

The Effect of Dietary Protein on Body Composition and Renal Function in Geriatric Dogs

Nolan Z. Frantz, PhD
Ryan M. Yamka, PhD
Kim G. Friesen, PhD

*Hill's Pet Nutrition, Inc.
Topeka, Kansas*

KEY WORDS: body composition, dog, kidney, renal failure

ABSTRACT

Forty healthy geriatric beagles (≥ 10 years, initially 12.0 kg) were fed a control food during a 30-day pre-feeding period, and then blocked by age, gender, and body fat percentage. Dogs were randomly assigned to 1 of 4 foods (A = Experimental Food, B = Royal Canin Mature Medium Breed, C = Purina Dog Chow Senior, and D = Eukanuba Senior Maintenance) for the 6-month testing period. Blood chemistry, microalbuminuria, and DEXA were evaluated for changes in kidney health and body composition. At Day 180, body weight increased ($P < 0.01$) in dogs fed Food B and tended ($P < 0.07$) to increase in dogs fed Food A. No other differences in weight or changes in weight were detected ($P > 0.13$). Dogs fed Food B and Food D lost lean ($P < 0.05$) over the 180-day period. Dogs fed Food B also gained fat ($P < 0.01$) while the other 3 foods maintained fat. In addition, dogs fed Food B gained ($P < 0.01$) bone mineral content (BMC) while dogs fed Food C lost ($P < 0.05$) BMC. For kidney function markers, blood creatinine was unaffected by dietary treatment ($P > 0.25$). Dogs fed Foods B, C, and D had higher ($P < 0.03$) blood urea nitrogen (BUN) levels than dogs fed Food A. For BUN:creatinine ratio, dogs fed Foods B, C, and D had elevated ($P < 0.02$) ratios compared to dogs fed Food A. Dogs fed Food D had a greater percentage of animals with reduced

kidney function ($P < 0.05$) as indicated by microalbuminuria analysis compared to dogs fed Food A.

In conclusion, geriatric dogs fed experimental Food A with reduced protein/phosphorus showed less progression of kidney disease compared to the other commercial geriatric foods. In addition, dogs fed experimental Food A maintained lean and bone mass compared to other commercial formulations.

INTRODUCTION

Renal failure or chronic renal disease is an important condition, particularly in older animals, that may impact the quality of life and longevity of the animal.¹ Dietary management of this disease has become critical to modifying the progression and increasing survival rates.^{2,3} A reduction in dietary crude protein concentration has been shown to reduce the progression of kidney disease in companion animals.⁴⁻⁶ A similar response has also been observed to reductions in dietary phosphorus availability⁷⁻¹⁰ on renal patient survival. Other dietary factors such as antioxidants and polyunsaturated fatty acids have shown promise in reducing the rate of kidney disease progression and protecting the kidney from further damage.¹¹⁻¹³

Loss of lean muscle mass is also a concern among aging companion animals^{14,15} as in humans. Reductions in muscle mass with aging may lead to decreases in activity and general health,¹⁶ and may be associ-

ated with other age-related diseases such as obesity, diabetes, etc. Supplying the proper concentrations of the essential amino acids relative to lysine (protein quality) rather than a total dietary protein amount (protein quantity) is required for the synthesis of new muscle protein and to prevent its breakdown.^{17,18} In foods designed for weight loss, dietary protein is often increased to prevent reductions in muscle mass while providing positive effects on insulin sensitivity.^{19,20} However, increasing dietary crude protein may also increase the risk for developing kidney disorders due to the processing of excess nitrogen and mobilization of calcium to buffer the additional acid load.^{7,21} Increasing dietary protein may also have negative implications on bone preservation.²²⁻²⁴

Thus, the objective of this study was to determine the effect of 3 commercially available geriatric foods and 1 experimental geriatric food with various protein levels on quality of life in geriatric dogs as determined by measures of body composition and kidney health.

