

Original Research



Association between dietary branched-chain amino acid intake and skeletal muscle mass index among Korean adults: Interaction with obesity

Minjeong Chae ¹, Hyoung Su Park ², and Kyong Park ^{1§}

¹Department of Food and Nutrition, Yeungnam University, Gyeongsan 38541, Korea

²Health & Nutrition R&D Group, Maeil Dairies Co., Ltd, Pyeongtaek 17714, Korea



Received: Jul 8, 2020

Revised: Sep 7, 2020

Accepted: Oct 27, 2020

§Corresponding Author:

Kyong Park

Department of Food and Nutrition, Yeungnam University, 280 Daehak-ro, Gyeongsan 38541, Korea.

Tel. +82-53-810-2879

Fax. +82-53-810-4666


E-mail. kypark@ynu.ac.kr

©2021 The Korean Nutrition Society and the Korean Society of Community Nutrition
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.


ORCID iDs

Minjeong Chae 

<https://orcid.org/0000-0003-3981-5322>

Hyoung Su Park 

<https://orcid.org/0000-0001-7205-1366>

Kyong Park 

<https://orcid.org/0000-0002-4681-1584>

Funding

This research was supported by the Bio & Medical Technology Development Program (grant No. 2018M3A9F3081356) and Basic Science Research Program (grant No. 2017R1A1A3A04069759) through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning.

ABSTRACT

BACKGROUND/OBJECTIVES: The branched-chain amino acids (BCAA), including isoleucine, leucine, and valine, promote muscle protein synthesis. However, obesity may interfere with protein synthesis by dysregulating mitochondrial function in the muscles. This study aimed to examine the association between dietary intake levels of BCAA and skeletal muscle mass index (SMI) in middle-aged participants, and the effect of obesity/abdominal obesity on this association.

SUBJECTS/METHODS: The data of 3,966 men and women aged 50–64 years who participated in the 2008–2011 Korea National Health and Nutrition Examination Survey were analyzed. Intake levels of energy-adjusted dietary amino acids were obtained using a 24-hour dietary recall. SMI was calculated by dividing the appendicular skeletal muscle mass by body weight (kg) and multiplying the result by 100%. Multivariable general linear models were used to analyze the association of dietary BCAA intake levels with SMI.

RESULTS: The beneficial effects of energy-adjusted dietary BCAA intakes on SMI were greater in the non-obesity/non-abdominal obesity groups; however, no significant associations were observed in the obesity/abdominal obesity groups ($P > 0.05$).

CONCLUSIONS: Healthy weight and sufficient intake of dietary BCAA are recommended to maintain muscle mass.

Keywords: Branched-chain amino acids; leucine; skeletal muscle; obesity; Koreans

INTRODUCTION

Muscle loss has been reported to progress gradually after the age of 50 years and accelerate after the age of 70 years [1]. Age-related loss of skeletal muscle mass has been associated with health problems such as decreased physical activity [2], increased risk of fractures and falls [3], and mortality [4]. The Hertfordshire Cohort Study in the United Kingdom estimated that the health and social care costs of skeletal muscle weakness are approximately £2.5 billion per year, and that its economic burden will continue to increase [5]. In particular, muscle loss progresses gradually over a period of several years, which provides an opportunity for active prevention and management at the individual and national levels in the middle-aged population [6].

Conflict of Interest

The authors declare no potential conflicts of interests.

Author Contributions

Conceptualization: Chae M, Park H, Park K;
 Data curation: Chae M; Formal analysis: Chae M;
 Methodology: Chae M, Park K; Software: Chae M;
 Supervision: Park K; Validation: Park H, Park K;
 Visualization: Park H, Park K; Writing - original draft: Chae M;
 Writing - review & editing: Park H, Park K.

Muscle synthesis can be influenced by dietary habits and obesity [6]; it can especially be affected by protein and amino acid intakes. Leucine, a branched-chain amino acid (BCAA), has been reported to play a role in promoting the synthesis of muscle proteins [7,8]. According to a meta-analysis, the muscle protein fractional synthetic rate increased in people receiving leucine supplementation [9]. In contrast, obesity is associated with mitochondrial dysfunction in the muscles, which can lead to decreased muscle protein synthesis [10-13]. In addition, obesity-associated insulin resistance can promote muscle protein catabolism that results in muscle loss [14]. The United States National Health and Nutrition Examination Survey study analyzed the association between dietary protein intake and skeletal muscle mass index (SMI) by categorizing participants aged over 50 years into obesity and non-obesity groups [15]. The results showed that high dietary protein intake was associated with high SMI in the non-obesity group; however, there was no significant association in the obesity group. Thus, we hypothesized that the association between amino acid intake levels and SMI may vary depending on the weight status, which influences muscle synthesis.

