Medicine Insights

Review

Clinical Research Review on the Protective Effects of Perioperative Multimodal Anesthesia Interventions in Elderly Patients

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Abstract: Elderly patients experience a progressive decline in organ reserve function and a significant reduction in their perioperative stress tolerance. The dual physiological stimulation from both surgery and anesthesia can easily trigger multi-organ dysfunction, making this demographic a high-risk population for severe postoperative complications. Multimodal anesthesia intervention, based on a multi-target composite mechanism, can effectively block the transmission of perioperative noxious stimuli, suppress inflammatory and oxidative stress-induced cellular damage, and maintain systemic homeostatic stability. Consequently, it demonstrates clear protective efficacy for vital organs, including the heart, brain, lungs, and kidneys, in elderly patients. This article systematically reviews the complex pathological mechanisms underlying perioperative organ injury in the aging population. Furthermore, it elucidates the core theoretical framework and clinical application principles of multimodal anesthesia strategies. We summarize its substantial clinical value and practical implementation strategies for comprehensive multi-organ protection. Additionally, the review critically analyzes current research limitations, such as the lack of standardized protocols and individualized dosing, alongside future directions for investigation. By integrating advanced pharmacological agents with regional anesthesia techniques, this comprehensive analysis provides a robust theoretical foundation for precision perioperative anesthesia and targeted organ protective strategies in clinical practice, ultimately aiming to improve postoperative recovery outcomes and enhance the overall quality of life for elderly surgical patients undergoing major procedures.

Keywords: anesthesia; geriatrics; organ protection; perioperative care; multimodal anesthesia

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1. Introduction

The continuous deepening of societal aging has led to a year-on-year increase in the proportion of elderly surgical patients admitted to surgical care systems. Due to physiological degenerative changes, the elderly population generally exhibits certain pathophysiological characteristics, including insufficient multi-organ functional reserve, prolonged underlying chronic diseases, and diminished immune regulatory function. During the perioperative period, the combined effects of multiple pathological stimuli—such as tissue injury induced by surgical trauma, systemic effects resulting from anesthesia procedures, and abnormal hemodynamic fluctuations—significantly elevate the risk of organ function impairment and directly impact patients' postoperative recovery and long-term prognosis. Traditional single-modality anesthesia approaches have limited therapeutic targets and are unable to fully modulate the perioperative stress-induced inflammatory response; furthermore, administration of high-dose monotherapy can increase the metabolic burden on organs, which is incompatible with the fragile physiological tolerance of elderly patients. The multimodal anesthesia strategy, developed in alignment with the principles of precision anesthesia and Enhanced Recovery After Surgery (ERAS), integrates anesthetic techniques, analgesic agents, and

adjunctive protective measures with distinct mechanisms of action. This approach ensures both the safety and efficacy of anesthesia while delivering multiple clinical benefits—including stress modulation, attenuation of inflammation, and organ protection—and has thus become a focal point of research in the field of perioperative anesthesia management for elderly patients [1, 2]. Drawing upon cutting-edge research achievements in the field of anesthesia both domestically and internationally in recent years, this article systematically elaborates on the theoretical framework, mechanisms of action, and clinical application rationale of multimodal anesthesia strategies, providing an academic reference for optimizing perioperative organ protection strategies in elderly patients and refining individualized anesthesia management systems.

2. The Core Pathological Mechanisms of Perioperative Organ Injury in Elderly Patients

2.1. Physiological Aging Leading to Decline in Organ Reserve Function

The structural remodeling and functional decline of organs induced by physiological aging represent the intrinsic core etiological factor underlying the high susceptibility of elderly patients to organ injury during the perioperative period. With advancing age, solid organs throughout the human body undergo degenerative changes—including apoptosis of cells, tissue fibrosis, and diminished structural integrity—while the body's compensatory regulatory capacity and stress tolerance gradually decline. The cardiovascular system is characterized primarily by myocardial fibrosis, reduced vascular wall elasticity, and elevated peripheral vascular impedance; meanwhile, the autonomic nervous system's sensitivity in regulating heart rate and blood pressure is significantly diminished, rendering it incapable of effectively compensating for the hemodynamic fluctuations induced by various perioperative stimuli. The central nervous system exhibits alterations such as cerebral parenchymal atrophy, reduced cerebral blood flow, and dysregulation of neurotransmitter metabolism; consequently, the tolerance threshold for cerebral ischemia and hypoxia is markedly lowered, making the brain highly vulnerable to reversible neurological dysfunction. The respiratory system manifests as a reduction in alveolar gas exchange area, decreased pulmonary elastic recoil, and diminished respiratory muscle strength, alongside significantly impaired oxygenation reserve and postoperative lung reexpansion capacity. Additionally, in elderly populations, hepatic and renal metabolic functions as well as the glomerular filtration rate remain persistently reduced, leading to diminished metabolic clearance capacity for anesthetic agents and an increased risk of drug accumulation. Under the combined influence of multiple perioperative stresses, these factors can easily push the body's compensatory limits beyond their capacity, precipitating multi-organ functional injury [3, 4].

