

SARCOPENIA

THE BENEFITS OF DAIRY PROTEINS

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Sarcopenia in Rapidly Aging Societies

The World Health Organization (WHO) Department of Aging and Life Course reports that the world population of adults aged 60 and over has doubled since 1980 and is predicted to reach 2 billion by 2050, with 400 million being 80 and older (WHO, 2012a). This dramatic increase in the world's population of older adults is an indicator of improved global health. However, it is now more important than ever to address the specific wellness and nutrition needs of older adults to promote overall quality of life.

The term "sarcopenia" has been defined as the age-associated loss of skeletal muscle mass and function, sometimes

also seen in conjunction with increased fat mass. The causes of sarcopenia are complex and can include physical inactivity, changes in anabolic hormones, chronic disease, inflammation, insulin resistance and nutritional deficiencies such as inadequate calorie and protein intake (Fielding et al., 2011).

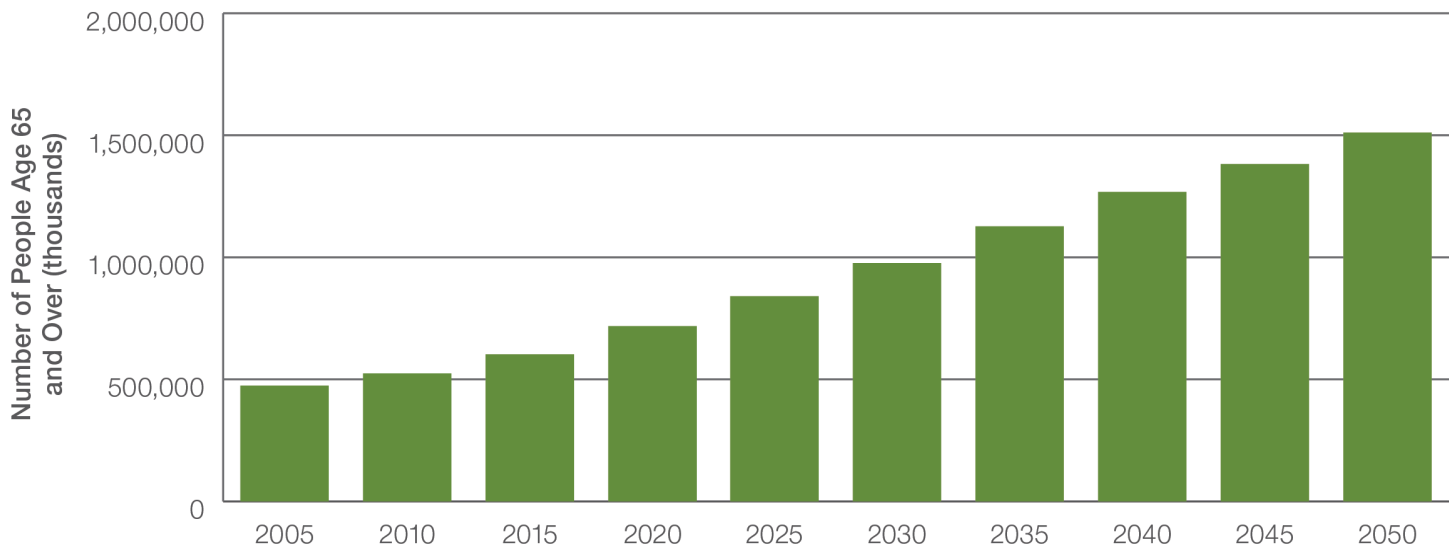
Health and research professionals propose that there are ways to combat this growing health problem via hormonal, physical and nutritional interventions. Protein consumption remains one of the most important factors in maintaining both muscle mass and functional capacity throughout the life-cycle.

This monograph will explain the etiology and implications of sarcopenia and highlight the most recent research on protein nutrition with and without exercise to provide strategies for combating this growing

global health problem. The impact of whey protein, particularly on both the building and maintenance of lean body mass, is presented along with its unique attributes in the prevention of sarcopenia.

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Projections of Global Aging Population Growth by Year



Source: Population Division of the Department of Economic and Social Affairs of the United Nations Secretariat, World Population Prospects: The 2010 Revision

Health Care Costs of Sarcopenia

It has been estimated that the direct health care cost attributable to sarcopenia in the United States in 2000 was \$18.5 billion, representing about 1.5% of health care expenditures for that year (Janssen et al., 2004). Since 2000, the U.S. population aged 65 and older has increased from 35 million to 40 million in 2010, representing about 13.1% of the population. It is projected to reach 55 million in 2020 and by 2030 reach 72.1 million persons or 19.3% of the U.S. population (Dept. of Health and Human Services, 2011). Overall the world population is aging. As stated by the World Health Organization (2012b) “while the shift to older populations started in wealthy regions such as Europe and North America, it is now low- and middle-income countries experiencing the greatest change.” “These trends are also evident for the oldest age groups. In the middle of the 20th century there were just over 14 million people on the whole

planet aged 80 years or older. By 2050, there will be 100 million living in China alone and 400 million people in this age group worldwide.” With rapid worldwide increases in the aging population, sarcopenia and its related health care costs will increase as a public health issue for years to come. A better understanding and management of sarcopenia would dramatically improve the health and quality of life in the elderly and help reduce healthcare costs associated with aging.

Sarcopenia: Definition, Etiology, and Implications

Sarcopenia refers to the loss of muscle mass and function that many adults experience with age. This decline in muscle can begin as early as age 40 and more commonly after age 55, when muscles begin to atrophy. As reviewed

by Rolland et al., (2008) researchers have estimated the rate of muscle loss to be 1-2% each year after the age of 50, with a decline in strength of 1.5% per year beginning at 50 years and accelerating to 3% after the age of 60. According to the European Society on Clinical Nutrition and Metabolism and the Special Interest Needs Group on Geriatric Nutrition and Cachexia (Muscaritoli, 2010), an adult can be diagnosed with sarcopenia if both of the following are present:

1. The person presents with a percentage of muscle mass more than two standard deviations below the mean obtained from a group of young, healthy adults of the same sex and ethnic background.
2. The person exhibits low gait speed, i.e., is unable to walk faster than 0.8 meters per second in a four-meter walk test.

