

Amino Acid Supplementation and Postoperative Recovery After Orthopedic and Abdominal Surgery: A Systematic Review

Affan Naufal Ahmada*, Patricia Amanda

Balaraja District Hospital, Tangerang, Indonesia

Email: affanaufal@gmail.com*, patricia.amanda712@gmail.com

Keywords:

aesthetic surgery;
health tourism;
Indonesia;
clinical accreditation;
policy framework

Abstract

Postoperative recovery following major orthopedic and abdominal surgery is frequently complicated by metabolic stress, hypercatabolism, skeletal muscle loss, and prolonged hospitalization. Surgical trauma triggers inflammatory and neuroendocrine responses that accelerate muscle protein breakdown and impair functional recovery. Amino acid supplementation, particularly formulations enriched with essential amino acids (EAAs) and branched-chain amino acids (BCAAs), has been proposed as a targeted nutritional strategy to preserve muscle mass and enhance postoperative outcomes. However, evidence across surgical specialties remains heterogeneous. This systematic review aimed to evaluate the effectiveness of perioperative amino acid supplementation in improving muscle-related recovery, enhancing functional outcomes, and reducing hospital length of stay (LOS) in adult patients undergoing orthopedic or abdominal surgery. A systematic literature search was conducted following the PRISMA 2020 guidelines using the PubMed/MEDLINE, ScienceDirect, and Embase databases. Eligible studies included randomized controlled trials and comparative retrospective studies involving adults (≥ 18 years) receiving enteral or parenteral amino acid supplementation during the perioperative period. Primary outcomes included postoperative muscle mass, muscle strength, functional recovery indicators, and hospital LOS. Risk of bias was assessed using the Cochrane RoB 2 tool and ROBINS-I. From 200 identified records, 10 studies comprising 1,061 patients met the inclusion criteria. The included studies involved patients undergoing orthopedic procedures (total hip arthroplasty, total knee arthroplasty, hip fracture surgery) and abdominal surgeries (gastrectomy, colectomy, gastrointestinal cancer resection). Evidence suggests that EAA and BCAA supplementation contributes to better preservation of skeletal muscle mass and faster recovery of muscle strength, particularly when combined with postoperative rehabilitation.

INTRODUCTION

Major surgical procedures, including orthopedic and abdominal operations, trigger a complex physiological stress response characterized by metabolic disruption and systemic hypercatabolism. Surgical trauma stimulates the release of counter-regulatory hormones such as cortisol, glucagon, and catecholamines, together with increased production of inflammatory cytokines including interleukin-6, interleukin-1 β , and tumor necrosis factor- α . This neuroendocrine and inflammatory cascade induces a hypermetabolic state that prioritizes tissue repair over normal metabolic homeostasis (Schricker & Lattermann, 2015; Popescu et al., 2025; Tipton et al., 2021).

A key consequence of this perioperative response is the development of insulin resistance accompanied by accelerated skeletal muscle protein breakdown. Skeletal muscle serves as the largest reservoir of amino acids, and during severe surgical stress, protein degradation exceeds protein synthesis, resulting in net amino acid release. These amino acids are redirected toward hepatic gluconeogenesis, acute-phase protein synthesis, immune activation, and wound healing (Schricker & Lattermann, 2015; Jaconelli et al., 2022).

Although this redistribution is adaptive, excessive muscle catabolism is associated with delayed mobilization, impaired recovery, increased infection risk, and prolonged hospital stay (Tipton et al., 2021; Gillis & Carli, 2024; Cruz-Jentoft & Sayer, 2019). Therefore, strategies aimed at reducing perioperative muscle loss have become an important focus of modern perioperative care.

While the systemic metabolic response to surgical trauma is broadly similar across surgical specialties, the clinical and nutritional challenges differ substantially between orthopedic and abdominal surgical populations.

Orthopedic surgery, including total hip arthroplasty, total knee arthroplasty, and hip fracture repair, is associated not only with surgical trauma but also with immobilization-related muscle atrophy. Reduced mechanical loading rapidly accelerates muscle loss and may delay functional recovery, particularly in elderly patients (Tipton et al., 2021; Baldwin et al., 2024; Yoshimura et al., 2020). In this population, perioperative muscle wasting may lead to prolonged disability and loss of independence.

In contrast, patients undergoing major abdominal and gastrointestinal surgeries face distinct nutritional challenges. These procedures frequently involve mandatory preoperative fasting, postoperative ileus, and varying degrees of gastrointestinal dysfunction or malabsorption. Together, these factors can exacerbate pre-existing deficits in energy and protein intake (Gillis & Carli, 2024). The situation is particularly pronounced in patients with gastrointestinal malignancies, who often present with baseline cachexia and significant malnutrition prior to surgery, rendering them highly vulnerable to the hypercatabolic effects of surgical stress (Jaconelli et al., 2022; Marano et al., 2024).

Although Enhanced Recovery After Surgery (ERAS) protocols have been widely implemented to improve perioperative outcomes, emphasizing reduced preoperative fasting and early postoperative oral feeding (Ljungqvist et al., 2017; Weimann et al., 2021), many patients remain unable to meet their nutritional and protein requirements during the immediate postoperative period through standard hospital diets alone. This nutritional gap highlights the need for targeted metabolic and nutritional interventions to support recovery (Weimann et al., 2025; Cederholm et al., 2017).

To counteract perioperative muscle catabolism, targeted amino acid supplementation has been proposed as a potential nutritional intervention. Essential amino acids (EAAs), particularly the branched-chain amino acids (BCAAs) leucine, isoleucine, and valine, play a critical role in regulating skeletal muscle protein metabolism (Wolfe, 2017; Shimomura et al., 2014).

Among these, leucine functions not only as a substrate for protein synthesis but also as a key intracellular signalling molecule. Elevated intracellular leucine levels activate the mechanistic target of rapamycin complex 1 (mTORC1), a central regulator of cellular growth and protein synthesis. Activation of this pathway stimulates translation initiation and enhances

muscle protein synthesis even under catabolic conditions (Wilkinson et al., 2013; Kimball & Jefferson, 2006).

By increasing circulating amino acid availability during the perioperative period, these nutrient-sensing pathways may promote anabolic signalling while simultaneously suppressing protein degradation, even under conditions of surgical stress. In addition to their anabolic effects, BCAAs have also been associated with improved glucose metabolism, enhanced immune function, and modulation of inflammatory responses, thereby potentially supporting overall postoperative recovery (Stechmiller, 2021; Wu, 2013; Nicastro et al., 2014).

Despite the strong biological rationale supporting perioperative amino acid supplementation, the clinical evidence regarding its effectiveness remains fragmented and inconsistent. Several randomized clinical trials have investigated amino acid supplementation across diverse surgical populations; however, reported outcomes vary considerably, particularly with respect to functional recovery, muscle preservation, and long-term clinical outcomes (Gillis & Carli, 2024; Baldwin et al., 2024).

While some studies demonstrate substantial benefits in maintaining skeletal muscle mass and improving strength recovery, others report minimal impact on functional independence or postoperative complication rates. This inconsistency underscores the need for a comprehensive synthesis of the available evidence.

