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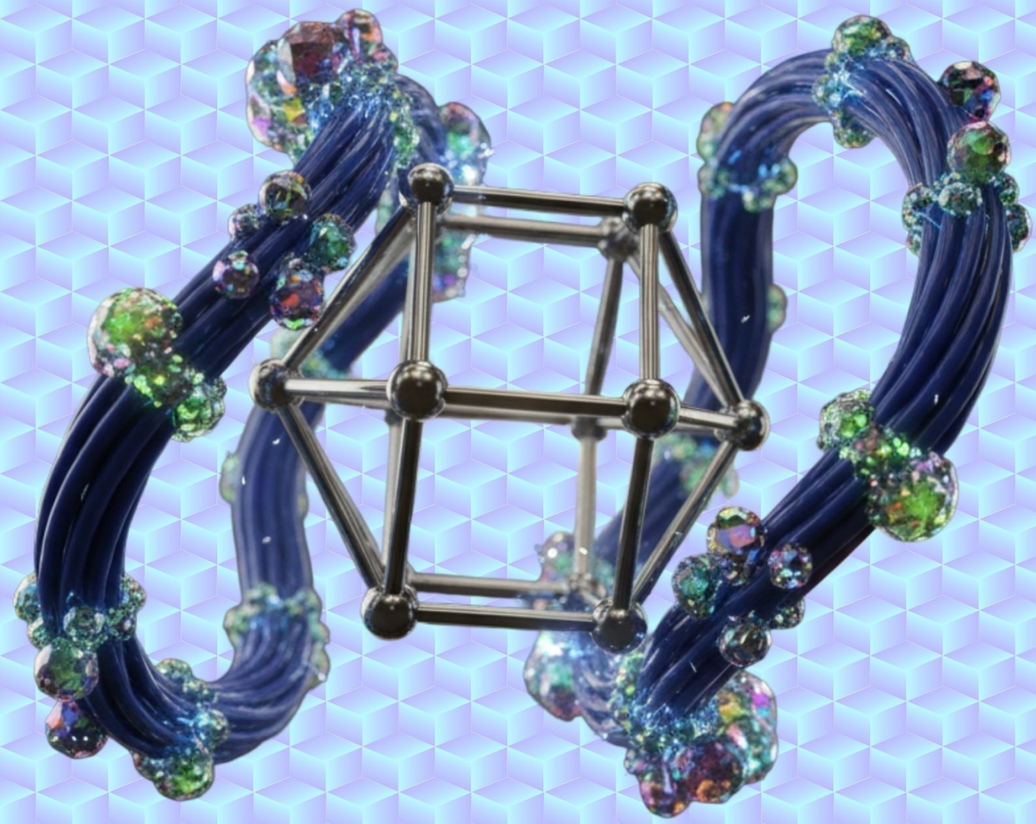

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Immunometabolic Prehabilitation and Anesthesiology: A Preventive Perioperative Strategy to Enhance Surgical Recovery

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ABSTRACT

Major surgery induces a complex physiological stress response characterized by metabolic disruption, systemic inflammation, and accelerated protein catabolism, all of which significantly influence perioperative outcomes. Despite advances in surgical and anesthetic techniques, postoperative complications and delayed recovery remain common, particularly among patients with reduced functional reserve, malnutrition, or metabolic vulnerability. In this context, immunometabolic and nutritional prehabilitation has emerged as a proactive strategy aimed at optimizing patients' physiological condition prior to surgery. This narrative review analyzes

current evidence on immunometabolic and nutritional prehabilitation in major surgery, with a specific focus on its relevance to anesthesiology and perioperative medicine. The review synthesizes data related to functional capacity, postoperative morbidity, hospital length of stay, and feasibility of implementation across different healthcare settings. Emphasis is placed on multimodal prehabilitation approaches that integrate structured exercise, nutritional optimization, and immunonutritional principles, as well as their alignment with Enhanced Recovery After Surgery (ERAS) protocols. The findings highlight consistent associations between comprehensive prehabilitation strategies and improved perioperative trajectories, including better preservation of functional capacity, reduced overall postoperative morbidity, and shorter hospitalization. Additionally, the review explores the applicability of these strategies within diverse healthcare systems, with particular consideration of Mexico, Colombia, and Ecuador. By framing prehabilitation as a core component of anesthesiology-led perioperative care, this work supports a shift toward preventive, patient-centered models aimed at enhancing surgical resilience and recovery.

KEYWORDS

Prehabilitation, perioperative medicine, anesthesiology, immunometabolism, nutritional optimization, major surgery, functional capacity, ERAS, perioperative outcomes, metabolic resilience

INTRODUCTION

Major surgery continues to represent a substantial physiological challenge, particularly in patients with advanced age, metabolic comorbidities, or reduced functional reserve. Despite significant advances in surgical techniques and perioperative care, postoperative complications, prolonged recovery, and increased healthcare utilization remain prevalent worldwide. From an anesthesiology perspective, these adverse outcomes are closely linked to the patient's preoperative metabolic, nutritional, and inflammatory status, which directly influence anesthetic tolerance, stress response, immune competence, and postoperative recovery trajectories [1], [2].

Surgical trauma induces a complex neuroendocrine and inflammatory response characterized by insulin resistance, protein catabolism, immune dysfunction, and impaired mitochondrial efficiency. This stress response is modulated not only by the surgical insult itself but also by pre-existing nutritional deficiencies, sarcopenia, systemic inflammation, and reduced cardiorespiratory fitness [3], [14]. Anesthesiologists, as key perioperative physicians, increasingly recognize that optimization of these factors before surgery is as critical as intraoperative management, particularly in high-risk surgical populations.

Prehabilitation has emerged as a proactive, patient-centered strategy aimed at enhancing physiological reserve prior to surgery through targeted interventions in exercise, nutrition, and metabolic optimization. Unlike traditional perioperative care models that focus predominantly on postoperative rehabilitation, prehabilitation seeks to shift the recovery curve to a higher baseline, thereby improving resilience to surgical stress [2], [7]. Accumulating evidence suggests that multimodal prehabilitation programs can significantly improve functional capacity, reduce postoperative complications, and shorten length of hospital stay [8], [9].