The European Working Group on Sarcopenia in Older People extends the diagnosis for sarcopenia to include

adults who have low muscle mass and either low physical performance or low muscle strength (Cruz-Jentoft, et al., 2010). While these consensus definitions provide quantitative cut-offs for the diagnosis of sarcopenia, it is important to acknowledge that aging adults not meeting these measures may still experience visible decreases in both muscle mass, functional ability and strength.

A Complex Etiology

The etiology of sarcopenia has not been fully elucidated. The loss of muscle mass with aging is the result of decreased protein synthesis, increased protein breakdown or the combination of both (Boirie, 2009; Lang et al., 2010). Many metabolic factors may be involved in



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this imbalance including changes in anabolic hormones, catabolic stimuli resulting from inflammation or disease, nutritional factors such as inadequate protein intake and physical inactivity. (Rolland et al., 2008; Boirie, 2009).

The Role of Hormones

Anabolic hormones such as insulin, growth hormone (GH) and sex hormones can impact protein synthesis and breakdown rates. Moreover, alterations in hormone production and/or sensitivity can occur with aging. Insulin has been shown to increase muscle protein synthesis and decrease breakdown, but its actions on muscle may become impaired with aging (Boirie, 2009). Insulin plays an important role in the body by controlling amino acid uptake, decreasing proteolysis and increasing protein synthesis. Thus, older adults with impaired ability to utilize insulin are likely to experience decreased anabolism and increased protein breakdown (Walrand et al., 2011). Insulin-like growth factor (IGF-1), a hormone similar in structure to insulin, also has anabolic effects on muscle in adults and the elderly. With aging, IGF-1 levels decrease as a result of decreased production at the muscle locally and also due to reductions of GH which stimulate its production by the liver. Lower levels of IGF-1 impair this hormone's ability to stimulate protein synthesis and lower the breakdown of proteins in muscle (Lang, et al., 2010). Decreases in GH and IGF-1 also are associated with increased visceral fat. Testosterone and estrogen both have anabolic effects on muscle. Serum testosterone gradually declines with age and is directly correlated to muscular strength and anabolism, partly via its effects on increased expression of IGF-1. In women, estrogen levels decline sharply after menopause. Cytokines associated with inflammation can reduce protein synthesis and increase protein breakdown and result in the loss of muscle mass. In addition, chronically low levels of inflammatory cytokines in the

blood may occur in individuals who are overweight or obese and have increased amounts of abdominal fat accumulation. These low but chronic levels of inflammatory cytokines can have adverse effects on muscle mass and have been associated with a variety of health disorders including sarcopenia and insulin resistance (Walrand et al., 2011). Insulin resistance has been shown to increase with age and can have adverse effects on the balance between protein synthesis and breakdown via the impaired ability to utilize insulin and increased levels of pro-inflammatory cytokines.

Higher Protein Intake May be Necessary

Both quantity of food intake and macronutrients consumed can impact the development of sarcopenia. Lower food intakes resulting from physiological age-related reductions in appetite can result in reduced weight and muscle mass (Ahmed and Haboubi, 2010). It has also been hypothesized that protein requirements vary between younger and older adults, given differences in utilization of amino acids. Older adults have an impaired ability to utilize dietary protein to build muscle and strength. While discrepancies exist in the literature, it is generally believed that basal (fasting) protein synthesis rates do not decline with age (Koopman and van Loon, 2009; Breen and Phillips 2011). When compared to their younger counterparts, protein synthesis rates in the elderly are more resistant to factors stimulating muscle building such as amino acids (Fry and Rasmussen, 2011).

As a result, aging muscle is less sensitive to lower doses of amino acids than the young indicating that higher protein diets may be needed to stimulate protein synthesis. While not clearly understood, this anabolic resistance seen in aging muscle may be a result of a decline in physical activity or an age-related decline in the processes

associated with inflammation, which can interfere with protein turnover (Breen and Phillips 2011). Studies have found that anabolism can be maintained with administration of high doses of protein, especially essential and branched chain amino acids (Volpi et al., 2003), providing additional evidence that older adults may require more protein to achieve the same increase in muscle growth. Thus, both quantity and quality of proteins consumed may impact protein synthesis in the elderly; this will be discussed in more detail later in this monograph.

Importance of Physical Activity

Physical inactivity also plays a role in the loss of muscle mass and functional ability, and remaining physically active with aging is important for maintaining muscle as well as overall health. It is important to acknowledge the benefits of each type of physical activity— aerobic versus anaerobic or resistive. While aerobic exercise such as walking, jogging, cycling or swimming does have positive

effects in terms of weight management, increased maximum oxygen uptake and improved cardiovascular health, it does not elicit the same gains in strength or increase of muscle mass as resistance exercise. Both are important to overall health; aerobic exercise decreases intramuscular body fat and improves muscle function, and resistance exercise increases muscle protein synthesis, mass and strength (Rolland et al., 2008).

In addition to lower muscle mass, it is well established that a decline in strength occurs with aging and is correlated with the loss of muscle (Doherty, 2003). Loss of muscle strength may be the result of loss in both the quantity and quality of muscle. The resultant loss in muscle power and function associated with aging can hinder actions such as rising from a chair, climbing steps or regaining balance (Lang et al., 2010). Moreover, loss of muscle also reduces the ability to burn calories which may help promote increased body fat with age (Koopman and van Loon, 2009).

