
Management of Overweight Dogs and Cats with Cancer

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Introduction

Obesity is the most common form of malnutrition diagnosed in dogs and cats in North America. Estimates of the proportion of affected animals vary, but it is generally accepted that between 20 and 45% of dogs and cats are overweight.¹

At the same time, necropsy surveys suggest that as many as 45% of dogs older than 10 years will die of cancer.² Given this background, it is not surprising that many dogs and cats are overweight at the time they are diagnosed with cancer. Management of these patients can be challenging not only because of their complex clinical presentation but also because of widespread misconceptions regarding optimal nutritional management of animals with neoplastic disease in general. This paper will first examine what is known about the relationship between obesity and cancer in both people and animals. A practical step-wise approach that can be used to manage individual animals with cancer and concurrent obesity will then be presented.

Relationship Between Obesity and Cancer in People

The type of malnutrition historically considered most typical of the tumor-bearing state is not obesity but rather the form of protein-energy malnutrition termed “cancer cachexia.” Cancer cachexia in people and animals is characterized clinically by weight loss, fatigue, anemia, and loss of both lean body mass and adipose stores,³ and can be classified as either primary or secondary.⁴ Primary cancer cachexia is an incompletely understood paraneoplastic syndrome in which the intermediary metabolism of fat, protein and carbohydrate is altered by an aberrant systemic inflammatory response to the underlying tumor, ultimately leading to inefficient energy utilization and weight loss. Secondary cancer cachexia is caused by functional abnormalities that are not necessarily specific to neoplastic disease, such as treatment-related nausea and vomiting or compromised gastrointestinal function caused by the physical presence of neoplastic cells, which can cause weight loss as well. Regardless of whether it is primary or secondary, the negative impact of cancer cachexia on quality of life and survival is well-documented and accepted in people and is becoming increasingly well understood in dogs and cats.^{3,5}

Despite the classic association of cachexia with malignant disease, however, it is increasingly evident that there also is a

Glossary of Abbreviations

BCS: Body Condition Score

CEA: Carcinoembryonic Antigen

IGF-1: Insulin-Like Growth Factor 1

IMRT: Intensity Modulated Radiation Therapy

PSA: Prostate Specific Antigen

SRT: Stereotactic Radiotherapy

strong and complex association between obesity and malignant disease. Obese people are documented to have significantly increased risk of developing neoplasms of the esophagus, pancreas, colon, endometrium, breast, and kidney, and they are also more likely to develop multiple myeloma, non-Hodgkin’s lymphoma and some types of leukemia.⁶ A number

of different mechanisms have been proposed to explain the observed increase in cancer incidence in this population. Increased secretion of insulin-like growth factor 1 (IGF-1) induced by the insulin resistance associated with obesity may promote induction and progression of malignant disease by stimulating cell proliferation, inhibiting apoptosis and enhancing angiogenesis.⁷ Higher levels of sex hormones, especially the estrogen synthesized by excess adipose tissue, are hypothesized to increase cancer risk by disrupting normal cellular growth and differentiation and inhibiting apoptosis.⁸ Increased synthesis of the polypeptide hormone leptin by the increased mass of adipose tissue in obese individuals could also promote tumor development because it stimulates cell proliferation and inhibits apoptosis.⁹ Finally, obesity itself is a chronic inflammatory disease and, as such, is recognized to have wide-ranging effects on the production and function of various cytokines and other mediators of inflammation. These may have a permissive effect on tumor development.⁸

In addition to the role that it plays in the pathogenesis of cancer on the cellular level, once a tumor is present, obesity can have a number of significantly negative consequences with respect to both the diagnosis and treatment of neoplastic disease in people.¹⁰ Obese people are less likely to participate in cancer-screening programs, so a definitive diagnosis of cancer may be delayed or missed altogether. It also has been suggested that obesity can decrease levels of tumor biomarkers, such as prostate specific antigen (PSA) and carcinoembryonic antigen (CEA), through increased plasma volume and hemodilution, leading to false negative or equivocal screening test results.^{11,12} The quality and accuracy of ultrasound, CT and MRI images can be compromised by the presence of excessive adipose tissue, making it difficult to define the location and extent of neoplastic disease.¹⁰