To date, there has been no systematic review specifically focused on adult patients undergoing major orthopedic or abdominal surgery who receive targeted, high-dose amino acid supplementation. Considering the increasing global volume of these surgical procedures and the significant healthcare burden associated with postoperative complications, a rigorous evaluation of the existing literature is warranted to clarify the potential role of amino acid supplementation in improving postoperative recovery outcomes and to inform future clinical practice guidelines.

The principal aim of this systematic review is to determine whether targeted amino acid supplementation contributes to improved postoperative recovery outcomes among adults undergoing major orthopedic or abdominal surgical procedures. Specifically, this review seeks to evaluate whether perioperative administration of amino acid supplementation, given preoperatively, intraoperatively, or postoperatively, contributes to preservation of skeletal muscle mass, improvement of muscle strength, enhancement of functional recovery, and reduction in hospital length of stay when compared with placebo, standard care, or no supplementation.

RESEARCH METHOD

This systematic review was planned, implemented, and reported in full alignment with the internationally recognized Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, ensuring a high level of methodological transparency and rigor throughout the research process.

Eligibility Criteria

The eligibility parameters for study inclusion and exclusion were predefined using the Population, Intervention, Comparator, Outcomes, and Study Design (PICOS) framework, allowing the review to be conducted in a systematic and highly focused manner.

Inclusion Criteria

Population:

Eligible studies included adult human participants aged 18 years or older who underwent either elective or emergency orthopedic procedures, such as joint arthroplasty, total hip or knee replacement, and surgical fixation of severe fractures, or major abdominal surgeries, including extensive gastrointestinal resections, colorectal operations, and oncological abdominal procedures.

Intervention:

The intervention of interest involved the administration of targeted amino acid supplementation. Acceptable formulations included purified essential amino acids (EAAs), branched-chain amino acids (BCAAs), as well as nutritional formulas or elemental diets enriched with high concentrations of amino acids. These supplements could be delivered through enteral routes, such as oral liquid preparations, amino acid gels, or tube feeding, or via parenteral administration, including intravenous infusion. The timing of supplementation encompassed a broad peri-surgical timeframe, including preoperative (prehabilitation), perioperative, or postoperative periods.

Comparator:

Control groups consisted of participants receiving placebo preparations (for example, starch or lactose-based powders), standard hospital care, routine rehabilitation protocols without additional nutritional supplementation, or standard iso-caloric nutritional formulas.

Outcomes:

Postoperative recovery outcomes were defined using several objective domains. These included quantitative measurements of skeletal muscle mass or volume, assessments of muscle strength under isometric or isotonic conditions, and validated indicators of functional mobility and recovery, such as the 6-Minute Walking Distance, Harris Hip Score, and the ability to perform activities of daily living. In addition, clinical administrative outcomes, including length of hospital stay (LOS) and rates of short-term postoperative complications, were considered.

Study Design:

Only studies employing methodologically rigorous designs were eligible. These included Randomized Controlled Trials (RCTs), pragmatic clinical trials, and high-quality retrospective comparative studies utilizing matched cohorts, such as those applying propensity score matching techniques.

Language:

To ensure precise interpretation and reliable data extraction, only studies published in the English language were included.

Exclusion Criteria

Studies were excluded when participants were younger than 18 years of age, since developmental physiology, including variations in growth hormone regulation and metabolic activity, may substantially alter amino acid metabolism in pediatric populations. Articles were also excluded if the study design was purely observational without a clearly defined comparative intervention, such as large cohort analyses, case-control investigations, or cross-sectional studies, because these designs provide limited ability to infer causal relationships.

In addition, studies involving individuals with clinical malnutrition, cachexia, or other

conditions associated with impaired nutritional status were excluded, as alterations in protein turnover, nitrogen balance, and amino acid metabolism in these populations could confound the interpretation of metabolic outcomes.

Furthermore, publications consisting of single case reports, case series, narrative reviews, editorials, or conference abstracts without complete peer-reviewed data were not considered eligible. Articles published in languages other than English were also excluded to minimize the risk of misinterpretation arising from translation.

Information Sources

A systematic and comprehensive literature search was conducted across several major biomedical electronic databases, specifically PubMed/MEDLINE, ScienceDirect, and Embase. The search strategy was structured to identify all relevant peer-reviewed publications available from the initial indexing of each database up to the time of the search.

To further ensure that all potentially eligible studies were captured, the reference lists of the included articles and relevant narrative reviews identified during the search process were also manually examined using a backward snowballing approach.

Search Strategy

The literature search strategy was systematically developed by integrating standardized Medical Subject Headings (MeSH) with a broad set of free-text keywords related to the nutritional intervention, the target population, and the surgical procedures of interest. The search syntax was subsequently tailored to align with the Boolean operators and indexing structures applied within each individual database.

For the PubMed/MEDLINE database, the principal search query was formulated as follows:

("Essential Amino Acids"[Mesh] OR "essential amino acid*" OR EAA OR leucine OR isoleucine OR valine) AND ("Orthopedic Procedures"[Mesh] OR orthopedic surgery OR hip surgery OR knee surgery OR fracture surgery OR "Abdominal Surgery"[Mesh] OR abdominal surgery OR gastrointestinal surgery OR colorectal surgery) AND ("Postoperative Period"[Mesh] OR postoperative OR perioperative OR preoperative) AND ("Randomized Controlled Trial" OR randomized OR clinical trial).

Additionally, standard database filtering functions were strictly applied to ensure that the retrieved studies were limited to human participants, adult populations (≥ 18 years), and publications written in English.

Study Selection Process

All records initially retrieved from the database searches were exported into a reference management software system for organization and management. During this stage, duplicate entries were removed through both automated detection and manual verification procedures.

The screening of studies was conducted through two sequential stages. In the first stage, two researchers independently assessed the titles and abstracts of all unique records according to the predefined PICOS eligibility criteria. Studies considered potentially relevant, as well as those with abstracts lacking sufficient information to determine eligibility, were advanced to the subsequent stage of evaluation.

In the second stage, the full-text versions of the remaining articles were obtained and independently reviewed by the same two researchers. Any discrepancies in study selection were resolved through detailed academic discussion. If consensus could not be reached, a third

senior reviewer conducted an independent adjudication to determine the final decision. The entire selection procedure was carefully documented to construct the PRISMA flow diagram.

Data Collection Process and Data Items

Data extraction from the included studies was conducted using a standardized electronic data extraction form that had been pre-tested prior to use. This form facilitated the systematic collection of both quantitative and qualitative information from the eligible full-text articles.

To ensure accuracy and reliability, two reviewers independently performed the data extraction process. Upon completion, the extracted data were cross-checked to verify consistency and minimize potential errors.

The information extracted from each study included the following categories:

Study Metadata: first author, publication year, and study design.

Patient Demographics: type of surgical procedure performed, total sample size (clearly stratified into intervention and control groups), and participant age characteristics reported as mean $\pm$ standard deviation.