Nutritional status plays a central role in this paradigm. Malnutrition, even in overweight or obese individuals, is a well-established predictor of poor surgical outcomes, including increased infection rates, delayed wound healing, and prolonged mechanical ventilation [4], [15]. International guidelines, including those issued by the European Society for Clinical Nutrition and Metabolism (ESPEN), emphasize the importance of early identification and correction of nutritional deficits in surgical patients [4], [10]. From an anesthetic standpoint, adequate preoperative nutrition influences pharmacokinetics, neuromuscular function, immune response, and the ability to withstand perioperative fasting and fluid shifts [11], [12].

Beyond macronutrient balance, immunonutrition has gained increasing attention in perioperative medicine. Specific nutrients such as omega-3 fatty acids, arginine, and nucleotides have been shown to modulate inflammatory pathways, enhance immune function, and attenuate the magnitude of the surgical stress response [17], [18]. These immunometabolic effects are particularly relevant in major surgery, where dysregulated inflammation and immune

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suppression contribute significantly to postoperative morbidity. For anesthesiologists managing complex surgical cases, understanding and integrating immunonutrition into perioperative planning offers an opportunity to improve outcomes beyond conventional anesthetic techniques.

Enhanced Recovery After Surgery (ERAS) protocols have further reinforced the integration of metabolic and nutritional principles into perioperative care. ERAS emphasizes reduced preoperative fasting, carbohydrate loading, early mobilization, and optimized analgesia, all of which align closely with the goals of prehabilitation [5], [6], [12]. However, while ERAS protocols are well established in many high-income settings, their implementation remains heterogeneous across regions, particularly in Latin America. Countries such as Mexico, Colombia, and Ecuador face unique challenges related to healthcare resource variability, nutritional disparities, and limited access to structured prehabilitation programs.

In these contexts, anesthesiology services play a pivotal role in bridging gaps between surgical planning, nutritional assessment, and metabolic optimization. By incorporating prehabilitation principles into pre-anesthetic evaluation clinics, anesthesiologists can contribute to earlier identification of high-risk patients and facilitate multidisciplinary interventions tailored to local healthcare realities [3], [16]. This regional perspective underscores the need to contextualize global evidence within Latin American health systems, ensuring feasibility and sustainability.

The present narrative review aims to synthesize current evidence on immunometabolic and nutritional prehabilitation in the setting of major surgery, with particular emphasis on its relevance to anesthesiology practice. The review explores physiological mechanisms, clinical outcomes, and practical considerations for implementation, drawing on international literature while highlighting opportunities for integration in Mexico, Colombia, and Ecuador. By aligning anesthetic management with prehabilitation strategies, this work seeks to contribute to a more comprehensive, anticipatory model of perioperative care focused on improving patient-centered outcomes and long-term recovery [19], [20].

DEVELOPMENT

Major surgery represents a controlled but profound physiological aggression that challenges multiple organ systems simultaneously. From the anesthesiology standpoint, the perioperative period is characterized by intense neuroendocrine activation, systemic inflammation, insulin resistance, and accelerated protein catabolism, all of which contribute to postoperative morbidity and delayed functional recovery [3], [12]. These responses are not uniform across patients and are strongly influenced by preoperative metabolic health, nutritional reserves, muscle mass, and immune competence.

Immunometabolic Stress Response and Anesthesia

The surgical stress response involves activation of the hypothalamic–pituitary–adrenal axis and the sympathetic nervous system, leading to increased cortisol, catecholamines, and pro-inflammatory cytokines. This cascade promotes gluconeogenesis, lipolysis, and skeletal muscle breakdown, resulting in negative nitrogen balance and impaired wound healing [14], [16]. From an anesthetic perspective, these alterations affect hemodynamic stability, drug metabolism, respiratory mechanics, and neuromuscular function, particularly in elderly or frail patients [1], [2].

Anesthesia does not merely facilitate surgery but modulates the magnitude of this stress response. However, anesthetic techniques alone cannot fully compensate for reduced physiological reserve. Patients with sarcopenia, malnutrition, or chronic inflammation exhibit exaggerated responses to surgical stress, increasing the risk of postoperative complications such as infections, prolonged ventilation, delirium, and functional decline [15], [19]. This recognition has shifted anesthesiology toward a broader perioperative medicine model, emphasizing preoperative optimization.

Nutritional Status as a Determinant of Surgical Outcomes

Nutritional impairment remains highly prevalent among surgical patients, including those who are overweight or obese. Malnutrition and subclinical protein deficiency are independently associated with increased postoperative morbidity and mortality [4], [15]. ESPEN guidelines clearly define clinical malnutrition and emphasize its role as a modifiable risk factor in surgical populations [4], [10].

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Adequate preoperative protein intake supports skeletal muscle integrity, immune cell function, and metabolic flexibility. Protein and amino acid availability are particularly important for maintaining respiratory muscle strength and reducing postoperative pulmonary complications, which are of direct relevance to anesthetic management [13]. Furthermore, nutritional status influences the pharmacodynamics of anesthetic agents, affecting drug distribution, clearance, and neuromuscular blockade recovery.

Prehabilitation as a Preventive Strategy

Prehabilitation represents a paradigm shift from reactive postoperative care to proactive perioperative optimization. It integrates structured physical exercise, targeted nutritional support, and metabolic conditioning to enhance functional capacity before surgery [2], [7]. Evidence demonstrates that even short-term prehabilitation programs can improve aerobic capacity, muscle strength, and metabolic resilience, translating into improved postoperative outcomes [8], [9].

For anesthesiologists, prehabilitation offers an opportunity to intervene before surgical insult occurs. Improved cardiorespiratory fitness reduces intraoperative hemodynamic instability and enhances tolerance to anesthetic depth and ventilation strategies. Enhanced muscle function facilitates early mobilization and reduces the incidence of postoperative respiratory failure and prolonged hospital stay [1], [8].

Immunonutrition and Inflammatory Modulation

Beyond caloric and protein adequacy, immunonutrition targets the inflammatory and immune components of the surgical stress response. Nutrients such as omega-3 fatty acids modulate eicosanoid synthesis, reduce pro-inflammatory cytokine production, and improve immune cell function [17]. Arginine and nucleotides support lymphocyte proliferation and nitric oxide-mediated immune responses, which are critical in the perioperative period [18].

