Effect of Diet on Loss and Preservation of Lean Body Mass in Aging Dogs and Cats

Dottie Laflamme, DVM, PhD, DACVN
Floyd, VA
JunqueDr@yahoo.com

Abstract
Sarcopenia may be defined as an age-related loss of lean body mass (LBM) unrelated to disease. It is a long-term process that becomes evident later in life, it has a complex and multifactorial etiology, and it increases the risks for morbidity and mortality. Dietary factors play a role in minimizing this age-related loss of LBM. Specifically, increased intake of protein and vitamin D has shown benefits. Other nutrients that appear to be important are those related to acid/base balance and inflammation. Most of the research into sarcopenia has been done in humans and rodent models, but some aspects have been confirmed in dogs or cats. More research is needed to determine optimum nutrient levels to reduce or prevent sarcopenia in aging dogs and cats.

Muscle and lean body mass (LBM) are determined by the balance between the rates of de novo protein synthesis and protein degradation. During growth, protein synthesis exceeds degradation and muscle mass increases, while in mature subjects protein synthesis and degradation are roughly equal so that muscle mass remains constant. With age this balance is lost and LBM decreases, leading to sarcopenia, which may be defined as an age-related loss of LBM unrelated to disease.

Sarcopenia is a lifelong process that becomes evident later in life, and it has a complex and multifactorial etiology. In most cases, the loss of LBM is offset by an increase in fat mass, resulting in little or no change in body weight. The age-related loss of LBM occurs in all species evaluated to date, including humans, dogs and cats.

In cachexia, a 15% reduction in LBM interferes with organic and physiological functions, while a decrease beyond 30% is usually fatal. Although there is no agreed upon cutoff to define sarcopenia, one study identified sarcopenia as a 3% loss in muscle mass or a 40% loss of grip strength over a three-year timeframe.

Functional measures of muscle strength are not conducted in dogs or cats, but significant loss of LBM has been demonstrated in aging dogs and cats. A cross-sectional study of 256 cats showed that apparently healthy cats lose approximately one-third of their LBM between about 10 and 15 years of age. This was confirmed in a longitudinal study following mature and geriatric cats over an eight-year period, wherein mean LBM decreased by 34%. In aging dogs, there was approximately a 10% loss in LBM and corresponding increase in fat mass. These effects appeared to be more pronounced in dogs beginning at age 8 to 9 years. Lifelong limited feeding or increased dietary protein intake reduced or delayed this age-related loss of LBM. Another longitudinal study in Labrador Retrievers confirmed loss of LBM with age and identified that the longest-lived dogs in the study experienced the slowest loss of LBM. Similar results were observed in cats. As with humans, loss of LBM in dogs and cats is associated with increased mortality.

Etiology of Sarcopenia
The etiology of sarcopenia is multifactorial and complex. Elderly people, especially those who are sarcopenic, have a blunted anabolic response to nutritional stimuli, such as amino acids and insulin. Some of the factors involved in sarcopenia include altered protein turnover with decreased muscle protein synthesis, due in part to decreased functionality of the mTOR pathway, and a relative increase in protein catabolism; chronic low-grade inflammation with increased cytokines such as TNF and IL-6; mitochondrial dysfunction; increased oxidative stress; insulin resistance; and altered neuromuscular junction structure and function. Regardless of the mechanisms, the result is a decrease in endogenous protein synthesis, possibly coupled with increased protein catabolism, leading to decreased muscle mass and strength.

Although exercise is the most efficient therapy for managing sarcopenia, it is recognized that nutrition also plays a role in the development and management of this condition. Specifically, adequate dietary protein, specific amino acids and vitamin D have been shown to play a role. Protein supplementation coupled with exercise achieves the best results in sarcopenic people. Other dietary factors that...
may be important include nutrients impacting metabolism, inflammatory mediators and acid/base balance.