Developments in the Management of Sarcopenia

Intake Recommendations for Lean Muscle Preservation

In the United States, the current Recommended Dietary Intake for protein remains at 0.8g/kg body weight/d for adults. However, new research shows that this may not be enough, especially in an older population (Wolfe, 2012). Given the hypothesis that older adults may have a blunted anabolic response to dietary protein and likely need more to preserve lean muscle mass and functional ability, current research now shows that protein intake of at least 1.0 and as high as 1.5g/kg may be optimal. This would mean as much as 102 grams of protein daily for a 150 pound person (Morley et al., 2010).

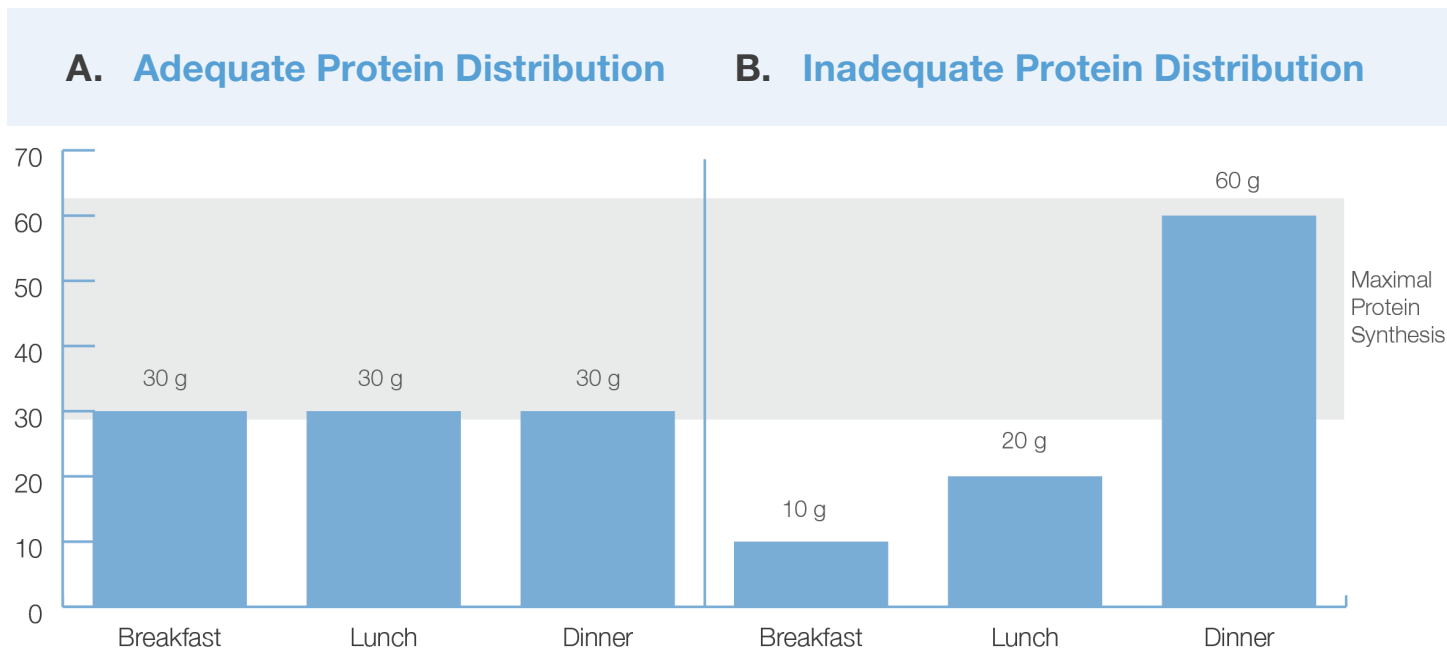


Figure 1: A pictorial example of the proposed relationship between the amount of protein ingested per meal and the resultant anabolic response.

(A) Ingestion of 90g of protein, distributed evenly over 3 meals. **(B)** Ingestion of 90g of proteins unevenly distributed throughout the day. Stimulating muscle protein synthesis to a maximal extent during the meals shown in Figure A is more likely to provide a greater 24 hour protein anabolic response than an unequal protein distribution (Paddon Jones and Ramusen 2009).

Quality of Dietary Protein

While older adults do need to consider the amount of protein in their diets, it is also important to consider both the timing and the quality of the protein they are consuming. Eating moderate amounts of protein at each meal, spread throughout the day, may be the most effective way to stimulate muscle anabolism. Ingesting 25-30g of protein at breakfast, lunch and dinner may allow for maximal utilization of dietary protein while consuming amounts in excess of 30g at once may not result in any further gains in lean mass, Figure 1.(Paddon-Jones and Rasmussen, 2009).

The quality of protein ingested has also been shown to play a role in improving muscle anabolism in the aging population. Proteins that contain the essential amino acids, most importantly leucine, have been shown to best stimulate muscle protein anabolism and decrease protein



Supplementation with whey or high protein diets containing whey and other milk proteins may serve as a viable treatment to induce muscle mass following atrophy in the elderly.

breakdown (Waters 2010). Leucine plays an important role in stimulating the mTOR pathway, which regulates cell proliferation and protein synthesis (Blomstrand et al., 2006; Fengna et al., 2011; Farnfield et al., 2012). Whey protein has a high concentration of leucine and has been shown to stimulate a rapid, acute rise in muscle protein synthesis (Churchward-Venne et al., 2012; Breen and Phillips 2011; Waters et al., 2010). Other vitamin and hormonal therapies are also being studied to help delay, treat or prevent age-associated muscle loss. However, these have not proved to be consistently as effective as dietary protein intake and physical activity.

