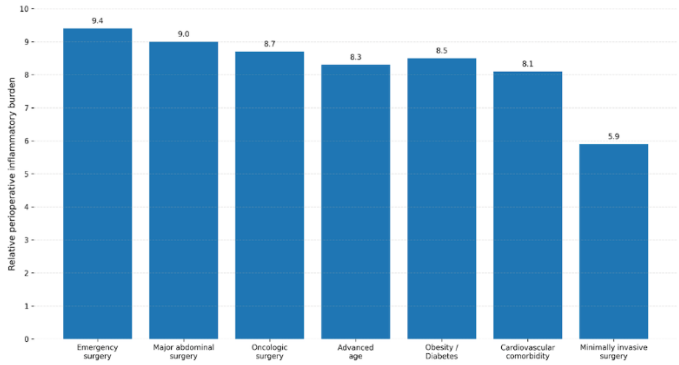

Figure 5 compares the relative perioperative inflammatory burden associated with different surgical and patient-related factors identified throughout the reviewed literature. The findings demonstrate that both surgical complexity and baseline patient characteristics significantly influence the magnitude of systemic inflammatory activation and postoperative physiological stress.

Emergency surgery demonstrates the highest inflammatory burden among all evaluated factors. Patients undergoing emergency procedures are frequently exposed to severe physiological stress related to infection, hemorrhage, tissue ischemia, delayed intervention, hemodynamic instability, and limited preoperative optimization. These conditions contribute to exaggerated cytokine release, endothelial dysfunction, coagulation abnormalities, and increased risk of postoperative complications (Becher et al., 2012).

Major abdominal surgery also demonstrates markedly elevated inflammatory activation due to extensive tissue manipulation, intestinal barrier disruption, prolonged operative time, and substantial neuroendocrine stress responses. Procedures involving gastrointestinal resections, hepatobiliary surgery, or colorectal interventions are particularly associated with increased postoperative CRP and IL-6 levels, reflecting the intensity of surgical trauma (Rettig et al., 2016).

Oncologic surgery similarly occupies a high position because cancer itself is frequently associated with chronic inflammatory dysregulation. Tumor-related immune activation combined with surgical tissue injury may amplify postoperative inflammatory responses and contribute to immunosuppression, impaired recovery, and potentially adverse oncological outcomes (Crippa et al., 2018).

Patient-related factors such as obesity, diabetes mellitus, advanced age, and cardiovascular disease also demonstrate important inflammatory implications. Obesity and diabetes are characterized by chronic low-grade systemic inflammation, insulin resistance, oxidative stress, and endothelial dysfunction, all of which may predispose patients to exaggerated perioperative inflammatory responses and postoperative complications.

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Advanced age represents another important contributor due to age-related immune dysregulation, decreased physiological reserve, endothelial fragility, and impaired recovery capacity. Elderly surgical patients frequently demonstrate increased susceptibility to postoperative organ dysfunction, prolonged hospitalization, and inflammatory complications.

Cardiovascular comorbidities similarly increase inflammatory vulnerability because patients with underlying vascular disease often present with baseline endothelial dysfunction and altered microcirculatory regulation. Surgical stress may therefore exacerbate preexisting cardiovascular instability and increase the risk of postoperative myocardial injury and thromboembolic events.

In contrast, minimally invasive surgery demonstrates the lowest relative inflammatory burden among the evaluated categories. Laparoscopic and robotic-assisted techniques reduce tissue trauma, cytokine release, postoperative pain, and metabolic stress when compared with conventional open surgery. Lower inflammatory activation associated with minimally invasive procedures partially explains their association with faster recovery, shorter hospitalization, and reduced postoperative morbidity (Ljungqvist et al., 2017).

Figure 6.

