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Association of Body Weight and Body Condition with Survival in Dogs with Heart Failure

J.L. Slupe, L.M. Freeman, and J.E. Rush

Background: Obesity is a risk factor for cardiovascular disease in people, but overweight and obese human heart failure patients have improved survival compared with normal- or underweight controls—the obesity paradox. The purpose of this study was to determine if there is an association of body weight and body condition with survival in dogs with heart failure.

Hypothesis: That body condition and changes in body weight are predictors of survival in dogs with heart failure.

Animals: One hundred and eight dogs with heart failure (International Small Animal Cardiac Health Council stages 2, 3a, or 3b) secondary to dilated cardiomyopathy or chronic valvular disease.

Methods: Medical records were reviewed, and data regarding initial body weight and body condition score (BCS), subsequent changes in body weight, and treatment were collected. Survival times were determined for dogs that were discharged from the hospital and lived >24 hours.

Results: Survival was significantly different between dogs that gained, lost, or maintained body weight over the course of their disease ($P = .04$), with dogs that gained weight surviving the longest. BCS and medications were not significantly associated with survival time; however, n-3 fatty acid intake was associated with longer survival time ($P = .009$).

Conclusions and Clinical Importance: These results suggest that changes in body weight might be an important consideration in the survival of dogs with heart failure.

Key words: Cachexia; Cardiac disease; Obesity.

Cardiac disease is one of the most common problems encountered in companion animals, with approximately 3 million of the 62 million dogs in the United States being diagnosed with cardiac disease every year and more than 10% of all dogs having some form of heart disease.^{1–3} New medications have improved the care of dogs with cardiac disease, but a diagnosis of heart failure still carries a poor prognosis for survival. In addition to medications, another important aspect of therapy for dogs with cardiac disease is nutritional modification, such as preventing nutrient deficiencies, including taurine and B vitamins, and nutritional excesses, such as sodium. In addition, certain nutrients can have benefits above and beyond their nutritional effects, for example, antioxidants and n-3 fatty acids. However, one of the most important aspects of optimal care for dogs with heart failure is maintaining optimal weight and body condition. Cardiac cachexia, a loss of lean body mass, is a common syndrome in dogs with heart failure, with more than 50% of dogs with dilated cardiomyopathy (DCM) and heart failure having some degree of cachexia.⁴ Cardiac cachexia is a multifactorial problem that results from decreased food intake, increased energy requirements, and an increased production of inflammatory cytokines.⁵ The lean body mass loss that occurs in cardiac cachexia affects strength, immune function, and survival.^{5–7,a}

As common as cardiac cachexia is in dogs with heart failure, an even more common problem in the general

population of dogs is obesity. More than one-third of the dogs in the United States are overweight or obese.⁸ Obesity does not increase the risk for coronary artery disease in dogs as it does in humans, but it can have adverse effects on cardiac output, pulmonary function, blood pressure, and heart rate in a variety of species.^{9,10} Therefore, weight loss is typically recommended for obese dogs with heart failure.¹¹

Keeping these aspects of obesity and cachexia in mind, it seems logical that the ideal goal is to maintain a dog with cardiac disease in ideal body weight and body condition. Several recent studies, however, have shown that obesity actually is associated with a longer survival time for people with heart failure.^{12–16} This inverse relationship between weight or body mass index (BMI) and survival time has been coined the “obesity paradox.” Results of a 2001 study of more than 1,000 patients with heart failure (New York Heart Association [NYHA] Class II–IV) showed that a higher BMI was associated with improved survival at 2 years.¹³ Patients with NYHA Class I–III heart failure and the highest BMI had the lowest incidence of clinical cardiac events, including cardiovascular death and urgent transplantations.¹⁴ A study of more than 500 human patients with NYHA Class I–IV heart failure demonstrated that cachectic patients had the lowest survival whereas those in the 2 highest BMI quantiles had the best survival.¹⁵ Finally, among humans with acute decompensated heart failure, obese patients have a higher rate of survival during a single hospitalization for heart failure.¹⁶

Proposed reasons for the obesity paradox include confounding effects of medications used to treat diseases associated with obesity, such as hypertension, or neuroendocrine factors elaborated by adipose tissue.^{13,14} It also might be that obese patients present at an earlier, less severe stage of disease than their normal weight counterparts because of the more prominent symptoms or signs as a result of excess body weight.^{12,13}

The effects of body condition or changes in body weight on survival have not been described in dogs with

From the Department of Clinical Sciences, Tufts Cummings School of Veterinary Medicine, North Grafton, MA.