Resistance and Aerobic Exercises for Better Quality of Life

Proper nutrition plays a crucial role in the maintenance of lean body mass with age, physical activity remains an equally important part of aging. Resistance exercise such as weight training, yoga or other body weight activity has been shown effective in increasing muscle mass and strength. Numerous studies have shown that resistance exercise training is effective in enhancing skeletal muscle mass, increasing muscle strength, improving functional capacity in the elderly and attenuating the development of sarcopenia (Koopman and van Loon 2008; Burton and Sumukadas, 2010). Progressive resistance training, a type of resistance exercise whereby individuals progressively increase resistance as strength increases, may be particularly effective. A recent Cochran review found evidence from 121 randomized controlled trials that older people who exercise their muscles against force or resistance become stronger and can improve performance in simple activities such as walking, standing or more complex activities such as bathing or meal preparation (Liu and Latham, 2009). Endurance-type exercise such as running, walking, swimming, biking and aerobics

have been shown to improve skeletal muscle oxidative capacity, meaning muscles are better able to utilize oxygen to contract and sustain movement over longer intervals. Aerobic exercise also increases mitochondrial function, enzyme activity and decreases body fat, resulting in improvements in functional mobility (Koopman and van Loon 2008; Burton and Sumukadas, 2010).

Dairy Protein for Prevention and Treatment

While new vitamin and hormone therapies are under investigation to mitigate the effects of sarcopenia, physical activity and dietary protein intake, especially whey protein from dairy products, and particularly when combined with exercise, provide a strategy for combating or preventing this global health problem. Two recent publications support this:

- Malafarina et al., (2012) conducted a systematic review on the impact of protein based nutritional supplementation on muscle. The review which included 17 studies with a total of 1287 subjects between the ages of 65 to 85 on average found that supplementation is effective in increasing both muscle mass and function. This effect increased when combined with physical activity.
- Cermak et al., (2012) conducted a meta-analysis to examine if protein supplementation augments the effects of resistance exercise in younger and older subjects. Focusing on the studies in older subjects, data from six randomized clinical trials that examined the impact of protein supplementation in untrained older subjects were combined. All six studies used a dairy based protein; five exclusively used a source of dairy protein (whey, milk or casein) and the remaining study used a combination approach (egg+meat+dairy). When studies were examined individually, all

studies reported no significant benefit of protein supplementation versus placebo on fat free mass gain. However, when combined data from 215 older subjects were examined, protein supplementation resulted in 38% more fat free mass and a 33% increase in strength when compared to placebo. Authors concluded that “protein supplementation increases muscle mass and strength gains during prolonged resistance exercise training in both younger and older subjects”.

Whey Protein in the Management of Sarcopenia

Research has shown that dietary protein plays an important role in the maintenance of lean body mass. Moreover, protein source remains an important piece. Whey protein, found exclusively in dairy products, whey supplements and ingredients, is an excellent protein source to use in combating sarcopenia for a variety of reasons.

High BCAA Content

Whey protein has a high concentration of the branched chain amino acids; leucine, isoleucine and valine, all important for muscle anabolism and tissue repair. Whey protein also contains all of the essential amino acids in higher concentrations than those found in vegetable protein sources (Marshall 2004; Hayes and Cribb, 2008). Whey is also a rich source of cysteine, up to four times higher than other proteins such as casein or soy, which may regulate whole body protein metabolism and changes in muscle mass (Hays and Cribb, 2008).

Fast Protein

Whey protein comprises 20% of the protein in milk, with the other 80% being casein. Casein forms curds in the stomach, which slows digestion and entrance into the small intestine. In contrast, whey protein is quickly digested and produces a rapid rise in circulating amino acid levels in the blood and has been designated as a “fast” protein (Boirie et al., 1997). This rapid rise in plasma amino acids makes whey a superior protein for postprandial utilization for the building of lean body mass and preservation of positive nitrogen balance (Marshall, 2004; Phillips et al., 2009; Hulmi et al., 2010).

Greater Rate of Muscle Synthesis

A beneficial effect of whey protein compared to casein, however, does not appear to be simply due to its faster absorption rate. Pennings et al., (2011) compared dietary protein digestion and absorption rates with muscle protein accretion after the ingestion of 20 g of whey, casein or casein hydrolysate in 48 older men (~74 yrs.). Casein hydrolysate was used as a comparison in this study, as researchers had found that hydrolyzed casein is altered in such a way as to resemble whey in terms of rate of digestion. As expected, both whey protein and casein hydrolysate exhibited greater digestion and absorption rates than casein, but the consumption of whey protein resulted in a greater rate of muscle protein synthesis. The greater muscle protein synthesis, which resulted from the ingestion of whey compared to casein, was likely due to both its faster rate of digestion and absorption and its higher leucine content.

Branch Chain Amino Acids and Protein Metabolism

While the absorption rate of whey protein likely plays a role in its superiority in building and preserving lean body mass, whey protein's higher concentration of branched chain amino acids (BCAA), in particular leucine also remains a primary contributor. Leucine is one of the most abundant dietary amino acids, accounting for more than 20% of total protein in the human diet and is the most effective BCAA for stimulating the building of lean body mass (Fengna et al., 2011). In addition to contributing to skeletal muscle growth, leucine supplementation has also been shown to attenuate lean body mass losses, when supplemented as part of an overall balanced diet. Whey protein remains a rich source of leucine, having higher concentrations of this amino acid than either casein or soy (Wilson et al., 2011).

The human body metabolizes BCAA, (leucine, isoleucine and valine) in a unique way that allows for a greater amount of these amino acids to reach systemic circulation. The liver is responsible for most amino acid catabolism but has low levels of the enzymes responsible for the degradation of BCAA. As a result, 70% of BCAA appear in the circulation for incorporation into proteins or metabolism by muscle other tissues (Brosnan and Brosnan, 2006; Wilson et al., 2011). Leucine, in particular, directly stimulates muscle protein synthesis, and may also have anti-catabolic effects, contributing to the attenuation of muscle protein catabolism.