With respect to cancer treatment, dosing of the appropriate cytotoxic chemotherapy drugs can be challenging in obese individuals. Many drugs are dosed on a body surface area basis,

and some studies examining frequency of chemotherapy dose reductions as well as incidence and severity of treatment-related side effects, such as myelosuppression, suggest that obese people receiving chemotherapy for treatment of their cancers may be undertreated.^{13,14} Obesity is likely to have a negative effect on the pharmacokinetics of some chemotherapy agents as well, altering important factors such as the volume of drug distribution and hepatic drug metabolism.¹⁰ Problems are often encountered in the delivery of radiotherapy in obese people. In particular, the precise and repeatable positioning that is essential for safe and effective delivery of intensity modulated radiation therapy (IMRT) and stereotactic radiotherapy (SRT) can be challenging in obese individuals because of increased skin mobility, increased motion of intra-abdominal organs within abdominal adipose tissue, and obscured bony landmarks.¹⁰ Finally, although major complications and short-term mortality do not appear to be increased, minor complications are reported to be more likely after cancer surgery in obese people.¹⁵ Based on all these considerations, it should not be surprising that there is evidence that people with established obesity have shorter survival times and higher all-cause, cancer-specific and cardiovascular death rates after they are diagnosed with a variety of types of cancer.^{16,17} They also tend to have compromised health-related quality of life.¹⁰

The authors of a recent review identified four major challenges associated with the clinical management of obese people with cancer: obesity-related comorbidities, such as hypertension, cardiovascular disease and type 2 diabetes mellitus; polypharmacy often directed at obesity-related comorbidities along with its associated drug interactions; development of sarcopenic obesity; and further weight gain after cancer diagnosis and treatment.¹⁰ Of these four challenges, sarcopenic obesity was felt to be of particular clinical significance. This is a condition described in some overweight people with neoplastic disease. Sarcopenic obesity is characterized by severe excess of body fat with a concurrent decrease in muscle mass and is believed to be initiated by the chronic inflammation associated with obesity. Sarcopenic obesity is important because it has a negative impact on outcome and survival. Affected individuals have significant loss of muscle and muscle function, reduced performance scores, and increased risk of cancer treatment-related toxicity compared to obese people with normal muscle mass. Early diagnosis and appropriate treatment is important for prognosis, and high-protein diets combined with physical exercise were proposed as effective potential interventions.¹⁰

Relationship Between Obesity and Cancer in Dogs and Cats

Although the relationship between obesity and cancer in dogs and cats could be similar in many respects to that seen in people, this has not been thoroughly investigated or proved. Early work shows that some of the endocrine changes believed to be involved in the pathogenesis of malignant disease in people are also present in obese dogs and cats. For instance, circulating leptin

concentrations are increased in obese dogs and cats, as they are in people.^{18,19} Canine adipocytes also possess the genes needed to synthesize the proinflammatory cytokine interleukin-6, and obese dogs have been shown to have increased serum concentrations of tumor necrosis factor- α and IGF-1.^{20,21} However, a link between these specific changes and increased cancer risk has yet to be established.

Several authors have investigated the potential role of body condition over time in the pathogenesis of cancer in the dog. Dogs with mammary gland tumors have been most frequently studied. One case control study investigated the effect of body condition and diet on the risk of mammary cancer in dogs and found that risk was decreased in both spayed and unspayed dogs that had been thin at 9 to 12 months of age.²² A similar study found that obesity at 12 months of age was associated with an increased risk of mammary cancer. This study also implicated regular consumption of human foods in tumor development because dogs with breast cancer were more likely to have high intake of red meat.²³ The authors of a third study were unable to find an association between survival and obesity in dogs with malignant mammary tumors, though they did not specifically evaluate the impact of historical obesity on tumor development later in life.²⁴ Overall, these studies suggest a possible role for fat intake and obesity in the pathogenesis of canine mammary tumors, as is the case in women.

Published surveys, so far, confirm that concurrent obesity is relatively common among dogs with cancer but have been unable to definitively prove that there is a cause-and-effect relationship between overweight and cancer incidence. In one study, 29% of dogs treated at a referral oncology practice were obese based on body condition score. Weight loss was documented in 68% of dogs, but it represented less than 5% of the precancer body weight in 31% of cases.²⁵ The distribution of body condition scores among dogs with a variety of types of cancer was also investigated and compared to dogs without cancer in a much larger study.²⁶ The overall prevalence of overweight (BCS>6/9) and obese (BCS>7/9) dogs in the total population in this study was 21.6% and 14.8%, respectively. However, the authors were unable to find an association between obese body condition and tumor development. In fact, there was a slight but significantly lower prevalence of overweight (BCS>6/9) and obese (BCS>7/9) dogs in the group with malignant disease as compared to dogs without cancer. Age, breed, neuter status, tumor type, and a history of corticosteroid administration were identified as important confounding factors affecting nutritional status in this study.

