Multicenter veterinary practice assessment of the effects of omega-3 fatty acids on osteoarthritis in dogs

James K. Roush, DVM, MS, DACVS; Chadwick E. Dodd, DVM; Dale A. Fritsch, MS; Timothy A. Allen, DVM, DACVIM; Dennis E. Jewell, PhD, DACAN; William D. Schoenherr, PhD; Daniel C. Richardson, DVM, DACVS; Phillip S. Leventhal, PhD; Kevin A. Hahn, DVM, PhD, DACVIM

Objective—To assess the effect of food containing high concentrations of fish oil omega-3 fatty acids and a low omega-6–omega-3 fatty acid ratio on clinical signs of osteoarthritis in dogs.

Design—Randomized, double-blinded, controlled clinical trial.

Animals—127 client-owned dogs with osteoarthritis in 1 or more joints from 18 privately owned veterinary clinics.

Procedures—Dogs were randomly assigned to be fed for 6 months with a typical commercial food or a test food containing a 31-fold increase in total omega-3 fatty acid content and a 34-fold decrease in omega-6–omega-3 ratio, compared with the control food. Dog owners completed a questionnaire about their dog's arthritic condition, and investigators performed a physical examination and collected samples for a CBC and serum biochemical analyses (including measurement of fatty acids concentration) at the onset of the study and at 6, 12, and 24 weeks afterward.

Results—Dogs fed the test food had a significantly higher serum concentration of total omega-3 fatty acids and a significantly lower serum concentration of arachidonic acid at 6, 12, and 24 weeks. According to owners, dogs fed the test food had a significantly improved ability to rise from a resting position and play at 6 weeks and improved ability to walk at 12 and 24 weeks, compared with control dogs.

Conclusions and Clinical Relevance—Ingestion of the test food raised blood concentrations of omega-3 fatty acids and appeared to improve the arthritic condition in pet dogs with osteoarthritis. (*J Am Vet Med Assoc* 2010;236:59–66)

Arthritis is generally diagnosed and classified clinically into 2 broad categories: degenerative arthritis and osteoarthritis. The main features of degenerative arthritis are the degradation of articular cartilage and the presence of inflammatory arthropathies, in which synovitis is the main pathological feature.[1] Osteoarthritis is associated with degenerative joint disease and is the most common form of arthritis in humans and veterinary species. It is generally a chronic, progressive disease characterized by the degeneration of articular cartilage, with loss of proteoglycan and collagen and periarticular proliferation of new bone.[2,3] Variable inflammatory responses also develop within the synovial membrane.[1,4]

Osteoarthritis affects up to 20% of dogs > 1 year of age.[2] Although osteoarthritis commonly develops in older, overweight, and large-breed dogs, the disease can affect dogs of all ages, sizes, and breeds. Treatments are aimed at prevention, slowing progression, and controlling clinical signs of disease. Adequate nutrition, bodyweight control, controlled exercise, physical therapy, anti-inflammatory and analgesic medications, and other disease-modifying methods are often incorporated in the management of osteoarthritis.[5] Nonsteroidal anti-inflammatory drugs and corticosteroid medications are effective modes of treatment, but they have potential adverse effects, including gastrointestinal ulceration, renal failure, hepatic failure, and death.[6] In addition, the long-term use of NSAIDs and corticosteroid medication may accelerate cartilage degeneration.[6]

Results of several studies[7–13] have suggested that omega-3 fatty acids have beneficial effects in the treatment of rheumatoid arthritis. Dietary supplementation with fish oil reportedly increases the concentrations of the omega-3 fatty acids EPA and DHA in inflammatory cells and results in a corresponding decrease in omega-6 fatty acid concentrations, particularly AA. Eicosanoids produced from omega-3 fatty acids appear to be less

Abbreviations

AA	Arachidonic acid
DHA	Docosahexaenoic acid
EPA	Eicosapentaenoic acid

From the Department of Clinical Sciences, College of Veterinary Medicine, Kansas State University, Manhattan, KS 66506 (Roush); Pet Nutrition Center, Hill's Pet Nutrition Inc, PO Box 1658, Topeka, KS 66601 (Dodd, Fritsch, Allen, Jewell, Schoenherr, Richardson, Hahn); and 4Clinics, 8 rue de la Terrasse, 75017 Paris, France (Leventhal).

