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# Mini Review

# **Nutritional Interventions for Surgical Patients**

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#### ABSTRACT -

During a state of trauma, such as injury or surgery, the body's nutritional needs are expected to increase. The body enters a higher metabolic state and requires more energy, the immune system is weakened due to stress, and persistent inflammation delays full return to normal function. Surgical nutritional interventions have demonstrated that targeted nutrition can enhance outcomes in acute patients and chronic conditions. This paper reviews the state of the clinical evidence on nutrition as a remedy for improving musculoskeletal and surgical patient outcomes.

#### Keywords

Nutrition; Orthopedics; Cosmetic; Surgery; Outcomes; Supplementation; Healing; Recovery.

#### INTRODUCTION |

lobally, healthcare costs have increased in the last few de-Jcades, most notably in the United States-where healthcare costs have climbed to nearly a quarter of the Gross Domestic Product.<sup>1</sup> Each year an estimated 126.6 million American, one in every two adults, are affected by musculoskeletal conditions. This costs an estimated \$213 billion in annual treatments and in lost wages.<sup>2</sup> These costs are compounded by delays due to bruising and slow wound healing. New approaches in the field of musculoskeletal injury treatment and management are attempting to alleviate these treatment complications for reduced costs and improved patient outcomes. One area that is showing considerable promise is targeted nutrition. A rapidly expanding body of evidence suggests that surgical patient outcomes can be enhanced through supplementation with amino acids, protein and other natural compounds. Stressing the body, whether through exercise or trauma, increases metabolic demands as an adaptive response to energy utilization and recovery. During a state of trauma, such as injury or surgery, the body's nutritional needs are expected to increase. The body enters a higher metabolic state and requires more energy, the immune system is weakened due to stress, and persistent inflammation delays full return to normal function. Clinically, the metabolic consequences to stress response includes changes in energy expenditure, among other physical and behavioral complications. Evidence continues to support the use of clinical nutrition to improve healing and recovery, especially in musculoskeletal conditions.<sup>3-7</sup> This paper reviews the state of the clinical evidence on nutrition as a remedy for improving musculoskeletal and surgical patient outcomes.

Overall malnutrition or nutritional deficiencies impede the natural progression of healing. A study has shown that most Americans are not at optimal nutritional status to prevent complications post-trauma and that nearly 50% of patients are undernourished or malnourished.<sup>8</sup> Another study which involved 16,000 subjects reported that many Americans were not meeting the minimum recommended thresholds for micronutrient intake.9 It showed the percentages of American people who are deficient in some minerals and vitamins as follows: vitamin D, 93%; vitamin E, 91%; magnesium 55%; calcium 49%; vitamin A 45%; and vitamin C 37%. Thus, undernourished patients face greater complications than properly nourished patients, which include longer hospital stays, greater risk of infection, and increased mortality. The combination of increased baseline nutritional needs postinjury or surgery and prevalent undernourishment suggests that most Americans are not nutritionally equipped to heal optimally. In some enhanced recovery after surgery (ERAS) protocols, carbohydrate loading improves patient well-being and metabolism. Carbohydrate loading alone, however, is not currently recommended as an essential routine intervention because it has not shown evidence of accelerating discharge criteria or reducing surgical complications.<sup>10</sup> Thus, a more targeted, complete nutrition approach is required to optimize patient recovery and reduce healthcare costs.

Clinical trials on nutritional interventions in surgery demonstrated that targeted nutrition could enhance outcomes in patients of acute patients and chronic conditions. Enhanced wound healing, lowered inflammation response, increased muscle mass

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and strength, and decreased muscle atrophy are crucial recovery objectives for surgical patients, and nutrition has been shown to support these healing processes. To illustrate the concept of targeted nutrition approach in terms of surgical outcomes and wound healing, a representative sample of randomized clinical trials from the literature is presented to detail the key factors involved in a targeted nutrition.