Although fewer studies have been published that evaluate nutritional status in cats with cancer, work to date suggests that obesity may be less common in cats with cancer than it is in dogs. In one study looking at body condition and weight loss in cats with cancer, almost half the cats evaluated were underweight or very thin and over 90% of them had clinically detectable evidence of muscle wasting. Body condition score was strongly correlated with survival time and prognosis in this study, with cats that had

low body condition scores having markedly shorter survival times.²⁷ Preliminary data suggest that sick cats are more likely to experience a decline in nutritional status than sick dogs, regardless of whether they have cancer (Mauldin GE, unpublished data). Further work is needed to determine if the lower body condition scores and relatively decreased incidence of obesity reported to date in the cats with cancer is specifically related to the presence of underlying neoplastic disease or whether weight loss is simply a more generic feline response to illness.

Practical Management of Obesity in Dogs and Cats with Cancer

The clinical approach to achieving successful weight loss in a dog or cat with uncomplicated obesity involves six relatively standard steps as outlined below. However, underlying neoplastic disease presents some unique and specific challenges that must also be taken into account in these animals.

1. Conduct a thorough patient assessment.

The biggest initial challenge associated with the management of overweight dogs and cats with cancer is deciding whether a weight-loss program is actually indicated. Is it reasonable to expect that weight loss will provide objective clinical benefit for the animal? Simply stated, will weight loss either prolong survival time or improve quality of life? If the answer to these questions is “no” or “likely not,” then the time, effort and expense necessary for successful weight loss will not be worthwhile for the animal or its owner. There is no doubt that the health risks of obesity in otherwise normal small animals are well-established and include musculoskeletal disease, glucose intolerance, diabetes mellitus, immunosuppression, and respiratory compromise.¹ Dogs that are maintained in optimal body condition have been shown to live longer than dogs that are overweight.²⁸ Although not specifically proven, it seems likely that obesity poses the same health risks in dogs and cats that also have cancer. Furthermore, it is intuitive that the negative impact of obesity on outcome, as suggested for people with cancer, exists in small animals as well. This includes inaccurate diagnostic test results, altered physiology and drug pharmacokinetics, suboptimal chemotherapy dosing and radiotherapy delivery, and the necessity of managing conflicting comorbidities (i.e., the need to administer corticosteroids to an obese cat with lymphoma that is also diabetic).

Based on these considerations, it would then seem that weight loss would be indicated in many or even most overweight dogs and cats with cancer. However, this is not necessarily the case. Some animals may have what is termed “metabolically healthy obesity.” In people this condition is not associated with deleterious comorbidities, and it is not clear that weight loss in these individuals can provide significant clinical benefit.¹⁰ Arguably, even more important than the hypothetical advantages that could be gained from achieving more optimal body condition is the expected survival time associated with the animal’s underlying cancer. Effective weight-loss programs are labor-intensive and can be

stressful and difficult for a devoted owner to implement. The expected survival time for an overweight pet with neoplastic disease must be long enough to justify the time and effort necessary to achieve optimal body condition. Finally, it is also important to recognize and accept that if the owner has made an informed decision to pursue palliative treatment alone for their pet’s malignant disease, a stringent weight-loss program is unlikely to improve quality or quantity of life for anyone. Obviously, the animal’s quality of life is of paramount concern, but the owner’s quality of life as he or she struggles to implement a weight-loss program for his or her pet with potentially incurable malignancy should also be considered.

Once a decision to implement a weight-loss program has been made, a clinical baseline including all diagnostics indicated for management of the animal’s obesity as well as tumor staging should be carefully established. A minimum database should always include screening reference laboratory bloodwork (complete blood count, serum biochemical profile and urinalysis) and will often include endocrine testing, imaging (radiographs, ultrasonography and/or cross-sectional imaging), and fine-needle aspiration cytologies.