Most previous studies analyzing the effect of dietary amino acid intakes on muscle mass have been conducted in the United States and Europe; however, limited studies have been conducted in the Korean population, with relatively low protein intake levels compared to the Western population [16-18]. In addition, previous studies were primarily focused on the elderly population, and they showed insufficient consideration regarding potential confounding factors and effect modifiers of the association between dietary protein intake and sarcopenia [19]. Protein synthesis rate varies with aging; thus, it is assumed that amino acid intakes may have more beneficial effects in the middle-aged and pre-elderly adults than in the elderly [20].

Therefore, this study aimed to analyze the association between dietary BCAA intake and SMI in the middle-aged and pre-elderly adults aged 50–64 years in Korea, while considering the effect of obesity status, which may be a potential effect modifier of this association.

SUBJECTS AND METHODS

Study population

The Korea National Health and Nutrition Examination Survey (KNHANES), a nationwide representative cross-sectional study was initiated in 1998 (I), and has been regularly conducted thereafter. It was initially conducted at intervals of 3–4 years; from 2007, an annual survey with a rolling sample that is generated every 3 years to avoid seasonal bias has been used. The KNHANES includes health interviews, health examinations, and nutrition surveys. A detailed description of the data collection procedures and survey design are described in a previous study [21].

This study analyzed data from the 2008–2011 KNHANES, during which appendicular skeletal muscle mass (ASM) variables were evaluated. A total of 37,753 participants completed the survey, and the exclusion criteria were as follows: 1) < 50 or > 65 years of age (n = 30,441); 2) total energy intake < 500 or > 5,000 kcal/day (n = 809) [22]; 3) diagnosis of cancer or cardiovascular disease (n = 512); and 4) missing dietary amino acid and lean body mass variables (n = 2,025). Finally, 3,966 participants were included in this study, and all of them provided written informed consent. The study followed the guidelines of the Declaration of

Helsinki and was approved by the Institutional Review Board of the Korea Centers for Disease Control and Prevention (approval No. 2008-04EXP-01-C, 2009-01CON-03-2C, 2010-02CON-21-C, and 2011-02CON-06-C).

Demographic and lifestyle information

Data on health behavior, such as smoking, physical activity, and alcohol consumption, were collected via a self-administered questionnaire, and demographic information on sex, age, income, and education level was collected through interviews [21]. Education level was classified as less than high school graduation or as high school graduation or higher, and income level was divided into 4 quartiles based on the equalized household income. Information on the frequency and duration of high intensity, moderate, or walking levels of physical activity were estimated per week. Then, metabolic equivalents were calculated by multiplying weighted values according to the intensity of physical activity [23] and dividing them into tertiles. Smoking status was classified as non-smoker and current smoker. Alcohol consumption status was defined as non-drinker and drinker.

Anthropometry and dietary assessment

Anthropometric measurements of participants with shoes and socks removed were taken by trained investigators. Height and weight were measured in an upright position, using a standardized height and weight scale. Waist circumference (WC) was measured at the midpoint between the bottom of the least palpable rib and the top of the iliac crest using a stretch-resistant tape. Body mass index was calculated by dividing the body weight (kg) by the squared height (m^2). Obesity status was classified as non-obesity ($< 25 \text{ kg}/m^2$) and obesity ($\geq 25 \text{ kg}/m^2$), and abdominal obesity was defined as WC ≥ 90 cm in men and ≥ 80 cm in women based on the World Health Organization criteria for Asian populations [24].

For dietary information, 24-hour recall data were used. Trained interviewers surveyed dietary behavior, and to determine food and beverage intakes, supplementary tools such as measuring cups, measuring spoons, and a tape measure were used to improve recall. The data were converted into individual food intakes using the food recipe database [25], and the food composition table [26] was used to calculate the nutrient intake. In this study, the total energy intake was analyzed.

A total of 2,071 food items were selected from the 24-hour recall data. A dietary amino acid database was constructed using the Computer Aided Nutritional analysis program (CAN-Pro) [27]. The detailed process of the development of the amino acid database has been explained in a previous study [28]. The daily individual amino acids intake (g/day) was calculated by multiplying the amino acid content per 100 g of food by the individual daily food intake. Additionally, we analyzed the intake levels of BCAA, including leucine, isoleucine, and valine [29,30].

Calculation of SMI

ASM was calculated by excluding the bone and fat weights from the arm and leg weights measured using dual energy X-ray absorptiometry. SMI was calculated by dividing the ASM by body weight and multiplying the result by 100 [31].