2.2. Surgical Trauma-Mediated Inflammation and Oxidative Stress-Induced Cascade Injury

Mechanical tissue injury resulting from surgical procedures represents a significant exogenous factor triggering perioperative systemic pathological damage. Surgical maneuvers—such as tissue dissection, tissue traction, and wound hemostasis—affect local tissue homeostasis, activate the body's innate immune response, and induce the massive release of various pro-inflammatory cytokines (e.g., tumor necrosis factor-α and interleukin-6), thereby initiating a persistent inflammatory cascade. Excessive inflammatory mediators compromise the systemic vascular endothelial barrier, increase microvascular permeability, and precipitate tissue edema and disordered organ microcirculatory perfusion, ultimately leading to ischemic-hypoxic pathological changes in multiple organs. Traumatic stress also alters the dynamic balance between the body's oxidative and antioxidant systems, inducing excessive generation and accumulation of reactive oxygen species, which triggers cellular membrane lipid peroxidation, mitochondrial structural damage, and programmed cell apoptosis. In elderly patients, the function of the endogenous antioxidant system is impaired, and the efficiency of reactive oxygen species scavenging is insufficient; consequently, oxidative stress-induced damage

accumulates and amplifies inflammatory pathological effects, promoting the onset and progression of multi-organ functional impairment.

2.3. Risk of Iatrogenic Organ Injury Associated with Traditional Single-Anesthesia Modalities

Technical limitations and adverse drug reactions associated with conventional single-anesthesia approaches constitute a significant iatrogenic factor in perioperative organ injury among elderly patients. Conventional general anesthesia requires substantial intravenous anesthetic and opioid analgesic administration to maintain intraoperative anesthesia depth; however, this high pharmacologic burden directly impairs myocardial contractility, depresses respiratory center activity, reduces effective renal perfusion, and attenuates immune defense function, thereby markedly increasing the risk of postoperative complications such as circulatory instability, respiratory suppression, and infections. Moreover, general anesthesia provides central sedation and analgesia only and cannot fully prevent peripheral nociceptive signal transmission to the central nervous system; persistent intraoperative sympathetic activation thus hinders effective modulation of the perioperative inflammatory stress response. In contrast, epidural or peripheral nerve block techniques used alone may yield insufficient analgesia and suboptimal sedation stability, potentially triggering abrupt sympathetic hyperactivity, severe hemodynamic variability, and worsening ischemia-reperfusion injury in highly vascularized organs—including the heart, brain, and kidneys [5]. Collectively, these isolated methods fall short of fulfilling clinical requirements for perioperative organ protection in elderly patients.

3. Core Theories and Interventional Principles of Perioperative Multimodal Anesthesia Management

3.1. Core Interventional Theory of Multi-Target Synergistic Enhancement

Multimodal anesthesia represents a contemporary perioperative management strategy developed to support precision anesthesia and align with Enhanced Recovery After Surgery (ERAS) principles. Its theoretical foundation rests on multi-mechanistic complementarity, multi-target coverage, and multi-effect synergy. This strategy moves beyond traditional approaches centered exclusively on intraoperative sedation and analgesia, integrating multiple therapeutic modalities—including peripheral nerve modulation, central sedation regulation, multi-target analgesia, and anti-inflammatory/anti-oxidative strategies—to form a comprehensive perioperative injury mitigation framework. Peripheral nerve modulation interrupts nociceptive signal transmission at the site of tissue trauma, thereby attenuating aberrant sympathetic nervous system activation; short-acting, low-toxicity general anesthetics preserve intraoperative central nervous system homeostasis, ensuring stable and titratable anesthesia control; adjunctive agents such as dexmedetomidine and lidocaine selectively modulate inflammatory cascades, oxidative stress responses, and organ microcirculatory function [5, 6]. These coordinated modalities act synergistically, offsetting the inherent limitations of any single technique. By concurrently optimizing anesthesia safety and efficacy, this strategy interrupts key pathological pathways underlying perioperative organ injury at their origin, delivering integrated clinical outcomes that unify anesthesia delivery with end-organ protection.