Corresponding author: Dr Lisa Freeman, Department of Clinical Sciences, Tufts Cummings School of Veterinary Medicine, 200 Westboro Road, North Grafton, MA 01536; e-mail: Lisa.Freeman@Tufts.edu.

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heart failure. Therefore, the purpose of the current study was to evaluate the relationship between survival and initial body condition or changes in body weight over time in dogs with heart failure. We hypothesize that body condition in dogs with heart failure is a predictor of survival time, with overweight or obese dogs having a longer survival time than underweight and normal weight individuals. Furthermore, we hypothesize that those dogs that maintain or gain weight during the course of disease will have a longer survival time than those that lose weight.

Materials and Methods

Case Selection

Eligible cases were identified from a computer database search of dogs with DCM or chronic valvular disease (CVD) evaluated by the Cardiology Service at the Foster Hospital for Small Animals at Tufts Cummings School of Veterinary Medicine (TCSVM) between 2004 and 2006. Dogs that had a first-time diagnosis of heart failure (International Small Animal Cardiac Health Council [ISACHC] score of 2, 3a, or 3b) at the TCSVM during this time period were eligible. Dogs that were diagnosed with heart failure at <1 year of age were excluded, because growth would interfere with the evaluation of body weight. Dogs that did not have a body weight recorded at the initial visit were also excluded.

Study Design

The medical records for the initial presentation of each eligible dog were reviewed, and the following information was collected for the dogs' initial visit using a standardized data collection form: signalment; body condition score (BCS; on a 1–9 scale where 1 = emaciated, 5 = ideal, and 9 = obese)¹⁷; body weight; underlying disease (ie, DCM or CVD); presence of arrhythmia; hematocrit; serum glucose, urea nitrogen, creatinine, sodium, chloride, and potassium concentrations; and ISACHC stage. Medications, dietary supplements, and diet used during the course of the disease were also recorded. Information was also collected from the medical record regarding change in body weight over time (from the time of initial diagnosis of heart failure until the last available body weight), survival time, and cause of death/euthanasia. The same electronic scale was used for many, but not all, of the dogs, so comparison of body weight both between and within patients was not always on the same scale. If ascites were noted at the time of a body weight measurement, that body weight was not used. If the date of death was not available from the medical record, referring veterinarians or owners were contacted for this information.

Data Analysis

Data were examined graphically. Data that were normally distributed are presented as mean \pm standard deviation, whereas skewed data are presented as median (range). Data that were not normally distributed were mathematically transformed before analysis. Baseline comparison between BCS and weight change categories was performed using analysis of variance with Tukey's post hoc analysis. Kaplan-Meier curves and log-rank tests were used to compare potential prognostic variables on survival time. This included baseline BCS, body weight changes, age (categorized by those younger than the median age of the study population and those older than the median age), medication use, dietary supplement use (n-3 fatty acids and taurine), underlying disease (ie DCM or CVD), baseline hematologic and serum biochemical parameters (categorized by those above and below the median value), presence of arrhythmia, and ISACHC stage (ie, 2, 3a, or 3b). Body

condition was categorized as emaciated (BCS = 1–2), underweight (BCS = 3–4), normal weight (BCS = 5), overweight (BCS = 6–7), or obese (BCS = 8–9), based on their initial BCSs. Weight changes were categorized as weight loss (loss of >0.2 kg to account for scale variation), weight gain (gain of >0.2 kg), or no change (weight within 0.2 kg of initial weight). Weight changes were also compared on a percentage basis. Because of the relatively small sample size, subgroup analysis for BCS and weight change categories was not performed. Medications and dietary supplements were evaluated as categorical variables (ie, the dog was receiving the medication or not) and the following ones were evaluated: furosemide, angiotensin-converting enzyme (ACE) inhibitors pimobendan, digoxin, β -blocker, diltiazem, sotalol, spironolactone, hydrochlorothiazide/spironolactone, taurine, and n-3 fatty acids. A medication or dietary supplement was considered to be administered to an individual dog if the dog received the medication/supplement chronically (ie, >1 week and not just during hospitalization for an episode of congestive heart failure). Survival times were included for dogs that were discharged from the hospital and that lived >24 hours. Dogs that were still alive at the time of data analysis and dogs lost to follow-up were censored for the purposes of survival analysis, with the last known date alive used for dogs lost to follow-up. Multivariate analysis also was performed to identify confounding variables. Death from any cause was included in the analysis. Statistical analysis was performed using a commercial statistical software package.^b *P* values < .05 were considered statistically significant.