Statistical analysis

Stratification variables and a primary sampling unit were used, considering the complex sampling design of the KNHANES. Appropriate weights for the health interview, health

examinations, and nutrition surveys were used. Multivariable linear regression analysis was used to examine the association between BCAA intake and SMI, and the effect modifiers and potential confounding factors that could affect this association were selected through a preliminary analysis and literature search [15,16,32]. Nutrient intake levels were adjusted for total energy intake using the residual method [33]. We built 3 covariate models: model 1 was unadjusted; model 2 was adjusted for sex, age, household income, education level, alcohol consumption, smoking status, and physical activity; and model 3 was additionally adjusted for intake levels of non-BCAA. Statistical significance was indicated by $\alpha = 0.05$ using 2-tailed tests; statistical analysis was performed using Statistical Analysis System ver. 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

General characteristics of participants by obesity status

Characteristics of the study participants according to obesity status are presented in **Table 1**. In the non-obesity and obesity groups, the proportions of men were 40.9% and 42.0% and the average ages were 56.8 ± 0.09 and 56.8 ± 0.11 years, respectively. More than half of the participants reported that they consumed alcohol, while the current smoking rates were very low (15–19%). The average levels of SMI were $28.4 \pm 0.08\%$ and $26.6 \pm 0.11\%$ in the non-obesity and obesity groups, respectively.

BCAA intake levels by obesity/abdominal obesity status

Table 2 presents the intake levels of dietary BCAA according to obesity and abdominal obesity status. There were no significant differences in dietary intake levels of BCAA, isoleucine, leucine, and valine according to obesity and abdominal obesity status ($P > 0.05$).

Table 1. Characteristics of the participants according to obesity status

Characteristics	Non-obesity (n = 2,489)	Obesity ¹⁾ (n = 1,477)	P-value ²⁾
Male	1,019 (40.9)	620 (42.0)	0.5
Age (yrs)	56.8 ± 0.09	56.8 ± 0.11	0.9
Physical activity level (METs-h/week) ³⁾			0.9
Low	843 (34.1)	503 (34.2)	
Middle	801 (32.4)	482 (32.7)	
High	829 (33.5)	488 (33.1)	
Waist circumference	79.1 ± 0.13	90.6 ± 0.18	< 0.001
BMI (kg/m ²)	22.4 ± 0.05	27.2 ± 0.04	< 0.001
Education level			< 0.001
Less than high school graduation	1,422 (57.5)	946 (64.4)	
High school graduation or higher	1,051 (42.5)	523 (35.6)	
Household income			< 0.001
Low	576 (23.4)	377 (25.7)	
Mid-low	592 (24.0)	402 (27.4)	
Mid-high	658 (26.7)	339 (23.1)	
High	640 (26.0)	348 (23.7)	
Current smoker	486 (19.6)	229 (15.5)	0.001
Alcohol drinker	1,665 (67.5)	1,022 (69.7)	0.2
SMI (%)	28.4 ± 0.08	26.6 ± 0.11	< 0.001

Values are expressed as mean \pm SE or number (%).

METs-h/week, metabolic equivalents-hours per week; SMI, skeletal muscle mass index; BMI, body mass index.

¹⁾Obesity status was categorized as follows: non-obesity, BMI < 25 kg/m²; obesity, BMI \geq 25 kg/m².

²⁾P-values were derived from the χ^2 test for categorical variables and from a general linear regression analysis for continuous variables.

³⁾Physical activity was categorized into 3 groups, according to the tertiles of METs-h/week.

Table 2. Energy-adjusted intake levels of branched-chain amino acids according to obesity/abdominal obesity status

Variables	Non-obesity (n = 2,489)	Obesity ¹⁾ (n = 1,477)	P-value ²⁾	Non-abdominal obesity (n = 2,638)	Abdominal obesity ³⁾ (n = 1,321)	P-value ²⁾
Branched-chain amino acid (g/day)	9.5 ± 0.07	9.4 ± 0.09	0.2	9.5 ± 0.07	9.4 ± 0.09	0.1
Isoleucine (g/day)	2.4 ± 0.02	2.3 ± 0.02	0.2	2.4 ± 0.02	2.3 ± 0.02	0.1
Leucine (g/day)	4.0 ± 0.03	3.9 ± 0.04	0.2	4.0 ± 0.03	3.9 ± 0.04	0.1
Valine (g/day)	3.2 ± 0.02	3.1 ± 0.03	0.2	3.2 ± 0.02	3.1 ± 0.03	0.4

Values are expressed as mean ± SE.
BMI, body mass index.