Intervention Characteristics: detailed information regarding the nutritional intervention, including the type of amino acid formulation (e.g., EAA, BCAA, or specific leucine ratios), the administered dosage, the method of administration (enteral or parenteral), the duration of the intervention, and the timing of administration relative to the surgical procedure.

Control Characteristics: description of the comparator condition, such as the type of placebo used or standard care protocols implemented.

Outcomes: primary and secondary outcomes evaluated in the studies. Extracted outcome data included quantitative means, standard deviations, standard errors, percentage changes from baseline, estimated treatment effects, and the corresponding p-values reported in the studies.

Risk of Bias Assessment

To ensure the methodological robustness of the synthesized evidence, a comprehensive risk-of-bias evaluation was conducted for each included study. This assessment was performed independently by two reviewers to maintain objectivity and reliability in the evaluation process. Randomized controlled trials were evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool and non-randomized comparative studies were assessed using the ROBINS-I instrument.

Data Analysis

A quantitative meta-analysis was not undertaken because the included studies demonstrated considerable clinical and methodological heterogeneity. These variations were observed in several aspects, including the types of surgical procedures performed, the specific amino acid formulations used, differences in dosing strategies, the timing of supplementation, and the methods applied to measure outcomes. Consequently, the findings were synthesized through a structured narrative approach to systematically summarize and interpret the available evidence.

The narrative synthesis was conducted in accordance with established methodological recommendations for systematic reviews that do not include meta-analysis. Initially, the studies were categorized based on the principal outcomes investigated: (1) skeletal muscle mass and muscle strength, (2) measures of functional recovery, and (3) length of hospital stay and associated clinical outcomes.

Within each outcome category, the major characteristics and findings of the included

studies were presented using descriptive summaries. The direction and consistency of the reported effects were evaluated by comparing the results between intervention and control groups across the studies. Consideration was given to factors such as the type of amino acid supplementation, route of administration, timing of the intervention (preoperative, perioperative, or postoperative), and the surgical population involved (orthopedic or abdominal surgery).

When available, effect estimates, levels of statistical significance, and clinical interpretations reported by individual studies were described. In addition, variations in study design, outcome measurement techniques, and intervention protocols were considered when interpreting the overall evidence base.

The purpose of this narrative synthesis was to identify recurring trends, areas of consistency, and points of divergence across the studies, thereby enabling a comprehensive interpretation of the potential role of perioperative amino acid supplementation in improving postoperative recovery outcomes.

RESULTS AND DISCUSSION

Study Selection

A comprehensive search conducted across multiple databases identified a total of 200 records, consisting of 37 records retrieved from PubMed/MEDLINE, 17 from ScienceDirect, and 146 from Embase. Prior to the screening stage, 2 duplicate entries were detected and removed. The remaining 198 unique records underwent title and abstract screening, resulting in the exclusion of 173 records that did not satisfy the predefined PICOS criteria, mainly due to irrelevant interventions or the inclusion of non-surgical populations.

Subsequently, full-text versions were requested for the 25 articles considered potentially relevant. However, 14 reports could not be obtained despite extensive efforts through institutional access, leaving 12 full-text articles available for eligibility assessment. During the independent and detailed full-text evaluation, 2 studies were excluded: one did not strictly meet the intervention inclusion criteria, while the other used an observational design without a comparator group, making it incompatible with the study requirements.

In the final stage, 10 studies fulfilled all eligibility criteria and were included in the systematic review. These studies were conducted by Baldissarro et al., Aquilani et al., Ikeda et al., Ueyama et al., Kikuchi et al., Fujimoto et al., Shichinohe et al., Ma et al., Wang et al., and Kang et al. (Yoshimura et al., 2020; Kinoshita et al., 2018; Okamoto et al., 2022; Tieland et al., 2025; Hirose et al., 2019; Kang et al., 2025; Ida et al., 2016; Baldissarro et al., 2016; Sugawara et al., 2024; Liu et al., 2024). The complete process of article identification, screening, eligibility assessment, and inclusion is illustrated in Figure 1.

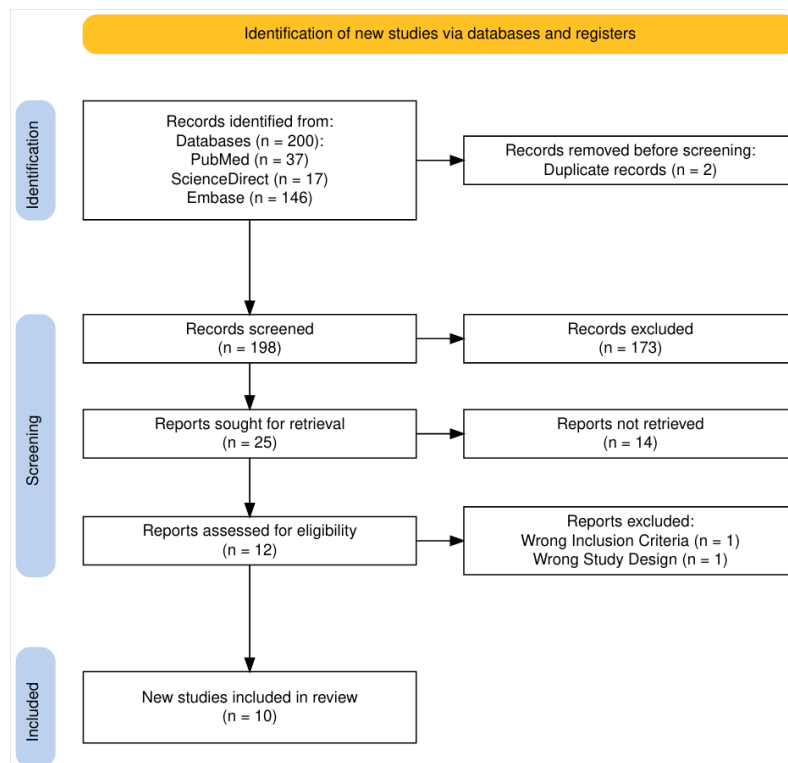


Figure 1. PRISMA Literature Search and Study Selection Flow.
Source: Author's illustration based on PRISMA 2020 guidelines

Characteristics of Included Studies

The ten studies included in this review were published between 2016 and 2025 and involved a combined total of 1,061 adult participants. The surgical populations represented in these studies covered both major orthopedic procedures and highly invasive abdominal operations, thereby providing a comprehensive representation of conditions associated with substantial surgical stress. The orthopedic groups consisted of patients undergoing elective total hip arthroplasty (THA), total knee arthroplasty (TKA), as well as urgent surgical management for severe hip fractures. Meanwhile, the abdominal and gastrointestinal groups included patients who underwent laparoscopic colectomy, radical gastrectomy, and extensive gastrointestinal cancer resections (Yoshimura et al., 2020; Kinoshita et al., 2018; Okamoto et al., 2022; Tieland et al., 2025; Hirose et al., 2019; Kang et al., 2025; Ida et al., 2016; Baldissarro et al., 2016; Sugawara et al., 2024; Liu et al., 2024).