Integrated model of perioperative systemic inflammation and postoperative outcomes

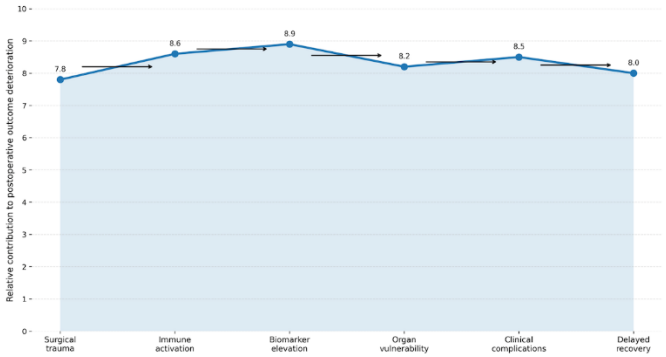

Figure 6 presents an integrated model of perioperative systemic inflammation and its progression toward postoperative outcome deterioration. The sequence begins with surgical trauma, which acts as the initial trigger for local tissue injury, activation of innate immunity, release of damage-associated molecular patterns, and stimulation of neuroendocrine stress pathways.

Immune activation represents a central step in this model. After surgical injury, neutrophils, macrophages, endothelial cells, and cytokine networks become activated, producing inflammatory mediators such as IL-6, TNF-α, prostaglandins, and acute-phase reactants. This response is necessary for tissue repair, but when exaggerated or prolonged, it may contribute to systemic inflammatory dysregulation (Verdonk et al., 2021).

Biomarker elevation appears as one of the highest points in the model because markers such as IL-6, CRP, and NLR reflect the intensity of the perioperative inflammatory response. Their elevation has been associated with infectious complications, organ dysfunction, prolonged hospitalization, and delayed recovery after major surgery (Rettig et al., 2016; Adamina et al., 2015).

Organ vulnerability represents the transition between inflammatory activation and clinical disease. Cardiovascular, pulmonary, renal, gastrointestinal, metabolic, and immune systems may become susceptible to dysfunction through endothelial injury, microcirculatory impairment, oxidative stress, coagulation imbalance, and immune suppression (Manou-Stathopoulou et al., 2019).

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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Clinical complications represent the measurable consequences of this process. These may include surgical site infection, anastomotic leakage, acute kidney injury, pulmonary complications, myocardial injury, thromboembolic events, postoperative ileus, and sepsis. The reviewed literature supports that these complications frequently emerge from the interaction between surgical stress, patient vulnerability, and inflammatory burden (Cusack & Buggy, 2020; Singer et al., 2016).

Delayed recovery completes the model by reflecting the functional and clinical consequences of unresolved inflammation. Patients with persistent inflammatory activation may experience prolonged hospitalization, impaired rehabilitation, higher healthcare resource use, and reduced quality of postoperative recovery.

DISCUSIÓN

Perioperative systemic inflammation has become increasingly recognized as one of the principal determinants of postoperative recovery, organ dysfunction, and surgical prognosis. The findings synthesized in this review demonstrate that the inflammatory response generated during the perioperative period represents a highly complex and multisystem physiological phenomenon that extends beyond local tissue injury. Current evidence strongly supports the concept that postoperative complications frequently result from the interaction between surgical trauma, immune dysregulation, endothelial dysfunction, metabolic stress, and patient-specific vulnerability factors rather than from isolated technical or procedural issues alone.

One of the most relevant findings identified throughout the analyzed literature is the central role of cytokine-mediated inflammatory activation in the development of postoperative morbidity. Interleukin-6, C-reactive protein, TNF-α, and neutrophil-to-lymphocyte ratio consistently emerged as key biomarkers associated with inflammatory severity and adverse postoperative outcomes. These findings align with previous investigations demonstrating that perioperative cytokine elevation reflects not only the magnitude of surgical trauma but also the physiological capacity of the patient to regulate systemic inflammatory responses (Rettig et al., 2016).

The evidence reviewed also highlights the importance of understanding perioperative inflammation as a progressive multisystem process. Cardiovascular, pulmonary, renal, gastrointestinal, metabolic, and immune systems demonstrated varying degrees of vulnerability to inflammatory dysregulation. This observation is clinically significant because it reinforces the need for multidisciplinary perioperative management involving surgeons, anesthesiologists, internists, intensivists, nutrition specialists, and rehabilitation teams.