## Vitamins and Amino Acids

Vitamins and essential amino acids (EAAs) play key roles in healing post-surgery. EAAs are a group of amino acids that humans cannot synthesize and must be supplied from an exogenous diet.<sup>11</sup> Patients given EAAs starting 7-days before surgery showed increased satellite cells on the day of surgery and a more favorable inflammatory environment post-surgery (operative leg p=0.03 for satellite cells/fiber and p=0.05 for satellite cell proportions for Type I-associated cells and p=0.05 for satellite cells/fiber for Type II-associated cells.), indicating that EAA ingestion before surgery reduces inflammation and improves healing.<sup>12</sup> In a double-blind, placebo-controlled, randomized trial on patients undergoing total knee arthroplasty (TKA), it was found that EAA supplementation (20 g/day) was a safe and effective method to reduce the loss of muscle volume in older adults recovering from TKA.3 These studies emphasize the importance of targeted nutritional supplements for muscle preservation and return to function-critical in any patient with a surgery that results in significant muscle atrophy such as anterior cruciate ligament reconstruction or anterior cruciate ligament (ACL) surgery. Essential amino acids are critical in this role due to their ability to enhance muscle protein synthesis, especially during acute inflammatory stages.<sup>13</sup> Non-essential amino acids are also crucial for surgical healing. One study found that the addition of glutamine supplementation in surgical patient care reduced infection rates and shortened the length of hospital stay. <sup>14</sup> Additionally, glutamine supplementation (~0.4 g/kg body weight/day) decreased the production of pro-inflammatory cytokines in this population; by decreasing inflammation, glutamine supplementation effectively improved the healing process.

Vitamins have also shown key benefits with regards to wound healing and reduction of inflammation and pain. A prospective double-blind, placebo-controlled pilot study found that supplementation of vitamin C and vitamin E, along with zinc was able to enhance protection against oxidative stress and reduce the time necessary for wound healing (p<0.001). This is a critical point, as it shows that nutrition plays a major part in preventing the adverse effects of the stress response. The combination of some of these key nutrients, for example combinations like glutamine, arginine, and omega-3 fatty acids, have been shown to improve recovery. <sup>16</sup>

The combination of EAAs and vitamins can have an additive benefit. In a study, thirteen-weeks of nutritional supplementation with Vitamin D and leucine-enriched whey protein attenuates the progression of chronic low-grade inflammatory profile in older sarcopenic persons with mobility limitations. This was shown partially by an overall decrease in IL-8 (p=0.03) after 13-weeks, a key cytokine involved in attracting and activating

neutrophils in inflammatory regions.<sup>17</sup>

Combinations including vitamins, EAAs, and other key ingredients like alpha lipoic acid (ALA), CoQ10, or resveratrol, similarly showed enhanced healing. Another study found that twice daily consumption of a mix containing EAA, creatine, vitamin D and ALA, coenzyme Q10 (CoQ10), and resveratrol for 12-weeks aids in sarcopenia prevention without physical exercise by improving muscle aging-related outcomes such as muscle mass, strength, and power.<sup>6</sup> This study involved 38 healthy, elderly subjects who were randomized and allocated into the supplement or placebo group. Significant improvements in vitamin D blood levels (+11,72 ng/ml; p<0.001), leg fat-free mass(+443.7 g; p < 0.05), appendicular lean mass (+0.53 kg; p < 0.05), maximal voluntary contraction (+1.38 kg; p<0.05) and peak power (+9.87 W; p < 0.05) were found in the supplement group compared to placebo. This type of study shows not only the physiological changes that occur after targeted nutritional combination supplementation, but also the types of functional improvements that are crucial factors in healing from surgery, especially for orthopedic conditions.