MATERIALS AND METHODS

Animal Care and Health

Prior to the studies, dogs were determined to be healthy by physical exam and blood chemistry screen. The dogs were located in the Hill's Pet Nutrition Center (Topeka, KS) and cared for in accordance with Institutional Animal Care and Use Committee protocols. Additionally, dogs were offered enrichment toys, received routine grooming and had daily opportunities for socialization with other dogs and people.

Study Design

Forty healthy geriatric dogs were fed a control food during a 30-day pre-feeding period, and then blood samples and dual-energy x-ray absorptiometry (DEXA; DXA-QDR-4500, Hologic, Inc., Waltham, MA) scans were performed. The dogs were blocked by age, gender, and body fat percentage and randomly assigned to 1 of 3 commercially available geriatric foods or the experimental

geriatric food for the 6-month testing period. Dogs were weighed weekly and food intake monitored daily.

Foods

Dogs were assigned to 1 of 4 foods (A-D): Food A (Experimental Food), Food B (Royal Canin Mature Medium Breed), Food C (Purina Dog Chow Senior), or Food D (Eukanuba Senior Maintenance) (Table 1). All foods were formulated to meet or exceed Association of American Feed Control Officials²⁵ nutrient recommendations.

Serum and Urine Analysis

Blood and urine samples were taken at Days 0, 30, 90, and 180. Collected serum was stored at -20°C in 1-mL aliquots. Serum was analyzed for chemistry screens and vital organ markers at the Hill's Pet Nutrition Center (Topeka, KS) (Table 2). Urine was sampled and microalbuminuria (Heska ERD kit) analysis conducted.

Statistical Analysis

Data were analyzed using General Linear Models procedure of SAS²⁶ to determine treatment means. The experimental unit was dog, and Day 0 used as a covariate. Four geriatric foods were compared (A-D). Differences were considered significant when $P < 0.05$ and trends were determined when $P \leq 0.10$.

RESULTS

Body Composition (Table 3)

At Day 90, dogs fed Food A and Food B had increased ($P < 0.01$) weight. No differences ($P > 0.72$) in lean or bone mineral content (BMC) were detected between foods; however, dogs fed Food B had increased ($P < 0.01$) fat. At Day 180, dogs fed Food B had increased ($P < 0.01$) weight and fat while dogs fed Food A tended ($P < 0.07$) to have increased weight compared to Day 0. Dogs fed Food B and Food D had reduced ($P < 0.05$) lean while dogs fed Food A and Food C maintained lean. Dogs fed Food B had increased ($P < 0.01$) BMC while dogs fed Food C had reduced ($P < 0.05$) BMC.

Table 1. Analyzed Nutrient Composition of the 4 Geriatric Foods.

Nutrient, 100% Dry Matter Basis	Control^a	Food A^b	Food B^c	Food C^d	Food D^e
Crude protein, %	21.53	18.64	27.65	25.51	27.47
Fat, %	17.00	15.24	13.52	10.19	12.70
Crude fiber, %	3.30	2.20	1.60	5.10	2.23
Ca, %	0.79	0.66	0.79	1.18	1.28
P, %	0.64	0.57	0.68	0.85	1.07
Ash, %	4.37	4.08	4.41	6.32	7.73
Moisture, %	7.40	7.36	8.38	8.12	6.55
Sodium, %	0.18	0.15	0.33	0.27	0.47
Potassium, %	0.68	0.64	0.73	0.65	1.00
Magnesium, %	0.11	0.11	0.08	0.14	0.12
Chloride, %	0.58	0.50	0.86	0.46	1.06
DHA, %	<0.01	0.04	0.15	<0.01	0.03
EPA, %	<0.01	0.30	0.10	<0.01	0.10
Linoleic acid, %	3.02	3.71	2.92	1.96	2.43
Total omega-3 fatty acids, %	0.83	1.21	0.48	0.12	0.38
Total omega-6 fatty acids, %	3.02	3.68	3.10	1.65	2.48
Taurine, ppm	1180	1400	1090	<100	1500
Carnitine, ppm	14	291	55	41	78
Lysine, %	0.97	1.00	1.28	1.08	1.61
Arginine, %	1.27	1.08	1.56	1.33	1.71
Methionine, %	0.40	0.93	0.49	0.47	0.61
Cystine, %	0.26	0.23	0.43	0.44	0.32
Threonine, %	0.74	0.72	1.06	0.92	1.09
Tryptophan, %	0.24	0.24	0.28	0.20	0.24
Leucine, %	1.62	1.58	3.01	2.89	2.09
Valine, %	0.91	0.86	1.37	1.17	1.27
Isoleucine, %	0.70	0.65	1.07	0.98	1.00
Manganese, ppm	17	81	77	66	63
Vitamin E, IU/kg	158	1378	594	822	393
Vitamin C, ppm	21	118	288	79	20
Lipoic acid, ppm	-	101	-	-	-
Atwater metabolizable energy, kcal/kg	3823	3785	3672	3326	3557
Lysine:calorie ratio	2.54	2.64	3.49	3.25	4.53