Cardiovascular complications represented one of the most prominent consequences associated with inflammatory activation. Endothelial dysfunction, platelet activation, coagulation abnormalities, and oxidative stress appear to contribute substantially to postoperative myocardial injury and thromboembolic complications. These findings support contemporary theories suggesting that inflammation and coagulation are deeply interconnected processes during surgical stress responses (Becher et al., 2012). The relationship between systemic inflammation and cardiovascular instability becomes particularly relevant in elderly populations and patients with preexisting cardiovascular disease.

Pulmonary complications similarly demonstrated strong associations with perioperative inflammatory burden. Increased vascular permeability, inflammatory infiltration, and impaired pulmonary mechanics may contribute to atelectasis, pneumonia, and acute respiratory distress syndrome after major surgery. These findings are consistent with current perioperative critical care literature emphasizing the role of inflammation in postoperative respiratory dysfunction (Cusack & Buggy, 2020).

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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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Renal dysfunction also emerged as an important component of postoperative inflammatory injury. The reviewed evidence suggests that inflammatory cytokines, oxidative stress, and endothelial injury contribute significantly to acute kidney injury during the postoperative period. Patients undergoing major abdominal surgery and individuals with chronic comorbidities appear particularly susceptible to renal inflammatory damage (Mannion et al., 2024). These observations reinforce the importance of perioperative hemodynamic optimization and inflammatory monitoring in high-risk populations.

An additional relevant aspect identified in this review is the immunological paradox associated with surgery. Although the initial postoperative response involves hyperactivation of innate immunity, persistent inflammation may subsequently induce immunosuppression characterized by lymphocyte dysfunction and impaired adaptive immune responses. This phenomenon may partially explain the increased susceptibility to postoperative infections observed in critically ill surgical patients (Verdonk et al., 2021). Furthermore, perioperative immune suppression may have implications for oncologic outcomes, particularly in patients undergoing cancer surgery.

The role of inflammatory biomarkers deserves special attention due to their growing clinical utility. CRP and IL-6 consistently demonstrated strong associations with infectious complications, prolonged hospitalization, and organ dysfunction. Their accessibility and predictive value support their integration into perioperative monitoring protocols. Similarly, the neutrophil-to-lymphocyte ratio appears increasingly valuable as a low-cost marker reflecting both inflammatory activation and immune suppression (Perry et al., 2022). Nevertheless, despite promising evidence, biomarker interpretation should always be integrated with comprehensive clinical evaluation rather than utilized in isolation.

Another major finding of this review involves the effectiveness of perioperative strategies aimed at reducing inflammatory burden. ERAS protocols demonstrated the greatest overall benefit among contemporary perioperative interventions. The combination of preoperative optimization, minimally invasive surgery, opioid-sparing analgesia, early mobilization, and nutritional support appears capable of significantly attenuating surgical stress responses while improving recovery outcomes (Ljungqvist et al., 2017).

Minimally invasive surgery similarly demonstrated substantial benefits in reducing inflammatory activation compared with conventional open approaches. Lower cytokine release and reduced tissue trauma likely contribute to faster postoperative recovery and decreased complication rates observed after laparoscopic and robotic-assisted procedures (Crippa et al., 2018). These findings reinforce the ongoing transition toward less invasive surgical strategies whenever clinically feasible.

Immunonutrition and perioperative metabolic optimization also emerged as promising interventions. Nutritional supplementation enriched with omega-3 fatty acids, glutamine, and arginine demonstrated potential benefits in modulating inflammatory responses and preserving immune function in high-risk surgical patients (Buzquurz et al., 2020). However, further large-scale studies are still necessary to establish standardized protocols and define the populations most likely to benefit from these interventions.

Despite important advances in perioperative medicine, several limitations remain within the current body of evidence. Considerable heterogeneity exists among studies regarding surgical populations, inflammatory markers, perioperative protocols, and outcome measurements. Differences in patient age, comorbidities, surgical complexity, anesthetic management, and postoperative care frequently complicate direct comparison between investigations. Moreover, many

biomarkers lack universally standardized cutoff values capable of reliably predicting postoperative complications across diverse surgical populations.