3.2. Age-Appropriate, Tiered Intervention Principle

Elderly patients exhibit significant physiological heterogeneity, with marked individual variations in organ reserve function, baseline disease status, and degree of frailty; thus, a uniformly standardized anesthesia approach is often inadequate to meet the diverse clinical needs of all patients. Consequently, personalized, tiered adaptation represents the core principle for implementing multimodal anesthesia strategies in elderly patients [7]. Prior to clinical application, a systematic assessment of the patient's overall condition must be conducted, incorporating factors such as age, frailty score, control status of underlying diseases, multi-organ function parameters, and the extent of surgical

trauma, to precisely determine the perioperative risk of organ injury. Based on this assessment, appropriate anesthesia techniques, analgesic approaches, and adjunctive protective strategies should be tailored. During clinical application, the principle of low-dose combined drug administration must be strictly adhered to—reducing the dosage of any single anesthetic agent through the combined use of multiple techniques and medications—to minimize the risk of toxic injury to vital organs induced by anesthetic agents. Additionally, quantitative monitoring techniques—such as the Bispectral Index (BIS) and dynamic hemodynamic monitoring—should be utilized to dynamically adjust anesthesia depth and drug infusion rates in real time, mitigating the risks of organ dysfunction associated with excessive anesthesia depth and the risk of stress activation associated with insufficient anesthesia depth, thereby enabling precise, individualized perioperative anesthesia management in elderly patients.

3.3. Principles of Comprehensive Closed-Loop Organ Protection during the Perioperative Period

Multimodal anesthesia strategies extend beyond traditional intraoperative management by implementing an integrated, closed-loop framework that spans preoperative optimization, intraoperative precise organ support, and postoperative sustained care—thereby systematically mitigating perioperative organ injury pathways. Preoperatively, comprehensive organ function evaluation and individualized preparation optimize baseline physiological status, enhance endogenous anti-inflammatory and antioxidant defenses, and lower organ vulnerability to procedural stressors. Intraoperatively, this framework serves as the pivotal phase for organ preservation: multimodal coordinated strategies stabilize circulatory dynamics, attenuate inflammatory and stress responses, ensure adequate organ perfusion, and limit progression of acute organ dysfunction [7, 8]. Postoperatively, sustained multimodal analgesia and anti-inflammatory support suppress delayed inflammatory activation, prevent homeostatic imbalances triggered by nociceptive stimuli, and decrease the risk of persistent organ complications. This integrated, closed-loop approach addresses all major contributors to perioperative organ injury; relative to conventional anesthesia practices, it delivers more consistent, coordinated protection across multiple organ systems in older adults and supports accelerated functional recovery.

4. The Protective Effect of Multimodal Anesthesia Intervention on Vital Organs in Elderly Patients

4.1. Neuroprotective Effect

Postoperative neurocognitive dysfunction is a highly prevalent perioperative complication among elderly surgical patients, characterized primarily by postoperative delirium, memory impairment, and deficits in cognitive attention. Its pathogenesis is closely associated with the neurotoxic effects of anesthetic agents, cerebral inflammatory responses, imbalances in cerebral perfusion, and disruptions in central metabolic homeostasis. Multimodal anesthesia strategies, through optimized selection and administration of anesthetic techniques, significantly reduce the risk of neurological injury in elderly patients. This approach emphasizes short-acting, low-persistence general anesthetics combined with regional anesthesia to minimize total exposure to general anesthetics and opioid analgesics, thereby reducing accumulation in brain tissue and attenuating anesthesia-related neuronal apoptosis and central nervous system suppression [2, 9].

Intraoperative electroencephalographic (EEG) monitoring enables precise titration of anesthesia depth, supporting stable central nervous system inhibition and preventing metabolic imbalances and stress-related injuries arising from inadequate or excessive anesthesia [10]. Adjunctive use of dexmedetomidine helps modulate central inflammatory activity, suppress pro-inflammatory factor expression in brain tissue, enhance cerebral microcirculatory perfusion, maintain dynamic equilibrium between cerebral oxygen supply and demand, and alleviate central inflammatory injury triggered by surgical stress. Concurrently, multimodal analgesia avoids central nervous system complications linked

to high-dose opioid administration, markedly lowers the incidence of postoperative delirium and cognitive decline in elderly patients, and promotes rapid restoration of neurological function after surgery.