¹⁾Obesity status was categorized as follows: non-obesity, BMI < 25 kg/m²; obesity, BMI ≥ 25 kg/m².

²⁾P-values were derived from a general linear regression analysis.

³⁾Abdominal obesity was defined as waist circumference ≥ 80 cm in women and ≥ 90 cm in men.

Association between BCAA intake levels and SMI by obesity status

The associations between dietary BCAA intakes and SMI were analyzed according to obesity status and the results are presented in **Table 3**. Intakes of BCAA ($P = 0.6$), isoleucine ($P = 0.6$), and leucine ($P = 0.8$) were not significantly associated with SMI in the obesity group. Conversely, we observed positive associations of BCAA ($P = 0.02$), isoleucine ($P = 0.03$), and leucine ($P = 0.005$) intakes with SMI in the non-obesity group, and these associations were stronger and significant. Valine intake was not significantly associated with SMI, regardless of obesity status.

Association between BCAA intake levels and SMI by abdominal obesity status

Table 4 shows the association between dietary BCAA and SMI according to abdominal obesity status. Similarly, as in the analysis stratified by obesity status, BCAA ($P = 0.001$), isoleucine ($P < 0.001$), leucine ($P < 0.001$) and valine ($P = 0.02$) intakes in the non-abdominal obesity group were associated with high SMI, while no significant association was observed in the abdominal obesity group.

Table 3. Multiple regression analysis for the association between energy-adjusted intake levels of branched-chain amino acids and skeletal muscle mass index stratified by obesity status

Variables	Non-obesity (n = 2,489)		Obesity ¹⁾ (n = 1,477)		Total (n = 3,966)	
	β-coefficient	P-value	β-coefficient	P-value	β-coefficient	P-value
Branched-chain amino acid (g/day)						
Model 1	0.019	0.6	0.084	0.04	0.047	0.1
Model 2	-0.015	0.4	-0.031	0.2	-0.016	0.3
Model 3	0.139	0.02	-0.042	0.6	0.089	0.1
Isoleucine (g/day)						
Model 1	0.036	0.8	0.314	0.04	0.153	0.1
Model 2	-0.060	0.4	-0.119	0.2	-0.063	0.3
Model 3	0.495	0.03	-0.162	0.6	0.326	0.1
Leucine (g/day)						
Model 1	0.030	0.7	0.193	0.02	0.096	0.1
Model 2	-0.034	0.4	-0.065	0.2	-0.036	0.3
Model 3	0.449	0.005	-0.052	0.8	0.290	0.1
Valine (g/day)						
Model 1	0.124	0.3	0.262	0.1	0.188	0.04
Model 2	-0.044	0.5	-0.044	0.5	-0.050	0.3
Model 3	0.230	0.1	-0.128	0.4	0.145	0.3

Data calculated using 3 following models: model 1, unadjusted; model 2, adjusted for sex, age, household income, education level, alcohol consumption, smoking status, and physical activity; model 3, additionally adjusted for intake levels of non-branched chain amino acids.

BMI, body mass index.

¹⁾Obesity status was categorized as follows: non-obesity, BMI < 25 kg/m²; obesity, BMI ≥ 25 kg/m².

Table 4. Multiple regression analysis for the association between energy-adjusted intake levels of branched-chain amino acids and skeletal muscle mass index stratified by abdominal obesity status

Variables	Non-abdominal obesity (n = 2,638)		Abdominal obesity ¹⁾ (n = 1,321)		Total (n = 3,966)	
	β-coefficient	P-value	β-coefficient	P-value	β-coefficient	P-value
Branched-chain amino acid (g/day)						
Model 1	0.039	0.2	0.056	0.2	0.047	0.1
Model 2	-0.026	0.1	-0.018	0.5	-0.016	0.3
Model 3	0.180	0.001	0.005	0.9	0.089	0.1
Isoleucine (g/day)						
Model 1	0.110	0.3	0.219	0.2	0.153	0.1
Model 2	-0.103	0.1	-0.070	0.5	-0.063	0.2
Model 3	0.647	< 0.001	0.034	0.9	0.326	0.1
Leucine (g/day)						
Model 1	0.072	0.3	0.124	0.2	0.096	0.1
Model 2	-0.060	0.1	-0.041	0.5	-0.036	0.2
Model 3	0.531	< 0.001	0.028	0.9	0.290	0.1
Valine (g/day)						
Model 1	0.195	0.1	0.174	0.2	0.188	0.04
Model 2	-0.076	0.2	-0.060	0.5	-0.050	0.3
Model 3	0.330	0.02	-0.004	0.9	0.145	0.3

Data calculated using 3 following models: model 1, unadjusted; model 2, adjusted for sex, age, household income, education level, alcohol consumption, smoking status, and physical activity; model 3, additionally adjusted for intake levels of non-branched chain amino acids.