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Address correspondence to Dr. Hahn (kevin_hahn@hillspet.com).

potent at inducing inflammation than those produced from AA.[14] Omega-3 fatty acids may also reduce serum concentrations and activities of proteoglycan-degrading enzymes, cyclooxygenase-2, and inflammation-inducible cytokines.[15] Also, feeding fish oil, which is rich in omega-3 fatty acids, reduces the serum concentrations of inflammatory factors in mice with experimentally induced rheumatoid arthritis,[16] and oral administration of the omega-3 fatty acids EPA and DHA reduces streptococcal cell wall arthritis in Lew/SsN rats.[17]

Accordingly, we hypothesized that dietary supplementation with fish oil omega-3 fatty acids would improve the osteoarthritic condition of dogs. The purpose of the study reported here was to compare the effects of a test food supplemented with fish oil omega-3 fatty acids and a control food on serum fatty acid concentrations and owner- and investigator-assessed severity of osteoarthritis.

Materials and Methods

Dogs—Dogs were recruited for the study from among the patients of 18 privately owned veterinary hospitals in the United States. To be eligible for inclusion, dogs were required to have osteoarthritis as diagnosed on the basis of history, clinical signs, and radiographic evidence of arthritis in 1 or more joints on the clinically affected limb as detected in orthogonal survey radiographs of the joints before enrollment. Dogs also had to be at least 1 year of age, weigh at least 11.4 kg (≥ 25.0 lb), have a body condition score > 1 (1 = very thin; 2 = underweight; 3 = ideal; 4 = overweight; and 5 = obese), consume dry dog food, not be enrolled in any other clinical study, and be free of systemic disease as determined by history and results of physical examination, CBC, serum biochemical analysis, and urinalysis. Results of laboratory tests were either required to be within reference limits provided by the analytic testing facility or acceptable as judged by the investigators.

Exclusion criteria included the following: acute traumatic injuries (including acute osteoarthritis) or complicating systemic diseases that could interfere with or prevent the evaluation of the dog's response in this study; treatment with topical or systemic pharmaceuticals or biologics (other than routine antiparasitic medication), corticosteroids, NSAIDs, or antimicrobials within 14 days before enrollment; arthrocentesis within 30 days before enrollment; treatment with injectable depot corticosteroids, polysulfated glycosaminoglycan, glucosamine, or chondroitin sulfate nutritional supplements within 30 days before enrollment; intra-articular injection of any material into any joint within 90 days before enrollment; surgery on any joint within 180 days before enrollment; fractious behavior; and pregnancy or likelihood of becoming pregnant during the study.

Participating dogs were dismissed from the study for the following reasons: development of an adverse reaction, injury, or illness that warranted treatment or surgical intervention, thereby establishing noncompliance with study restrictions or requiring disclosure (unmasking) of the type of food to which the dog had been assigned; unblinding of the investigator; determination by the investigator that the dog was unable to continue in the study because of excessive pain or other complications; lack of dog cooperation with study procedures or of owner compliance with study restrictions; owner withdrawal from the study; failure of owner to comply with feeding instructions or to adhere to the study protocol; and death of the dog because of natural causes or owner-elected euthanasia. In addition, data from dogs were removed from statistical analyses if it was determined ex post facto that they did not meet eligibility criteria. Each participating veterinary hospital followed guidelines established for Good Clinical Practice, and all dog owners provided written consent for participation.