Sarcopenia and Obesity

Sarcopenia is an important and prevalent global health issue. The ramifications of this muscle loss on overall health, quality of life and health care costs are serious. Age-related loss of muscle mass has a negative impact on strength, power, functionality and daily living. It is also associated with undesirable conditions associated with aging such as:

- osteoporosis
- increased susceptibility to illness falls and related injuries (Dutta, 1997; Janssen, 2002; Doherty, 2003).

Sarcopenia is often masked by an increase in fat mass that occurs in old age. This condition is termed “sarcopenic obesity” and is more debilitating than either obesity or sarcopenia alone. Older adults also experience a redistribution of fat, from subcutaneous areas and the extremities toward intra-abdominal, intra-hepatic and intra-muscular areas. This redistribution is associated with increased waist circumference and increased risk for metabolic disorders such as heart disease and diabetes (Walrand et al., 2011). Other research has shown independent associations between both increased central obesity and decreased muscle mass on increased mortality in older men (Wannamethee et al., 2007).

Protein Intake Most Beneficial at 35g/day for Muscle Synthesis

Pennings et al., (2012) also conducted a dose response study to examine the impact of the amount of whey ingested on the absorption and subsequent use of amino acids in older subjects. Thirty three men aged ~73 years were randomized to consume 10, 20 or 35g of intrinsically labeled whey protein. Ingestion of the protein supplement led to a rapid rise in both essential amino acid and leucine uptakes. When compared to 10g of whey, the ingestion of 35g of whey resulted in significantly higher peak concentrations of both essential amino acids and leucine. Overall protein oxidation was also highest in subjects who consumed 35g. Whole body protein balance significantly increased in a stepwise manner as the amount of whey protein ingested increased. Whole body protein synthesis rates increased with the ingestion of 20g or 35g while muscle protein synthesis rates were only greater after ingestion of 35 g when compared to the 10g of whey protein. The authors conclude that 35 g of whey protein resulted in the absorption and delivery of more amino acids for use in building muscle in older subjects. Thus, higher doses of whey protein may be beneficial in combating age associated muscle loss.

Benefits Beyond Essential Amino Acid Content

A study by Katsanos et al., (2008) was conducted to assess whether the beneficial effects of whey protein on skeletal muscle accrual could be explained by whey's essential amino acid content. Older subjects (65-85 yrs.) received a bolus of 15 grams of whey protein, 7.57 g of essential- or 6.72 g non-essential amino acids (n=5 per group). Researchers found that the ingestion of whey protein improved phenylalanine balance, a marker of protein accretion, to the greatest extent. Subjects who consumed whey protein experienced a greater insulin response, which has been shown to inhibit muscle breakdown and increase protein synthesis. Increased insulin levels may be the result of the effects of non-essential amino acids or bioactive peptides formed during whey's digestion that enhance its secretion. The authors also speculate that whey protein increases the plasma concentration of cysteine which, in addition to leucine, may also have a role in augmenting muscle protein accretion (Hays and Cribb, 2008). Regardless of mechanism, results of this study indicate a beneficial impact of whey consumption on muscle accretion in older subjects that extends beyond its leucine or essential amino acid content.

Role of Leucine in Muscle Synthesis

Recent research reveals that leucine, found most abundantly in whey protein, is effective in increasing anabolism and helping protect against sarcopenia. Mange et al., (2012) examined whether supplementation with free leucine following muscle loss during immobilization in aged rats would improve protein synthesis during the recovery phase. In this study, the hind leg of each subject rat was immobilized for 8 days, with a 40 day recovery period. Rats were supplemented with either casein + alanine or casein + leucine following immobilization. Researchers found that free leucine supplementation had a positive impact on protein synthesis in the postprandial state, resulting in higher protein synthesis and earlier normalization of proteolysis. However, despite increased synthesis rates, the diet failed to increase muscle mass. Authors believe that the free leucine, which is absorbed rapidly, induced an anabolic signal prior to the arrival of additional amino acids from digestion of the casein. To confirm this hypothesis a pilot study was conducted using leucine rich diets consisting of either whey or high protein (casein plus whey) which would deliver both leucine and other amino acids

together. Both whey and high protein diets produced greater rates of protein synthesis than the earlier diets tested and resulted in a progressive muscle mass recovery. Thus, supplementation with whey or high protein diets containing whey and other milk proteins may serve as a viable treatment to induce muscle mass following atrophy in the elderly.

Rieu et al., (2006) assessed protein kinetics in 20 healthy elderly men aged 70 (\pm 1) years old, both before and after ingestion of a balanced casein based diet supplemented or not with leucine. The leucine group was given 0.052g leucine per kg body weight, doubling plasma leucine concentration. Subjects were asked to consume this diet every 20 minutes over a 5 hour period. The leucine diet was also supplemented with isoleucine and valine, while the control diet was supplemented with alanine, which previously was shown to have no effect in protein anabolism. Whole body protein turnover was not affected but fractional synthesis rates increased with supplemental leucine. It was concluded from this that the supplementation of leucine in the diets of the elderly enhances protein synthesis and may represent an effective strategy to limit muscle protein losses during aging.

Whey Protein vs. Plant Protein

Yang et al., (2012) also examined the impact of soy protein consumption on muscle metabolism in older men. Thirty subjects (~71 yrs.) consumed 0, 20g or 40g of soy protein following a unilateral knee exercise to allow assessment of protein metabolism in both the exercised leg and the leg at rest. Results were then compared to responses obtained following ingestion of whey protein isolate previously obtained in a similar group of men. Total, essential and branched chained amino acids and whole body leucine oxidation increased with increased protein intake. However, peak blood leucine levels were higher for whey. Muscle fractional synthesis rates in unexercised legs (rest) were not increased as a result of ingestion of soy protein isolate but it was increased with ingestion both 20g and 40g of whey protein. With exercise muscle fractional synthesis rates were increased only with 40 g of soy. In contrast both 20g and 40 g of whey increased synthesis rates with 40g whey having the greatest impact. Results indicate that ingestion of whey protein isolate may have advantages for enhancing muscle protein synthesis in older men.