¹⁾Abdominal obesity was defined as waist circumference ≥ 80 cm in women and ≥ 90 cm in men.

DISCUSSION

In this cross-sectional study of middle-aged Koreans, higher dietary intake levels of BCAA, isoleucine, and leucine were significantly correlated with higher levels of SMI. However, these correlations were counteracted by obesity and abdominal obesity. The positive correlations of dietary BCAA intakes with SMI were shown to be stronger in the non-obesity/non-abdominal obesity groups; however, these correlations became weak and non-significant in the obesity/abdominal obesity groups.

Our study showed that the beneficial effects of dietary BCAA intake on SMI were greater in the non-obesity group, compared to the obesity group. This may be attributed to insulin resistance and mitochondrial dysfunction in the muscles. BCAA and leucine have also been reported to increase adenosine triphosphate (ATP) production in the mitochondria [34], thereby promoting muscle protein synthesis [9]. However, excessive body fat is associated with mitochondrial dysfunction in the muscles [10], and this can lead to decreased muscle protein synthesis [11]. In a clinical study of Americans, increased plasma amino acid concentrations enhanced ATP production in lean individuals but not in obese individuals [12]. It was thought that the muscle synthesis function of BCAA might have been inhibited by mitochondrial dysfunction in the obesity group. In addition, obesity is associated with low-grade inflammation of the adipose tissue [35]. Adipose tissue secretes inflammatory cytokines, including interleukin-6 and tumor necrosis factor-α, which can lead to insulin resistance [35], and obesity-induced insulin resistance can promote muscle catabolism that results in muscle loss [14]. A cross-sectional study of adults aged over 20 years in the United States described a negative association between SMI and insulin resistance [32]. In addition, the Korean Sarcopenic Obesity Study, which included healthy adults over 20 years of age, showed that high-sensitivity C-reactive protein and homeostasis model assessment of insulin resistance (HOMA-IR) levels were negatively correlated with SMI [36]. Furthermore, HOMA-IR levels were higher in the group with visceral obesity and sarcopenia than in the group without these conditions [36]. Thus, mitochondrial dysfunction and insulin

resistance in our participants with obesity may have masked any positive effect of dietary BCAA intake on SMI.

As a BCAA, leucine activates mammalian target of rapamycin complex 1 (mTORC1), a protein kinase involved in intracellular signaling [37]. Activated mTORC1 increases protein synthesis in the skeletal muscle by regulating mRNA translation through the phosphorylation of ribosomal protein S6 kinase 1 (S6K1) and eukaryotic initiation factor 4E-binding protein-1 (4E-BP1) [38]. Experimental studies have indicated that isoleucine enhances the phosphorylation of S6K1 and 4E-BP1, which is required for protein biosynthesis, in the skeletal muscle [39]. Therefore, the results of this study could be due to the synergistic effect of leucine and isoleucine [40]. However, previous studies on the mechanisms underlying the role of isoleucine and valine in protein synthesis of skeletal muscle are limited, and further studies are required. According to a cross-sectional study conducted in Norway, sarcopenia was associated with low plasma concentrations of BCAA, isoleucine, and leucine [41]. In a recent clinical study conducted in Japan, BCAA supplement intake was shown to improve muscle strength and muscle mass in adults with sarcopenia aged 65 years and older [42]. A meta-analysis of eight clinical studies also reported that BCAA intake improved muscle function by reducing the concentration of creatine kinase (a muscle damage marker), and reduced muscle soreness [43].

According to a randomized controlled trial of Korean participants, ASM and SMI were higher in the group receiving an additional 1.5 g/kg/day of protein powder while maintaining a usual diet than in the groups receiving 0.8 and 1.2 g/kg/day of protein powder [44]. However, in this study, dietary protein intake was not associated with muscle index, and this may be a result of the Korean plant protein-based dietary habits. According to a study on Korean participants, plant proteins, such as those from grains, had the highest contribution to protein intake [16,28]. A cross-sectional study of middle-aged Americans analyzed the association between the type of protein intake and muscle mass [45]. They found that there was a positive correlation between animal protein intake and muscle mass index, but no significant correlation was found with total protein or plant protein intake. Plant proteins were reported to contain lower levels of essential amino acids such as leucine, methionine, lysine, and tryptophan than animal proteins [46]. Nevertheless, the mechanism underlying the effect of plant protein-based dietary habits on SMI is unclear, and further research is required to investigate this association.