DHA = docosahexaenoic acid; EPA = eicosapentaenoic acid.

^aControl food ingredient list: corn meal, poultry meal, animal fat, soybean meal, flaxseed, corn gluten meal, egg, pal enhancer, potassium chloride, calcium carbonate, choline chloride, iodized salt, vitamin premix, preservative, L-tryptophan, taurine, dicalcium phosphate, L-lysine, glucosamine, mineral premix, L-arginine, and chondroitin sulfate.

^bExperimental food ingredient list: corn meal, poultry meal, soybean meal, animal fat, pal enhancer A, flaxseed, soybean oil, fish oil, beet pulp, corn gluten meal, DL-methionine, pal enhancer B, potassium chloride, dicalcium phosphate, calcium carbonate, L-carnitine, choline chloride, vitamin E, L-lysine, vitamin premix, iodized salt, taurine, L-tryptophan, L-threonine, mineral premix, preservative, manganese sulfate.

^cRoyal Canin Mature Medium Breed.

^dPurina Dog Chow Senior.

^eEukanuba Senior Maintenance.

Table 2. Vital Organ Markers Measured in Blood in Dogs.

Metabolite	Food A	Food B	Food C	Food D	SE	Probability, <i>P</i>			
						Treatment	Food A vs Food B*	Food A vs Food C*	Food A vs Food D*
BUN:creatinine									
Day 30	19.7	29.9	28.6	29.3	1.26	0.01	<0.01	<0.01	<0.01
Day 90	20.2	27.2	27.0	29.7	1.82	0.01	<0.01	<0.01	<0.01
Day 180	20.1	25.1	25.5	26.3	1.53	0.02	0.02	0.02	<0.01
BUN, mg/dL									
Day 30	10.8	15.3	15.1	15.7	0.69	0.01	<0.01	<0.01	<0.01
Day 90	11.9	14.3	14.0	14.6	0.80	0.06	0.03	0.05	0.02
Day 180	12.0	14.6	15.5	14.5	0.80	0.01	0.02	<0.01	0.03
Creatinine, mg/dL									
Day 30	0.56	0.51	0.54	0.54	0.019	0.32	0.07	0.58	0.63
Day 90	0.59	0.52	0.54	0.54	0.023	0.20	0.04	0.18	0.20
Day 180	0.59	0.57	0.63	0.57	0.020	0.25	0.47	0.22	0.73

BUN = blood urea nitrogen.

*Probability of greater F-value.

