Submitted: 18.11.2022
Accepted: 20.12.2022
Early publication date: 11.04.2023

Endokrynologia Polska
DOI: 10.5603/EP.a2023.0016
ISSN 0423–104X, e-ISSN 2299–8306
Volume/Tom 74; Number/Numer 2/2023

Protein, amino acid, and peptide supplementation for the treatment of sarcopaenia

Peng-Ju Liu*, Fang Wang*, Shu-Li He, Fang Ma

Department of Clinical Nutrition, Peking Union Medical College Hospital, China Academic Medical Science and Peking Union Medical College, Beijing, China
**The authors contributed equally to this study.*

Abstract
Sarcopaenia is an age-related disease affected by many factors, nutrition being one. Reduced protein intake and decreased diet quality are correlated with sarcopaenia. Protein, amino acid, or peptide supplementation is a commonly used clinical practice to increase protein intake. However, whether supplementation plays a key role in preventing and treating sarcopaenia and whether it needs to be combined with other interventions is worthy of study. This review focuses on protein, amino acid, and peptide supplementation for the prevention and treatment of sarcopaenia. **(Endokrynol Pol 2023; 74 (2): 140–143)**

Key words: *protein; amino acid; peptide; sarcopenia; supplement; old age*

Introduction

Muscle attenuation syndrome was named sarcopaenia by Rosenberg in 1989. The European Working Group on Sarcopaenia in Older People (EWGSOP) published its consensus report on sarcopaenia in 2010 [1]. Since then, the International Working Group on Sarcopaenia and the Asian Working Group on Sarcopaenia have published their consensus reports [2, 3], and the Osteoporosis and Bone Mineral Disease Branch of the Chinese Medical Association published its consensus report in 2016 [4]. In 2018, the EWGSOP revised the diagnostic criteria [5]. Sarcopaenia is officially recognized as a disease characterized by muscle failure, which is common in the elderly but also affects younger people [6]. Low muscle strength is the key feature of sarcopaenia, so diagnosis is based on muscle quantity and quality, and poor physical function signifies severe sarcopaenia [5]. One study showed that sarcopaenia is associated with a range of adverse clinical outcomes, including an increased risk of falls and fractures, a reduced ability to cope with routine tasks, reduced quality of life, an increased risk of early death, and an increased risk of hospitalization with greater costs [5].

Sarcopaenia is a progressive, widespread disease of the skeletal muscles. The original definition of EWGSOP was based on the reduction of muscle mass; however, the revised consensus emphasizes muscle strength and recognizes that it is more important than muscle mass in predicting adverse outcomes [1, 5]. Both decreasing muscle mass and changing muscle strength involve macro and micro changes to muscle structure and composition. The amount of skeletal muscle remains constant for a long time after adulthood in healthy people, indicating a strong homeostasis mechanism [7]. Muscle is in dynamic equilibrium, and the inflow of amino acids and the resulting increase in muscle protein synthesis from dietary protein intake offset the outflow of amino acids caused by muscle protein degeneration between meals [7]. However, with increased age, especially after 60 years old, imbalanced protein homeostasis becomes obvious. It has been reported that the muscle mass of 75-year-old women and men is reduced by 0.7% and 1.0% per year, respectively, and decreasing muscle mass can accelerate muscle strength loss 2- to 5-fold. Therefore, the factors that disrupt the muscle protein homeostasis system could be a therapeutic target to alleviate sarcopaenia. In recent years, the main areas of interest have been investigating how aging damages the amino acid anabolic response and identifying strategies to alleviate the damage [7].

Fang Ma, Department of Clinical Nutrition, Peking Union Medical College Hospital, China Academic Medical Science and Peking Union Medical College, No. 1 Shuaifuyuan, Dongcheng District, Beijing, 100730, China, tel: 8610-69155550, fax: 8610-69155550; e-mail: fang_06master@163.com

Protein intake and sarcopaenia

The aetiology of sarcopaenia is multifaceted and includes increased inflammatory mediators (cytokines), prolonged stays in bed or low levels of physical activity, hormone disorders, and malnutrition (especially insufficient carbohydrate, protein, or both) [8–12]. Nutrition is a modifiable risk factor for sarcopaenia. One study showed that increasing the quantity and quality of dietary protein promoted muscle protein synthesis in the elderly [13, 14], while insufficient protein intake contributed to muscle mass reduction and impeded their physical functions [15]. Another study showed that a higher intake of branched-chain amino acids negatively correlated with senile sarcopaenia risk [16].