2. Calculate appropriate energy intake for safe weight loss.

The weight-reduction protocols that are routinely applied in otherwise healthy animals¹ are not necessarily suitable for overweight dogs and cats with cancer. A very conservative reduction in caloric intake below the calculated maintenance energy requirement at estimated ideal body weight is probably most appropriate to start for animals that are clinically stable and self-supportive, especially if cancer therapy and weight loss are planned to occur simultaneously. The goal is to gradually and safely achieve a more optimal body condition score and nutritional status, even if that process takes longer than would normally be expected in a case of uncomplicated obesity. Aggressive weight-loss programs are contraindicated during cancer-related critical illness, even in dogs and cats that are very obese. Severe caloric restriction in a sick animal could contribute to clinically significant protein-calorie malnutrition with loss of lean body mass, including skeletal muscle atrophy, hypoproteinemia, delayed wound healing, immunosuppression, and compromised organ function. This situation would be similar to “sarcopenic obesity,” as described in detail above.

3. Choose a weight-loss ration.

The most consistent features of available prescription diets intended for weight loss in dogs and cats are decreased caloric density and an optimized essential nutrient profile that takes into account the decreased calories that will be consumed during the course of weight loss. Decreased caloric density is achieved by decreasing the fat content of the diet and in some cases through the addition of various types of fiber that are intended to increase gut fill and satiety. Most weight-loss rations are also relatively high in protein in order to spare lean body mass while adipose tissue is lost.

Unfortunately, the characteristics of a typical prescription weight-loss ration may not necessarily be considered ideal for a dog or cat with cancer, even when that animal is significantly overweight. Whether true or not, it is a commonly held belief of owners and veterinarians alike that dogs and cats with malignant disease should consume high levels of protein and fat. The rations typically recommended deliver 35 to 50% of calories as protein, contain as few carbohydrate calories as possible, and are high in fat. The purpose of this recommendation is twofold. First, it seeks to provide all the protein and amino acids that might possibly be needed to protect and expand lean body mass, including synthesis of various enzymes, clotting factors, immunoglobulins, and support of tissue healing. Second, it also attempts to provide ample energy for an animal generally assumed to be at risk for weight loss and in a form that is less likely to be usable by cells that have undergone malignant transformation. Since neoplastic cells oxidize fat inefficiently, a high-fat, low-carbohydrate diet could preferentially supply energy to host tissues while avoiding inadvertent “feeding” of the tumor. In one study, a high-fat ration was successful in normalizing some aspects of carbohydrate metabolism and appeared to prolong survival in a subset of dogs with lymphoma.²⁹ However, it is important to recognize that a convincing clinical association among documented metabolic abnormalities, actual weight loss and poor prognosis has yet to be demonstrated in dogs or cats with any type of cancer. More work is needed to prove that high-fat diets can provide an objective benefit for dogs and cats with neoplastic disease.

It can be extremely difficult to reconcile the competing dietary recommendations for weight loss and malignant disease in dogs and cats. This will be especially true when the pet owner is convinced that feeding a high-fat diet will result in a survival benefit for his or her animal, regardless of its current body condition. In the end, the most appropriate diet is recommended based on an objective as possible assessment of the risk to benefit ratio of weight loss. When obesity is significant (i.e., body condition score 7/9 or greater) and the expected survival time after cancer therapy is relatively prolonged (i.e., a year or more), it seems logical that a prescription weight-loss ration would be the safest and most-efficient way to achieve optimal body condition along with its associated health benefits. Open, rational and nonjudgmental discussion of the compromised survival documented in obese people with cancer will be helpful in convincing skeptical owners of the benefits of weight loss. They may also be reassured to find that most weight-loss products contain ample protein, just like “cancer diets.” In cases where overweight is less severe or cancer survival times are anticipated to be shorter, incrementally decreased intake of a high-quality complete and balanced commercial ration with a somewhat higher fat content may be an acceptable compromise.