Kidney Health (Table 4)

At Day 30, dogs fed Food B tended ($P < 0.07$) to have lower creatinine compared to dogs fed Food A. Dogs fed Food A had lower ($P < 0.01$) blood urea nitrogen (BUN) and lower BUN:creatinine ratio compared to dogs fed the other 3 commercial foods. Dogs fed Food A had a lower ($P < 0.04$) percentage of animals with early signs of kidney damage as indicated by microalbuminuria analysis compared to dogs fed Food B and Food D and tended ($P < 0.08$) to have a lower percentage with early signs of kidney damage compared to dogs fed Food C. At Day 90, dogs fed Food B had lower ($P < 0.04$) creatinine compared to dogs fed Food A. Dogs fed Food A had lower ($P < 0.05$) BUN and BUN:creatinine ratio ($P < 0.01$) compared to dogs fed the other 3 commercial foods. No differences ($P > 0.17$) in the percentage of dogs with early signs of kidney damage by microalbuminuria analysis were detected at Day 90. At Day 180, creatinine levels were similar ($P > 0.25$) for the 4 foods. Dogs fed Food A had lower ($P < 0.03$) BUN levels and BUN:creatinine

($P < 0.02$) compared to the other 3 commercial foods. Finally, dogs fed Food D had a greater ($P < 0.01$) percentage of animals with early signs of kidney damage and dogs fed Food B tended ($P < 0.08$) to have greater damage as indicated by microalbuminuria analysis compared to dogs fed Food A.

DISCUSSION

In geriatric dogs, renal failure is a common process and leads to death in approximately 5% of the dog population.²⁷ One of the main treatment strategies in the management of dogs with renal disease is to reduce dietary protein and phosphorus in foods.²⁸ However, decreased dietary protein concentrations have been implicated in reducing lean muscle in aging animals¹⁸ and during weight loss.^{14,19} Thus, dietary intervention for one purpose may be counterproductive to another in the geriatric animal. Even so, balancing diets based on ideal amino acid ratios^{17,29} should allow a reduction in dietary crude protein while maintaining lean muscle mass of the dog. The objective of this experiment was to compare commercially available geriatric foods to an experimental

Table 3. Body Composition Measured in Dogs Fed 4 Different Foods.

Body Parameter Measured	Food A	Food B	Food C	Food D	Probability, P				
					SE	Treatment	Food A Vs Food B*	Food A Vs Food C*	Food A Vs Food D*
Weight									
Day 0, kg	12.07	11.91	12.20	11.68	0.695	0.96	0.86	0.90	0.69
Day 90, kg	12.63	12.55	12.29	11.98	0.747	0.92	0.94	0.74	0.53
Day 180, kg	12.63	12.98	12.25	12.07	0.798	0.84	0.75	0.73	0.61
Change Day 0 to 90, kg	0.56	0.64	0.09	0.30	0.203	0.21	0.75	0.11	0.36
Change Day 0 to 180, kg	0.56	1.08	0.03	0.41	0.309	0.13	0.22	0.23	0.73
Day 0 vs Day 90*	<0.01	<0.01	0.66	0.16			-	-	-
Day 0 vs Day 180*	0.07	<0.01	0.91	0.20			-	-	-
Lean									
Day 0, g	7792	7842	7768	7691	475.5	0.99	0.94	0.97	0.88
Day 90, g	7790	7672	7814	7544	488.2	0.98	0.87	0.97	0.72
Day 180, g	7718	7581	8048	7202	469.9	0.65	0.83	0.61	0.43
Change Day 0 to 90, g	-2	-170	46	-147	112.4	0.45	0.30	0.76	0.37
Change Day 0 to 180, g	-74	-260	46	-262	129.8	0.26	0.29	0.51	0.30
Day 0 vs Day 90*	0.98	0.14	0.69	0.20			-	-	-
Day 0 vs Day 180*	0.55	0.04	0.73	0.05			-	-	-
Fat									
Day 0, g	3936	3647	3576	3942	394.4	0.87	0.61	0.52	0.99
Day 90, g	4133	4289	3465	3872	402.9	0.50	0.78	0.25	0.65
Day 180, g	4311	4792	3615	4173	470.5	0.36	0.45	0.29	0.83
Change Day 0 to 90, g	196	642	-111	-70	239.2	0.12	0.20	0.37	0.44
Change Day 0 to 180, g	375	1145	20	299	332.5	0.10	0.09	0.44	0.87
Day 0 vs Day 90*	0.42	0.01	0.64	0.77			-	-	-
Day 0 vs Day 180*	0.24	<0.01	0.95	0.38			-	-	-
Bone mineral content									
Day 0, g	429.2	422.0	430.1	433.2	23.77	0.99	0.83	0.98	0.91
Day 90, g	428.4	429.2	427.7	437.8	24.27	0.99	0.98	0.98	0.79
Day 180, g	426.9	436.8	431.8	421.6	25.38	0.98	0.77	0.89	0.88
Change Day 0 to 90, g	-0.8	7.2	-2.4	4.6	5.00	0.50	0.26	0.83	0.45
Change Day 0 to 180, g	-2.3	14.8	-9.8	0.1	4.78	0.01	0.01	0.26	0.73
Day 0 vs Day 90*	0.87	0.16	0.64	0.36			-	-	-
Day 0 vs Day 180*	0.62	<0.01	0.05	0.99			-	-	-