**Role of Diet in Sarcopenia**

**Protein:**

Insufficient protein intake can contribute to loss of LBM. Multiple studies have confirmed lower protein intakes were associated with increased risk for sarcopenia in elderly people.\(^{13,16,20}\) Likewise, in dogs and cats, lower protein intake was associated with greater loss of LBM.\(^{6,16,17,22-24}\) Dietary protein supports both endogenous protein turnover and gluconeogenesis. When dietary protein intake is inadequate, mammals will gradually deplete proteins from their LBM, particularly skeletal muscle, to support these metabolic functions.\(^{25-27}\)

Aging impacts the physiological response to protein intake. Muscle protein synthesis in response to protein intake is attenuated in older people compared to younger people.\(^{12-14,21,23}\) Increasing the amount of protein consumed may help to overcome this anabolic resistance. For example, muscle-protein synthesis was stimulated in young adults with <10g of whey protein, but older men required >20g whey protein to achieve similar protein synthesis.\(^{22}\) It appears that the recommended daily allowance (RDA) (0.8g/kg bodyweight), which was established using data from young adult men, is not adequate to maintain nitrogen balance nor preserve muscle mass in elderly people.\(^{17}\) Although not universally accepted, there is a growing consensus that older people should consume more protein. Daily intake of at least 1.0 to 1.2g/kg body weight is recommended, an increase of 50% over the RDA.\(^{21,23,25}\)

The amount of protein that is “adequate” for dogs and cats also remains controversial. Traditionally, nitrogen balance studies were used to determine minimum protein requirements. However, nitrogen balance studies do not account for maintenance of muscle mass, and multiple studies have indicated that the amount of protein required to maintain LBM or protein turnover far exceeds that needed to maintain nitrogen balance.\(^{15-17,21,26-30}\) For example, cats need only about 1.5g protein/kg body weight to maintain nitrogen (protein) balance but need over 5g protein/kg body weight to maintain LBM.\(^{21}\) Dogs required about three times more protein to maintain protein/DNA ratios (an indicator of protein reserves) compared to that needed to maintain nitrogen balance, and old dogs needed 50% more protein than young dogs regardless of the measure used.\(^{27}\) As in humans, greater protein intake helps reduce the age-related loss of LBM in dogs and cats.\(^{5-21,26}\)

Specific types of protein and amino acids also can impact LBM. “Fast” proteins, such as whey, contribute to greater endogenous protein synthesis compared to “slow” proteins, such as casein. Whey, a soluble protein, is rapidly digested and absorbed. Casein protein clots in the stomach, delaying gastric emptying and slowing uptake of the amino acids.\(^{31}\) The greatest anabolic effect of protein appears dependent on reaching a threshold concentration. Rapidly absorbed proteins achieve this threshold, while slower absorption of the same amino acids fails to achieve the threshold, resulting in less protein synthesis.\(^{31}\) In healthy young adults, post-prandial protein synthesis was increased 68% by whey but only 31% by casein. Although casein protein reduced protein catabolism to a greater extent compared to whey, net protein balance was more positive for the whey protein.\(^{31}\)

Similar findings were observed in old rats, in elderly men and following exercise.\(^{20,33}\)

Whey protein is rich in branched-chain amino acids including leucine, which is recognized to have important regulatory actions on protein turnover. Among other functions, leucine reduces proteolysis and enhances protein synthesis.\(^{15,36}\) Whey protein also triggers insulin release, which promotes protein synthesis.\(^{20,36}\) When the effect of whole whey protein was compared to an infusion equivalent to its essential amino-acid content, the intact whey protein resulted in greater muscle protein accrual.\(^{25}\

Based on the numerous studies showing beneficial effects from either leucine or whey protein on muscle protein synthesis, studies in sarcopenic humans have been conducted using leucine-enriched whey protein (along with vitamin D) supplements.\(^{36,37}\) In the first of these multicenter trials, elderly sarcopenic subjects received a supplement containing 20g whey protein (including 3g leucine), 800IU vitamin D and a mixture of vitamins, minerals and fiber twice daily, or they received an isocaloric placebo containing carbohydrates, fat and some trace elements. The baseline protein intake in both groups averaged 1.0g protein/kg body weight daily. Over the 13-week study, the treated group showed significantly greater improvement in the chair-stand test, indicating greater strength and balance, and also in muscle mass.\(^{25}\)

Another study evaluated subjects given a once daily supplement containing 22g whey protein, 9g essential amino acids, and 100IU vitamin D compared to those receiving a placebo, while both groups underwent a similar exercise program for 12 weeks.\(^{37}\) The treated group showed significant improvements in muscle mass and muscle strength. In addition, the treated group showed reduced body fat, improved fat distribution, increased insulin-like growth factor, and reduced C-reactive protein, an inflammatory mediator.\(^{25}\)