4.2. Cardiovascular System Protective Effect

Elderly patients frequently exhibit pronounced degenerative changes in the cardiovascular system, including diminished myocardial contractile reserve, reduced vascular compliance, and impaired autonomic regulatory function; consequently, perioperative hemodynamic instability may readily trigger adverse cardiovascular events such as myocardial ischemia, arrhythmias, or myocardial injury. Multimodal anesthesia strategies, by synergistically modulating multiple physiological pathways, help sustain perioperative circulatory homeostasis and deliver continuous myocardial protection. Combining general anesthesia with regional nerve blockade interrupts peripheral nociceptive signaling induced by surgical trauma, attenuates excessive sympathetic activation, limits stress hormone surges, prevents abrupt heart rate and blood pressure fluctuations, reduces myocardial oxygen consumption, and preserves the equilibrium between myocardial oxygen supply and demand [11, 12].

Compared with general anesthesia alone, multimodal approaches significantly reduce requirements for general anesthetic agents and opioids, thereby minimizing their depressive effects on myocardial contractility. Intraoperative administration of adjuncts such as lidocaine or magnesium salts stabilizes myocardial cell membrane potential, enhances myocardial microcirculation, and lowers arrhythmia risk. Integrated with real-time dynamic hemodynamic monitoring, these interventions permit prompt correction of pathological states—including intraoperative hypoperfusion or blood pressure dysregulation—thus mitigating myocardial ischemia-reperfusion injury, comprehensively safeguarding perioperative cardiovascular function in elderly patients, and reducing the incidence of severe postoperative cardiovascular complications.

4.3. Respiratory System Protection Effect

In elderly patients, pulmonary tissue elasticity declines, respiratory muscle strength diminishes, and airway mucosal defense capacity weakens. When combined with factors such as anesthesia-related suppression of respiratory drive, inflammatory responses to surgical trauma, and postoperative immobility, these physiological changes increase susceptibility to perioperative respiratory complications—including atelectasis, hypoxemia, and pulmonary infections. Multimodal anesthesia strategies support pulmonary function preservation by optimizing anesthetic management, minimizing pharmacologic adverse effects, attenuating pulmonary inflammation, and enhancing postoperative ventilation. Combining regional nerve blockade with light general anesthesia significantly reduces requirements for opioid and sedative agents, thereby avoiding respiratory suppression, accelerating recovery of spontaneous breathing after surgery, and lowering the incidence of perioperative hypoxemia and respiratory suppression [13].

Perioperative intravenous lidocaine infusion demonstrates anti-inflammatory and antioxidant properties, inhibits pulmonary inflammatory cascades, mitigates alveolar endothelial injury and interstitial edema, and improves ventilation and gas exchange. Furthermore, multimodal analgesia effectively manages postoperative incisional pain, alleviates pain-induced restriction of thoracic mobility, supports effective deep breathing and productive coughing for airway clearance, decreases sputum retention and atelectasis, strengthens airway defense mechanisms, reduces postoperative pulmonary infection rates, and maximizes maintenance of respiratory functional integrity throughout the perioperative period in elderly patients.

4.4. Renal and Digestive System Protective Effects

The progressive reduction in renal blood flow, sustained decline in glomerular filtration rate, and significant impairment of renal compensatory repair capacity in elderly patients—combined with perioperative hemodynamic instability, inflammatory stress,

and the toxic effects of anesthetic agents—constitute key risk factors for acute kidney injury [14, 15]. Multimodal anesthesia approaches help stabilize systemic circulatory status, maintain effective renal perfusion pressure, and prevent persistent renal ischemic and hypoxic injury; they also minimize the use of anesthetic agents to reduce renal metabolic burden, attenuate local renal inflammatory infiltration and oxidative stress, and support both glomerular filtration and tubular reabsorption functions—thereby contributing to the prevention and management of acute kidney injury during the perioperative period.

Regarding the digestive system, elderly patients frequently exhibit gastrointestinal mucosal atrophy and diminished barrier integrity; thus, excessive perioperative stress may readily induce mucosal ischemic injury, compromise barrier function, promote bacterial translocation, and impair gastrointestinal motility and secretion. Multimodal anesthesia strategies help modulate the systemic stress response, enhance gastrointestinal microcirculatory perfusion, and support mucosal barrier integrity. Furthermore, these strategies substantially reduce opioid requirements, thereby alleviating opioid-associated adverse effects—including delayed gastric emptying, nausea, vomiting, and abdominal distension—and lowering the incidence of postoperative complications such as gastrointestinal dysfunction and intra-abdominal infection, ultimately supporting digestive system homeostasis throughout the perioperative period [4].