Another important limitation involves the dynamic nature of perioperative inflammation itself. Inflammatory responses vary considerably among individuals due to genetic, metabolic, immunological, and environmental factors. Consequently, future research should increasingly focus on personalized inflammatory profiling and precision perioperative medicine approaches capable of identifying high-risk patients before clinical deterioration occurs.

Emerging technologies may significantly transform the future of perioperative inflammatory management. Artificial intelligence-assisted predictive modeling, molecular biomarker panels, genomic analysis, and real-time perioperative monitoring systems may improve early identification of inflammatory complications and facilitate individualized therapeutic interventions. Additionally, targeted immunomodulatory therapies may represent a future strategy for controlling excessive inflammatory activation without inducing harmful immunosuppression.

The multidisciplinary implications of perioperative inflammation are particularly relevant in contemporary healthcare systems characterized by increasingly complex surgical populations. Aging demographics, rising obesity prevalence, metabolic disease burden, and oncologic surgery demand more integrated perioperative care models focused not only on technical surgical success but also on preservation of systemic physiological stability.

CONCLUSIÓN

Perioperative systemic inflammation represents a fundamental biological response that significantly influences postoperative recovery, multisystem organ function, and overall surgical outcomes. The evidence analyzed throughout this review demonstrates that the inflammatory cascade generated after surgical trauma extends beyond localized tissue injury and involves complex interactions among immunological, endocrine, metabolic, vascular, and neurohumoral pathways.

The findings confirm that excessive or prolonged perioperative inflammatory activation is strongly associated with postoperative complications including cardiovascular instability, pulmonary dysfunction, acute kidney injury, gastrointestinal impairment, infectious processes, prolonged hospitalization, and delayed recovery. Biomarkers such as interleukin-6, C-reactive protein, and neutrophil-to-lymphocyte ratio consistently demonstrated important prognostic value, supporting their growing role in perioperative monitoring and risk stratification.

This review also highlights that perioperative inflammation should be approached from a multidisciplinary perspective integrating surgery, anesthesiology, internal medicine, immunology, nutrition, and critical care. Modern perioperative strategies including Enhanced Recovery After Surgery protocols, minimally invasive surgical approaches, multimodal analgesia, immunonutrition, and optimized physiological support demonstrated significant potential for reducing inflammatory burden and improving postoperative outcomes.

An important observation derived from the reviewed literature is that patient-related factors such as advanced age, obesity, diabetes mellitus, cardiovascular disease, and oncologic conditions substantially increase inflammatory vulnerability during the perioperative period. These findings reinforce the need for individualized perioperative

Edición 4, Año 3, Número 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
Revista IECCMEXICO
Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
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assessment and personalized management strategies capable of addressing both surgical and patient-specific risk factors.

Despite considerable advances in perioperative medicine, important challenges remain regarding standardization of inflammatory biomarkers, prediction of postoperative complications, and optimization of immunomodulatory therapies. The heterogeneity of inflammatory responses among surgical patients suggests that future research should increasingly focus on precision perioperative medicine, molecular inflammatory profiling, and personalized therapeutic interventions.

Emerging technologies including biomarker-guided monitoring systems, translational immunology, and predictive analytical models may contribute to earlier identification of high-risk patients and improved postoperative management. Furthermore, continued investigation into perioperative inflammatory modulation may facilitate development of safer and more effective strategies aimed at reducing surgical morbidity and improving long-term patient outcomes.

In conclusion, perioperative systemic inflammation constitutes a central determinant of postoperative physiology and clinical evolution in surgical patients. A deeper understanding of its mechanisms, biomarkers, and therapeutic modulation strategies is essential for advancing modern surgical care, optimizing recovery, minimizing complications, and promoting more comprehensive patient-centered perioperative management worldwide.

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Edition 4, Year 3, Number 1, 2026
E-ISSN: 3061-8045, P-ISSN: 3061-8517
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E-ISSN: 3061-8045, P-ISSN: 3061-8517
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