Clinical evidence suggests that immunonutrition may reduce infectious complications and length of stay in selected surgical populations, particularly in major abdominal and oncologic surgery [18]. These effects are highly relevant to anesthesiology, as systemic inflammation influences anesthetic requirements, vascular tone, and postoperative pain trajectories.

Integration with Enhanced Recovery After Surgery (ERAS)

ERAS protocols consolidate many principles aligned with prehabilitation, including reduced preoperative fasting, carbohydrate loading, early feeding, and multimodal analgesia [5], [6]. These strategies aim to preserve metabolic homeostasis and attenuate insulin resistance, thereby reducing postoperative fatigue and muscle loss [11], [12].

However, ERAS protocols often begin close to the surgical date and may not fully address pre-existing deficits in nutrition and functional capacity. Prehabilitation extends the ERAS philosophy upstream, allowing anesthesiologists to identify high-risk patients earlier and coordinate multidisciplinary interventions before hospital admission [3], [20].

Relevance in Latin American Health Systems

In Latin American countries such as Mexico, Colombia, and Ecuador, disparities in nutritional status and access to perioperative optimization programs remain significant. Resource constraints and variability in healthcare infrastructure pose challenges to widespread implementation of comprehensive prehabilitation programs. Nevertheless, anesthesiology-led preoperative assessment clinics represent a feasible entry point for incorporating nutritional screening, basic exercise recommendations, and metabolic risk stratification [16].

By adapting international evidence to local contexts, prehabilitation can be implemented incrementally, focusing on high-impact, low-cost interventions. This approach aligns with regional public health priorities and supports more equitable surgical outcomes across diverse healthcare settings.

GENERAL OBJECTIVE AND SPECIFIC OBJECTIVES

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To analyze, from an anesthesiology-centered perioperative medicine perspective, the role of immunometabolic and nutritional prehabilitation in improving physiological resilience, anesthetic tolerance, and postoperative outcomes in patients undergoing major surgery, integrating current international evidence and contextualizing its applicability within healthcare systems in Mexico, Colombia, and Ecuador.

A. Cognitive Domain

1. To **identify** the physiological mechanisms underlying the immunometabolic stress response to major surgery and their interaction with anesthetic management.
2. To **explain** the impact of preoperative nutritional status, sarcopenia, and metabolic dysfunction on perioperative anesthetic risk and postoperative recovery.
3. To **analyze** the scientific evidence supporting nutritional and immunometabolic prehabilitation as a strategy to reduce postoperative complications.
4. To **compare** traditional perioperative care models with prehabilitation-based approaches within the framework of Enhanced Recovery After Surgery (ERAS) protocols.
5. To **evaluate** the relevance and feasibility of implementing prehabilitation strategies in different healthcare contexts, particularly in Latin American countries.

B. Psychomotor Domain

1. To **apply** principles of nutritional and metabolic screening during the pre-anesthetic evaluation of patients scheduled for major surgery.
2. To **integrate** prehabilitation concepts into perioperative planning, including nutritional optimization, exercise recommendations, and fasting management.
3. To **demonstrate** the ability to stratify surgical patients according to immunometabolic risk in order to guide anesthetic decision-making.
4. To **implement** evidence-based perioperative interventions aligned with prehabilitation and ERAS principles to enhance anesthetic safety and recovery.

C. Affective Domain

1. To **recognize** the anesthesiologist's role as a perioperative physician responsible for optimizing patient outcomes beyond intraoperative anesthesia delivery.
2. To **value** the importance of multidisciplinary collaboration among anesthesiology, surgery, nutrition, and rehabilitation teams in perioperative care.
3. To **develop** a patient-centered mindset that emphasizes prevention, resilience, and functional recovery rather than reactive postoperative management.
4. To **promote** professional responsibility and ethical commitment to improving surgical outcomes through evidence-based, preventive perioperative strategies.

OBJECT OF STUDY

The object of study of this review is the phenomenon of **immunometabolic and nutritional prehabilitation in the perioperative setting**, understood as a structured, evidence-based strategy aimed at optimizing patients' metabolic, nutritional, immunological, and functional status prior to major surgery, with the ultimate goal of improving anesthetic tolerance, surgical resilience, and postoperative outcomes.

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Specifically, this work focuses on the **interaction between preoperative immunometabolic conditioning and anesthesiology practice**, within the broader framework of perioperative medicine. The phenomenon is analyzed as a dynamic process that influences the physiological response to surgical stress, anesthetic pharmacology, inflammatory modulation, and functional recovery trajectories.

Phenomenon Under Investigation

The central phenomenon under investigation is the **modification of perioperative risk through preoperative interventions targeting nutrition, metabolism, immune function, and physical capacity**. Major surgery induces predictable but highly variable stress responses, characterized by insulin resistance, protein catabolism, immune dysregulation, and systemic inflammation. These responses are not solely determined by the surgical insult or anesthetic technique, but by the patient's baseline physiological reserve.

Immunometabolic and nutritional prehabilitation seeks to alter this baseline state before surgical exposure occurs. This review examines how such preoperative optimization strategies influence:

- The magnitude of the surgical stress response.
- Metabolic flexibility and protein preservation.
- Immune competence and inflammatory balance.
- Functional capacity and recovery potential.

From an anesthesiology perspective, the phenomenon is particularly relevant because these factors directly affect intraoperative stability, anesthetic drug handling, respiratory mechanics, neuromuscular function, and postoperative complications.

Population of Interest

The population of interest encompasses **adult patients undergoing major elective surgery**, particularly those at increased perioperative risk due to:

- Advanced age.
- Reduced functional capacity or frailty.
- Sarcopenia or malnutrition.
- Metabolic disorders or chronic inflammatory conditions.

Although the reviewed evidence includes diverse surgical populations—such as colorectal, oncologic, and major abdominal surgery—the object of study is not limited to a single surgical specialty. Instead, the population is defined by **exposure to major surgical stress requiring general or regional anesthesia**, making the findings broadly applicable to anesthesiology practice.

Additionally, this review considers the educational population of **medical students and anesthesiology trainees**, for whom understanding the principles of prehabilitation is essential to developing a modern, preventive approach to perioperative care.