These studies provide examples of the combined effect of whey protein and resistance exercise in combating sarcopenia. While other strategies such as vitamin and hormonal supplementation may play a role, whey protein and exercise remain key factors for helping older adults preserve lean body mass and retain an optimal level of physical functioning.

Conclusion

Sarcopenia is a prevalent global health problem, with numbers affected continuing to climb as people live well into old age. Whey protein has been shown to be an effective tool in combating age-related skeletal muscle mass loss, largely due to its high concentration of leucine and its ability for fast and efficient absorption when compared with casein or soy protein. Especially in combination with resistance exercise, consumption of whey protein may be a key strategy in preventing and managing age-related declines in muscle mass and functional ability, thereby improving quality of life and health of older adults.

Exercise, Whey Protein and Their Combined Effects in Managing and Preventing Sarcopenia

While whey protein can positively affect skeletal muscle mass in older adults, its effects are amplified with the addition of physical activity. It is well-accepted that aerobic exercise improves cardiovascular health, regulates body weight/body fatness, and contributes to overall reduction in risk factors for the development of diabetes and cardiovascular disease (Koopman and van Loon 2008; Burton and Sumukadas, 2010). However, resistance exercise, in combination with whey protein, is the combination most frequently studied by researchers and health experts.

Prevention of Age-Related Muscle Loss

Drummond et al., (2008) examined whether supplementation of essential amino acids would stimulate similar rates of muscle protein synthesis in both young (n=7) and older men (n=6) between the ages of 24-77 yr. One hour after a bout of leg resistance exercise, each of the subjects was given 20 grams of essential amino acids, found in high concentrations in whey protein. Muscle biopsies were taken prior to testing and at 1, 3 and 6 hours post-ingestion. Muscle protein synthesis increased in younger men at both 1-3 hr. and 3-6 hr. post exercise, while older participants demonstrated the same response only during the 3-6 hr. post-exercise period. Thus, essential amino acids were able to increase muscle protein synthesis to a similar extent in both young and older men, albeit the time to muscle protein synthesis activation and peak was delayed in the elderly. Thus, the combination of resistance exercise

and dietary supplementation of essential amino acids (e.g. whey) can be a useful strategy to the prevention of age-related loss of muscle.

Increased Muscle Synthesis

In a study by Burd et al., (2011), 14 healthy elderly men aged ~72 years were divided into two groups and ingested either 20 grams of whey protein isolate (WPI) or 20 grams of micellar casein (MC) following a unilateral leg resistance exercise (3 sets of 10 repetitions on a leg extension machine). Blood essential amino acids and leucine concentrations peaked 60 min post drink, and both were higher after ingestion of WPI. Both rested leg and resistance exercised-stimulated rates of muscle protein synthesis were greater after ingestion of the whey protein.

Whey Protein Dosage

A similar study by Yang, et al., (2012) indicates that ingestion of whey protein at levels higher than 20 g in elderly men may be beneficial following resistance exercise. A dose response study was conducted in 37 generally healthy older men aged ~71 years. Subjects were randomly assigned to one of four treatments and ingested a beverage containing 0, 10, 20, or 40 g of whey protein following a unilateral leg resistance exercise. Peak plasma leucine concentration occurred 1-1.5 hr. following ingestion for all doses but was greater with the highest dose of 40 g. Whole body leucine oxidation increased in a stepwise manner as the ingested dose of whey protein increased. Researchers found that muscle fractional synthesis rate in the non-exercised leg was increased in the 20g and 40g whey protein groups, when compared with

those ingesting 0 g of whey protein. In the exercised leg, muscle fractional synthesis rate was increased at all levels of whey protein ingestion when examined versus the non-exercised leg. Researchers further found that in the exercised leg, the 20g and 40g whey groups saw muscle fractional synthesis rates statistically greater than the 0g and 10g whey groups. Further, the 40g whey group experienced a muscle fractional synthesis rate 32% greater than the group consuming only 20g. Thus in older adults, up to 40g of whey protein ingested post-resistance exercise was shown to be an effective strategy for increasing muscle fractional synthesis rate and thereby attenuating sarcopenia-related muscle loss.

Chale et al., (2012) examined the efficacy of whey protein combined with progressive resistance training on lean mass, muscle strength and physical function. Eighty sedentary, mobility-limited older adult men and women (~78 yrs.) received either two 20 g servings of whey protein (total 40 g/d) or carbohydrate control. Both groups performed three bouts of resistance training per week. Total lean mass increased in both groups as a result progressive resistance training after six months. Total lean mass gains were 1.3% for the whey group and 0.6% for the control group; however these differences were not statistically different. Examination of the overall diet indicated only a net increase of 18 g/d of protein consumed by the group receiving 40 g of whey protein. Researchers concluded that further research with higher whey protein doses, single versus multiple dose administration and longer times are needed to understand the role of protein supplementation in older aged-limited mobility individuals.