5. Clinical Implementation Strategies for Multimodal Anesthesia Interventions in Elderly Patients during the Perioperative Period

With organ protection in elderly patients as the core objective, multimodal anesthesia approaches should be implemented throughout the entire perioperative period. These approaches should be tailored to the patient's individual physiological characteristics and surgical risks, adopting a stratified, precise, and systematic methodology. Preoperative assessment of multi-dimensional organ function is essential; this involves systematically screening for underlying cardiac, cerebral, pulmonary, and renal pathologies as well as evaluating the patients' functional reserve status, standardizing the management of underlying medical conditions, optimizing the patients' nutritional and physiological status, and implementing individualized preanesthetic preparation. Through low-dose anti-inflammatory and antioxidant strategies, the body's organ protection mechanisms can be activated, thereby reducing perioperative injury susceptibility.

The intraoperative period represents a critical window for organ protection; therefore, a three-dimensional strategy combining "precision general anesthesia + targeted regional anesthesia blocks + adjuvant pharmacological modulation" should be implemented in clinical practice [16]. The appropriate regional anesthesia technique should be selected based on the surgical procedure and the extent of trauma to block the transmission of noxious stimuli at the source; short-acting, low-toxicity general anesthetic agents should be used to maintain optimal anesthesia depth, while multimodal monitoring techniques should be employed to dynamically adjust anesthesia parameters; additional medications such as dexmedetomidine or lidocaine may be administered for continuous modulation of inflammatory stress and microcirculatory status, ensuring hemodynamic stability throughout the procedure and preventing the activation of acute organ injury pathways.

Postoperative multimodal analgesia combined with organ-protective strategies—utilizing regional nerve block analgesia alongside intravenous multi-target analgesic approaches in place of single opioid-based approaches—provides sustained attenuation of postoperative delayed inflammatory stress responses and mitigates pain-induced imbalances in the body's internal environment. Concurrently, dynamic monitoring of postoperative organ function, early ambulation, and respiratory rehabilitation strategies consolidate perioperative organ protection outcomes, prevent the development of long-term complications, and achieve an integrated approach that harmonizes anesthetic management, organ protection, and enhanced recovery after surgery (ERAS).

6. Research Limitations and Future Directions

Current research on perioperative multimodal anesthesia strategies for organ protection in elderly patients has established a comprehensive theoretical framework; its core mechanisms and clinical benefits have been validated by numerous clinical studies. However, significant gaps in research and limitations in clinical application remain. Most existing studies focus on observing the protective effects on individual organs, yet they lack investigation into the molecular pathways and regulatory mechanisms underlying coordinated multi-organ protection; consequently, a standardized protocol tailored to elderly patients with varying risk profiles has not yet been developed. Elderly patients exhibit considerable individual heterogeneity—characterized by differences in frailty status, underlying medical conditions, and organ reserve—which means there is currently no unified stratified approach, and the precision of personalized clinical anesthesia plans still requires improvement [17]. Furthermore, while most clinical studies use postoperative short-term complications as primary endpoints, follow-up studies examining long-term organ function outcomes and quality of life in these patients are scarce; thus, evidence supporting long-term protective effects still needs to be further supplemented and refined.

Future research should focus on three core aspects—systematic approach, precision, and long-term sustainability—to further refine the multimodal organ protection strategy for elderly patients under anesthesia. Subsequent studies could delve deeper into the underlying mechanisms of multi-target synergistic protection, clarify the dose–effect relationships and signaling regulatory pathways associated with different anesthesia techniques and drug combinations, and solidify the theoretical foundation [5, 8]. Additionally, by integrating frailty assessment scales, organ reserve function, and surgical risk stratification in elderly patients, standardized, personalized, and tiered criteria should be established to enhance the precision and standardization of clinical anesthesia planning. Furthermore, large-scale, long-term prospective cohort studies should be conducted to systematically analyze the impact of multimodal anesthesia strategies on long-term organ function and survival outcomes in elderly patients, thereby strengthening the evidence-based research framework and promoting the standardized adoption of these approaches in precision anesthesia for older adults.

7. Conclusion

Multimodal anesthesia approaches—characterized by coordinated effects across multiple physiological targets, low toxicity, minimal invasiveness, and integrated perioperative risk management—can effectively attenuate excessive perioperative inflammatory stress and hemodynamic instability in elderly patients. These approaches help interrupt pathways associated with acute multi-organ injury, lower the incidence of perioperative organ complications, and enhance clinical outcomes. Such strategies are particularly well-suited to the physiological profile of older adults, who commonly experience reduced organ reserve and limited compensatory capacity. Compared with conventional single-modality anesthesia techniques, multimodal approaches demonstrate superior safety and organ protection. Future work should focus on optimizing personalized protocols and deepening mechanistic understanding, establishing multimodal anesthesia as a foundational strategy for perioperative organ protection in elderly surgical patients—and thereby supporting faster recovery and improved long-term outcomes.

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