Regarding methodological design, eight studies were conducted as Randomized Controlled Trials (RCTs) with structured designs, including double-blind, single-blind, and pragmatic trial formats, while two studies employed retrospective comparative approaches using rigorously matched cohorts, such as propensity score matching techniques (Yoshimura et al., 2020; Kinoshita et al., 2018; Okamoto et al., 2022; Tieland et al., 2025; Hirose et al., 2019; Kang et al., 2025; Ida et al., 2016; Baldissarro et al., 2016; Sugawara et al., 2024; Liu et al., 2024).

Although the exact biochemical composition of the nutritional interventions differed among studies, all protocols consistently emphasized the administration of high-density, targeted amino acid supplementation. The interventions mainly involved purified essential amino acids (EAAs), branched-chain amino acid (BCAA) formulations with high leucine

content, total amino acid enriched parenteral nutrition, or enteral elemental diet preparations. The timing of supplementation varied across studies, ranging from preoperative administration up to 14 days as part of a prehabilitation strategy, perioperative intravenous infusion protocols, and postoperative supplementation lasting up to six weeks combined with structured physical rehabilitation programs (Yoshimura et al., 2020; Kinoshita et al., 2018; Okamoto et al., 2022; Tieland et al., 2025; Hirose et al., 2019; Kang et al., 2025; Ida et al., 2016; Baldissarro et al., 2016; Sugawara et al., 2024; Liu et al., 2024).

A detailed summary of the primary studies focusing on muscle-related outcomes and functional recovery is presented in Table 1.

Table 1. Characteristics and Design of Included Studies. Int: Intervention; Con: Control; PSM: Propensity Score Matched. Asterisk denotes multi-arm control in Aquilani.

Author (Year)	Surgery Type	Study Design	Sample Size (Int / Con)	Intervention Type	Control Type	Primary Outcomes Measured
Ikeda et al. (2019)	Total hip arthroplasty	Single-blinded RCT	18 / 13	3.4g BCAA (post-exercise)	1.2g Starch	Knee extension strength, upper arm muscle area
Ueyama et al. (2020)	Total knee arthroplasty	Double-blind RCT	30 / 30	9g/day EAA (perioperative)	Powdered Lactose	Rectus femoris area, quadriceps strength
Fujimoto et al. (2025)	GI cancer surgery	Prospective RCT	18 / 27	AA jelly + resistance training (14 days pre-op)	Standard Care	Knee extension strength, Skeletal muscle index, Complications
Kikuchi et al. (2022)	Radical gastrectomy	Retrospective	40 / 43	PPN + ONS (Amino Acids)	PPN (Glucose)	% Skeletal muscle loss, % Body weight loss
Aquilani et al. (2018)	Hip fracture surgery	RCT	28 / 55*	8g/day EAA + Rehab	Placebo / Rehab only	6-Min Walking Distance (6MWD)
Baldissarro et al. (2016)	Elective hip arthroplasty	RCT	30 / 30	8g/day EAA (14 days)	Maltodextrin	Harris Hip Score (HHS), Plasma AA levels
Shichinohe et al. (2016)	Laparoscopic colectomy	Multicenter RCT	45 / 49	Elemental Diet (AA)	Conventional Diet	Estimated minimum LOS (emLOS), Time to defecation
Ma et al. (2024)	Gastric cancer surgery	Double-blind RCT	70 / 67	Early IV BCAA	Standard Nutrition	Length of stay, Time to defecation
Wang et al. (2024)	Gastrointestinal tumor	Pragmatic RCT	204 / 203	High IV AA (2.0 g/kg/day)	Standard AA (1.2 g/kg/day)	Infection incidence, Length of stay
Kang et al. (2025)	Hip fracture surgery	Retrospective (PSM)	53 / 53	12g/day BCAA (6 weeks post-op)	Standard Care	Postoperative serum albumin recovery

Source: Compiled from included studies

Risk of Bias in Included Studies

Among the eight randomized controlled trials assessed with the RoB 2 framework, three studies (Wang et al., Ueyama et al., and Ma et al.) were clearly categorized as having an overall low risk of bias, supported by well-implemented randomization procedures, effective double-blinding involving both participants and outcome assessors, and complete as well as transparent reporting of study outcomes (Yoshimura et al., 2020; Sugawara et al., 2024; Liu et al., 2024). Four trials were judged to present some concerns, mainly due to single-blind study designs in which full blinding of participants was difficult to achieve, or because of limited clarity regarding the pre-specified selection of reported outcomes (Kinoshita et al., 2018; Okamoto et al., 2022; Hirose et al., 2019; Ida et al., 2016). One study (Shichinohe et al.) was classified as having a high risk of bias, largely attributable to unavoidable limitations related to objective outcome measurement and the practical difficulty of maintaining adequate blinding when comparing a clearly distinguishable oral elemental diet intervention with standard hospital nutrition (Tieland et al., 2025).

The two retrospective comparative studies assessed using the ROBINS-I instrument were both determined to have an overall moderate risk of bias (Okamoto et al., 2022; Kang et al., 2025). Although Kikuchi et al. and Kang et al. implemented advanced cohort matching methods, particularly Kang et al., who applied propensity score matching to balance baseline characteristics such as pre-fracture functional status, the retrospective nature of these designs inherently carries unavoidable risks of residual confounding and possible bias in the retrospective classification of interventions (Kang et al., 2025).

Overall, the included evidence was derived predominantly from randomized studies of acceptable methodological quality, although the certainty of findings for some outcomes should be interpreted with caution because several trials had some concerns and one trial had high risk of bias, while the non-randomized studies remained vulnerable to confounding.

A comprehensive, domain-specific summary of the risk of bias evaluations for all included studies is presented in Tables 2 and 3.

Table 2. Risk of Bias Assessment for Randomized Controlled Trials Using Cochrane RoB 2 Tool.

Study	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Risk of Bias
Ikeda et al., 2019	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Wang et al., 2024	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Shichinohe et al., 2016	Some concerns	Low risk	Low risk	High risk	Low risk	High risk
Ueyama et al., 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Fujimoto et al., 2025	Some concerns	Some concerns	Some concerns	Low risk	Some concerns	Some concerns
Aquilani et al., 2018	Some concerns	Some concerns	Low risk	Low risk	Some concerns	Some concerns

Study	Randomization Process	Deviations from Intended Interventions	Missing Outcome Data	Measurement of the Outcome	Selection of the Reported Result	Overall Risk of Bias
Baldissarro et al., 2016	Some concerns	Low risk	Low risk	Low risk	Some concerns	Some concerns
Ma et al., 2024	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

Source: Author's analysis using Cochrane RoB 2 tool (2025)

Table 3. Risk of Bias Assessment for Retrospective Studies Using ROBINS-I.

Study	Confounding	Selection of Participants	Classification of Interventions	Deviations from Intended Interventions	Missing Data	Measurement of Outcomes	Selection of Reported Results	Overall Risk of Bias
Kikuchi et al., 2022	Moderate	Low	Low	Unclear	Low	Low	Low	Moderate
Kang et al., 2025	Low	Low	Low	Low	Moderate	Low	Moderate	Moderate

Source: Author's analysis using ROBINS-I tool (2025)

Primary Outcome: Skeletal Muscle Mass and Muscular Strength Dynamics

The preservation of skeletal muscle mass and the prevention of postoperative muscle weakness constitute the primary and most important targets in perioperative nutritional optimization. Four included studies reported explicit quantitative and objective measurements related to muscle morphology as well as isotonic and isometric strength parameters (Yoshimura et al., 2020; Okamoto et al., 2022; Tieland et al., 2025; Hirose et al., 2019).