The amino acid lysine also may impact LBM. Studies in swine and rats show that lysine deficiency leads to increased protein degradation and decreased protein synthesis in muscle, whereas supplementation with lysine decreased muscle protein degradation.\(^{38,39}\)

Since lysine is limited (low relative to requirements) in many vegetable-source proteins, supplementation may be most important for vegetarians or for those whose diets are based on vegetable-source proteins. A study in young adult dogs fed diets containing mixtures of corn gluten or poultry as the protein sources evaluated changes in LBM and body fat, and changes in the 20S proteasome of the ubiquitin proteasome pathway involved in protein catabolism.\(^{19}\

While most dogs
lost LBM, those with the highest lysine intake gained LBM. In dogs fed 12% protein diets, there appeared to be an inverse linear correlation between lysine intake and LBM loss. Further, the 20S proteasome was decreased in dogs fed the high-lysine diet, suggesting a reduction in protein catabolism via this mechanism. This is consistent with pigs, where lysine-deficient diets trigger upregulation of this catabolic pathway.9

Similarly, in aging cats, lysine appears to protect LBM. One published study in aging cats evaluated the impact of diets containing protein ranging from 6.87 to 10.22g/100Kcal, and lysine (lysine:calorie ratio) ranging from 2.71 to 6.30 on changes in LBM. Although there were limitations to the study, it showed that increasing dietary lysine, independent of total protein, helped reduce loss of LBM in aging cats.10

**Vitamin D:**

Multiple epidemiological studies have identified an association between low serum vitamin D concentrations and an increased prevalence of sarcopenia in aging people.11,12,13 Coupled with low vitamin D were increased concentrations of parathyroid hormone (PTH), which also has been associated with loss of muscle mass and strength.9

Vitamin D metabolites can influence muscle cell metabolism by mediating gene transcription as well as by other mechanisms.9 Vitamin D affects the transcription rate of thousands of genes, including insulin receptors.42 Activation of insulin receptors contributes to increased muscle protein synthesis, and supplemental vitamin D results in increased vitamin D receptors within muscle.14-16 In aged rats, vitamin D deficiency reduced the rate of protein synthesis by 40% compared to vitamin-D replete rats.42 In both rodents and humans, vitamin D deficiency induced greater body fat and intramuscular lipids, a finding linked with compromised neuromuscular function.14 Intramuscular fat also may contribute to reduced protein synthesis via activation of eukaryotic initiation factor 2a (eIF2α).42 Activated eIF2α inhibits initiation of protein translation and the rate of protein synthesis. Whether this specific mechanism applies to humans, dogs or cats remains to be determined.

Low serum vitamin D may impact muscle function via PTH, which can be increased due to lack of inhibition from vitamin D. PTH increases intracellular calcium concentrations, which may disrupt muscle structure or function. PTH also may stimulate release of inflammatory mediators such as IL-6. Elevated IL-6 in aging humans is associated with lower muscle mass and strength.9 Independent of PTH, studies have shown an inverse association between serum vitamin D and IL-6 and between intramuscular vitamin D receptor density and intramuscular IL-6 in aging humans.16

Studies in humans evaluating vitamin D supplementation have generally yielded beneficial results with improvements in muscle strength as well as muscle mass.14-17 These effects were primarily observed in individuals with initially low serum vitamin D concentrations, which is common in sarcopenia. Provision of vitamin D along with supplemental protein may yield the best results, but additional research is needed.14,36,37 Currently, data on vitamin D supplementation to preserve LBM in dogs or cats is lacking.

**Acid/Base Balance:**

Acidosis is associated with increased protein catabolism, negative nitrogen balance and muscle protein wasting. It appears to promote muscle protein catabolism via the ubiquitin proteasome pathway and to inhibit protein synthesis via promotion of insulin resistance.44-46 Insulin normally promotes protein synthesis, but this effect is hindered in insulin resistance. Metabolic acidosis induces insulin resistance and interferes with insulin-signaling pathways, leading to reduced phosphatidylinositol 3-kinase (PI3K) activity and increased protein degradation.46

The role of acidosis in LBM wasting is best recognized in patients with chronic kidney disease (CKD), but the same or similar mechanisms may play a role in other conditions, including sarcopenia.47,48 Correction of acidosis in subjects with CKD eliminated the muscle-protein degradation and improved muscle mass.47