The relationship between protein intake and muscle protein synthesis

Early studies showed that the amino acids in proteins are bioactive components of anabolism and are necessary for muscle protein synthesis. Many studies have shown that leucine, phenylalanine, valine, and threonine (essential amino acids) stimulate muscle protein synthesis in humans; in contrast, non-essential amino acids such as arginine, glycine, and serine do not [17, 18]. Leucine plays a key regulatory role in muscle protein synthesis, and a study showed that a small dose of leucine (3 g) without other amino acids could strongly stimulate muscle protein synthesis [19]. Furthermore, a recent study compared 20 g of whey protein with an essential amino acid mixture containing low-dose leucine (1.2 g) and found that leucine was more effective at stimulating muscle protein synthesis [20]. Leucine, valine, and isoleucine are branched-chain amino acids. Unlike other essential amino acids, leucine is mainly metabolized in skeletal muscle [21]; therefore, it is speculated that its metabolites could promote muscle protein synthesis. Leucine is regulated by branched-chain aminotransferase, through which most leucine in the body is metabolized and reversibly transformed into α-ketoisocaproic acid; a study showed that this metabolite could stimulate muscle protein synthesis [22]. In addition, some leucine is converted to β-hydroxyl-β-methylbutyrate (HMB), a metabolite with anabolic and anti-catabolic potential [7, 23]; a study showed that 3 g of HMB taken orally produced an effect equivalent to leucine supplementation on muscle protein synthesis and inhibited the degeneration of leg muscles [19]. However, the benefit of taking HMB remains controversial because using the same low dosage of leucine (3 g) could maximize muscle protein synthesis [19]. The anabolic responses to protein and essential amino acids are dose-dependent and transient. At present, it is generally believed that the anabolic response to nutrition is maximized by ingesting 20 to 40 g of high-quality protein, such as meat or whey protein, or 10 to 20 grams of essential amino acids [24–26]. When the intake of essential amino acids exceeds the dosage needed for muscle protein synthesis, excess amino acids are oxidized and enter the urea synthesis pathway [27]. The remaining carbon skeletons are used for gluconeogenesis and ketogenesis in other tissues.

Muscle protein synthesis in the elderly

There was no significant difference in muscle protein synthesis rates between the elderly and young adults under fasting [25, 28]. However, muscle protein synthesis in the elderly decreased significantly after the intake of essential amino acids (anabolic resistance) [25]. Additionally, decomposition and catabolism were weakened due to the reduced secretion of insulin caused by carbohydrate, protein, or essential amino acid intake [29]. Metabolic factors that could be associated with sarcopaenia in the elderly include the following: decreased intake of protein/essential amino acids, decreased blood flow to muscle tissue after meals, increased metabolism of essential amino acids in the spleen, and decreased anabolic signal pathway activity. These factors cause the muscle protein metabolism to be at a net loss [7], which could mean that the elderly need more protein intake than the young [30]. However, although this reduced sensitivity to nutrient-driven anabolic stimuli (essential amino acids and insulin) may promote the development of sarcopaenia, it does not represent the full picture of senile sarcopaenia [7].

Protein, amino acid, or peptide supplementation for the prevention and treatment of sarcopaenia

Supplementing protein, essential amino acids, or peptides is common in clinical practice and can compensate for a lack of protein in the diet. In recent years, several studies have evaluated protein and amino acid supplementation, either alone or in combination with other nutrients, for the prevention and treatment of sarcopaenia. In addition, protein supplementation combined with exercise has also been reported in the prevention and treatment of sarcopaenia [31]. Some cohort studies have also shown that a lower protein intake is associated with sarcopaenia [13, 32, 33]. In addition to observational studies, randomized controlled studies using protein or amino acids alone or combined with exercise are increasing. In most randomized controlled studies, different doses of whey protein or amino acids (or their metabolites, e.g. HMB) were used as

interventions; participants were all elderly and were either healthy and living in the community, suffering from muscle weakness or sarcopaenia, or frail. The intervention period of most studies was no more than 24 weeks; however, one had an intervention period of 12 months [34]. Many randomized controlled studies showed inconsistent results due to different regions, ages, health statuses, intervention methods, supplement doses, or intervention cycles.