*Probability of greater F-value.

Table 4. Percentage of Dogs Without Kidney Damage Measured by Urine Microalbuminuria in Dogs.

	% Without Damage				Probability, <i>P</i>		
	Food A	Food B	Food C	Food D	Food A vs Food B*	Food A vs Food C*	Food A vs Food D*
Day 0	50	60	40	20	0.34	0.34	0.08
Day 30	90	40	60	50	0.02	0.08	0.04
Day 90	40	50	60	30	0.34	0.17	0.34
Day 180	70	44	67	22	0.08	0.35	0.01

*Probability of a greater F-value compared to Food A.

geriatric food for dogs on measures of body composition and kidney health.

Dogs fed experimental Food A had lower BUN and BUN:creatinine ratios at all 3 time points compared to the 3 commercial foods. In addition, dogs fed Food A had a lower percentage of animals with renal damage at Day 30 compared to 3 commercial foods and at Day 180 compared to dogs fed Food D. In the current study, dietary protein was lower in the experimental food compared to the 3 commercial foods. These data suggest improved measures of kidney function and reduced progression of kidney disease in dogs fed the experimental food compared to the 3 commercially available foods.^{30,31} Similarly, Polzin et al⁴ also observed reduced serum urea nitrogen and mortality rates in dogs fed reduced protein foods (8% and 17%) compared to a high protein food (44%). Jacob et al⁶ reported a reduced rate of renal disease progression and mortality rate in dogs fed a reduced protein diet. Restricting both dietary protein and calories resulted in improved measures of kidney function in cats with surgically induced renal failure.⁵ Furthermore, lower dietary protein intakes were associated with reduced mortality rate in a retrospective human study.³² On the other hand, Bovee³³ and Finco et al³⁴ observed no definitive relationship between dietary protein intake and measures of kidney function in dogs. Reducing the dietary protein concentration may slow renal disease progression by reducing negative effects of increased protein metabolism.

In addition to lower dietary protein, the experimental food contained lower

concentrations of phosphorus which has also been implicated in improving renal disease status.^{7,21} Brown et al³⁵ described improved survival rates and reduced kidney deterioration in dogs fed a low phosphorus food compared to a high phosphorus food. Similarly, Finco et al¹⁰ fed dogs a reduced phosphorus food (0.4%) compared to a high phosphorus food (1.4%) which increased survival time. Elliot et al³⁶ and Ross et al³⁷ reported increased survival time when cats with chronic renal failure were fed a diet with reduced protein and phosphorus. Both reduced protein and phosphorus diets have shown positive effects on renal function and chronic renal patient survival time, and may help improve healthy aging in geriatric animals by slowing renal disease progression.