Results

One hundred and sixteen dogs with DCM or CVD were diagnosed with an initial episode of stage 2, 3a, or 3b heart failure between 2004 and 2006. Eight dogs were excluded from all analyses because no initial BCS was recorded nor was there a follow-up body weight recorded at any subsequent visit. All remaining analyses will refer only to the remaining 108 dogs. The median age of dogs was 10.0 years (range, 1.3–16.4 years) and the most commonly represented breeds were mixed breed (*n* = 14), Doberman Pinscher (*n* = 14), Boxer (*n* = 7), Shih Tzu (*n* = 6), and Pomeranian (*n* = 6). A variety of other breeds were represented in smaller numbers. Sixty-two male dogs (56 castrated) and 46 female dogs (42 spayed) were included. Dogs were classified in ISACHC stage 2 (*n* = 41), stage 3a (*n* = 26), and stage 3b (*n* = 41) at the time of their initial diagnosis at TCSVM. Medications administered over the course of the dogs' disease were variable and included ACE inhibitors (*n* = 101), furosemide (*n* = 99; median dose = 2.8 mg/kg [range, 0.8–11.0 mg/kg/day]), pimobendan (*n* = 56), digoxin (*n* = 18), β -blocker (*n* = 16), diltiazem (*n* = 11), sotalol (*n* = 8), spironolactone (*n* = 8), hydrochlorothiazide/spironolactone (*n* = 6), and procainamide (*n* = 1). Most dogs were receiving multiple medications. Many dogs had concurrent diseases, with hypothyroidism (*n* = 15), osteoarthritis (*n* = 7), and seizures (*n* = 7) being the most common.

Median body weight was 19.5 kg (range, 1.7–81.8 kg), with the change in weight over time ranging from a loss of 16.2 kg to a gain of 7.6 kg (median = –0.3 kg). On a percentage basis from the initial body weight, the median weight change was –2.2% (range, –43.8 to +21.6%). A change in body weight was available for 90 dogs, and the median time from the first to last body weight was 88 days (range, 3–926 days). Fifty dogs lost weight over the course of their disease, 25 dogs gained weight, and 15 dogs had a change in body weight of <0.2 kg. Dogs

in the 3 weight change category groupings (ie, weight loss, weight gain, and no change) were not significantly different in any variables measured, including age, sex, breed, ISACHC stage, underlying disease (ie, DCM versus CVD), echocardiographic measurements, medications, or presence of arrhythmia. An initial BCS was available for 73 of 108 dogs. Median BCS was 5 (range, 2–9) and included the predefined categories emaciated ($n = 4$), underweight ($n = 18$), normal weight ($n = 21$), overweight ($n = 28$), or obese ($n = 2$). Dogs in the different BCS categories were not significantly different in any variables measured. A total of 46 dogs (43%) were noted to be anorectic at the time of the initial visit. For dogs whose medical records included diet information, the main diet for the majority of dogs at the time of the initial onset of heart failure was a maintenance dry or canned dog food, but 11 ate therapeutic commercial diets designed for dogs with heart disease and 4 dogs ate homemade diets. Twenty-seven dogs were receiving one or more dietary supplements: taurine ($n = 14$), n-3 fatty acids ($n = 11$; 6 from a fish oil supplement; 4 from a therapeutic diet enriched with n-3 fatty acids; and 1 receiving both the supplement and the diet), L-carnitine ($n = 3$), coenzyme Q10 ($n = 2$), and antioxidants ($n = 2$).