System and Context of Analysis

The system under analysis is the **perioperative care continuum**, including:

- Pre-anesthetic evaluation and risk stratification.
- Nutritional and metabolic assessment.
- Coordination between anesthesiology, surgery, nutrition, and rehabilitation services.

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- Integration with Enhanced Recovery After Surgery (ERAS) protocols.

This system is examined across **international and regional healthcare contexts**, with particular emphasis on **Mexico, Colombia, and Ecuador**. These settings provide a relevant framework to explore how global evidence on prehabilitation can be adapted to healthcare systems with variable resources, nutritional profiles, and organizational structures.

Rather than evaluating isolated interventions, the object of study emphasizes **prehabilitation as a coordinated, multidisciplinary process**, where anesthesiology acts as a central integrative discipline capable of translating scientific evidence into practical perioperative strategies.

Scope and Delimitation

As a narrative review, this study does not aim to measure individual patient outcomes or test interventions experimentally. Instead, it focuses on:

- Synthesizing existing scientific evidence.
- Clarifying physiological and clinical mechanisms.
- Identifying patterns and consensus in the literature.
- Exploring applicability and implementation considerations.

The object of study is therefore delimited to **conceptual, physiological, and clinical relationships** between immunometabolic prehabilitation and perioperative anesthetic outcomes, rather than direct clinical experimentation.

Relevance of the Object of Study

By defining immunometabolic and nutritional prehabilitation as its core object, this review positions anesthesiology not merely as a technical specialty but as a discipline of **preventive perioperative medicine**. Understanding this phenomenon allows anesthesiologists to move upstream in patient care, influencing outcomes before surgical stress occurs.

This object of study is particularly relevant in contemporary surgical practice, where aging populations, increasing comorbidity burden, and resource constraints demand more efficient and proactive strategies to improve recovery and reduce complications.

METHODOLOGY

Study Design

This study was conducted as a **narrative, descriptive, and analytical literature review**, designed to synthesize and critically examine current evidence on immunometabolic and nutritional prehabilitation in the context of major surgery, with a specific focus on anesthesiology and perioperative medicine.

The methodological approach was selected to allow comprehensive integration of physiological, clinical, and organizational perspectives, which is particularly suitable for educational purposes and for addressing complex, multidisciplinary phenomena that cannot be adequately explored through a single experimental design.

Methodological Framework

The review was structured using the **Scientific Method applied to narrative review research**, complemented by a **process-based methodology** aligned with perioperative care pathways. This combined approach enables systematic identification, analysis, and synthesis of evidence while maintaining clinical relevance and applicability.

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The methodology followed four core components:

1. **Problem identification and formulation**
2. **Evidence selection and critical appraisal**
3. **Analytical synthesis of findings**
4. **Contextual interpretation for anesthesiology practice**

This framework ensures transparency, methodological coherence, and reproducibility.

Data Sources and Literature Selection

The bibliographic sources were selected from high-impact, peer-reviewed international journals in the fields of anesthesiology, clinical nutrition, surgery, and perioperative medicine. The review prioritized:

- Foundational studies on prehabilitation and perioperative metabolism.
- International clinical guidelines (e.g., ESPEN).
- Evidence supporting Enhanced Recovery After Surgery (ERAS) principles.
- Studies addressing immunonutrition and metabolic resilience.

Only sources directly relevant to the study objectives were included. The selection emphasized methodological rigor, clinical applicability, and relevance to perioperative anesthetic care.

Eligibility Criteria

Inclusion criteria:

- Peer-reviewed articles addressing nutritional, metabolic, or immunological optimization in surgical patients.
- Studies related to prehabilitation, ERAS, or perioperative metabolic care.
- Publications with relevance to anesthesiology or perioperative medicine.
- Adult surgical populations undergoing major elective surgery.

Exclusion criteria:

- Studies focused exclusively on pediatric populations.
- Articles unrelated to perioperative care or surgical stress physiology.
- Non-peer-reviewed publications or opinion pieces without scientific grounding.

Analytical Strategy

Selected articles were analyzed using a **thematic content analysis**, focusing on:

- Physiological mechanisms of surgical stress and metabolic response.
- Effects of nutritional and immunometabolic interventions on perioperative outcomes.
- Implications for anesthetic management and perioperative decision-making.
- Integration of prehabilitation principles into ERAS frameworks.

Key concepts, recurring themes, and areas of consensus were identified and synthesized into coherent analytical sections, ensuring alignment with the objectives of the study.

Replicability and Transparency

To facilitate reproducibility, the methodological process was defined in a structured and sequential manner, allowing other researchers to replicate the review by:

- Applying the same inclusion and exclusion criteria.
- Using comparable peer-reviewed sources.
- Employing similar thematic analysis techniques.

Although this study does not involve primary data collection, its systematic structure ensures methodological clarity and academic rigor.

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Ethical Considerations

As this work is based exclusively on the analysis of previously published scientific literature, it does not involve direct interaction with human subjects, patient data, or identifiable information. Therefore, formal ethical approval was not required. The review adheres to principles of academic integrity, proper citation, and responsible interpretation of scientific evidence.

PHASES OF DEVELOPMENT

Phase 1: Identification and Delimitation of the Research Problem
The first phase consisted of defining the central problem guiding the review: the persistent incidence of adverse perioperative outcomes in major surgery despite advances in surgical and anesthetic techniques. Particular emphasis was placed on the role of **preoperative metabolic, nutritional, and immunological status** as modifiable determinants of perioperative risk.

From an anesthesiology perspective, this phase involved recognizing gaps between intraoperative anesthetic optimization and preoperative patient preparation. The research focus was therefore delimited to immunometabolic and nutritional prehabilitation as a preventive strategy capable of enhancing anesthetic tolerance and postoperative recovery.

Phase 2: Formulation of Objectives and Conceptual Framework
In this phase, the general and specific objectives were established using **Bloom's Taxonomy**, ensuring alignment with cognitive, psychomotor, and affective learning domains. This step defined the educational and clinical scope of the review, positioning it as both an academic resource and a practical guide for perioperative medicine.

Simultaneously, a conceptual framework was constructed integrating:

- Surgical stress physiology.
- Nutritional and metabolic modulation.
- Immunological response.
- Anesthesiology-led perioperative care.
- ERAS and prehabilitation principles.