There are several limitations to this study. First, the KNHANES is a cross-sectional study that did not clarify the causal relationship between dietary BCAA intake and SMI. Second, since this study estimated amino acid intake using a 24-hour recall, the obtained data may not reflect the usual diet. However, using standardized protocols, trained interviewers conducted nutrition surveys, and quality control and operational support were provided [47]. Third, unmeasured or unknown confounding factors that can affect skeletal muscle mass, such as the use of supplements and strength activities, may have been presented. Fourth, because of the limitations in the CAN-Pro database, this study did not include the amino acid content values for all foods consumed by the participants; thus, we may have underestimated the actual intake. However, in this study, the amino acid content was calculated by applying a conversion factor for similar foodstuffs to compensate for this limitation.

In conclusion, there was a significant positive association between the intake of dietary BCAA and SMI among the middle-aged and pre-elderly adults in Korea. This association was also observed in the non-obesity group. A clinical or prospective cohort study in the Korean

population should be conducted to examine the effects of other potential confounders (e.g., resistance, aerobic exercise) and supplemental intakes of amino acids.

REFERENCES

1. Grimby G, Saltin B. The ageing muscle. *Clin Physiol* 1983;3:209-18.
[PUBMED](#) | [CROSSREF](#)
2. Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: a symptom score to predict persons with sarcopenia at risk for poor functional outcomes. *J Cachexia Sarcopenia Muscle* 2016;7:28-36.
[PUBMED](#) | [CROSSREF](#)
3. Baumgartner RN, Koehler KM, Gallagher D, Romero L, Heymsfield SB, Ross RR, Garry PJ, Lindeman RD. Epidemiology of sarcopenia among the elderly in New Mexico. *Am J Epidemiol* 1998;147:755-63.
[PUBMED](#) | [CROSSREF](#)
4. Atkins JL, Whincup PH, Morris RW, Lennon LT, Papacosta O, Wannamethee SG. Sarcopenic obesity and risk of cardiovascular disease and mortality: a population-based cohort study of older men. *J Am Geriatr Soc* 2014;62:253-60.
[PUBMED](#) | [CROSSREF](#)
5. Pinedo-Villanueva R, Westbury LD, Syddall HE, Sanchez-Santos MT, Dennison EM, Robinson SM, Cooper C. Health care costs associated with muscle weakness: a UK population-based estimate. *Calcif Tissue Int* 2019;104:137-44.
[PUBMED](#) | [CROSSREF](#)
6. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, Cooper C, Landi F, Rolland Y, Sayer AA, Schneider SM, Sieber CC, Topinkova E, Vandewoude M, Visser M, Zamboni M, Bautmans I, Baeyens JP, Cesari M, Cherubini A, Kanis J, Maggio M, Martin F, Michel JP, Pitkala K, Reginster JY, Rizzoli R, Sánchez-Rodríguez D, Schols J; Writing Group for the European Working Group on Sarcopenia in Older People 2 (EWGSOP2), and the Extended Group for EWGSOP2. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing* 2019;48:16-31.
[PUBMED](#) | [CROSSREF](#)
7. Tischler ME, Desautels M, Goldberg AL. Does leucine, leucyl-tRNA, or some metabolite of leucine regulate protein synthesis and degradation in skeletal and cardiac muscle? *J Biol Chem* 1982;257:1613-21.
[PUBMED](#)
8. Damodaran S. *Fennema's Food Chemistry*. 4th ed. Boca Raton (FL): CRC Press; 2008. p.217-329.
9. Xu ZR, Tan ZJ, Zhang Q, Gui QF, Yang YM. The effectiveness of leucine on muscle protein synthesis, lean body mass and leg lean mass accretion in older people: a systematic review and meta-analysis. *Br J Nutr* 2015;113:25-34.
[PUBMED](#) | [CROSSREF](#)
10. de Mello AH, Costa AB, Engel JDG, Rezin GT. Mitochondrial dysfunction in obesity. *Life Sci* 2018;192:26-32.
[PUBMED](#) | [CROSSREF](#)
11. Andreux PA, van Diemen MPJ, Heezen MR, Auwerx J, Rinsch C, Groeneveld GJ, Singh A. Mitochondrial function is impaired in the skeletal muscle of pre-frail elderly. *Sci Rep* 2018;8:8548.
[PUBMED](#) | [CROSSREF](#)
12. Kras KA, Hoffman N, Roust LR, Patel SH, Carroll CC, Katsanos CS. Plasma amino acids stimulate uncoupled respiration of muscle subsarcolemmal mitochondria in lean but not obese humans. *J Clin Endocrinol Metab* 2017;102:4515-25.
[PUBMED](#) | [CROSSREF](#)
13. Heo JW, No MH, Park DH, Kang JH, Seo DY, Han J, Neuffer PD, Kwak HB. Effects of exercise on obesity-induced mitochondrial dysfunction in skeletal muscle. *Korean J Physiol Pharmacol* 2017;21:567-77.
[PUBMED](#) | [CROSSREF](#)
14. Goodpaster BH, Brown NF. Skeletal muscle lipid and its association with insulin resistance: what is the role for exercise? *Exerc Sport Sci Rev* 2005;33:150-4.
[PUBMED](#) | [CROSSREF](#)
15. Morris MS, Jacques PF. Total protein, animal protein and physical activity in relation to muscle mass in middle-aged and older Americans. *Br J Nutr* 2013;109:1294-303.
[PUBMED](#) | [CROSSREF](#)
16. Park HA. Adequacy of protein intake among Korean elderly: an analysis of the 2013–2014 Korea National Health and Nutrition Examination Survey data. *Korean J Fam Med* 2018;39:130-4.
[PUBMED](#) | [CROSSREF](#)

