

Age-Related Muscle Loss: Sarcopenia and Cachexia

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Abstract

Sarcopenia and cachexia are two important syndromes that occur in aging and in animals with diseases, respectively. Cachexia is a common finding that is associated with increased morbidity and mortality. Sarcopenia is similar to cachexia in that it is characterized by muscle loss, but sarcopenia occurs during aging in the absence of disease. Both syndromes are becoming increasingly important in dogs and cats because of their high prevalence and deleterious effects. A better understanding of these syndromes is critical to optimize patient care.

Sarcopenia

Significant loss of lean-body mass occurs with aging. This loss of lean-body mass, termed sarcopenia, occurs in the absence of disease (although sarcopenia and cachexia can occur concurrently, see below).¹ In people, sarcopenia actually begins early in life, around 30 years of age, and from 20 to 80 years of age, there is a 30% reduction in muscle mass.² In sarcopenia, the loss of lean-body mass often is accompanied by an increase in fat mass so the total weight may not change (or may even increase), thus masking the sarcopenia. Sarcopenia has important clinical implications because it is associated with increased mortality.^{1,2} The mechanisms of sarcopenia appear to be multifactorial and involve physical inactivity, elevated cytokine production, decreased concentrations of growth hormone and testosterone, changes in type II muscle fibers, insulin resistance, and decreased protein synthesis. Few studies investigating sarcopenia have been conducted in dogs and cats, but available information shows that dogs and cats also lose lean-body mass during aging.³ This is an important area for future research with potential opportunities for prevention and treatment.

Cachexia

Cachexia, a loss of lean-body mass, has been described since the time of Hippocrates.¹ It is estimated to affect 0.5 to 1.0% of the populations of the United States, Europe, and Japan, or 6 to 12 million people.⁴ Cachexia occurs in a variety of acute and chronic diseases in people, including heart failure (cardiac cachexia), cancer (cancer cachexia), chronic

Glossary of Abbreviations

BCS: Body Condition Score
CHF: Congestive Heart Failure
CKD: Chronic Kidney Disease
DEXA: Dual-Energy X-Ray Absorptiometry
IL-1: Interleukin-1
MCS: Muscle Condition Score
TNF: Tumor Necrosis Factor

kidney disease (CKD; renal cachexia), and chronic obstructive pulmonary disease, as well as in people with acute illnesses and injuries. The syndrome of cachexia also is common in companion animals with these conditions.¹

The weight loss associated with cachexia is unlike that seen in a healthy dog, cat or person who loses weight. In a healthy animal that is receiving insufficient calories

to meet requirements, metabolic adaptations allow fat to be used as the primary fuel source, thus preserving lean-body mass. In animals with illnesses or injury, the primary fuel source is amino acids from muscle so these animals quickly catabolize muscle and lean-body mass. Therefore, loss of lean-body mass is a hallmark of cachexia, and fat is lost to a lesser degree. The loss of lean-body mass has direct and deleterious effects on strength, immune function, and survival. In people, cachexia is an independent predictor of mortality.

Current definitions of cachexia in people rely primarily on loss of body weight (typically 5% over a period of 6 to 12 months).⁵ Total weight loss is an insensitive measure of muscle loss, so using weight loss as a diagnostic criterion reduces the ability to identify cachexia until its more advanced stages and results in an underdiagnosis of the prevalence of this syndrome. In addition, there are certain types of cachexia (e.g., cardiac cachexia with fluid accumulation) in which weight loss is masked by the accumulation of fat or water. Therefore, waiting until weight loss occurs often prevents an early diagnosis and misses the underlying issue of lean-body mass losses and inflammation. Another reason for using factors other than total weight loss for a diagnosis of cachexia is that cachexia is a process, i.e., a loss of lean-body mass, and not necessarily an end-stage syndrome. Lean-body mass loss occurs before significant weight loss can be detected. If a loss of lean-body mass was used as a criterion for the diagnosis of cachexia, the prevalence of this syndrome in chronic diseases would be even higher.

In addition to the insensitivity of weight loss as the criterion for cachexia, it is not only the quantitative loss of muscle that results in deleterious effects.¹ There also are qualitative changes in muscle function including increased collagen content, altered mitochondrial function, and a shift in fibers from type I (oxidative) to type IIb (glycolytic).

This shift may further predispose muscle fibers to atrophy as part of the mechanism for cachexia as glycolytic fibers are less resistant to atrophy.