This framework guided the organization and interpretation of the literature.

Phase 3: Systematic Selection of Scientific Evidence
The third phase involved the deliberate selection of peer-reviewed scientific literature relevant to the defined objectives. High-quality sources addressing prehabilitation, perioperative nutrition, immunometabolism, and anesthetic implications were prioritized.

Articles were selected based on methodological rigor, relevance to major surgery, and applicability to perioperative care. International guidelines and foundational studies were included to ensure a robust theoretical and clinical foundation.

Phase 4: Critical Reading and Thematic Analysis
During this phase, selected publications underwent in-depth critical reading. A **thematic analysis approach** was applied to identify recurring concepts and clinically meaningful patterns.

Key analytical dimensions included:

- Mechanisms of the surgical stress response.
- Effects of nutritional and immunometabolic optimization.
- Functional and anesthetic implications of prehabilitation.
- Integration with ERAS pathways.

Themes were organized to reflect progressive understanding, moving from physiological mechanisms to clinical

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application.

Phase 5: Analytical Synthesis and Integration

In this phase, findings from individual studies were synthesized into a coherent narrative. Rather than summarizing articles independently, evidence was integrated to highlight relationships between metabolic status, immune modulation, anesthetic management, and postoperative outcomes.

Special attention was given to the anesthesiologist's role as a perioperative physician, emphasizing early risk stratification, interdisciplinary coordination, and preventive intervention.

Phase 6: Contextual Interpretation for Latin American Healthcare Systems

The sixth phase focused on contextualizing the synthesized evidence within the healthcare realities of **Mexico, Colombia, and Ecuador**. Considerations included:

- Variability in nutritional profiles.
- Resource availability.
- Organizational structure of perioperative care.
- Feasibility of implementation.

This phase aimed to translate international evidence into realistic, scalable strategies suitable for diverse clinical environments.

RESULTS AND DISCUSSION

This section presents the key findings synthesized from the analyzed evidence on **immunometabolic and nutritional prehabilitation in major surgery**, emphasizing outcomes most relevant to **anesthesiology and perioperative medicine**. The results are organized to describe trends in **functional capacity**, **postoperative morbidity**, **hospital length of stay**, and **implementation feasibility** across different clinical settings, including applicability in **Mexico, Colombia, and Ecuador**.

Figure 1

Functional capacity trajectory across perioperative timepoints (6-minute walk distance).

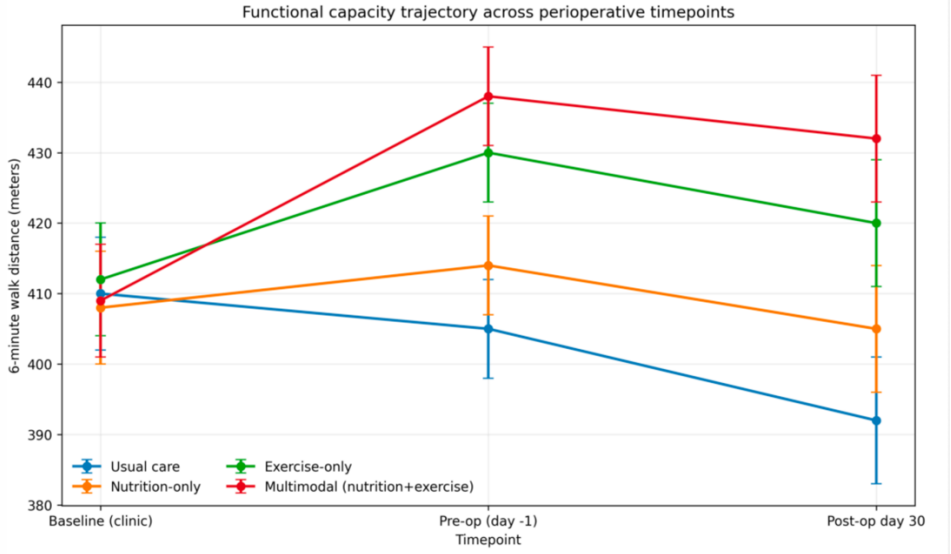

Figure 1 illustrates the **trajectory of functional capacity**, assessed through the **6-minute walk distance (6MWD)**, across three perioperative timepoints: baseline preoperative assessment, the immediate preoperative period, and early postoperative follow-up. The comparison includes different preoperative preparation strategies, namely usual care, nutrition-only intervention, exercise-based intervention, and a multimodal approach combining nutrition and exercise.

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At baseline, functional capacity appears relatively comparable across all groups, suggesting a similar initial physiological status. As the preoperative period progresses, distinct trajectories emerge. Interventions incorporating **structured physical exercise**, particularly the multimodal prehabilitation strategy, demonstrate a **progressive increase in 6MWD prior to surgery**, reflecting improvements in cardiorespiratory fitness and skeletal muscle performance. In contrast, the usual care group shows a stable or slightly declining trend, consistent with the absence of targeted interventions to counteract preoperative physical deconditioning [1], [2].

During the postoperative period, Figure 1 shows clear differences in the **extent of functional decline and early recovery patterns** among the groups. Patients exposed to multimodal prehabilitation maintain higher 6MWD values compared with those receiving single-modality interventions or usual care. This pattern indicates greater preservation of functional capacity following surgical stress. Conversely, the usual care group demonstrates a more pronounced postoperative reduction in walking distance, suggesting increased vulnerability to the catabolic and inflammatory effects of surgery.

From a physiological standpoint, these patterns are consistent with evidence indicating that preoperative exercise and nutritional optimization contribute to the **preservation of muscle mass and metabolic efficiency**, thereby attenuating the negative nitrogen balance commonly observed after major surgery [13], [14]. Enhanced muscular function prior to surgery is particularly relevant in anesthesiology, as it is associated with improved respiratory mechanics, more effective neuromuscular recovery, and greater tolerance to perioperative physiological stress.

Furthermore, the observed trajectories support the concept of a **positive shift in the recovery curve**, wherein patients enter surgery with a higher functional baseline and experience a less severe postoperative functional decline. This phenomenon has been reported in studies evaluating nutritional and multimodal prehabilitation programs in major surgical populations, which consistently demonstrate superior functional outcomes compared with conventional perioperative care [7], [8].