Within orthopedic surgery settings, Ikeda et al. specifically investigated elderly female patients undergoing total hip arthroplasty (THA). Subjects assigned to the intervention group received 3.4 g of branched-chain amino acids (BCAAs) immediately after completing a standardized postoperative rehabilitation protocol consisting of three daily exercise sets. This group demonstrated a statistically significant increase in upper-arm muscle cross-sectional area ($p = 0.012$) and showed a markedly greater improvement in knee extension strength of the contralateral, non-operated limb ($p = 0.028$) compared with the iso-caloric starch placebo group. However, no statistically significant improvement was observed in the hip abductor strength of the operated limb. This finding suggests that extensive local surgical trauma together with the complex biological processes related to implant integration may temporarily override systemic anabolic responses at the surgical site (Hirose et al., 2019).

Strong long-term evidence was reported by Ueyama et al. in patients undergoing total knee arthroplasty (TKA). In a double-blind randomized controlled trial, perioperative supplementation with 9 g/day of essential amino acids (EAAs) significantly reduced rectus femoris muscle atrophy during the first four postoperative weeks, a period considered highly vulnerable to catabolic loss. At a two-year follow-up, the intervention group maintained a rectus femoris muscle area equivalent to $134\% \pm 31\%$ of baseline, which was significantly

higher than the placebo group value of $114\% \pm 27\%$ ($p < 0.05$). In addition, recovery of isometric quadriceps strength reached $159\% \pm 54\%$ in the EAA group compared with $125\% \pm 40\%$ in the control group (Yoshimura et al., 2020).

In patients undergoing major abdominal oncologic surgery, the metabolic stress response is substantially more pronounced. Kikuchi et al. demonstrated that early administration of amino acids through peripheral parenteral nutrition combined with high-protein oral nutritional supplementation significantly reduced early postoperative muscle loss after radical gastrectomy. Using computed tomography for precise measurement, total skeletal muscle loss at postoperative day 7 was $-4.1\% \pm 3.8\%$ in the amino-acid group, compared with $-6.5\% \pm 3.8\%$ in the glucose control group ($p = 0.006$) (Okamoto et al., 2022).

Similarly, Fujimoto et al. examined a frail population undergoing gastrointestinal cancer surgery. A 14-day preoperative prehabilitation program consisting of resistance exercise and intake of leucine-enriched amino acid jelly resulted in better preservation of knee extension strength at hospital discharge ($119.3\% \pm 72.0\%$ of baseline in the intervention group versus $86.7\% \pm 22.0\%$ in the control group, $p = 0.044$), although no significant difference was observed in overall skeletal muscle index measured by bioelectrical impedance. These findings indicate that amino acid supplementation may maintain functional strength and neuromuscular performance even before detectable morphological changes in muscle mass occur (Tieland et al., 2025).

Secondary Outcome: Functional Recovery and Rehabilitation Metrics

The preservation of skeletal muscle mass must ultimately translate into meaningful improvements in functional capacity, as real-world recovery outcomes are essential for maintaining patient independence and overall quality of life. Several well-designed randomized controlled trials assessed validated functional recovery parameters following targeted amino acid supplementation (Yoshimura et al., 2020; Kinoshita et al., 2018; Tieland et al., 2025; Hirose et al., 2019; Ida et al., 2016; Baldissarro et al., 2016).

Aquilani et al. performed an important randomized controlled trial involving 83 elderly patients recovering from hip fracture surgery, a population known to be at high risk for long-term disability, institutionalization, and increased mortality. Participants who received 8 g/day of essential amino acids (EAAs) in combination with a standard rehabilitation program demonstrated a substantial improvement in physical endurance, as measured by the 6-Minute Walk Distance (6MWD). The intervention group showed an average increase of $+118.2 \pm 100.3$ meters from baseline, which was significantly greater than the improvement observed in the placebo group ($+73.6 \pm 66.3$ m, $p = 0.024$) and the rehabilitation-only group ($+65.4 \pm 52.4$ m, $p = 0.034$) (Kinoshita et al., 2018).

In patients undergoing elective total hip arthroplasty, Baldissarro et al. assessed recovery using the widely accepted Harris Hip Score (HHS). After a controlled 14-day course of EAA supplementation, the intervention group achieved a significantly higher functional recovery score, reaching a mean HHS of 76.37, compared with 70.0 in the maltodextrin placebo group ($p = 0.006$). Similarly, Ueyama et al. reported that perioperative EAA supplementation not only preserved thigh muscle mass but also reduced the time required to regain basic Activities of Daily Living (ADLs) and significantly improved standardized gait performance ($p = 0.005$) (Yoshimura et al., 2020; Baldissarro et al., 2016).

Ikeda et al. assessed functional outcomes using the Functional Independence Measure

after total hip arthroplasty. Although the supplemented group showed improvement in functional scores during rehabilitation, the overall difference between groups was not statistically significant, indicating that functional recovery may depend on multiple factors beyond nutritional intervention alone (Hirose et al., 2019).

In abdominal surgical populations, functional recovery is primarily characterized by the restoration of gastrointestinal function and metabolic stability rather than mobility. Fujimoto et al. observed that preoperative amino acid supplementation combined with resistance exercise reduced the decline in activities of daily living at follow-up compared with standard care, although the difference did not reach statistical significance. These findings suggest a potential long-term benefit of perioperative nutritional support in frail surgical populations (Tieland et al., 2025).

Functional recovery in abdominal surgery is also reflected by the restoration of gastrointestinal activity. Shichinohe et al. demonstrated that administration of an amino acid–based elemental diet, which does not require complex enzymatic digestion, led to faster gastrointestinal recovery in patients undergoing laparoscopic colectomy. The time to first postoperative defecation averaged 2.2 days in the elemental diet group, compared with 3.1 days in the conventional hospital diet group, representing a statistically significant difference ($p = 0.005$) (Ida et al., 2016).

Secondary Outcome: Length of Hospital Stay and Clinical Complications

Prolonged hospital length of stay (LOS) represents a major contributor to increased healthcare costs, limited hospital bed availability, and prolonged patient morbidity. Three large, well-powered studies reported consistent evidence that optimized amino acid supplementation can significantly reduce the duration of hospitalization (Ida et al., 2016; Sugawara et al., 2024; Liu et al., 2024).

In the large pragmatic clinical trial AMIGITS, Wang et al. randomized 407 patients undergoing gastrointestinal tumor surgery to receive either high-dose intravenous amino acids with a target intake of 2.0 g/kg/day or standard nutritional care providing 1.2 g/kg/day. Patients in the high-dose amino acid group showed a significantly lower rate of severe infections during hospitalization and within the first 30 postoperative days ($p = 0.024$). This reduction in infectious complications was associated with a statistically significant decrease in total postoperative hospital stay ($p < 0.001$), suggesting that adequate amino acid provision may support immune function and accelerate recovery after major abdominal surgery (Liu et al., 2024).