In one study, frail elderly people were given 15 g of milk protein concentrate or an isoenergetic placebo for 24 weeks. Compared with exercise alone, the lean weight of the participants in the protein supplementation group increased, but no improvement in strength or physical function was observed [35]. In another study, a protein supplement from red meat combined with resistance exercise improved the muscle mass and strength of elderly women after 4 months [36]. In a study by Kang et al. [37], 115 elderly people received whey protein (32.4 g/day), had their diet controlled, and partook together in 30-minute resistance training sessions taught by professional physiotherapists for 12 weeks. At the end of the experiment, the whey protein supplementation group's grip strength and walking speed increased significantly. In another study, whey protein combined with vitamin D supplementation or exercise improved sarcopaenia patients' muscle mass; however, there was no improvement in patients with normal muscle mass but low muscle strength [38]. Another multicentre, double-blind, randomized controlled study also showed that leucine-rich whey protein combined with vitamin D increased muscle mass and lower limb function in elderly patients with sarcopaenia [39]. Two other studies showed that protein or amino acid supplementation combined with exercise benefits the elderly in terms of muscle strength or lean weight [40, 41]. In addition, there are relevant reports on branched-chain amino acid supplementation interventions for sarcopaenia. A systematic review and meta-analysis concluded that leucine could improve muscle protein synthesis in the elderly and address the age-related decline in muscle mass [42]. Although there are few recent studies on peptides and sarcopaenia, a randomized controlled study showed that combining collagen peptides with resistance training could improve elderly people's body composition by increasing lean muscle and reducing body fat [43].

However, not all randomized controlled studies showed positive results. Chale et al. and Amasene et al. did not show that whey protein supplementation improved physical function or increased muscle mass [44, 45]. In addition, a recent 12-month randomized controlled study showed that supplementing with milk protein (40 g/day) did not improve physical function or reduce muscle loss in elderly people with low grip strength or walking speed when compared with a group taking a placebo with equal energy [35].

Conclusion

Many factors affected these randomized controlled studies, leading to inconsistent results. Many studies showed that gender could be relevant, but this has not been studied. Cultural food preparation methods, diets, and ethnic differences could also have affected the results [46]. In addition, gene variability could also help explain the inconsistencies [47]. The genetic basis of sarcopaenia has attracted the attention of researchers, and some genes related to physical function and muscle mass have been identified [48]. In summary, whether supplementing with protein, amino acid, or peptides plays a key role in preventing and treating sarcopaenia and whether it needs to be combined with other interventions should be studied further.

Conflict of interest

The authors declared no conflict of interest.

Funding

This study was supported by China National Key R&D Program during the 13th Five-year Plan Period (No. 2020YFC2005604).

References

1. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010; 39(4): 412–423, doi: 10.1093/ageing/afq034, indexed in Pubmed: 20392703.
2. Morley JE, Abbatecola AM, Argiles JM, et al. Society on Sarcopenia, Cachexia and Wasting Disorders Trialist Workshop. Sarcopenia with limited mobility: an international consensus. J Am Med Dir Assoc. 2011; 12(6): 403–409, doi: 10.1016/j.jamda.2011.04.014, indexed in Pubmed: 21640657.
3. Chen LK, Liu LK, Woo J, et al. Sarcopenia in Asia: consensus report of the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2014; 15(2): 95–101, doi: 10.1016/j.jamda.2013.11.025, indexed in Pubmed: 24461239.
4. Chinese Society of Osteoporosis and Bone Mineral Research. Sarcopenia Consensus. Chinese J Osteoporosis Bone Mineral Res. 2016; 9: 215–227.
5. Cruz-Jentoft A, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age and Ageing. 2018; 48(1): 16–31, doi: 10.1093/ageing/afy169, indexed in Pubmed: 31081853.
6. Vellas B, Fielding RA, Bens C, et al. Implications of ICD-10 for Sarcopenia Clinical Practice and Clinical Trials: Report by the International Conference on Frailty and Sarcopenia Research Task Force. J Frailty Aging. 2018; 7(1): 2–9, doi: 10.14283/jfa.2017.30, indexed in Pubmed: 29412436.
7. Mitchell WK, Wilkinson DJ, Phillips BE, et al. Human Skeletal Muscle Protein Metabolism Responses to Amino Acid Nutrition. Adv Nutr. 2016; 7(4): 828S–838S, doi: 10.3945/an.115.011650, indexed in Pubmed: 27422520.
8. Mitchell WK, Phillips BE, Williams JP, et al. Development of a new Sonovue™ contrast-enhanced ultrasound approach reveals temporal and age-related features of muscle microvascular responses to feeding. Physiol Rep. 2013; 1(5): e00119, doi: 10.1002/phy2.119, indexed in Pubmed: 24303186.
9. Arnal MA, Mosoni L, Boirie Y, et al. Protein feeding pattern does not affect protein retention in young women. J Nutr. 2000; 130(7): 1700–1704, doi: 10.1093/jn/130.7.1700, indexed in Pubmed: 10867039.
10. Bouillanne O, Curis E, Hamon-Vilcot B, et al. Impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients: a randomized controlled trial. Clin Nutr. 2013; 32(2): 186–192, doi: 10.1016/j.clnu.2012.08.015, indexed in Pubmed: 22992307.

