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# The Role of Branched-Chain Amino Acid (BCAA) Supplementation in Sarcopenia among the Elderly

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**A B S T R A C T**

**Background:** Sarcopenia is a syndrome characterized by loss of skeletal muscle mass, strength, and skeletal muscle function that occurs as a result of aging. To maintain muscle mass, a dynamic balance is needed between muscle protein synthesis (MPS) and its breakdown. BCAAs, including leucine (Leu), isoleucine (Ile), and valine (Val), have been found to have important mediating effects in protein synthesis, glucose homeostasis. **Methods:** This literature review aims to explain further the role of BCAAs in sarcopenia. **Results:** Numerous studies have demonstrated the advantages of BCAAs for maintaining or improving skeletal muscle mass and performance in both healthy elderly people and those with other comorbidities. It was also shown that resistance training and vitamin D supplementation enhanced the benefits of BCAAs. **Conclusion:** There are still study results that contradict the role of BCAAs in sarcopenia, hence more research with homogeneity in supplementation dosage and outcome measurement methods is required in order to obtain stronger evidence to support its claims.

## 1. Introduction

Sarcopenia, characterized by the progressive loss of skeletal muscle mass, strength, and function, is a condition commonly associated with aging. Muscle mass is a critical determinant of muscle strength and is closely linked to the performance of daily activities and the level of independence among the elderly. Maintaining muscle mass requires a dynamic equilibrium between muscle protein synthesis (MPS) and its breakdown. Studies have indicated that older individuals exhibit a diminished MPS response to low doses of amino acids compared to younger counterparts. Consequently, adequate dietary protein intake, encompassing essential amino acids found in meat, poultry, fish, and dairy products, is crucial. This intake is necessary to prevent negative nitrogen balance, delay or inhibit sarcopenia progression, and maintain energy balance, physical function, and life quality.[1,2] The overall prevalence of sarcopenia is estimated to be between 6 and 22% among adults over 65, with variations across different healthcare settings and an increase with age. The number of elderly individuals with sarcopenia is expected to rise due to the rapid increase in the elderly population globally, with a slight male predominance. In Asia, using the 2014 criteria set by the Asia Working Group for Sarcopenia (AWGS) for diagnosing sarcopenia, prevalence rates range from 5.5 to 25.7%. However, when considering larger studies with sample sizes over 1000, the estimated prevalence narrows to between 7.3 and 12%.[3,4]

Nutrition plays a pivotal role in preventing sarcopenia in the elderly, with protein being one of the most crucial nutrients. Among the various amino acids, branched-chain amino acids (BCAAs) such as leucine (Leu), isoleucine (Ile), and valine (Val) are

essential amino acids that have significant roles in protein synthesis, glucose homeostasis, and nutrient signaling pathways like phosphoinositide 3-kinase-protein kinase B (PI3K-AKT) and mammalian target of rapamycin (mTOR), which are key regulators of protein synthesis and autophagy. BCAAs serve not only as substrates for protein synthesis but also stimulate protein synthesis and inhibit proteolysis. They have been studied in various diseases, including liver cirrhosis, renal failure, sepsis, trauma, burns, and cancer, and have been found to play roles in preventing or slowing the progression of sarcopenia. This literature review aims to further elucidate the role of BCAAs in sarcopenia.[1,5]

## 2. Methods

This study is a literature review focused on assessing the impact of branched-chain amino acids (BCAAs) on sarcopenia. The review process involved a comprehensive search for relevant studies using databases such as PubMed, ScienceDirect, Google Scholar, and ResearchGate, with the keywords "branched-chain amino acid" and "sarcopenia." The retrieved journal articles were meticulously analyzed by the authors. References within these articles were also reviewed to identify additional pertinent studies, which were included if they aligned with the research objective. The findings from these studies were then compiled and presented in a descriptive format.

## 3. Results and Discussion

### Sarcopenia overview

Sarcopenia, derived from the Greek words "Sarx" meaning flesh and "Penia" for loss, refers to the reduction in muscle mass and function that occurs with aging. Defined as a progressive and age-related skeletal muscle disorder, sarcopenia encompasses the loss of muscle mass, strength, and/or a decline in physical performance. Since 2016, the International Statistical Classification of Diseases and Related Health Problems (ICD) by the World Health Organization (WHO) has recognized sarcopenia as a disease, designated by the ICD-10-CM code M62.84. Sarcopenia is an inevitable part of the aging process, though its severity can vary significantly based on certain risk factors, including a sedentary lifestyle, hormonal imbalances (involving growth factors, testosterone, thyroid hormones, and insulin-like growth factor-1 (IGF-1)), cytokines, and a decrease in protein synthesis due to inadequate intake or lack of physical activity. In sarcopenia, the increased oxidation of proteins in skeletal muscle with age leads to the accumulation of lipofuscin and cross-linked proteins not adequately cleared by the proteolysis system, resulting in the buildup of non-contractile dysfunctional proteins in skeletal muscle. This accumulation is one of the reasons for the significant decline in muscle strength observed in sarcopenia.[6,7] Currently, there are no pharmacological treatments available that can cure sarcopenia. However, physical activities, particularly resistance training, have been shown to effectively reduce muscle mass loss and increase strength in sarcopenic conditions, thus helping to prevent and manage the syndrome. Additionally, enhancing total protein intake through supplementation or dietary sources has been found to aid in the prevention and management of sarcopenia. Elderly individuals are advised to consume 1-1.5 grams of protein per day to prevent sarcopenia, as this amount provides sufficient amino acid content to maximize muscle protein synthesis (MPS).[8,9]