One final consideration in the choice of a weight-loss ration for use in a dog or cat with cancer may be its level of enrichment with omega-3 fatty acids. It is interesting to note that the high-fat ration used in the study cited above that demonstrated

improved survival among some dogs with lymphoma was also heavily enriched with omega-3 fatty acids. Changing the dietary ratio of omega-6 to omega-3 fatty acids alters the fatty acid composition of cell membranes throughout the body, and this, in turn, impacts cell membrane eicosanoid production, cytokine synthesis and the inflammatory cascade. Although supplementation with omega-3 fatty acids is often proposed as an adjunct for the management of cancer cachexia, it seems possible that it may paradoxically provide benefit for obese animals with cancer as well. Both cancer cachexia and obesity are considered to be chronic inflammatory conditions. If they were added to a weight-loss ration, care would obviously have to be taken to ensure that omega-3 fatty acids did not increase caloric intake above that required for weight loss or significantly dilute the concentration of any essential nutrients. Another option may be to choose a complete and balanced commercial prescription product based primarily on its enrichment with omega-3 fatty acids. For instance, some rations intended for chronic management of dogs with degenerative joint disease contain high levels of omega-3 fatty acids and are also designed to help maintain optimal body condition.

4. Institute an individualized weight-loss program.

Although the ration chosen and the initially recommended level of caloric intake may differ between obese dogs and cats that have cancer and those that do not, the fourth step in the process of weight loss is essentially the same in both groups. Here, the owner is given explicit written instructions regarding exactly how much of what type of food to feed, including all treats and supplements. Specific instructions for physical activity are also provided, taking care to begin slowly in previously sedentary animals. Ten minutes of supervised activity each day is a reasonable starting point in such cases, with an increase of five to 10 minutes per day each week if tolerated. Extrapolation from studies performed in people with malignant disease suggests that physical activity will help to maintain lean body mass and avoid sarcopenic obesity in overweight dogs and cats with cancer and may improve quality of life as well as cancer-specific and overall survival. Encouraging pet owners to keep a diary to record body weight, type and amount of food consumed, all treats and supplements, exercise and other observations, including clinical signs and side effects of cancer therapy, will make monitoring simpler. It will also facilitate troubleshooting in cases where problems are encountered.

5. Carefully monitor response to energy restriction.

Obese dogs and cats with cancer that are undergoing weight loss should be thoroughly re-evaluated on a regular basis. Two to four initial biweekly rechecks, followed by monthly visits for the duration of the weight-loss program, are a reasonable schedule in most cases. Frequent re-evaluation allows the animal's response to anti-cancer therapy to be assessed and permits treatment-related toxicities to be identified and addressed. Reg-

ularly scheduled rechecks also facilitate the serial measurements of body weight and body condition score that are essential in confirming successful weight loss. Repeat bloodwork is recommended to ensure that weight loss is well-tolerated, though the potential side effects of caloric restriction will have to be distinguished from changes secondary to cancer therapy in some cases. Obese cats should be monitored for biochemical evidence of hepatic lipidosis; subtle changes, such as normocytic, normochromic anemia and lymphopenia, in both dogs and cats can also reflect development of protein-calorie malnutrition.

Although weight loss will be slower if a relatively conservative decrease in caloric intake has been recommended as described above, there should still be a clear and consistent downward trend in both body weight and body condition score. As much as possible, muscle mass should be carefully assessed to make sure there is no evidence of atrophy as adipose tissue is lost. Caloric intake should be increased if weight loss is too rapid or if evidence of muscle atrophy or protein-calorie malnutrition develops; intake should obviously be decreased if weight loss does not occur as planned.

6. Transition to maintenance ration or maintenance energy intake.

Once the target weight has been reached in a previously obese dog or cat with concurrent cancer, food intake must be adjusted to maintain the target weight and stop additional weight loss. In some cases, the target weight will correspond to an optimal body condition score of 5/9, but in others, the decision will reasonably be made based on underlying cancer diagnosis or other factors to stop weight loss at a slightly overweight body condition (i.e., body condition score of 6/9). If a prescription weight-loss product was used to allow weight loss, transition to a maintenance product may have to be made. Rations containing ample protein are likely to be preferred in order to maintain lean body mass most effectively; however, use of a “cancer diet” with high-protein and -fat content may simply promote regain of all weight that was lost. Alternatively, if weight loss was accomplished through decreased intake of a complete and balanced commercial ration not specifically designed for weight loss, then all that is required to maintain stable weight may be a slight increase in intake of the same diet. Regardless, more frequent rechecks (i.e., biweekly) during this transition phase will help to ensure that a healthy weight and body condition score are maintained and that all new dietary recommendations are well-accepted.

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