Similarly, Ma et al. reported that early intravenous administration of a branched-chain amino acid (BCAA)–enriched formulation in patients undergoing gastric cancer surgery resulted in faster postoperative recovery. The intervention group had a median length of stay of 8.0 days, compared with 8.5 days in the control group receiving standard nutritional management (mean difference 0.38 days; 95% CI 0.02–0.74; $p < 0.001$) (Sugawara et al., 2024).

In addition, Shichinohe et al. applied a composite outcome measure known as the estimated minimum length of stay (emLOS), which was defined according to strict clinical criteria including adequate oral intake, controlled pain, and absence of fever. Using this metric, patients receiving an elemental amino acid–based diet achieved emLOS by postoperative day 4, whereas the control group reached this endpoint on postoperative day 7, demonstrating a

statistically significant difference ($p = 0.018$) (Ida et al., 2016).

To better interpret these clinical findings, objective biochemical indicators reflecting nutritional status and systemic inflammatory activity offer important mechanistic explanations. In a propensity score–matched retrospective analysis involving 106 elderly patients recovering from severe hip fracture surgery, Kang et al. demonstrated that a six-week postoperative supplementation protocol using high-dose BCAAs (12 g/day) produced a statistically significant improvement in serum albumin levels at the sixth postoperative week compared with standard treatment. Because hypoalbuminemia is strongly associated with an increased risk of postoperative complications, this improvement in biochemical parameters carries substantial clinical significance (Kang et al., 2025).

Consistent with these metabolic effects, Baldissarro et al. also reported comparable findings, showing that a 14-day course of essential amino acid supplementation effectively restored plasma amino acid concentrations depleted by surgery and was associated with a rapid reduction in elevated C-reactive protein (CRP) levels, indicating attenuation of the systemic inflammatory response (Baldissarro et al., 2016).

Overall, the available evidence indicates that perioperative amino acid supplementation may shorten hospital stay, reduce postoperative complications, and improve metabolic recovery, particularly in patients undergoing major abdominal surgery or in elderly individuals at high risk of catabolic stress (Kang et al., 2025; Ida et al., 2016; Baldissarro et al., 2016; Sugawara et al., 2024; Liu et al., 2024).

Summary of Main Findings

The present systematic review synthesizes evidence from ten clinical studies involving patients undergoing major orthopedic and abdominal surgery and demonstrates that perioperative amino acid supplementation may provide clinically meaningful benefits in postoperative recovery. Across different surgical populations, targeted supplementation with essential amino acids or branched-chain amino acids consistently attenuated muscle catabolism, improved functional recovery, and in several studies reduced hospital length of stay (Tipton et al., 2021; Baldwin et al., 2024; Liu et al., 2024).

Loss of skeletal muscle mass is a well-recognized consequence of surgical stress and immobilization, particularly in elderly or frail patients. Previous nutritional and rehabilitation studies have shown that insufficient protein intake during the perioperative period contributes to delayed recovery, increased complications, and prolonged hospitalization (Tipton et al., 2021; Cruz-Jentoft & Sayer, 2019; Nicastro et al., 2014). The findings of the present review support these observations, as most included trials reported improved preservation of muscle strength or muscle mass when amino acid supplementation was combined with rehabilitation or adequate nutritional support (Yoshimura et al., 2020; Hirose et al., 2019; Baldissarro et al., 2016).

The beneficial effects observed across the included studies are consistent with prior clinical investigations demonstrating that essential amino acid supplementation enhances muscle protein synthesis and accelerates functional recovery after surgery (Ferrando et al., 2010). In orthopedic populations, supplementation appears particularly effective when combined with exercise or structured rehabilitation, which may enhance anabolic signaling and promote faster restoration of mobility (Kinoshita et al., 2018; Hirose et al., 2019). In abdominal surgery, where patients frequently experience severe metabolic stress and inadequate oral

intake, high-dose amino acid administration has been associated with improved postoperative recovery and fewer complications (Sugawara et al., 2024; Liu et al., 2024).

The present findings are also in agreement with previous clinical nutrition trials showing that specialized nutritional supplementation in hospitalized patients can reduce complications and improve recovery outcomes, particularly in older adults at risk of malnutrition (Ljungqvist et al., 2017). Furthermore, randomized trials in gastrointestinal surgery have demonstrated that optimized amino acid intake may improve short-term clinical outcomes, including reduced infection rates and faster recovery of gastrointestinal function (Liu et al., 2024; Ljungqvist et al., 2017).

Taken together, the evidence suggests that perioperative amino acid supplementation represents a biologically plausible and clinically effective strategy to counteract surgery-induced hypercatabolism. Although the magnitude of benefit varies across studies, the overall direction of effect is consistent, supporting the integration of targeted amino acid supplementation into modern perioperative nutritional care (Baldwin et al., 2024; Wall et al., 2024).

Mechanistic Interpretation of Amino Acid Efficacy

The effectiveness of amino acid supplementation during the perioperative period can be explained by its dual role as both a substrate for protein synthesis and a regulator of cellular signalling. Surgical stress triggers a strong metabolic response characterized by increased levels of cortisol, catecholamines, and inflammatory cytokines, which lead to insulin resistance and activation of the ubiquitin–proteasome pathway, resulting in accelerated muscle protein breakdown (Schricker & Lattermann, 2015; Jacconelli et al., 2022). In this hypercatabolic condition, muscle proteins are degraded to release free amino acids that are used for hepatic gluconeogenesis and acute phase protein synthesis, immune activation, and wound healing, leading to rapid loss of muscle mass if adequate nutritional support is not provided (Schricker & Lattermann, 2015; Tipton et al., 2021).

Administration of essential amino acids (EAAs), especially branched-chain amino acids (BCAAs) such as leucine, can counteract this catabolic process through specific molecular mechanisms (Wolfe, 2017; Shimomura et al., 2014). Leucine acts as an important nutrient signal that directly activates the mechanistic target of rapamycin complex 1 (mTORC1). Activation of mTORC1 leads to phosphorylation of 4E-BP1, allowing the release of eIF4E and the formation of the eIF4F translation initiation complex. In addition, mTORC1 activates S6K1, which increases ribosomal activity and improves protein translation efficiency (Wilkinson et al., 2013; Kimball & Jefferson, 2006). Activation of this pathway increases ribosomal activity, enhances translation efficiency, and suppresses proteolysis, thereby counteracting the catabolic effects induced by surgical stress (Kimball & Jefferson, 2006).

Increasing plasma amino acid levels through oral or intravenous supplementation signals the body that sufficient nutrients are available. This condition stimulates muscle protein synthesis while suppressing autophagy and proteasomal degradation, thereby reducing the catabolic effects even during systemic inflammation caused by major surgery (Tipton et al., 2021; Wolfe, 2017).