Dietary supplementation with poly-unsaturated fatty acids and antioxidants are also believed to provide protective effects in renal failure patients.² The experimental food contained both higher concentrations of omega-3 fatty acids and antioxidants. Brown et al¹¹ demonstrated that omega-3 fatty acids were renal protective when fed to dogs while omega-6 fatty acids were detrimental to renal function. Brown et al³⁸ proposed that providing omega-3 fatty acids functioned to reduce prostaglandin production and reduce glomerular capillary pressure. Furthermore, a retrospective study evaluating commercial diets noticed that cats survived the longest on a diet containing high levels of the omega-3 fatty acid eicosapentanoic acid.³⁹ Using rat renal reduction models, Barcelli et al⁴⁰ and Clark et al⁴¹ reported preservation of renal function in those fed greater concentra-

tions of omega-3 fatty acids. The addition of L-carnitine to the diet of rats in renal injury models also has been found to reduce the severity of renal damage and enhance renal function.⁴²⁻⁴⁴ High levels of antioxidants vitamin E and C have been shown to reduce oxidative stress and DNA damage in cats with renal insufficiency.¹³ Finally, the experimental Food A contained lipoic acid, a potent antioxidant, which has been shown to reduce tissue injury and renal dysfunction in rats with acute renal failure.⁴⁵ The addition of these dietary ingredients to low protein/phosphorus foods may aid in the protection kidney function and slow progression of kidney disease in aging dogs.

Dogs fed Food B gained weight, fat, BMC, and lost lean over the 180-day feeding period; however, the change in BMC might be due to the additional weight gain in dogs fed Food B. Dogs fed Food D lost lean and BMC over the feeding period. We have no explanation why dogs fed Food B and Food D lost lean during the course of this study. The importance of body condition in the development of aging diseases in companion animals has been described.¹⁵ In addition, a greater amount of lean muscle mass is associated with improved mobility and cognitive function in humans.¹⁶ In the current study, the loss of lean in the geriatric dog may be part of the aging process and could potentially be prevented by providing additional essential amino acids that promote protein synthesis and prevent protein degradation.

CONCLUSION

Reducing dietary protein and phosphorus along with the addition of omega-3 fatty acids, carnitine, and high levels of antioxidants in the experimental geriatric food resulted in improved markers of kidney function and preservation of muscle mass in the geriatric dog. High protein diets designed to minimize loss of lean muscle may increase the risk for development of renal disease.