Twenty-three dogs were still alive at the time of the analysis. For dogs that did not survive, 59 were euthanized and 24 died. The most common causes of death were worsening heart failure ($n = 60$), noncardiac causes ($n = 9$), and sudden death ($n = 7$). The cause of death could not be determined for 6 dogs, and 2 dogs were lost to follow-up. The median survival time for dogs that were discharged from the hospital and that lived for >24 hours was 174 days (3–1,274 days). Survival time was significantly related to body weight changes (overall P value = .04), with the dogs that gained weight having the longest survival (median = 219 days versus 210 days for dogs that lost weight and 74 days for dogs that had no weight change; Fig 1). If body weight changes are assessed as a percent change (ie, gain, loss, or no change, with a change $>2\%$ used as the criteria for a change in weight), the P value for survival = .07. Changes in BCSs were not available for a sufficient number of subjects, so only the initial BCS was used for analysis. For evaluation of survival times between baseline BCS categories, the emaciated category had the shortest survival time (median 115 days) and the obese category had the longest survival time (median = 275 days); however, there were few dogs in the obese and emaciated BCS categories and this comparison did not reach statistical significance (overall P value = .09; Fig 2).

In addition, n-3 fatty acid supplementation was associated with longer survival compared with dogs not receiving n-3 fatty acid supplementation ($P = .009$). Age was also significantly related to survival, with older dogs (dogs >10 years) having a longer survival time than younger dogs (<10 years; $P = .02$). No other variables, including ISACHC stage, medications, taurine supplementation, presence of arrhythmia, hematologic or serum biochemical parameters, or underlying cardiac disease, were associated with survival time on multivariate analysis. Weight change category, age, and n-3

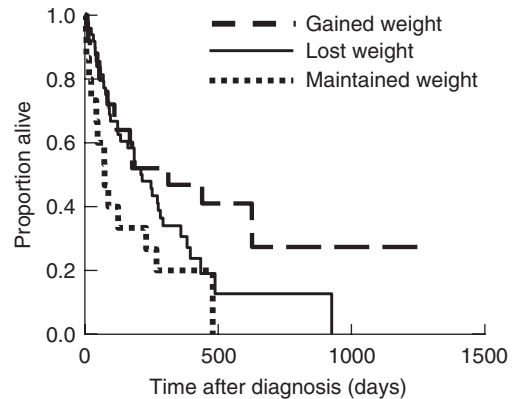


Fig 1. Survival plot of dogs with heart failure as a function of body weight change. Kaplan-Meier survival curves for dogs with heart failure that gained weight ($n = 25$), dogs that lost weight ($n = 50$), and dogs that maintained weight ($n = 15$) over time ($P = .04$).

fatty acid supplementation remained independent predictors of survival on multivariate analysis.

Discussion

This current study demonstrates that, as in humans, body weight changes are associated with survival in dogs with heart failure, with dogs gaining weight having the longest survival time. The obesity paradox is a relatively newly addressed phenomenon in cardiology, with the first paper from human medicine being published in 2001. There are a number of possible reasons that the obesity paradox may exist, and it is not yet clear whether this is just an association or whether a causal relationship exists. One possible explanation may be a cardioprotective role of adipose tissue-derived neuroendocrine molecules, including cytokines and hormones.^{14,18} Medications used to treat comorbidities seen with obesity in humans could also play a role, but the fact that our study's results mirror those in humans argues against this

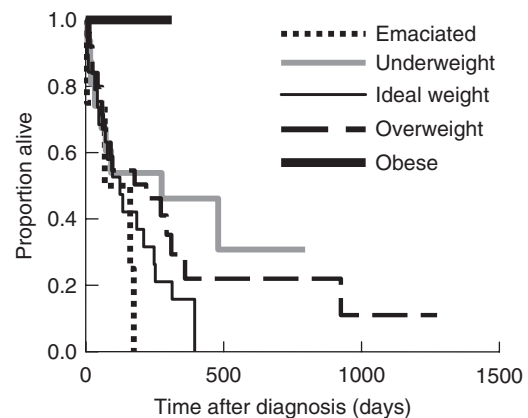


Fig 2. Survival plot of dogs with heart failure as a function of body condition score (BCS). Kaplan-Meier survival curves for dogs with different BCS categories on a 1–9 scale¹⁷ at the time of initial diagnosis ($P = .09$). BCS categories: emaciated, BCS = 1–2; underweight, BCS = 3–4; ideal, BCS = 5; overweight, BCS = 6–7; obese, BCS = 8–9.

explanation.^{14,18} Obese patients may present earlier for their heart disease than nonobese patients because of more pronounced clinical signs as a result of excess weight, resulting in a “healthier” heart failure population.¹⁴ Weight gain also may be an indicator of better response to treatment; ie, if dogs maintain or lose weight, they had a poor response to therapy. Finally, the obesity paradox may be more attributable to the lack of cachexia than to the actual gain in weight, given the adverse effects documented for cachexia in human heart failure patients.⁶ For further review of the obesity paradox in humans, readers are referred to recent review articles on this topic.^{14,18}

Although there was not a statistically significant difference in survival between BCS categories ($P = .09$) and individual BCS groups were not statistically compared, the results were consistent with studies of human heart failure patients in that dogs classified as emaciated (BCS = 1–2) had the shortest numerical survival time, while those animals classified as obese (BCS = 8–9) had the longest numerical survival time. Additional larger studies will be needed to determine whether initial BCS is predictive of survival in dogs with heart failure.