Overall, the available mechanistic evidence supports the clinical findings of the present review, indicating that perioperative amino acid supplementation can reduce surgery-induced catabolism, enhance anabolic signaling, and facilitate faster recovery of muscle mass and

function. These biological effects provide a strong rationale for the integration of targeted amino acid supplementation into perioperative nutritional strategies, particularly in elderly, malnourished, or high-risk surgical patients (Schricker & Lattermann, 2015; Tipton et al., 2021; Wu, 2013).

Divergent Paradigms: Orthopedic vs. Abdominal Surgery

In major orthopedic surgeries such as total hip arthroplasty (THA), total knee arthroplasty (TKA), and hip fracture repair, rapid muscle loss is mainly caused by localized disuse atrophy combined with direct tissue injury from surgery. Evidence from studies conducted by Aquilani et al. and Ikeda et al. shows that high-dose BCAA or EAA supplementation is most effective when it is carefully combined with resistance training or functional rehabilitation. Under these conditions, anabolic signaling can be maximized, leading to improved recovery of muscle strength and faster return to independent mobility (Tipton et al., 2021; Baldwin et al., 2024; Wall et al., 2024).

Aquilani et al. reported improved walking performance in elderly patients receiving essential amino acids during rehabilitation after hip fracture surgery, while Ikeda et al. and Ueyama et al. observed better recovery of muscle strength and functional performance when supplementation was administered during the postoperative rehabilitation period (Yoshimura et al., 2020; Kinoshita et al., 2018; Hirose et al., 2019). These findings indicate that anabolic stimulation provided by amino acids may enhance the adaptive response to physical training, resulting in faster restoration of muscle function.

In contrast, patients undergoing major abdominal or gastrointestinal surgery, including radical gastrectomy and complex colectomy, commonly experience severe caloric deficiency. This condition is caused by preoperative fasting, removal of absorptive intestinal surfaces during surgery, and prolonged postoperative ileus that limits nutrient intake (Jaconelli et al., 2022; Marano et al., 2024). In such cases, nutritional strategies often bypass the impaired gastrointestinal tract using peripheral parenteral nutrition (PPN) or specially formulated elemental diets. The abdominal surgery studies included in this review showed that amino acid supplementation may be particularly beneficial when administered early in the perioperative period or through parenteral or elemental formulations. Kikuchi et al. demonstrated reduced postoperative muscle loss with early amino acid supplementation after gastrectomy.

Shichinohe et al. reported that elemental diets, which consist of pre-digested free amino acids requiring minimal digestion and absorption, can accelerate the recovery of bowel function and reduce the duration of hospitalization. In addition, the AMIGITS trial conducted by Wang et al. demonstrated that increasing intravenous amino acid administration from the standard dose of 1.2 g/kg/day to a higher dose of 2.0 g/kg/day enhances immune function, resulting in fewer postoperative infections and improved recovery outcomes (Ida et al., 2016; Liu et al., 2024).

These differences between surgical populations are consistent with current clinical nutrition guidelines, which recommend individualized perioperative nutritional strategies based on the type of surgery, baseline nutritional status, and expected metabolic stress (Weimann et al., 2021; Weimann et al., 2025). In orthopedic patients, supplementation may be most effective when combined with rehabilitation to stimulate muscle protein synthesis, whereas in abdominal surgery early metabolic support may be required to prevent severe catabolism and support recovery of gastrointestinal function.

Integration with ERAS and Clinical Guidelines

The clinical implications of these findings are directly applicable to current surgical practice. Contemporary perioperative management is largely based on Enhanced Recovery After Surgery (ERAS) protocols. Existing guidelines from the European Society for Clinical Nutrition and Metabolism (ESPEN) and international ERAS organizations strongly recommend minimizing preoperative fasting and promoting early postoperative oral nutrition. However, the detailed evidence summarized in this review indicates that providing only standard hospital diets may not be adequate to meet the metabolic demands following major surgery. High-density and targeted amino acid supplementation appears to be necessary to counteract the severe catabolic state induced by surgical stress (Ljungqvist et al., 2017; Weimann et al., 2021).

The results of the present review suggest that targeted amino acid supplementation may represent an effective strategy to bridge this nutritional gap. Several included trials demonstrated improved muscle preservation, enhanced functional recovery, and shorter hospitalization when amino acids were administered in addition to standard care (Yoshimura et al., 2020; Kinoshita et al., 2018; Hirose et al., 2019; Sugawara et al., 2024; Liu et al., 2024). These findings are consistent with previous systematic reviews reporting that protein- or amino acid-based supplementation can improve postoperative recovery, particularly when combined with rehabilitation or adequate caloric intake (Baldwin et al., 2024).

Therefore, the routine integration of essential amino acid (EAA) or branched-chain amino acid (BCAA) supplementation into perioperative care protocols should be considered. This approach may be particularly beneficial for patients at high risk, including elderly individuals, frail patients, and those with sarcopenia, where the risk of postoperative muscle loss and delayed recovery is significantly increased.

Limitations of the Evidence Included

Although the available evidence supporting perioperative amino acid supplementation is strong, several methodological limitations within the included studies should be clearly recognized. First, considerable clinical heterogeneity exists in terms of the biochemical composition, dosage, and timing of the nutritional interventions. The analyzed studies applied a wide range of protocols, from relatively low doses such as 3.4 g of oral BCAAs administered only after surgery in combination with rehabilitation therapy, to high-dose intravenous administration reaching 2.0 g/kg/day initiated before the surgical procedure. This wide variation makes it impossible to determine a single standardized dosing regimen that can be universally applied to all patient populations (Okamoto et al., 2022; Tieland et al., 2025; Sugawara et al., 2024; Liu et al., 2024).

Second, different methods were used to assess muscle mass across the included studies. Ueyama measured the cross-sectional area of the rectus femoris using ultrasound, Kikuchi performed whole-body skeletal muscle evaluation using computed tomography (CT), while Fujimoto used bioelectrical impedance analysis (BIA) for body composition assessment (Yoshimura et al., 2020; Hirose et al., 2019). Although all methods consistently showed a protective effect against muscle loss, the differences in accuracy and sensitivity between these techniques may introduce variability when attempting to combine the results into a single pooled analysis (Tipton et al., 2021; Jaconelli et al., 2022).

Third, several of the included studies had relatively small sample sizes, which may limit

the strength of general conclusions. For instance, Ikeda et al. analyzed only 31 participants, and the final analysis by Fujimoto included 45 frail patients. In addition, some studies, such as those conducted by Kang et al. and Kikuchi et al., used retrospective designs despite applying advanced statistical approaches including propensity score matching and strict control methods. Although these methods improve reliability, retrospective studies still carry a risk of selection bias and unmeasured confounding factors (Okamoto et al., 2022; Tieland et al., 2025; Hirose et al., 2019; Kang et al., 2025).

Finally, functional recovery outcomes were not uniformly defined across studies. Some trials focused on muscle strength or imaging-based measurements, whereas others evaluated mobility, activities of daily living, or length of hospital stay (Baldwin et al., 2024). Because postoperative recovery is a multifactorial process influenced by surgical technique, rehabilitation, and baseline nutritional status, the isolated effect of amino acid supplementation may be difficult to quantify precisely.