Study foods—The control food consisted of typical adult commercial dry[a] and canned[b] foods, and the test food consisted of dry and canned formulations[c] (**Appendix 1**). The control foods were identified from a list of leading brands of commercial dog foods and selected because they most closely matched the macronutrient profile of the test foods. The foods all met or exceeded the complete and balanced nutrition guidelines of the Association of American Feed Control Officials for the maintenance of adult dogs (> 1 year old).[18] Identical packaging was used to mask the identity of the foods from all individuals directly involved with evaluating each dog.

Study protocol and assessments of osteoarthritis—This investigation was conducted as a 6-month prospective, randomized, double-blinded, controlled study. Eligible dogs were randomly assigned to receive control or test food. Neither pet owners nor investigators had knowledge of the food to which dogs were assigned. Owners had the choice of feeding dry food, canned food, or a mixture of the 2. Upon enrollment in the study, pet owners were instructed to transition their dogs to the assigned study food over 7 days by mixing increasing amounts of study food with decreasing amounts of the food used before entry in the study (week 0). Feeding guidelines were provided to owners with the intent for dogs to be fed according to their usual feeding regimen (free choice or meal) to maintain a constant body weight and condition.

At weeks 6, 12, and 24, owners completed a questionnaire in which they were asked to score the change in osteoarthritis severity from the previous to the present visit (1 = better; 2 = about the same; 3 = worse) for the following clinical signs: difficulty in rising from rest, limping, stiffness, soreness when touched, yelping or whimpering in pain, aggression, lagging on walks, reluctance to run, reluctance to walk, reluctance to jump, reluctance to climb stairs, reluctance to play, and activity level. Investigators reviewed all owner-submitted questionnaires for completeness.

In addition, clinical evaluations were conducted by attending veterinarians at weeks 0 (baseline), 6, 12, and 24 by use of a specific scoring system (**Appendix 2**). Evaluations consisted of a physical examination, wherein a 5-point scale was used to characterize the following clinical signs: lameness, pain on palpation, degree of weight bearing, range of joint motion, and willingness to hold up the contralateral limb. The same veterinarian performed all assessments for a given dog. Also, at all visits, a blood sample was collected for analysis of CBC, serum biochemical analysis, and serum fatty acid concentrations. Results from those analyses were used

to screen dogs for study eligibility and to monitor dogs for adverse effects.

Analysis of food nutrient content—Nutrient content of foods was assessed with standard methods by a commercial laboratory.[d]

Analysis of serum fatty acids—Serum concentrations of fatty acids were analyzed by use of gas chromatography. Extraction of fatty acids from the serum harvested from blood samples was performed as described elsewhere,[19] with modifications. Briefly, 50 µL of internal standard (2 mg of heptadecanoic acid/mL in methanol), 1 mL of saline (1% NaCl) solution, and 3 mL of a 2:1 (v/v) mixture of chloroform and methanol were added to test tubes containing 0.2 mL of serum. The content of the tubes was mixed with a vortex machine for 1 minute, and then the tubes were centrifuged at 3,200 × *g* for 15 minutes. The chloroform was evaporated to dryness under a stream of nitrogen in a water bath at 30°C (86°F). The fatty acids were subsequently methylated in a mixture of 3 mL of 12% boron trifluoride in methanol and 1 mL of isooctane at 70°C (158°F) for 1 hour. Water (1 mL) was added to extract fatty acid methyl esters. The isooctane extract was separated and dried with anhydrous sodium sulfate. Fatty acid methyl esters were separated and detected with a gas chromatograph[e] equipped with a flame ionization detector and a 30-m column[f] (internal diameter, 0.25 mm; film thickness, 0.2 µm). The column was operated with the following temperature program: initial oven temperature of 150°C (302°F), followed by an increase at 2°C/min to 200°C (392°F), 20 minutes at 200°C, increase at 3°C/min to 240°C (464°F), and 10 minutes at 240°C. The injector and detector temperatures were 250°C (482°F) and 260°C (500°F), respectively. Helium was used as the carrier gas. Chromatographic data were acquired with commercial computer software.[g] The peaks obtained were identified by comparison of their relative retention times with those of known standards of fatty acid methyl esters prepared from free fatty acids as described previously. Fatty acid concentrations were determined by comparison of peak areas with standard curves generated by use of the internal standard.