Whether weight gain or obesity is directly associated with survival benefits or it is the absence of cachexia that is the true explanation for the obesity paradox is not clear. It may be that, as in healthy humans, there is actually a J- or U-shaped curve for optimal survival: at very low and very high body weights, there is reduced survival, but those near optimal body weight have the best survival.^{19,20} The current study was limited by its retrospective nature in that an assessment of muscle loss or cachexia was not collected for each subject. This would provide additional information on the role of body condition on survival in heart failure.

The results of this study also show a significantly longer survival time for dogs receiving n-3 fatty acid supplementation; n-3 fatty acid supplementation reduces inflammatory cytokines and eicosanoids, reduces muscle loss, and has antiarrhythmic effects.^{4,21} A study in dogs with DCM and heart failure showed a significant relationship between reduced interleukin-1 concentrations and longer survival times.⁴ Further studies of potential beneficial effects of n-3 fatty acid supplementation on survival are warranted.

We were unable to detect any other significant relationships between survival and factors such as baseline hematologic or serum biochemical parameters, presence of arrhythmia, or baseline ISACHC classification. Some of these factors (eg, sodium, glucose, hematocrit, and arrhythmia) have been identified as prognostic factors in dogs²² or humans with heart failure.^{23–25}

Several important limitations to this study must be noted. BCSs are a subjective measure of obesity in animals. Although there are guidelines to determine the BCS and these have been validated against quantitative measures of body composition, there is some interobserver variation present among individuals assigning the score. Future studies should have a single investigator assigning BCS for all dogs in a prospective manner. Furthermore, BCS assesses only fat stores, so loss of lean body mass is

not being assessed in this study. Assessment of lean body mass (eg, cachexia or muscle scores; total body potassium) would provide valuable information. It is possible that many of the animals that had no change in weight simply did not have enough time to gain or lose weight before death or that we did not reevaluate dogs at optimal time points to be able to document weight changes. It is also not possible to determine which of the animals lost weight purposely because they were overweight or obese. However, considering how difficult and unsuccessful most weight loss programs are in dogs and other species, this is unlikely to have contributed to weight loss in the majority of animals exhibiting weight loss in this study. The same electronic scale may not have been used when assessing changes in weight and animals were not always weighed at the same times, eg, after diuretic doses or after emptying the bladder, so some variability is expected. The overall sample size also limits this study. Most studies regarding the obesity paradox in humans include far more than 300 patients. Further study with a larger group of dogs may provide additional information regarding the relationship between body weight change and body condition and survival in dogs with heart failure. The distribution of dogs among the different BCS categories was also a limitation. Only a small number of dogs were classified as emaciated or obese, 4 and 2 dogs, respectively. It must also be kept in mind that survival time in veterinary medicine is always a challenge because of the option for euthanasia. Although most dogs in the current study were euthanized for worsening heart failure, owners may have elected this option at different points in the process. Various factors, such as the prognosis given by the clinician, quality of life, recurrent clinical signs, and anorexia, influence owners' decisions to euthanize their dogs with heart failure.²⁶ Finally, because this study was retrospective, it was not possible to collect all the desired information for each dog and at the same time point. Because the time between body weight measurements ranged from 3 to 926 days, some dogs may not have had sufficient time to demonstrate a change in body weight. Nonetheless, the results of this study are consistent with those in humans and warrant further research, which could help determine the optimal management of dogs with heart failure.

Footnotes

^aFreeman LM, Rush JE. Relationship between cachexia and lymphocyte subpopulations and hematologic parameters in dogs with spontaneously-occurring congestive heart failure. Proceedings of the Third Cachexia Conference, Rome, Italy, December 8–10, 2005: 82 (abstract)

^bSystat 11.0, SPSS, Chicago, IL

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