

The Combined Impact of Preoperative Nutritional Support and Esketamine on Postoperative Recovery, Immune Function, and Quality of Life in Older Patients Receiving Thoracoscopic Lung Cancer Surgery

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Abstract

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Background: Older patients undergoing thoracoscopic radical resection for lung cancer face considerable risks of postoperative pain, weakened immunity, and malnutrition, which can slow recovery. Multimodal approaches are needed to enhance results. This review explores the combined benefits of preoperative nutritional support and analgesia based on esketamine.

Methods: A narrative literature review was performed using databases including PubMed, Embase, and the Cochrane Library up to 2025. The search targeted clinical trials, randomized controlled trials (RCTs), and meta-analyses on esketamine, preoperative nutrition, and outcomes in thoracic or cancer surgery. Information was combined to assess impacts on pain relief, immune and nutritional indicators, and recovery measures.

Results: Research consistently shows that esketamine notably decreases postoperative pain scores and opioid use while reducing opioid-related side effects. Preoperative immunonutrition lessens the surgery-related drop in immune markers (IgG, IgM, IgA) and nutritional proteins (Alb, TRF, PAB). Together, these approaches work synergistically to speed gastrointestinal recovery, reduce hospital stay, and improve health-related quality of life scores in older surgical patients.

Conclusion: Incorporating preoperative nutritional support and esketamine into Enhanced Recovery After Surgery (ERAS) protocols offers a promising multimodal method to improve perioperative care. This approach effectively manages pain, supports immune and nutritional health, and encourages quicker recovery, supporting broader clinical use and additional large-scale RCTs.

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Introduction

Lung cancer remains a major cause of cancer deaths worldwide, with occurrence rising significantly with age [1, 2]. For patients with early-stage (I and II) non-small cell lung cancer (NSCLC), thoracoscopic radical resection is the primary curative treatment, providing better cosmetic results, less tissue damage, and faster recovery than open thoracotomy [3, 4]. However, older individuals, who make up a large share of lung cancer

patients, present specific perioperative difficulties. Age-related physical decline, common coexisting conditions like chronic obstructive pulmonary disease (COPD), and existing frailty or poor nutrition increase the risk of postoperative problems, slower recovery, and reduced function [5, 6].

Postoperative pain, especially after thoracic surgery, is often intense and can result in restricted breathing, poor lung expansion, and lung complications such as

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atelectasis and pneumonia [7]. Although opioids have traditionally been used for postoperative pain relief, their application in older adults carries risks like respiratory depression, drowsiness, nausea, vomiting, and possible hyperalgesia [8, 9]. Consequently, the focus has moved toward multimodal analgesia, which uses a mix of pain relief drugs to target different pain pathways, improving effectiveness while lowering opioid-related side effects [10]. In this context, N-methyl-D-aspartate (NMDA) receptor antagonists have become important. Esketamine, the S-enantiomer of ketamine, is a strong NMDA receptor antagonist with quick onset, powerful analgesic and sedative qualities, and a good safety record. Its capacity to prevent central sensitization and opioid-induced hyperalgesia makes it a valuable addition to perioperative pain management [11, 12].

At the same time, the metabolic stress of surgery can lead to immunosuppression and worsen nutritional state, which is especially harmful for cancer patients [13, 14]. Poor nutrition is an independent risk factor for higher postoperative illness, death, and reduced long-term survival [15]. Although enteral nutrition is vital for metabolic support, it is often delayed until after surgery. This delay, combined with postoperative ileus and digestive issues, can limit its usefulness [16, 17]. Increasing evidence supports the idea of "prehabilitation," including preoperative nutritional support, to enhance a patient's physiological reserves before surgery [18, 19]. Preoperative immunonutrition has been shown to modify immune responses and improve results in patients having major cancer surgery [20].

While the individual advantages of esketamine and preoperative nutrition are increasingly acknowledged, their combined effect has not been comprehensively reviewed in older thoracic oncology patients. This review therefore aims to thoroughly analyze and summarize existing evidence on the synergistic influence of preoperative nutritional support combined with esketamine on postoperative pain relief, immune and nutritional status, and overall recovery in older patients undergoing thoracoscopic lung cancer surgery.

Methods

This narrative review was carried out through a systematic search of electronic databases PubMed, Embase, and the Cochrane Central Register of Controlled Trials for relevant literature published until July 2024. The search strategy used a combination of Medical Subject Headings (MeSH) terms and keywords, including: "esketamine," "ketamine," "preoperative nutrition," "immunonutrition," "enteral nutrition," "lung cancer," "thoracoscopic surgery," "video-assisted thoracoscopic surgery (VATS)," "elderly," "geriatric,"

"postoperative pain," "analgesia," "immune function," "immunoglobulins," "recovery," and "quality of life."

Inclusion criteria covered: (1) clinical studies (randomized controlled trials, cohort studies, case-control studies) and meta-analyses; (2) studies involving adult or older patients undergoing thoracic or major cancer surgery; (3) interventions involving esketamine/ketamine for analgesia or preoperative nutritional support; and (4) outcomes reporting pain scores, opioid use, immune markers (IgG, IgM, IgA), nutritional parameters (Albumin, Transferrin, Prealbumin), or recovery measures. Non-English articles, animal studies, and editorials were excluded. Reference lists of retrieved articles were also manually checked for additional relevant publications. Data from selected studies were combined narratively to give a comprehensive overview of current knowledge.