11. Katsanos CS, Kobayashi H, Sheffield-Moore M, et al. Aging is associated with diminished accretion of muscle proteins after the ingestion of a small bolus of essential amino acids. Am J Clin Nutr. 2005; 82(5): 1065–1073, doi: 10.1093/ajcn/82.5.1065, indexed in Pubmed: 16280440.
12. Phillips BE, Hill DS, Atherton PJ. Regulation of muscle protein synthesis in humans. Curr Opin Clin Nutr Metab Care. 2012; 15(1): 58–63, doi: 10.1097/MCO.0b013e32834d19bc, indexed in Pubmed: 22037010.
13. Houston DK, Nicklas BJ, Ding J, et al. Health ABC Study. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr. 2008; 87(1): 150–155, doi: 10.1093/ajcn/87.1.150, indexed in Pubmed: 18175749.
14. Børsheim E, Bui QUT, Tissier S, et al. Effect of amino acid supplementation on muscle mass, strength and physical function in elderly. Clin Nutr. 2008; 27(2): 189–195, doi: 10.1016/j.clnu.2008.01.001, indexed in Pubmed: 18294740.
15. Cerri AP, Bellelli G, Mazzone A, et al. Sarcopenia and malnutrition in acutely ill hospitalized elderly: Prevalence and outcomes. Clin Nutr. 2015; 34(4): 745–751, doi: 10.1016/j.clnu.2014.08.015, indexed in Pubmed: 25263170.
16. Ma WJ, Zhang W, Zhai J, et al. Branched chain and other amino acid intakes are inversely associated with sarcopenia among community elders in Qingdao, China. Asia Pac J Clin Nutr. 2022; 31(1): 97–107, doi: 10.6133/apjcn.202203_31(1).0011, indexed in Pubmed: 35357108.
17. Smith K, Barua JM, Watt PW, et al. Flooding with L-[1-13C]leucine stimulates human muscle protein incorporation of continuously infused L-[1-13C]valine. Am J Physiol. 1992; 262(3 Pt 1): E372–E376, doi: 10.1152/ajpendo.1992.262.3.E372, indexed in Pubmed: 1550230.
18. Smith K, Reynolds N, Downie S, et al. Effects of flooding amino acids on incorporation of labeled amino acids into human muscle protein. Am J Physiol. 1998; 275(1): E73–E78, doi: 10.1152/ajpendo.1998.275.1.E73, indexed in Pubmed: 9688876.
19. Wilkinson DJ, Hossain T, Hill DS, et al. Effects of leucine and its metabolite β-hydroxy-β-methylbutyrate on human skeletal muscle protein metabolism. J Physiol. 2013; 591(11): 2911–2923, doi: 10.1113/jphysiol.2013.253203, indexed in Pubmed: 23551944.
20. Bukhari SSI, Phillips BE, Wilkinson DJ, et al. Intake of low-dose leucine-rich essential amino acids stimulates muscle anabolism equivalently to bolus whey protein in older women at rest and after exercise. Am J Physiol Endocrinol Metab. 2015; 308(12): E1056–E1065, doi: 10.1152/ajpendo.00481.2014, indexed in Pubmed: 25827594.
21. Wagenmakers AJ. Protein and amino acid metabolism in human muscle. Adv Exp Med Biol. 1998; 441: 307–319, doi: 10.1007/978-1-4899-1928-1_28, indexed in Pubmed: 9781336.
22. Escobar J, Frank JW, Suryawan A, et al. Leucine and alpha-ketoisocaproic acid, but not norleucine, stimulate skeletal muscle protein synthesis in neonatal pigs. J Nutr. 2010; 140(8): 1418–1424, doi: 10.3945/jn.110.123042, indexed in Pubmed: 20534881.
23. Van Koevering M, Nissen S. Oxidation of leucine and alpha-ketoisocaproate to beta-hydroxy-beta-methylbutyrate in vivo. Am J Physiol. 1992; 262(1 Pt 1): E27–E31, doi: 10.1152/ajpendo.1992.262.1.E27, indexed in Pubmed: 1733247.
24. Symons TB, Sheffield-Moore M, Wolfe RR, et al. A moderate serving of high-quality protein maximally stimulates skeletal muscle protein synthesis in young and elderly subjects. J Am Diet Assoc. 2009; 109(9): 1582–1586, doi: 10.1016/j.jada.2009.06.369, indexed in Pubmed: 19699838.