Severe weight loss in a patient with advanced heart failure or cancer represents a classical picture of cachexia and offers little diagnostic dilemma. However, identification of cachexia is more difficult when it is more subtle. Therefore, developing clinically applicable techniques is necessary to identify lean-body mass loss at an early stage in which treatments are much more likely to be successful. Some of the currently used research tools, such as dual-energy X-ray absorptiometry (DEXA), have limitations for measurement of lean-body mass due to inherent assumptions. However, clinically applicable methods of assessing muscle, such as muscle condition score (MCS), can and should be evaluated in every patient at every visit, in addition to body weight, body condition score (BCS), and diet history. Additional techniques for quantification of muscle loss, such as ultrasound, are being developed.

There are many mechanisms that are consistent across all types of cachexia, including underlying mechanisms (i.e., inflammation) and effects on body composition and food intake. However, there also are some details specific to individual types of cachexia. The three most common forms of cachexia are cardiac, cancer, and renal.

Cardiac Cachexia

Cardiac cachexia is common in dogs and cats with congestive heart failure (CHF), with >50% of patients affected by some degree of cachexia. Anorexia, hyporexia, or dysrexia are extremely common in dogs and cats with CHF, which limits the substrates available for maintaining weight and lean-body mass.¹ However, inflammatory cytokines, such as tumor necrosis factor (TNF) and interleukin-1 (IL-1), are primary mediators of cachexia. These inflammatory cytokines are known to directly cause anorexia, to increase energy requirements, and to increase the catabolism of lean-body mass. Of particular pertinence to heart disease, TNF and IL-1 also cause cardiac myocyte hypertrophy and fibrosis, and have negative inotropic effects. In addition, reduction of cytokines has been correlated with survival in dogs and cats with CHF.

Cancer Cachexia

In people, cancer is one of the most common diseases in which cachexia is present. In people with cancer, it is estimated that over 50% lose weight unintentionally, though the prevalence depends on the type of cancer. Although few dogs and cats with cancer have a thin BCS, weight loss (69% in dogs) and muscle loss (35% of dogs and 91% of cats) are much more common.^{6,7} Therefore, specific attention to changes in muscle mass, as well as changes in body weight, are important in order to detect cancer cachexia.

Renal Cachexia

Reduced food intake, weight loss and muscle loss are very common in dogs and cats with CKD. Thin body condition in dogs and weight loss in cats have been associated with shorter survival times.^{8,9}

New Interventions

Because of the important implications of sarcopenia and cachexia on morbidity and mortality in people, there is extensive research into the prevention, diagnosis, and treatment of this syndrome. Nutritional modification, hormone replacement, and exercise (both resistance and aerobic) are being actively studied to combat sarcopenia and to enhance healthy aging. There are exciting opportunities for new and effective targets in cachexia and sarcopenia to reduce energy requirements, enhance energy intake, improve nutrient absorption, and modify metabolic alterations to prevent and even reverse muscle loss as the mechanisms of these syndromes are becoming better understood (e.g., ghrelin receptor agonists, myostatin antagonists).

Practical Implications

One of the keys to the practical management of cachexia and sarcopenia in dogs and cats is recognizing it in its earliest stages, and to achieve this nutritional assessment (body weight, BCS, MCS, and diet history) must be consistently assessed. The goal for BCS in a healthy young- to middle-aged dog or cat should be 4 to 5 on a 9-point BCS scale. However, in certain diseases (e.g., CHF, CKD), a slightly higher BCS may be desirable. Obesity (>7/9 BCS) should be avoided.

MCS differs from the BCS in that it specifically evaluates muscle mass. Evaluation of muscle mass includes visual examination and palpation of the head, scapulae, thoracic and lumbar vertebrae, and pelvic bones. BCS and MCS are not directly related as an animal can be obese but still have significant muscle loss (or, conversely, be very thin but have a normal MCS). Palpation is required for accurately assessing BCS and MCS, especially in animals with medium- to long-hair coats. Consistently evaluating MCS in all patients will help to identify muscle loss at an early stage (i.e., mild) in aging or ill animals, rather than waiting until muscle loss is moderate or severe when it may be more difficult to successfully intervene.

New treatments are being evaluated in humans and companion animals to increase food intake, maintain body weight, and most importantly, maintain or increase lean-body mass. These include approaches such as cytokine antagonists, myostatin antagonists, and ghrelin agonists. However, a wide variety of approaches are currently being investigated that may hold promise for both humans and companion animals.

Conclusions

Sarcopenia and cachexia are becoming important in veterinary practice because of their high prevalence and deleterious effects, and a better understanding of these syndromes is critical to optimize patient care. New drugs, diets, and other treatments to specifically target sarcopenia and cachexia are being developed and are likely to benefit canine and feline, as well as human, patients.

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