References

- Ahmed T, Haboubi N.** Assessment and management of nutrition in older people and its importance to health. *Clinical Investigations in Aging*. 2010;5:207-216.
- Blomstrand E, Eliasson J, Karlsson HKR, and Kohnke R.** Branched-chain amino acids activate key enzymes in protein synthesis after physical exercise. *Journal of Nutrition* 2006;136:269S-273S.
- Boirie Y, Dangin M, Gachon P, Vasson MP, Maubois JL.** Slow and fast dietary proteins differently modulate postprandial protein accretion. *Proceedings of the National Academy of Sciences of the United States of America*. 1997 DEC 23;94(26):14930-14935.
- Boirie Y.** Physiopathological mechanisms of sarcopenia. *The Journal of Nutrition, Health and Aging*. 2009;13(8):717-723.
- Breen L, Phillips SM.** Skeletal muscle protein metabolism in the elderly: Interventions to counteract the 'anabolic resistance' of ageing. *Nutrition and Metabolism (London)*. 2011;8:68. doi:10.1186/1743-7075-8-68.
- Brosnan JT, Brosnan ME.** Branched-chain amino acids: enzyme and substrate regulation. *Journal of Nutrition*. 2006;136:207S-211S
- Burd N, Yang Y, Moore DR, Tang, JE, Tarnopolsky, MA, Phillips SM.** Greater stimulation of myofibrillar protein synthesis with ingestion of whey protein isolate v. micellar casein at rest and after resistance exercise in elderly men. *British Journal of Nutrition*. 2012 Sep 28;108(6):958-62.
- Burton LA, Sumukadas D.** Optimal management of sarcopenia. *Clinical Investigations in Aging*. 2010 Sep 7;5:217-228.
- Cermak NM, Res PT, de Groot LCPGM, Saris WHM, van Loon LJC.** Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training: a meta-analysis. *American Journal of Clinical Nutrition*. 2012;96:1454-1464.
- Chale A, Cloutier GJ, Hau C, Phillips EM, Dallal GE, Fielding RA.** Efficacy of whey protein supplementation on resistance exercise-induced changes in lean mass, muscle strength, and physical function in mobility-limited older adults. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*. 2012 Oct 31. [Epub ahead of print]. doi: 10.1093/gerona/gls221.
- Churchward-Venne TA, Burd NA. & Phillips SM.** Nutritional regulation of muscle protein synthesis with resistance exercise: strategies to enhance anabolism. *Nutrition and Metabolism (London)*. 2012 May 17;9:40. doi: 10.1186/1743-7075-9-40.
- Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, Martin FC, Michael JP, Rolland Y, Schneider SM et al.** Sarcopenia: European consensus on definition and diagnosis: Report of the European working group on sarcopenia in older people. *Age Aging*. 2010 Jul;39(4):412-423. doi:10.1093/aging/afq034
- Department of Health and Human Services.** USA. Administration on Aging. A profile of older Americans: 2011. www.aoa.gov/aoaroot/aging_statistics/Profile/index.aspx: p3.
- Doherty TJ.** Invited review: aging and sarcopenia. *Journal of Applied Physiology*. 2003; 95:1717-1727. Doi 10.1152/jappphysiol.00347.2003.
- Drummond MJ, Dreyer HC, Pennings B, Fry CS, Dhanani S, Dillon EL, Sheffield-Moore M, Volpi E, Rasmussen BB.** Skeletal muscle protein anabolic response to resistance exercise and essential amino acids is delayed with aging. *Journal of Applied Physiology*. 2008;104:1452-1461. doi: 10.1152/jappphysiol.00021.2008
- Dutta C.** Significance of sarcopenia in the elderly. *The Journal of Nutrition*. 1997;127:992S-993S.
- Farnfield MM, Breen LB, Carey KA, Garnham A, Cameron-Smith D.** Activation of mTOR signaling in young and old human skeletal muscle in response to combined resistance exercise and whey protein ingestion. *Applied Physiology, Nutrition and Metabolism*. 2012;37:21-30.
- Fengna L, Yin Y, Tan B, Kong X, Wu G.** Leucine nutrition in animals and humans: mTOR signaling and beyond. *Amino Acids*. 2011;41(5):1185-1193. doi: 10.1007/s00726-011-0983-2.
- Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, Abellan van Kan G, Andrieu S, Bauer J, Breuille D, et al.** Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *Journal of the American Medical Director's Association*. 2011 May;12(4):249-256.
- Fry CS, Rasmussen BB.** Skeletal muscle protein balance and metabolism in the elderly. *Current Aging Science*. 2011 Dec;4(3):260-268.
- Hayes A, Cribb PJ.** Effect of whey protein isolate on strength, body composition and muscle hypertrophy during resistance training. *Current Opinion in Clinical Nutrition and Metabolic Care*. 2008;11:40-44.
- Hulmi JJ, Lockwood CM, Stout JR.** Effect of protein/essential amino acids and resistance training on skeletal muscle hypertrophy: a case for whey protein. *Nutrition and Metabolism (London)* 2010 June 17;7:51. doi: 10.1186/1743-7075-7-51
- Janssen I, Heymsfield SB, Ross R.** Low relative skeletal mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *Journal of the American Geriatrics Society*. 2002;50:889-896.
- Janssen I, Shepard DS, Katzmarzyk PT, Roubenoff, R.** The healthcare costs of sarcopenia in the United States. *Journal of the American Geriatrics Society*. 2004;52(1): 80-85. doi: 10.111/j.1532-5415.2004.52014.x.
- Katsanos CS, Chinkes DL, Paddon-Jones D, Zhang, X., Aarsland A, Wolfe RR.** Whey protein ingestion in elderly results in greater muscle protein accrual than its constituent essential amino acid content. *Nutrition Research*. 2008 Oct;28(10):651-658. doi: 10.1016/j.nutres.2008.06.007.
- Koopman R, van Loon, LJC.** Aging, exercise and muscle protein metabolism. *Journal of Applied Physiology*. 2009;106:2040-2048. doi: 10.1152/jappphysiol.91551.2008.
- Lang T, Streeper T, Cawthon P, Baldwin K, Taaffe DR, Harris TB.** Sarcopenia: etiology, clinical consequences, intervention and assessment. *Osteoporosis International*. 2010;21(4):543-559. doi: 10.1007/s00198-009-1059-y.