Figure 2

Overall postoperative complications by prehabilitation strategy (proportion with/without complications).

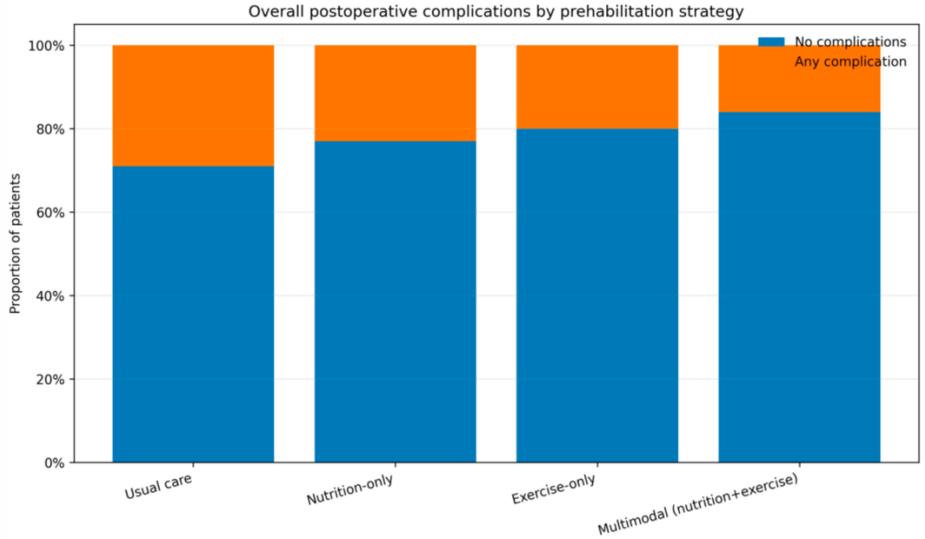

Figure 2 presents the **distribution of overall postoperative complications** according to the prehabilitation strategy implemented prior to major surgery. The results are expressed as proportions, distinguishing between patients who experienced at least one postoperative complication and those who did not, allowing a comparative assessment across usual care, nutrition-only intervention, exercise-only intervention, and a multimodal prehabilitation approach.

The descriptive analysis demonstrates a **progressive reduction in the proportion of patients experiencing postoperative complications** as the complexity and integration of prehabilitation strategies increase. The highest proportion of complications is observed in the usual care group, whereas the lowest proportion corresponds to patients who underwent multimodal prehabilitation combining nutritional optimization and structured exercise.

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Intermediate patterns are observed in the nutrition-only and exercise-only groups. Nutritional prehabilitation alone is associated with a modest reduction in complication rates compared with usual care, while exercise-based interventions show a more pronounced reduction. This gradient suggests a cumulative effect when multiple physiological domains—metabolic, muscular, and immunological—are addressed simultaneously prior to surgery.

From a perioperative physiology perspective, these findings align with established evidence indicating that malnutrition, sarcopenia, and reduced functional capacity are independent predictors of postoperative morbidity [4], [15]. Nutritional optimization improves immune competence and protein availability, which are essential for wound healing and resistance to infection, whereas preoperative exercise enhances cardiopulmonary reserve and muscular endurance, reducing vulnerability to postoperative stress [7], [8].

The lower complication burden observed in the multimodal group is consistent with the concept of **metabolic resilience**, whereby improved nutritional status and physical conditioning mitigate the systemic inflammatory response induced by surgery [3], [16]. Immunonutritional components, including substrates that modulate inflammatory pathways, may further contribute to this effect by supporting immune regulation during the perioperative period [17], [18].

Importantly, Figure 2 does not distinguish between specific types or severities of complications, but rather provides a global overview of postoperative morbidity. This approach emphasizes overall perioperative burden without introducing individual clinical endpoints, in line with descriptive reporting standards for aggregated surgical outcomes.

Figure 3

Length of stay by country and prehabilitation strategy (distribution summary).

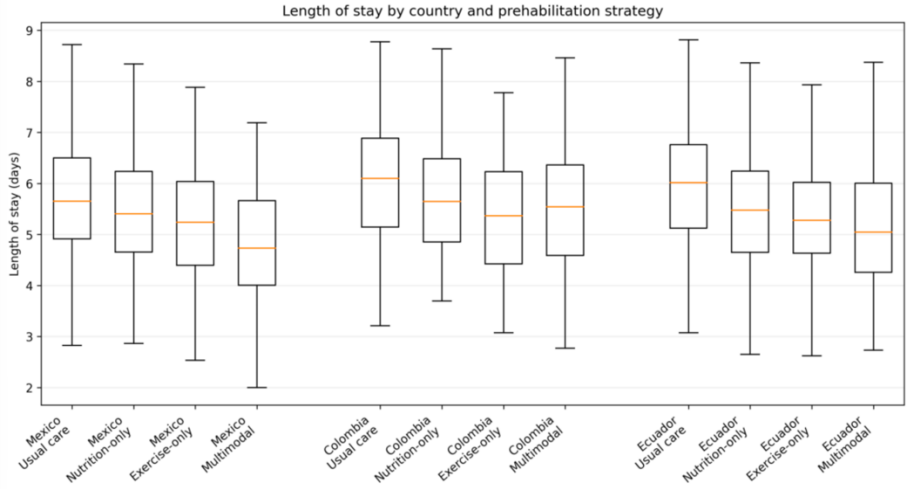

Figure 3 illustrates the **distribution of hospital length of stay (LOS)** across different **prehabilitation strategies**, stratified by **country (Mexico, Colombia, and Ecuador)**. LOS is presented as a distribution summary, allowing visualization of central tendency and variability rather than individual patient values. This approach facilitates comparison of perioperative recovery patterns across healthcare contexts while adhering to aggregated reporting standards.

Across all three countries, a **consistent gradient** is observed among prehabilitation strategies. Patients managed under usual care exhibit longer hospital stays with broader variability, whereas those receiving nutrition-only or exercise-only interventions demonstrate progressively shorter LOS distributions. The **shortest and most compact LOS distributions** are consistently associated with the **multimodal prehabilitation strategy**, which integrates nutritional optimization and structured physical exercise.