Animal proteins and cereal grains are metabolized to acidic residues, whereas fruits and vegetables are metabolized to alkaline residues, such as potassium bicarbonate. In non-CKD aging men and women, studies have established an association between greater intake of alkaline foods and greater LBM.48-50 A small, short-term study in elderly women showed that adding potassium bicarbonate to a high-protein diet significantly reduced nitrogen excretion compared to those fed the high-protein diet alone.49 A larger study confirmed the benefit of reducing dietary acid load on preservation of LBM in older women, but not in men.48

Even mild metabolic acidosis may contribute to a loss of LBM and sarcopenia.49,50 In a study of men with CKD, in which arterial pH was adjusted by oral intake of sodium citrate/citric acid and ammonium chloride, alterations of pH within the normal range (7.37 to 7.44) induced significant differences in nitrogen balance.50

While serum bicarbonate may be monitored in pets, evaluation of blood pH or blood gases to quantify acid/base balance is rarely done, especially in healthy aging pets. Future research should evaluate the importance of acid/base or dietary anion gap on LBM in aging dogs and cats.

**Omega-3 Fatty Acids:**

Increased markers of inflammation are common in sarcopenic humans and associated with subsequent decline in muscle strength and mobility.18 Inflammation may interfere with the mTOR signaling pathway, critical for normal protein synthesis.11 Although not specific to sarcopenia, studies in humans have shown that consumption of fish oil, a source of the long-chain omega-3 fatty acids eicos-
apenaenoic acid (EPA) and docosahexaenoic acid (DHA), results in reduction of the inflammatory mediators C-reactive protein, IL-6 and tumor necrosis factor-alpha.13

Independent of circulating markers of inflammation, EPA and DHA supplementation may influence the mTOR signaling pathway to overcome age-related anabolic resistance to protein synthesis.14 Using a hyperaminoacidemia-hyperinsulinemia clamp to study muscle-protein synthesis in healthy older humans, mTOR activation and protein synthesis were enhanced in those given fish oil over those given corn oil.15 Observational studies showed correlations between habitual fish oil intake and greater LBM. Some, but not all, interventional studies have shown improvements in strength and muscle mass in aging humans.16 Although fish oil can reduce inflammatory mediators in dogs and cats, there is no published data evaluating the impact of fish oil on muscle mass or function in these species.

Antioxidants:

Multiple epidemiological studies have shown associations between increased serum antioxidants or decreased markers of oxidative stress and reduced risk for sarcopenia.17 However, the few interventional studies that have been conducted have not found benefits. On the contrary, one study actually showed a detriment from supplementing vitamins E and C, with a reduced response to exercise on muscle mass.18

Other Nutrients:

Reduced calorie intake or reduced digestion and metabolic efficiency can contribute to loss of weight and LBM. Although energy requirements decrease with age in most species, in cats this appears to be true only up to about 10 to 12 years of age.3 With advancing age, geriatric feline energy requirements actually increase despite a decrease in body size. This effect appears to accelerate after approximately 13 years of age. The increased energy requirement in aging cats may be due, in part, to reduced digestive function.3 Older cats had an average reduction in energy digestion of about 8% and in protein digestion of about 6%.52 In other studies, 33% of healthy geriatric cats had a reduced ability to digest fat, and 20% had a reduced ability to digest protein.3

Concurrent with the reduced fat digestion, there is reduced absorption of numerous minerals and vitamins, including vitamin B12,53 potentially contributing to metabolic inefficiencies. Recent epidemiological evidence in humans suggests a possible role of minerals and trace nutrients in sarcopenia. Specifically, magnesium, phosphorus, selenium, and vitamin B12 intakes were lower in the sarcopenic subjects compared to age-matched adults without sarcopenia. Serum B12 was 15% lower in the sarcopenic group compared with controls.54,55 Given that B vitamins serve as cofactors in energy and protein metabolism, avoidance of deficiencies may be important in preserving LBM.

Conclusions

Rapidly accumulating evidence in humans and other species suggests links between dietary nutrients and preservation of LBM in aging subjects. The data suggest that protein intake should increase with aging. For aging humans, it should exceed the RDA by at least 50%. Older dogs and cats also should receive more protein compared to standard recommendations. Although dietary protein has proven to play a role in the loss of LBM that occurs in aging dogs and cats, most other nutrients have not yet been evaluated for their role in sarcopenia in pets. As loss of LBM is common in both dogs and cats, future research should focus on some of these nutrients that have not been studied in other species.

References