25. Cuthbertson D, Smith K, Babraj J, et al. Anabolic signaling deficits underlie amino acid resistance of wasting, aging muscle. FASEB J. 2005; 19(3): 422–424, doi: 10.1096/fj.04-2640fje, indexed in Pubmed: 15596483.
26. Atherton PJ, Etheridge T, Watt PW, et al. Muscle full effect after oral protein: time-dependent concordance and discordance between human muscle protein synthesis and mTORC1 signaling. Am J Clin Nutr. 2010; 92(5): 1080–1088, doi: 10.3945/ajcn.2010.29819, indexed in Pubmed: 20844073.
27. Moore DR, Robinson MJ, Fry JL, et al. Ingested protein dose response of muscle and albumin protein synthesis after resistance exercise in young men. Am J Clin Nutr. 2009; 89(1): 161–168, doi: 10.3945/ajcn.2008.26401, indexed in Pubmed: 19056590.
28. Kumar V, Selby A, Rankin D, et al. Age-related differences in the dose-response relationship of muscle protein synthesis to resistance exercise in young and old men. J Physiol. 2009; 587(1): 211–217, doi: 10.1113/jphysiol.2008.164483, indexed in Pubmed: 19001042.
29. Wilkes EA, Selby AL, Atherton PJ, et al. Blunting of insulin inhibition of proteolysis in legs of older subjects may contribute to age-related sarcopenia. Am J Clin Nutr. 2009; 90(5): 1343–1350, doi: 10.3945/ajcn.2009.27543, indexed in Pubmed: 19740975.
30. Moore DR, Churchward-Venne TA, Witard O, et al. Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. J Gerontol A Biol Sci Med Sci. 2015; 70(1): 57–62, doi: 10.1093/gerona/glu103, indexed in Pubmed: 25056502.
31. Denison HJ, Cooper C, Sayer AA, et al. Prevention and optimal management of sarcopenia: a review of combined exercise and nutrition interventions to improve muscle outcomes in older people. Clin Interv Aging. 2015; 10: 859–869, doi: 10.2147/CIA.S55842, indexed in Pubmed: 25999704.
32. Scott D, Blizzard L, Fell J, et al. Associations between dietary nutrient intake and muscle mass and strength in community-dwelling older adults: the Tasmanian Older Adult Cohort Study. J Am Geriatr Soc. 2010; 58(11): 2129–2134, doi: 10.1111/j.1532-5415.2010.03147.x, indexed in Pubmed: 21054294.
33. McLean RR, Mangano KM, Hannan MT, et al. Dietary Protein Intake Is Protective Against Loss of Grip Strength Among Older Adults in the Framingham Offspring Cohort. J Gerontol A Biol Sci Med Sci. 2016; 71(3): 356–361, doi: 10.1093/gerona/glv184, indexed in Pubmed: 26525088.
34. Björkman MP, Suominen MH, Kautiainen H, et al. Effect of Protein Supplementation on Physical Performance in Older People With Sarcopenia-A Randomized Controlled Trial. J Am Med Dir Assoc. 2020; 21(2): 226–232.e1, doi: 10.1016/j.jamda.2019.09.006, indexed in Pubmed: 31734121.
35. Tieland M, Dirks ML, van der Zwaluw N, et al. Protein supplementation increases muscle mass gain during prolonged resistance-type exercise training in frail elderly people: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc. 2012; 13(8): 713–719, doi: 10.1016/j.jamda.2012.05.020, indexed in Pubmed: 22770932.
36. Daly RM, O'Connell SL, Mundell NL. Protein-enriched diet, with the use of lean red meat, combined with progressive resistance training enhances lean tissue mass and muscle strength and reduces circulating IL-6 concentrations in elderly women: a cluster randomized controlled trial. Am J Clin Nutr. 2014; 99(4): 899–910, doi: 10.3945/ajcn.113.064154, indexed in Pubmed: 24477043.