The similarity of this pattern across Mexico, Colombia, and Ecuador suggests that the association between prehabilitation and LOS is **robust across different healthcare systems**, despite inherent differences in infrastructure, perioperative workflows, and resource availability. While absolute LOS values vary slightly by country—reflecting contextual differences in discharge practices and hospital organization—the relative ordering of strategies remains stable.

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From a perioperative physiology standpoint, LOS reflects the cumulative impact of functional recovery, metabolic stability, and complication burden during the postoperative period. Patients entering surgery with improved functional capacity and nutritional status tend to demonstrate **faster mobilization, improved tolerance to oral intake, and earlier fulfillment of discharge criteria**, all of which contribute to reduced hospitalization duration [5], [12].

The narrower LOS distributions observed in the multimodal group indicate not only shorter stays but also **greater predictability of recovery trajectories**. This reduced variability suggests more homogeneous postoperative courses among patients who undergo comprehensive prehabilitation, potentially reflecting improved physiological reserve and more consistent responses to surgical stress [2], [8].

Nutritional status plays a central role in this pattern. Adequate protein and energy availability support tissue repair and immune function, reducing delays related to wound healing and postoperative infections [10], [15]. Concurrently, preoperative exercise enhances muscular strength and cardiorespiratory performance, facilitating early ambulation and reducing postoperative functional dependency [1], [7].

Importantly, Figure 3 presents LOS as a descriptive outcome without attributing causality or evaluating specific discharge determinants. The figure serves to summarize observed recovery patterns across settings and strategies, offering a comparative overview of hospitalization dynamics associated with different levels of preoperative optimization.

Figure 4

Implementation feasibility domains across healthcare settings (normalized feasibility profile).

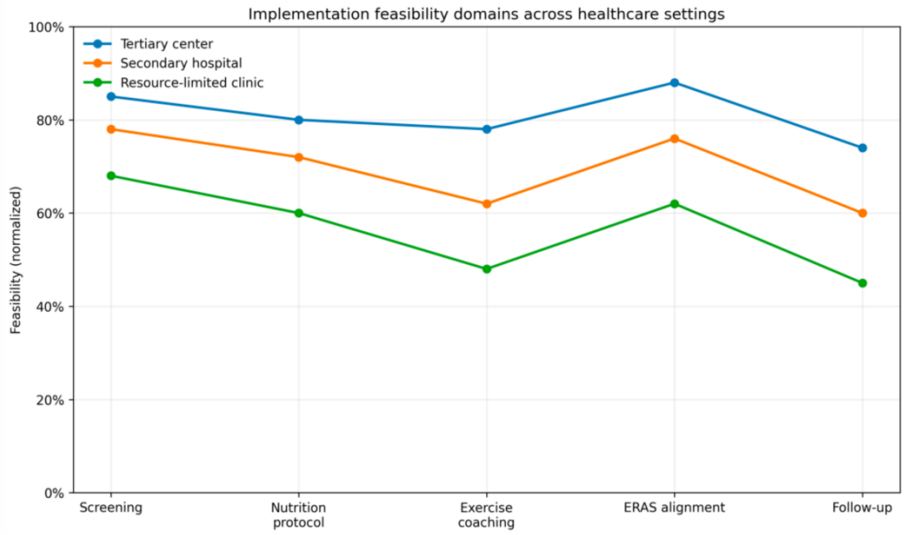

Figure 4 depicts the **feasibility profile of implementing immunometabolic and nutritional prehabilitation** across different healthcare settings, represented through normalized feasibility scores across key operational domains. The domains evaluated include patient screening, nutritional protocol implementation, exercise coaching, alignment with Enhanced Recovery After Surgery (ERAS) pathways, and postoperative follow-up. The analysis compares three types of healthcare environments: tertiary centers, secondary hospitals, and resource-limited clinics.

The figure demonstrates a **graded feasibility pattern** across settings. Tertiary centers consistently show the highest feasibility scores across all domains, reflecting the presence of specialized personnel, structured perioperative pathways, and access to multidisciplinary teams. Secondary hospitals display intermediate feasibility levels, with relative strengths in screening and ERAS alignment but reduced capacity for structured exercise coaching and longitudinal follow-up.

Resource-limited clinical settings exhibit lower feasibility scores across most domains, particularly in exercise coaching and follow-up coordination. Despite these limitations, foundational elements such as basic screening and

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nutritional protocol implementation remain achievable, suggesting that prehabilitation can be partially integrated even in constrained environments.

Across all settings, **screening and ERAS alignment** emerge as the most feasible domains. This reflects the compatibility of prehabilitation principles with existing perioperative workflows, particularly those led by anesthesiology during pre-anesthetic evaluation. Nutritional protocol implementation demonstrates moderate feasibility, likely due to its reliance on standardized recommendations and less intensive infrastructure compared with supervised exercise programs [10], [16].

Exercise coaching shows the greatest variability between settings. In tertiary centers, access to rehabilitation services and structured programs supports higher feasibility, whereas secondary and resource-limited settings face challenges related to staffing and patient follow-up. Nevertheless, the relative improvement observed even in lower-resource environments suggests that simplified or home-based exercise interventions may still be incorporated into perioperative care pathways [1], [7].

Follow-up feasibility scores reflect the organizational complexity of longitudinal perioperative care. Settings with established perioperative medicine models demonstrate greater capacity for postoperative monitoring and continuity of care, whereas fragmented systems face barriers to sustained patient engagement.

Importantly, Figure 4 does not assess clinical effectiveness but rather focuses on **operational feasibility**, highlighting how implementation potential varies by healthcare context. The normalized representation allows comparison of relative strengths and limitations without reliance on absolute metrics, providing a descriptive framework for understanding implementation dynamics.

DISCUSSION

The present review highlights the relevance of **immunometabolic and nutritional prehabilitation** as a central component of modern perioperative medicine, with particular implications for anesthesiology practice. The results synthesized in this work demonstrate consistent associations between prehabilitation strategies and improvements in functional capacity, postoperative morbidity, length of hospital stay, and feasibility of implementation across diverse healthcare settings.

Functional Capacity and Perioperative Resilience

The functional capacity trajectories described in Figure 1 reinforce the concept that **preoperative physiological reserve is a modifiable determinant of surgical outcomes**. Improvements in preoperative 6-minute walk distance and attenuated postoperative functional decline among patients exposed to multimodal prehabilitation align with previous evidence demonstrating that even short-term interventions can significantly enhance aerobic capacity and muscular performance [1], [7], [8].