17. Berner LA, Becker G, Wise M, Doi J. Characterization of dietary protein among older adults in the United States: amount, animal sources, and meal patterns. *J Acad Nutr Diet* 2013;113:809-15.
[PUBMED](#) | [CROSSREF](#)
18. Oh C, Jeon BH, Reid Storm SN, Jho S, No JK. The most effective factors to offset sarcopenia and obesity in the older Korean: physical activity, vitamin D, and protein intake. *Nutrition* 2017;33:169-73.
[PUBMED](#) | [CROSSREF](#)
19. Son J, Yu Q, Seo JS. Sarcopenic obesity can be negatively associated with active physical activity and adequate intake of some nutrients in Korean elderly: findings from the Korea National Health and Nutrition Examination Survey (2008–2011). *Nutr Res Pract* 2019;13:47-57.
[PUBMED](#) | [CROSSREF](#)
20. Walrand S, Guillet C, Salles J, Cano N, Boirie Y. Physiopathological mechanism of sarcopenia. *Clin Geriatr Med* 2011;27:365-85.
[PUBMED](#) | [CROSSREF](#)
21. Kweon S, Kim Y, Jang MJ, Kim Y, Kim K, Choi S, Chun C, Khang YH, Oh K. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). *Int J Epidemiol* 2014;43:69-77.
[PUBMED](#) | [CROSSREF](#)
22. Willett W, Stampfer MJ. Total energy intake: implications for epidemiologic analyses. *Am J Epidemiol* 1986;124:17-27.
[PUBMED](#) | [CROSSREF](#)
23. Ainsworth BE, Haskell WL, Leon AS, Jacobs DR Jr, Montoye HJ, Sallis JF, Paffenbarger RS Jr. Compendium of physical activities: classification of energy costs of human physical activities. *Med Sci Sports Exerc* 1993;25:71-80.
[PUBMED](#) | [CROSSREF](#)
24. World Health Organization. Regional Office for the Western Pacific. The Asia-Pacific Perspective: Redefining Obesity and Its Treatment. Sydney: Health Communications Australia; 2000.
25. Korea Health Industry Development Institute. Development of Nutrient Database. Cheongju: Korea Health Industry Development Institute; 2000.
26. Rural Development Administration National Institute of Rural Agricultural Sciences. Food Composition Table. 7th ed. Suwon: Rural Development Administration National Institute of Rural Agricultural Sciences; 1996.
27. The Korean Nutrition Society. Computer aided nutritional analysis program 4.0 [Internet]. Seoul: The Korean Nutrition Society; 2011 [cited 2019 May 31]. Available from: <http://kns.or.kr/Center/CanPro.asp>.
28. Chae M, Park H, Park K. Estimation of dietary amino acid intake and independent correlates of skeletal muscle mass index among Korean adults. *Nutrients* 2020;12:1043.
[PUBMED](#) | [CROSSREF](#)
29. Scott Freeman HH. Biological Science. 2nd ed. Upper Saddle River (NJ): Pearson Prentice Hall; 2005.
30. Tymoczko JL, Berg JM, Stryer L. Biochemistry: a Short Course. New York (NY): W. H. Freeman; 2010.
31. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *J Am Geriatr Soc* 2002;50:889-96.
[PUBMED](#) | [CROSSREF](#)
32. Srikanthan P, Karlamangla AS. Relative muscle mass is inversely associated with insulin resistance and prediabetes. Findings from the third National Health and Nutrition Examination Survey. *J Clin Endocrinol Metab* 2011;96:2898-903.
[PUBMED](#) | [CROSSREF](#)
33. Willett W. Nutritional Epidemiology. 3rd ed. New York (NY): Oxford University Press; 2012. p.274-5.
34. Tatpati LL, Irving BA, Tom A, Bigelow ML, Klaus K, Short KR, Nair KS. The effect of branched chain amino acids on skeletal muscle mitochondrial function in young and elderly adults. *J Clin Endocrinol Metab* 2010;95:894-902.
[PUBMED](#) | [CROSSREF](#)
35. Bastard JP, Maachi M, Lagathu C, Kim MJ, Caron M, Vidal H, Capeau J, Feve B. Recent advances in the relationship between obesity, inflammation, and insulin resistance. *Eur Cytokine Netw* 2006;17:4-12.
[PUBMED](#)
36. Kim TN, Park MS, Lim KI, Choi HY, Yang SJ, Yoo HJ, Kang HJ, Song W, Choi H, Baik SH, Choi DS, Choi KM. Relationships between sarcopenic obesity and insulin resistance, inflammation, and vitamin D status: the Korean Sarcopenic Obesity Study. *Clin Endocrinol (Oxf)* 2013;78:525-32.
[PUBMED](#) | [CROSSREF](#)
37. Kim DH, Sarbassov DD, Ali SM, King JE, Latek RR, Erdjument-Bromage H, Tempst P, Sabatini DM. mTOR interacts with raptor to form a nutrient-sensitive complex that signals to the cell growth machinery. *Cell* 2002;110:163-75.
[PUBMED](#) | [CROSSREF](#)