### Branched chain amino acids (BCAA)

Amino acids are the primary nutritional source for protein synthesis. Among them, branched chain amino acids (BCAAs), including leucine (Leu), isoleucine (Ile), and valine (Val), play a crucial role as nutritional signals with significant impacts on protein synthesis, glucose homeostasis, anti-obesity effects, and nutrient-sensitive signaling pathways. Isoleucine, an essential amino acid encoded by the codons AUU, AUC, and AUA, possesses a hydrophobic side chain and chirality in its side chain structure. Leucine, another essential hydrophobic branched-chain amino acid, is unique in directly stimulating muscle protein synthesis. It is encoded by six codons: UUA, UUG,

CUU, CUC, CUA, and CUG. Valine, a non-polar essential amino acid synthesized in plants, is encoded in the genetic code by the codons GUU, GUC, GUA, and GUG. These BCAAs are integral to various physiological processes, underscoring their importance in nutrition and metabolic regulation.[4,9]

**BCAA mechanism in sarcopenia**

In muscle tissue, branched chain amino acids (BCAAs) serve as vital energy substrates and precursors for other amino acids, playing a significant role in promoting protein synthesis. BCAAs are instrumental in reducing muscle damage and enhancing protein synthesis through the regulation of the mTOR pathway. While most amino acids are metabolized in the liver, BCAAs are primarily catabolized in extrahepatic tissues such as muscle, adipose tissue, kidneys, and the brain. This catabolism initiates through a transamination reaction with alpha-ketoglutarate to form glutamate and branched-chain keto acids (BCKAs), subsequently transforming glutamate into glutamine via glutamine synthetase enzyme action. Glutamine functions in various critical roles, including muscle protein synthesis, maintaining renal acid-base balance, glutathione production, heat shock protein expression, and detoxifying tissues of ammonia. Oxidative damage triggers inflammatory processes contributing to muscle mass catabolism through oxidative stress, activating heat shock proteins, and decreasing glutathione axis, which can be mitigated by BCAA supplementation to lower muscle lysis risk.[10,11]

**BCAA studies on sarcopenia**

Research has demonstrated a strong association between low BCAA concentrations, particularly leucine and isoleucine, and low protein intake with sarcopenia incidence among elderly individuals in nursing homes. Various global studies have highlighted BCAAs' beneficial effects on sarcopenia, including clinical trials showing significant muscle function improvements, such as increased grip strength, gait speed, and skeletal mass index, after BCAA supplementation. Studies also indicate that BCAA intake, especially when combined with dietary protein sources like milk protein, significantly enhances myofibrillar protein synthesis post-prandially. In addition to skeletal effects, BCAA supplementation has been found to benefit inflammatory processes, indicated by reduced cytokine levels such as IL-6 and TNF-alpha.[9] BCAAs synergize with resistance training, enhancing cardiometabolic health markers like LDL, serum insulin, and HDL cholesterol. Their effects have also been studied in sarcopenic patients with other conditions, showing significant improvements in muscle strength and functionality. However, not all studies report consistent benefits of BCAAs on sarcopenia, with some findings contradicting the effectiveness of BCAAs in muscle mass preservation and insulin sensitivity enhancement. These discrepancies may be attributed to factors like supplementation dosage, outcome measurement methods, etc., underscoring the need for further clinical trials and analysis of BCAAs in diverse elderly populations with varying comorbidities and potential BCAA effect alterations under specific conditions.[12]

**Clinical practice**

Branched chain amino acids (BCAAs) constitute approximately 15–25% of the amino acids found in common food sources, with milk protein (26%), eggs (22%), and maize (21%) being particularly rich in BCAAs. The current guidelines by the World Health Organization/Food and Agriculture Organization/United Nations University recommend a total BCAA intake of 85 mg per kg body weight per day for a healthy adult population, broken down as 39 mg/kg for leucine, 20 mg/kg for isoleucine, and 26 mg/kg for valine. Research indicates that to achieve the threshold dose of 3 g of leucine for optimal muscle protein synthesis (MPS) stimulation, 25-30 g of high-quality protein should be consumed per meal. For the elderly, it is recommended to consume protein in the range of 1 – 1.2 grams per kg body weight per day to meet these needs, with primary sources of BCAAs

including chicken, fish, cottage cheese, lentils, sesame, and peanuts. The safety and efficacy of consuming protein at levels of 1.4 grams per kg body weight or higher in the elderly population have been explored. However, it remains unclear whether protein needs should be elevated in the elderly to maintain nitrogen balance and prevent the loss of muscle mass and strength.[13,14]

**4. Conclusion**

BCAAs are crucial nutritional components in maintaining muscle protein synthesis in the elderly. Nutritional supplementation with BCAAs can be considered in clinical practice for both healthy elderly individuals and those with comorbid diseases, within the recommended dosage. Further research is needed, with a focus on dosage uniformity and outcome measurement methods, to strengthen the evidence base, given the existence of studies that contest the role of BCAAs in sarcopenia.

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