CONCLUSION

This systematic review, conducted through a comprehensive and detailed analysis, demonstrates that perioperative amino acid supplementation particularly formulations rich in essential amino acids and branched-chain amino acids represents an effective, safe, and biologically targeted nutritional intervention for adult patients undergoing major orthopedic as well as abdominal surgery. The incorporation of standardized high-dose amino acid supplementation into established Enhanced Recovery After Surgery (ERAS) protocols may provide substantial clinical benefits, including improved postoperative recovery, better long-term functional outcomes, and reduced healthcare burden related to prolonged hospitalization and postoperative complications. In conclusion, integration of targeted amino acid supplementation into modern perioperative care has the potential to improve recovery, reduce complications, and enhance functional outcomes, but further high-quality research is needed before universal clinical recommendations can be established.

REFERENCES

- Baldissarro, E., Sandri, M., et al. (2016). Functional recovery after elective hip surgery improved by essential amino acid supplementation: A randomized study. *Aging Clinical and Experimental Research*, 28(6), 1213–1220.
- Baldwin, C., et al. (2024). Post-operative protein supplementation following orthopaedic surgery: A systematic review. *Nutrients*, 16, 1092.
- Cederholm, T., Barazzoni, R., Austin, P., et al. (2017). ESPEN guideline on hospital nutrition. *Clinical Nutrition*, 36(3), 623–650.
- Cruz-Jentoft, A. J., & Sayer, A. A. (2019). Sarcopenia. *The Lancet*, 393(10191), 2636–2646.
- Ferrando, A. A., Paddon-Jones, D., Hays, N. P., et al. (2010). EAA supplementation facilitates recovery of muscle function after surgery. *American Journal of Physiology: Endocrinology and Metabolism*, 298(3), E558–E565.
- Gillis, C., & Carli, F. (2024). Protein-based perioperative nutrition interventions for improving muscle mass and functional outcomes following orthopaedic surgery. *Cochrane Database of Systematic Reviews*.
- Hirose, T., Tetsuka, K., Nagano, A., et al. (2019). Effect of exercise therapy combined with branched-chain amino acid supplementation on muscle strength after orthopedic surgery. *Journal of Orthopaedic Science*, 24(2), 329–334.

- Ida, S., Watanabe, M., Yoshida, N., et al. (2016). Impact of elemental diet on early recovery after laparoscopic gastrectomy. *Surgery Today*, 46(10), 1190–1197.
- Jaconelli, M., Greenhaff, P. L., Brook, M., & Atherton, P. J. (2022). The effects of elective abdominal surgery on protein turnover: A meta-analysis of stable isotope techniques to investigate postoperative catabolism. *Clinical Nutrition*, 41(4), 873–882.
- Kang, J. S., Lee, S. H., Kim, Y. H., et al. (2025). Impact of branched-chain amino acid supplementation on postoperative serum albumin recovery in older adults with hip fracture: A propensity score-matched study. *Nutrients*, 17(2), 345.
- Kimball, S. R., & Jefferson, L. S. (2006). Signaling pathways and molecular mechanisms through which branched-chain amino acids mediate translational control of protein synthesis. *Journal of Nutrition*, 136(1 Suppl), 227S–231S.
- Kinoshita, S., et al. (2018). Supplemented amino acids may enhance walking recovery after hip fracture surgery in elderly patients. *Journal of Nutrition, Health & Aging*, 22(3), 311–317.
- Ljungqvist, O., Scott, M., & Fearon, K. C. (2017). Enhanced recovery after surgery: A review. *JAMA Surgery*, 152(3), 292–298.
- Liu, X., Zhang, Y., Wang, H., et al. (2024). Effect of amino acid supplementation on short-term complications after gastrointestinal tumor surgery: The AMIGITS randomized clinical trial. *Clinical Nutrition*, 43(4), 890–898.
- Marano, L., Porfida, R., Pezzella, M., et al. (2024). Immunonutrition in operated gastric cancer patients: An update. *Biomedicines*, 12(12), 2876.
- Nicastro, H., Artioli, G. G., Costa, A., et al. (2014). Leucine supplementation accelerates connective tissue repair of injured skeletal muscle. *Journal of Nutrition*, 144(9), 1385–1391.
- Okamoto, Y., et al. (2022). Impact of amino acids nutrition following gastrectomy in gastric cancer patients. *Anticancer Research*, 42(7), 3637–3644.
- Popescu, G. A., Minca, D. G., et al. (2025). Multimodal prehabilitation in major abdominal surgery—rationale, modalities, results and limitations. *Medicina (Kaunas)*, 61(5), 908.
- Schricker, T., & Lattermann, R. (2015). Perioperative catabolism. *Canadian Journal of Anaesthesia*, 62(2), 182–193.
- Shimomura, Y., Kitauro, Y., Kadota, Y., et al. (2014). Branched-chain amino acids and muscle protein metabolism in humans: An update. *Nutrition Research Reviews*, 27(1), 1–15.
- Stechmiller, J. K. (2021). The effect of amino acids on wound healing: A systematic review and meta-analysis on arginine and glutamine. *Nutrients*, 13, 2840.
- Sugawara, K., Takahashi, S., et al. (2024). Early intravenous branched-chain amino acid-enriched nutrition supplementation in older patients undergoing gastric surgery: A randomized clinical trial. *Clinical Nutrition*, 43(5), 1021–1029.
- Tieland, M., Dirks, M. L., van der Zwaluw, N., et al. (2025). Pre-operative resistance training and amino acid supplementation in older adults undergoing surgery: A randomized trial. *Clinical Nutrition*, 44(1), 112–120.
- Tipton, K. D., et al. (2021). Pre- and post-surgical nutrition for preservation of muscle mass, strength, and functionality following orthopedic surgery. *Nutrients*, 13(5), 1675.
- Wall, B. T., et al. (2024). Selected nutrients to oppose muscle disuse following arthroscopic orthopedic surgery: A narrative review. *Nutrients*, 16, 1450.
- Weimann, A., Braga, M., Carli, F., et al. (2021). ESPEN practical guideline: Clinical nutrition in surgery. *Clinical Nutrition*, 40(7), 4745–4761.
- Weimann, A., Braga, M., Carli, F., et al. (2025). ESPEN guideline on clinical nutrition in surgery: Update 2025. *Clinical Nutrition*.
- Wilkinson, D. J., Hossain, T., Hill, D. S., et al. (2013). Effects of leucine and its metabolite β -hydroxy- β -methylbutyrate on human skeletal muscle protein metabolism. *Journal of*

- Physiology*, 591(11), 2911–2923.
- Wolfe, R. R. (2017). Branched-chain amino acids and muscle protein synthesis in humans: Myth or reality? *Journal of the International Society of Sports Nutrition*, 14, 30.
- Wu, G. (2013). Functional amino acids in growth, reproduction, and health. *Advances in Nutrition*, 4(1), 31–37.
- Yoshimura, Y., Wakabayashi, H., Yamada, M., et al. (2020). Impact of postoperative nutritional status on clinical outcomes following total knee arthroplasty. *Clinical Nutrition*, 39(3), 860–866.