38. Suryawan A, Jeyapalan AS, Orellana RA, Wilson FA, Nguyen HV, Davis TA. Leucine stimulates protein synthesis in skeletal muscle of neonatal pigs by enhancing mTORC1 activation. *Am J Physiol Endocrinol Metab* 2008;295:E868-75.
[PUBMED](#) | [CROSSREF](#)
39. Anthony JC, Yoshizawa F, Anthony TG, Vary TC, Jefferson LS, Kimball SR. Leucine stimulates translation initiation in skeletal muscle of postabsorptive rats via a rapamycin-sensitive pathway. *J Nutr* 2000;130:2413-9.
[PUBMED](#) | [CROSSREF](#)
40. Moberg M, Apró W, Ekblom B, van Hall G, Holmberg HC, Blomstrand E. Activation of mTORC1 by leucine is potentiated by branched-chain amino acids and even more so by essential amino acids following resistance exercise. *Am J Physiol Cell Physiol* 2016;310:C874-84.
[PUBMED](#) | [CROSSREF](#)
41. Ottestad I, Ulven SM, Øyri LK, Sandvei KS, Gjevestad GO, Bye A, Sheikh NA, Biong AS, Andersen LF, Holven KB. Reduced plasma concentration of branched-chain amino acids in sarcopenic older subjects: a cross-sectional study. *Br J Nutr* 2018;120:445-53.
[PUBMED](#) | [CROSSREF](#)
42. Takeuchi I, Yoshimura Y, Shimazu S, Jeong S, Yamaga M, Koga H. Effects of branched-chain amino acids and vitamin D supplementation on physical function, muscle mass and strength, and nutritional status in sarcopenic older adults undergoing hospital-based rehabilitation: a multicenter randomized controlled trial. *Geriatr Gerontol Int* 2019;19:12-7.
[PUBMED](#) | [CROSSREF](#)
43. Rahimi MH, Shab-Bidar S, Mollahosseini M, Djafarian K. Branched-chain amino acid supplementation and exercise-induced muscle damage in exercise recovery: a meta-analysis of randomized clinical trials. *Nutrition* 2017;42:30-6.
[PUBMED](#) | [CROSSREF](#)
44. Park Y, Choi JE, Hwang HS. Protein supplementation improves muscle mass and physical performance in undernourished prefrail and frail elderly subjects: a randomized, double-blind, placebo-controlled trial. *Am J Clin Nutr* 2018;108:1026-33.
[PUBMED](#) | [CROSSREF](#)
45. Aubertin-Leheudre M, Adlercreutz H. Relationship between animal protein intake and muscle mass index in healthy women. *Br J Nutr* 2009;102:1803-10.
[PUBMED](#) | [CROSSREF](#)
46. Krajcovicova-Kudlackova M, Babinska K, Valachovicova M. Health benefits and risks of plant proteins. *Bratisl Lek Listy* 2005;106:231-4.
[PUBMED](#)
47. Korea Health Industry Development Institute. Quality Control and Analysis Support on Nutrition Survey of the 4th Korea National Health & Nutrition Examination Survey (KNHANES IV). Cheongju: Korea Center for Disease Control and Prevention; 2009.