29. **Liu CJ, Latham NK.** Progressive resistance strength training for improving physical function in older adults. *Cochrane Database of Systematic Reviews*. 2009; Issue 3. Art. No: CD002759. doi:10.1002/14651858.CD002759.pub2.
30. **Magne H, Savary-Auzeloux I, Migne C, Peyron MA, Combaret L, Remond D, Dardevet D.** Contrarily to whey and high protein diets, dietary free leucine supplementation cannot reverse the lack of recovery of muscle mass after prolonged immobilization during aging. *The Journal of Physiology*. 2012;590.8:2035-2049. doi: 10.1113/jphysiol.2011.226266.
31. **Malafarina V, Uriz-Otano F, Iniesta R, Gil-Guerrero L.** Effectiveness of nutritional supplementation on muscle mass in treatment of sarcopenia in old age: a systematic review. *Journal of the American Medical Director's Association*. 2012;(In press):1-8.
32. **Marshall K.** Therapeutic applications of whey protein. *Alternative Medicine Review*. 2004; 9(2):136-156.
33. **Morley JE, Argiles JM, Evans WJ, Bhasin S, Cella D, Deutz NEP, Doehner W, Fearon KCH, Ferrucci L, Hellerstein MK, et al.** Nutritional recommendations for the management of sarcopenia. *Journal of the American Medical Director's Association*. 2010;11, 391-396. doi: j.jamda.2010.04.014.
34. **Muscaritoli M, Anker SD, Argiles J, Aversa Z, Bauer JM, Biolo G, Boirie Y, Bosaeus T, Cederholm T, Costelli P, et al.** Consensus definition of sarcopenia, cachexia and pre-cachexia: Joint document elaborated by Special Interest Groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics". *Clinical Nutrition*. 2010;29: 154-159.
35. **Paddon-Jones D, Rasmussen B.** Dietary protein recommendations and the prevention of sarcopenia. *Current Opinion in Clinical Nutrition and Metabolic Care*. 2009;12(1):86-90. doi: 10.1097/MCO.0b013e32831cef8b.
36. **Pennings B, Boirie Y, Senden JMG, Gijsen AP, Kuipers H, van Loon, LJC.** Whey protein stimulates postprandial muscle protein accretion more effectively than do casein and casein hydrolysate in older men. *American Journal of Clinical Nutrition*. 2011;93:997-1005.
37. **Pennings B, Groen B, de Lange A, Gijsen AP, Zorenc AH, Senden JMG, van Loon LJC.** Amino acid absorption and subsequent muscle protein accretion following graded intakes of whey protein in the elderly. *American Journal of Physiology, Endocrinology and Metabolism*. 2012;302:E992-E999. doi: 10.1152/ajpen-do.00517.2011
38. **Phillips SM, Tang JE, Moore DR.** The role of milk and soy-based protein in support of muscle protein synthesis and muscle protein accretion in young and elderly persons. *Journal of the American College of Nutrition*. 2009;28(4):343-354.
39. **Rieu L, Balage M, Sornet C, Giraudet C, Pujos E, Grizard J, Mosoni L, Dardevet D.** Leucine supplementation improves muscle protein synthesis in elderly men independently of hyperaminoacidemia. *The Journal of Physiology*. 2006;575.1:305-315. doi:10.1113/jphysiol.2006.110742.
40. **Rolland Y, Czerwinski S, Abellan Van Kan G, Morley JE, Cesari M, Onder G, Woo J, Baumgartner R, Pillard F, Boirie Y, et al.** Sarcopenia: its assessment, etiology, pathogenesis, consequences and future perspectives. *The Journal of Nutrition, Health and Aging*. 2008;12(7):433-450.
41. **Volpi E, Kobayashi H, Sheffield-Moore M, Mittendorfer B, Wolfe RR.** Essential amino acids are primarily responsible for the amino acid stimulation of muscle protein anabolism in healthy elderly adults. *American Journal of Clinical Nutrition*. 2003;78(2):250-258.
42. **Walrand S, Guillet C, Salles J, Cano N, Boirie Y.** Physiopathological mechanism of sarcopenia. *Clinical Geriatric Medicine*. 2011;27:365-385. doi:10.1016/j.cger.2011.03.005.
43. **Wannamethee SG, Shaper AG, Lennon L, Whincup PH.** Decreased muscle mass and increased central adiposity are independently related to mortality in older men. *American Journal of Clinical Nutrition*. 2007;86:1339-1346.
44. **Waters, D., Baumgartner, R., Garry, P. & Vellas, B.** Advantages of dietary, exercise-related, and therapeutic interventions to prevent and treat sarcopenia in adult patients: an update. *Clinical Interventions in Aging*. 2010;10(5):259-270.
45. **Wilson, G. et al. (2011).** Leucine dense whey proteins to optimize anabolic responses in skeletal muscle. *International Journal on Nutraceuticals, Functional Foods and Novel Foods from Research to Industrial Application*. 2011;10: 2-3.
46. **Wolfe RR.** The role of dietary protein in optimizing muscle mass, function and health outcomes in older individuals. *British Journal of Nutrition*. 2012;108(Suppl. 2):S88-S93. doi: 10.1017/S0007114512002590.
47. **World Health Organization.** Ten facts on aging and the life course. <http://www.who.int/features/factfiles/aging/en/index.html>. (2012a).
48. **World Health Organization.** Global brief for World Health Day 2012, Good health adds life to years. http://www.who.int/world_health_day/2012. Document number: WHO/DCO/WHD/2012.2. (2012b). p10.
49. **Yang Y, Breen L, Burd NA, Hector AJ, Churchward-Venne TA, Josse AR, Tar-nopolsky MA, and Phillips SM.** Resistance exercise enhances myofibrillar protein synthesis with graded intakes of whey protein in older men. *British Journal of Nutrition*. 2012; Available on CJO 2012 doi:10.1017/S000711451007422.

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