REFERENCES

- Allen TA, Polzin DJ, Adams LG. Renal disease. In: Hand MS, Lewis LD, eds. *Small Animal Clinical Nutrition*. 4th edition Topeka, KS: Mark Morris Institute; 2000:563-604.
- Brown SA, Finco DR, Bartges JW, Brown CA, Barsanti JA. Interventional nutrition for renal disease. *Clin Tech Small Anim Pract*. 1998;13:217-223.
- Pugliese A, Gruppillo A, Di Pietro S. Clinical nutrition in gerontology: chronic renal disorders of the dog and cat. *Vet Res Commun*. 2005;29:57-63.
- Polzin DJ, Osborne CA, Hayden DW, Stevens JB. Influence of modified protein diets on morbidity, mortality, and renal function in dogs with induced chronic renal failure. *Am J Vet Res*. 1984;45:506-517.
- Adams LG, Polzin DJ, Osborne CA, O'Brien TD. Effects of dietary protein and calorie restriction in clinically normal cats and in cats with surgically induced chronic renal failure. *Am J Vet Res*. 1993;54:1653-1662.
- Jacob F, Polzin DJ, Osborne CA, et al. 2002. Clinical evaluation of dietary modification for treatment of spontaneous chronic renal failure in dogs. *J Am Vet Med Assoc*. 2002;220:1163-1170.
- Ross LA, Finco DR, Crowell WA. Effect of dietary phosphorus restriction on the kidneys of cats with reduced renal mass. *Am J Vet Res*. 1982;43:1023-1026.
- Polzin DJ, Osborne CA, Adams LG. Effect of modified protein diets in dogs and cats with chronic renal failure: current status. *J Nutr*. 1991;121(Suppl 11):S140-S144.
- Finco DR, Brown SA, Crowell WA, Duncan RJ, Barsanti JA, Bennett SE. Effects of phosphorus/calcium-restricted and phosphorus/calcium-replete 32% protein diets in dogs with chronic renal failure. *Am J Vet Res*. 1992;53:157-163.
- Finco DR, Brown SA, Crowell WA, Duncan RJ, Barsanti JA, Bennett SE. Effects of dietary phosphorus and protein in dogs with chronic renal failure. *Am J Vet Res*. 1992;53:2264-2271.
- Brown SA, Brown CA, Crowell WA, et al. Beneficial effects of chronic administration of dietary omega-3 polyunsaturated fatty acids in dogs with renal insufficiency. *J Lab Clin Med*. 1998;131:447-455.
- Brown SA, Finco DR, Brown CA. 1998c. Is there a role for dietary polyunsaturated fatty acid supplementation in canine renal disease? *J Nutr*. 1998;128:2765S-2767S.
- Yu S, Paetau-Robinson I. Dietary supplementation of Vitamins E and C and beta-carotene reduce oxidative stress in cats with renal insufficiency. *Vet Res Commun*. 2006;30:403-413.
- Hannah SS, Laflamme DP. Increased dietary protein spares lean body mass during weight loss in dogs. *J Vet Intern Med*. 1998;12:224.
- Laflamme DP. Nutrition for aging cats and dogs and the importance of body condition. *Vet Clin North Am Small Anim Pract*. 2005;35:713-742.

16. Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *J Am Geriatr Soc.* 2005;50:889-896.
17. Baker DH, Czarnecki-Maulden GL. Comparative nutrition of cats and dogs. *Ann Rev Nutr.* 1991;11:239-263.
18. Wakshlag JJ, Barr SC, Ordway GA, et al. 2003. Effect of dietary protein on lean body wasting in dogs: correlation between loss of lean mass and markers of proteasome-dependent proteolysis. *J Anim Physiol Anim Nutr.* 2003;87:408-420/
19. Diez M, Nguyen P, Jeusette I, Devois C, Itasse L, Biourge V. Weight loss in obese dogs: evaluation of a high-protein, low-carbohydrate diet. *J Nutr.* 2002;132:1685S-1687S.
20. Laflamme DP, Hannah SS. Increased dietary protein promotes fat loss and reduces loss of lean body mass during weight loss in cats. *Int J Appl Res Vet Med.* 2005;3:62-68.
21. Klahr S, Buerkett J, Purkerson ML. Role of dietary factors in the progression of renal disease. *Kidney Int.* 1983;24:579-587.
22. Barzel US, Massey LK. Excess dietary protein can adversely affect bone. *J Nutr.* 1998;128:1051-1053.
23. Reddy ST, Wang CY, Sakhae K, Brinkley L, Pak CY. Effect of low-carbohydrate high-protein diets on acid-base balance, stone-forming propensity, and calcium metabolism. *Am J Kidney Dis.* 2002;40:265-274.
24. Ginty F. Dietary protein and bone health. *Proc Nutr Soc.* 2003;62:867-876.
25. Association of American Feed Control Officials (AAFCO). *Association of American Feed Officials: Official Publication.* Atlanta, GA: Association of American Feed Control Officials; 2005.
26. SAS. *SAS/STAT® User's Guide (Release 6.03).* Cary, NC: SAS Institute, Inc.; 1989.
27. Bronson RT. Variation in age at death of dogs of different sexes and breeds. *Am J Vet Res.* 1982;43:2057-2059.
28. Deveaux C, Polzin DJ, Osborne CA. What role does dietary protein restriction play in the management of chronic renal failure in dogs? *Vet Clin North Am.* 1996;26:1247-1266.
29. Frantz NZ, Yamka RM, Friesen, KG. The effect of diet and lysine:calorie ratio on body composition and kidney health in geriatric cats. *Int J Appl Res Vet Med.* 2007;5:25-36.
30. Case LP, Carey DP, Hirakawa DA, Daristotle L. Chronic renal failure. In: Case LP, Carey DP, Hirakawa DA, Daristotle L, eds. *Canine and Feline Nutrition.* St. Louis, MO: Mosby, Inc.; 2000:451-471.
31. Gary AT, Cohn LA, Kerl ME, Jensen WA. The effects of exercise on urinary albumin excretion in dogs. *J Vet Intern Med.* 2004;18:52-55.
32. Fouque D, Laville M, Boissel JP. Low protein diets for chronic kidney disease in non diabetic adults. *Cochrane Database Syst Rev.* 2006;2:CD001892.
33. Bovee KC. Influence of dietary protein on renal function in dogs. *J Nutr.* 1991;121:S128-S139.
34. Finco DR, Brown SA, Brown CA, Crowell WA, Sunvold G, Cooper TL. Protein and calorie effects on progression of induced chronic renal failure in cats. *Am J Vet Res.* 1998;59:575-582.
35. Brown SA, Crowell WA, Barsanti JA, White JV, Finco DR. Beneficial effects of dietary mineral restriction in dogs with marked reduction in renal mass. *J Am Soc Nephrol.* 1991;1:1169-1179.
36. Elliot J, Rawlings JM, Markwell PJ, Barber PJ. Survival of cats with naturally occurring chronic renal failure: effect of dietary management. *J Small Anim Prac.* 2000;41:235-242.
37. Ross SJ, Osborne CA, Kirk CA, Lowry SR, Koehler LA, Polzin DJ. Clinical evaluation of dietary modification for treatment of spontaneous chronic kidney disease in cats. *J Am Vet Med Assoc.* 2006;229:949-957.
38. Brown SA, Brown CA, Crowell WA, et al. Effects of dietary polyunsaturated fatty acid supplementation in early renal insufficiency in dogs. *J Lab Clin Med.* 2000;135:275-286.
39. Plantinga EA, Everts H, Kastelein AM, Beynen AC. Retrospective study of the survival of cats with acquired chronic renal insufficiency offered different commercial diets. *Vet Rec.* 2005;157:347-357.
40. Barcelli U, Maiyata J, Ito Y, et al. Beneficial effects of polyunsaturated fatty acids in partially nephrectomized rats. *Prostaglandins.* 1986;32:211-9.
41. Clark WF, Parbtani A, Philbrick DJ, Holub B, Huff MW. Chronic effects of omega-3 fatty acids (fish oil) in a rat 5/6 renal ablation model. *J Am Soc Nephrol.* 1991;1:1343-1353.
42. Kopple JD, Ding H, Letoha A, et al. 2002. L-carnitine ameliorates gentamicin-induced renal injury in rats. *Nephrol Dial Transplant.* 2002;17:2122-2131.
43. Gorur S, Bagdatoglu OT, Polat G. Protective effect of L-carnitine on renal ischaemia-reperfusion injury in the rat. *Cell Biochem Funct.* 2005;23:151-155.
44. Aydogu N, Atmaca G, Yalcin O, Taskiran R, Tastekin E, Kaymak K. Protective effects of L-carnitine on myoglobinuric acute renal failure in rats. *Clin Exp Pharmacol Physiol.* 2006;33:119-124.
45. Takaoka M, Ohkita M, Kobayashi Y, Yuba M, Matsumura Y. Protective effect of alpha-lipoic acid against ischaemic acute renal failure in rats. *Clin Exp Pharmacol Physiol.* 2002;29:189-194.