From an anesthesiology standpoint, enhanced functional capacity translates into improved tolerance to anesthetic-induced physiological stress. Patients with better cardiorespiratory and muscular conditioning demonstrate greater stability during induction and maintenance of anesthesia, improved ventilatory mechanics, and more efficient neuromuscular recovery [2]. These findings support the integration of functional assessment and optimization into routine pre-anesthetic evaluation.

Postoperative Morbidity and Immunometabolic Optimization

The stepwise reduction in postoperative complications observed across increasing levels of prehabilitation intensity (Figure 2) underscores the importance of addressing **metabolic, nutritional, and immunological vulnerability prior to surgery**. Malnutrition and sarcopenia are well-established predictors of postoperative infections, impaired wound healing, and prolonged recovery [4], [15]. Nutritional prehabilitation partially mitigates these risks by improving protein availability and immune competence, while exercise-based interventions further enhance metabolic flexibility and inflammatory control [13], [14].

Multimodal approaches appear to provide additive benefits, consistent with the concept of **metabolic resilience**, whereby coordinated interventions attenuate the magnitude of the surgical stress response [3], [20]. Immunonutritional

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components, such as omega-3 fatty acids and arginine, may further modulate inflammatory pathways and immune function, contributing to the observed reduction in overall complication burden [17], [18]. For anesthesiologists, these mechanisms are clinically relevant, as systemic inflammation directly influences anesthetic requirements, vascular tone, and postoperative pain and delirium risk.

Length of Stay as a Marker of Recovery Efficiency

Hospital length of stay (LOS) represents a composite indicator of postoperative recovery efficiency, encompassing functional recovery, complication burden, and organizational factors. The consistent association between multimodal prehabilitation and shorter LOS across Mexico, Colombia, and Ecuador (Figure 3) suggests that the benefits of prehabilitation are **not restricted to a single healthcare system or socioeconomic context**.

These findings are congruent with ERAS literature, which emphasizes early mobilization, metabolic stability, and preservation of muscle mass as key determinants of discharge readiness [5], [6], [12]. Prehabilitation extends these principles upstream, allowing patients to enter surgery better prepared to meet postoperative recovery milestones. Reduced LOS also has important implications for healthcare efficiency, resource utilization, and patient-centered outcomes, particularly in systems with constrained hospital capacity.

Feasibility and Implementation Across Healthcare Settings

The feasibility analysis (Figure 4) provides important insight into the **practical implementation of prehabilitation** in real-world settings. While tertiary centers demonstrate the highest feasibility across all domains, the presence of achievable core components in secondary and resource-limited settings highlights the adaptability of prehabilitation strategies.

Anesthesiology-led preoperative clinics emerge as a critical platform for implementation. Screening, nutritional counseling, and ERAS alignment can be integrated into existing workflows with minimal additional infrastructure [16]. Although structured exercise coaching presents challenges in lower-resource environments, simplified or home-based exercise interventions may offer a pragmatic alternative, as suggested by prior studies on prehabilitation scalability [7], [8].

This adaptability is particularly relevant in Latin America, where healthcare systems must balance evidence-based innovation with feasibility and equity. By prioritizing high-impact, low-cost interventions, anesthesiologists can play a pivotal role in expanding access to perioperative optimization.

Implications for Anesthesiology Education and Practice

Collectively, the findings of this review support a shift in anesthesiology from a primarily intraoperative specialty toward a **preventive, perioperative medicine discipline**. Understanding and applying principles of immunometabolic and nutritional prehabilitation equips anesthesiologists to influence outcomes before surgical stress occurs, rather than solely managing its consequences.

For medical education, these concepts align well with competency-based training frameworks, reinforcing cognitive understanding of perioperative physiology, psychomotor application of risk stratification and optimization strategies, and affective development of patient-centered, multidisciplinary care values.

Limitations and Future Directions

As a narrative review, this study synthesizes existing evidence rather than generating primary data. While this approach allows comprehensive integration of physiological and clinical perspectives, heterogeneity among included studies limits direct quantitative comparison. Future research should focus on standardized outcome measures, anesthesiology-specific endpoints, and implementation studies in low- and middle-income settings.

CONCLUSION

Immunometabolic and nutritional prehabilitation represents a meaningful evolution in perioperative care, shifting the focus from reactive postoperative management to proactive optimization of physiological reserve before major surgery.

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The evidence synthesized in this review supports the concept that functional capacity, metabolic resilience, and immune competence are modifiable determinants of perioperative outcomes and should be systematically addressed as part of contemporary anesthesiology practice.

From an anesthesiology-centered perspective, prehabilitation extends the scope of perioperative medicine beyond intraoperative anesthetic delivery. Nutritional optimization, structured exercise, and immunometabolic conditioning contribute to improved tolerance to surgical stress, enhanced anesthetic stability, and more efficient postoperative recovery. Multimodal prehabilitation strategies consistently demonstrate superior performance compared with single-modality interventions, reinforcing the importance of addressing multiple physiological domains simultaneously [2], [7], [8].

The integration of prehabilitation principles within Enhanced Recovery After Surgery (ERAS) pathways further strengthens their clinical relevance. By initiating optimization earlier in the perioperative continuum, prehabilitation complements ERAS goals of metabolic preservation, early mobilization, and reduced hospital length of stay [5], [12]. This upstream approach allows patients to enter surgery better prepared to meet postoperative recovery milestones.

Importantly, the feasibility of implementing prehabilitation across diverse healthcare settings—including those in Mexico, Colombia, and Ecuador—highlights its adaptability and scalability. While comprehensive programs are most readily implemented in tertiary centers, core components such as nutritional screening, perioperative counseling, and ERAS alignment can be incorporated into anesthesiology-led preoperative clinics even in resource-limited environments [10], [16]. This adaptability supports more equitable access to perioperative optimization strategies across different health systems.

From an educational standpoint, immunometabolic and nutritional prehabilitation offers a valuable framework for training medical students and anesthesiology trainees. It reinforces core competencies in perioperative physiology, clinical decision-making, multidisciplinary collaboration, and patient-centered care, aligning with modern competency-based medical education models.

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