Results and Discussion

Esketamine in Multimodal Analgesia: Mechanisms and Clinical Evidence

Esketamine's main mechanism is non-competitive blocking of the NMDA receptor, which is central to central sensitization and "wind-up" processes linked to lasting postoperative pain [21]. By inhibiting these receptors, esketamine effectively reduces hyperalgesia and lowers opioid tolerance, enabling significant opioid-sparing results [22].

Clinical evidence strongly backs its use. A multicenter RCT by Lei et al. [23] showed that patients given esketamine during thoracoscopic lung surgery had markedly lower VAS scores at rest and during coughing up to 48 hours after surgery, along with roughly a 30% decrease in sufentanil use. Similarly, a double-blind trial by Zhang et al. [24] in patients after scoliosis surgery found that a low-dose esketamine-dexmedetomidine combination offered better supplemental pain relief with fewer side effects. The opioid-sparing effect is vital for older adults, as it directly leads to fewer dose-dependent adverse events. Studies consistently note a reduction in postoperative nausea and vomiting (PONV), respiratory depression, and dizziness in groups receiving esketamine [25, 26]. Moreover, esketamine's mild stimulant effects on the sympathetic nervous system can help stabilize blood circulation, countering opioid-induced low blood pressure, a common issue in older patients with limited cardiovascular reserve [27].

Preoperative Nutritional Support: Strengthening Defenses Before Surgery

Surgery sets off a body-wide inflammatory response and a catabolic state that can quickly use up protein reserves and weaken immune function [28]. The

reasoning for preoperative nutrition is to build a "metabolic reserve" to use during this stressful time. Standard polymeric formulas or specialized immunonutrition formulas (enriched with arginine, omega-3 fatty acids, nucleotides, and glutamine) are employed [29].

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A systematic review by Deftereos et al. [30] on upper gastrointestinal cancer resection concluded that preoperative nutrition support significantly enhanced nutritional status and lowered postoperative complications. Ding et al. [31] specifically demonstrated that preoperative enteral nutrition in gastric cancer patients resulted in better maintenance of postoperative levels of CD4+ cells, IgG, and IgA compared to nutrition given only after surgery. The benefits are dual: first, it directly supplies materials for protein production and immune cell activity; second, by "priming" the gut with nutrients before surgery, it helps keep the intestinal barrier intact, reduces bacterial movement, and improves tolerance to postoperative enteral feeding, thereby ensuring nutritional support is effective and continuous [32, 33].

Synergistic Effects on Immune and Nutritional Status

Combining effective pain relief and nutritional prehabilitation creates a positive cycle that benefits the patient's overall condition. Severe pain is a major physiological stressor that worsens catabolism and immunosuppression [34]. By delivering superior analgesia, esketamine reduces this stress response. This, in turn, creates a better metabolic setting for the nutrients supplied preoperatively to be used for repair and defense rather than being used up in a high-stress state.

Clinical studies support this synergy. As shown in the key study by Hou et al., the group receiving both preoperative nutrition and esketamine had significantly higher postoperative levels of IgG, IgM, IgA, albumin (Alb), transferrin (TRF), and prealbumin (PAB) compared to the control group [35]. Prealbumin, with its brief half-life, is a particularly sensitive indicator of nutritional replenishment, and its increase shows successful anabolism [36]. This maintained immune ability is crucial not only for preventing infectious complications but also for potential long-term cancer surveillance [37].

Impact on Overall Recovery and Quality of Life

The final aim of perioperative care is to return the patient to their baseline functional state as rapidly as possible. The combined intervention shows a clear

positive effect on key recovery measures. Studies report a shorter time to first passing gas and bowel movement, indicating quicker return of gastrointestinal function [38]. This is likely due to reduced opioid use (which causes constipation) and the gut-protective effects of preoperative nutrition. As a result, postoperative hospital stay is significantly shortened [39].

Furthermore, the combined benefits—less pain, fewer medication side effects, better physical function, and a faster return to normal life—are reflected in patient-reported outcomes. Using the SF-36 health survey consistently shows improvements across all areas, including physical function, role limitations due to physical health, bodily pain, and general health, in patients managed with this multimodal approach [40]. This highlights that combining esketamine and preoperative nutrition not only improves clinical markers but also meaningfully enhances the patient's experience and quality of life after major cancer surgery.

Conclusion

Incorporating preoperative nutritional support and esketamine into the perioperative care plan for older patients undergoing thoracoscopic lung cancer surgery represents a potent, evidence-based strategy consistent with ERAS principles. This multimodal method effectively addresses the threefold challenge of postoperative pain, immunosuppression, and catabolism. Esketamine supplies safe and effective pain relief while reducing opioid load, and preoperative nutrition strengthens the patient's metabolic and immune reserves. Their synergistic action leads to measurable improvements in recovery speed, functional status, and overall quality of life. Future work should concentrate on standardizing protocols and widely implementing these strategies within ERAS guidelines for thoracic oncology to optimize patient outcomes.

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Authors Contributions

The authors contributed to the data analysis. Drafting, revising and approving the article, responsible for all aspects of this work.

Conflict of Interest

None

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