# **Other Key Ingredients**

**β-hydroxy β-methylbutyrate:** Whether used independently or in combination therapies, β-hydroxy β-methylbutyric acid (HMB) has been shown to promote wound healing and diminish muscle wasting in several studies. Elderly women treated for 12-weeks with a nutritional supplement containing HMB, arginine, and lysine had positively altered measurements of functionality, strength, and fat free mass (all p < 0.05).<sup>5</sup> At 12-weeks, there was also a 17% improvement in the "get-up-and-go" functionality test in the experimental group (-2.3  $\pm$ /- 0.5 s) but no change in the placebo group (0.0 +/- 0.5 s; p=0.002). This demonstrates both the functional metrics and the improvements in muscle mass possible by nutritional supplements. A double-blind, controlled 12-month study found that HMB in combination with Vitamin D had a significant benefit on lean body mass. Additionally, these patients showed improvement in knee extension peak torque versus controls even without an exercise regimen (p=0.04). Overall these findings showed that without exercise, the HMB and vitamin D supplemented group showed significant increases in functional outputs compared to those in the control group. Interestingly, HMB has also been shown to increase anabolic signaling and reduce muscle damage, while increasing muscle mass and strength. 18,19 Also, HMB has been suggested to directly stimulate protein synthesis, through an mechanistic target of rapamycin (mTOR) dependent mechanism.<sup>20</sup> With these enhanced functional outcomes, key targeted nutrients like HMB, are essential to consider in orthopedic and surgical nutritional interventions.

A combination of key ingredients in these nutritional therapies are essential to reduce inflammation and enhance healing. A randomized controlled study included 75 older female patients with hip fractures and investigated the effects of calcium HMB, vitamin D, and protein supplementation on wound healing and muscle strength. The study group received an enteral product containing 3 g Ca HMB, 1000 IU vitamin D, and 36 g

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protein, in addition to standard post-operative nutrition. Results indicated that patients on the supplement product demonstrated accelerated wound healing (p<0.05), shortened immobilization periods (p=0.001), and increased muscle strength (p=0.026) without changes in body mass index. This study also found reduced related complications after an orthopedic operation.<sup>4</sup>

There is a growing body of evidence suggesting that targeted nutritional supplements enriched with some of these specific nutrients can have a positive impact on those individuals under catabolic conditions. In hospitalized patients, supplementation with a high-protein oral nutrition supplement enriched with HMB was linked to significant improvements in patient related clinical outcomes. Another systematic review of randomized controlled trial (RCT) studies the effectiveness of HMB supplementation and found that HMB alone or in combination with amino acids, demonstrated a beneficial effect in mitigating loss of muscle mass and function in healthy older adults and those with various conditions.

#### **Proteases**

One key ingredient utilized in oral nutrition for wound healing in surgical procedures is the protease, bromelain. Proteases are enzymes that break down protein into amino acids. Bromelain, a protease derived from the pineapple plant, has clinical evidence supporting its use as an anti-inflammatory or analgesic, properties that qualify this protease as an adjunctive treatment for osteoarthritis.<sup>22</sup> One randomized, controlled double-blind clinical trial found that oral bromelain could be effective in pain reduction (p<0.05) and enhanced wound healing, without increasing the risk of postoperative bleeding.<sup>23</sup> Research has shown that bromelain can alter cell surface molecules involved in leukocyte homing, cell adhesion and activation thus, suggesting that bromelain is playing an anti-inflammatory role by multiple mechanisms.<sup>24</sup> Inflammation and slow wound healing are huge hurdles in surgical recovery. A randomized, crossover, placebo-controlled, clinical trial looked at patients given a forearm skin biopsy, along with an oral nutritional supplement containing proteases, antioxidants, and minerals versus placebo. This was to study wound healing. A 17% improvement in wound healing time in the treated group was attained, as compared to the control group (p<0.005). Also, wounds were less red, which has been associated with less inflammation.<sup>25</sup>

# CONCLUSION \_\_\_

In conclusion, a significant proportion of the surgical patient population is considered as being nutritionally compromised. With incidence of trauma, the body's nutritional needs increase above the normal requirements (baseline). An increasing body of scientific evidence suggests that targeted nutrition supplementation should be utilized in surgical patient care. Overall, such studies highlight the importance of nutritional supplementation in wound healing and surgical recovery. This awareness and utilization of nutritional regimens for trauma and surgical patients also can alleviate the high cost of medical care, in addition to the desirable outcomes. As more research studies and clinical trials are conducted, the significant role of nutrition in medical and

clinical care will be further emphasized.

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