37. Kang L, Gao Y, Liu X, et al. Effects of whey protein nutritional supplement on muscle function among community-dwelling frail older people: A multicenter study in China. Arch Gerontol Geriatr. 2019; 83: 7–12, doi: 10.1016/j.archger.2019.03.012, indexed in Pubmed: 30921603.
38. Yamada M, Kimura Y, Ishiyama D, et al. Synergistic effect of bodyweight resistance exercise and protein supplementation on skeletal muscle in sarcopenic or dynapenic older adults. Geriatr Gerontol Int. 2019; 19(5): 429–437, doi: 10.1111/ggi.13643, indexed in Pubmed: 30864254.
39. Bauer JM, Verlaan S, Bautmans I, et al. Effects of a vitamin D and leucine-enriched whey protein nutritional supplement on measures of sarcopenia in older adults, the PROVIDE study: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc. 2015; 16(9): 740–747, doi: 10.1016/j.jamda.2015.05.021, indexed in Pubmed: 26170041.
40. Kim HK, Suzuki T, Saito K, et al. Effects of exercise and amino acid supplementation on body composition and physical function in community-dwelling elderly Japanese sarcopenic women: a randomized controlled trial. J Am Geriatr Soc. 2012; 60(1): 16–23, doi: 10.1111/j.1532-5415.2011.03776.x, indexed in Pubmed: 22142410.
41. Vukovich MD, Stubbs NB, Bohlken RM. Body composition in 70-year-old adults responds to dietary beta-hydroxy-beta-methylbutyrate similarly to that of young adults. J Nutr. 2001; 131(7): 2049–2052, doi: 10.1093/jn/131.7.2049, indexed in Pubmed: 11435528.
42. Xu Zr, Tan Zj, Zhang Q, et al. 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(1): 25–34, doi: 10.1017/S0007114514002475, indexed in Pubmed: 25234223.
43. Zdzieblik D, Oesser S, Baumstark MW, et al. Collagen peptide supplementation in combination with resistance training improves body composition and increases muscle strength in elderly sarcopenic men: a randomised controlled trial. Br J Nutr. 2015; 114(8): 1237–1245, doi: 10.1017/S0007114515002810, indexed in Pubmed: 26353786.
44. Chalé A, Cloutier GJ, Hau C, et al. Efficacy of whey protein supplementation on resistance exercise-induced changes in lean mass, muscle strength, and physical function in mobility-limited older adults. J Gerontol A Biol Sci Med Sci. 2013; 68(6): 682–690, doi: 10.1093/gerona/gls221, indexed in Pubmed: 23114462.
45. Amasene M, Cadenas-Sanchez C, Echeverria I, et al. Effects of Leucine-Enriched Whey Protein Supplementation on Physical Function in Post-Hospitalized Older Adults Participating in 12-Weeks of Resistance Training Program: A Randomized Controlled Trial. Nutrients. 2019; 11(10), doi: 10.3390/nu11102337, indexed in Pubmed: 31581591.
46. Ganapathy A, Nieves JW. Nutrition and Sarcopenia-What Do We Know? Nutrients. 2020; 12(6), doi: 10.3390/nu12061755, indexed in Pubmed: 32545408.
47. Fenech M, El-Sohemy A, Cahill L, et al. Nutrigenetics and nutrigenomics: viewpoints on the current status and applications in nutrition research and practice. J Nutrigenet Nutrigenomics. 2011; 4(2): 69–89, doi: 10.1159/000327772, indexed in Pubmed: 21625170.
48. Tan LJ, Liu SL, Lei SF, et al. Molecular genetic studies of gene identification for sarcopenia. Hum Genet. 2012; 131(1): 1–31, doi: 10.1007/s00439-011-1040-7, indexed in Pubmed: 21706341.