Statistical analysis—Commercially available statistical software was used to assess results from investigators' clinical evaluations by construction of a generalized linear mixed model with a Poisson distribution and log-link function.[h] Clinic and clinic-by-food random effects were included in the model to adjust for random differences between the veterinary clinics. The model also included a random residual effect to adjust for data overdispersion. Food was the only fixed effect in the model. The day 0 value for each clinical sign was used as a covariate to adjust for differences in clinical-sign severity at the start of the study. In addition, data from dogs with a score of 1 (no clinical sign) for a given clinical sign at the start of the study were removed from the data set for that clinical sign prior to analysis. Data were analyzed separately for evaluations conducted at weeks 6, 12, and 24.

Results from owners' evaluations were also analyzed by construction of a generalized linear mixed model with a Poisson distribution and log-link function. The model was adjusted for overdispersion by inclusion of a random residual effect. Food was the only fixed effect in the model. Data from dogs with a frequency score of 5 (never observed) for a clinical sign at the start of the study were removed from the data set prior to analysis. The data were analyzed separately for evaluations made at weeks 6, 12, and 24. Values of serum fatty acids concentration were analyzed by use of a 1-way ANOVA, with food as the fixed effect.[i] A P value < 0.05 was considered as indicating a significant difference. All data are reported as group mean ± SE.

Results

Dogs—One hundred eighty-one dogs were screened for inclusion in the study. Of these, 14 were excluded for the following reasons: lack of radiographic confirmation of osteoarthritis in the lame limb (n = 7), exclusionary concurrent disease (3), body weight < 11.4 kg (2), scheduled surgery (1), and owner moving away (1). Of the 167 dogs that began the study, 127 completed 6 months of feeding (71 received the test food and 56 received the control food).

Forty dogs were lost to follow-up. Of these, 16 were fed the test food and 24 received the control food. The 16 dogs in the test-food group were lost to follow-up for the following reasons: nonarthritic conditions (n = 5), owner noncompliance with study protocol (3),

Table 1—Mean ± SD values of continuous characteristics and distributions (number [%] of dogs) of categorical characteristics for client-owned dogs with osteoarthritis assigned to receive a control food (n = 56) or a test food supplemented with omega-3 fatty acids (71) in a 6-month clinical trial to evaluate the effect of ingestion of omega-3 fatty acids on osteoarthritis.

Characteristic	Control food	Test food	*P* value
Age at study start (y)	8.4 ± 3.6	8.5 ± 3.7	0.88
Body weight (kg)			
Start of study	34.1 ± 13.0	32.4 ± 10.9	0.42
Week 24	34.7 ± 13.4	31.9 ± 11.0	0.20
Body condition score (scale of 1 to 5)			
Start of study	3.38 ± 0.68	3.37 ± 0.72	0.94
Week 24	3.38 ± 0.65	3.36 ± 0.77	0.88
Sex			0.72
Female	31 (56)	42 (59)	
Male	25 (44)	29 (41)	
Reproductive status			0.22
Neutered or spayed	45 (80)	63 (89)	
Sexually intact	11 (20)	8 (11)	
Primary affected joint at study start			0.26
Spinal column	3 (5)	2 (3)	
Elbow	6 (11)	8 (11)	
Hip	30 (54)	44 (62)	
Tarsus	4 (7)	0 (0)	
Stifle	12 (21)	14 (20)	
Shoulder	1 (2)	3 (4)	
Concurrent treatment			0.32
None	37 (66)	53 (75)	
Prescription NSAIDs	5 (9)	7 (10)	
Glycosaminoglycans or omega-3 fatty acids	4 (7)	6 (8)	
Combination of treatments	10 (18)	5 (7)	

A value of $P < 0.05$ was used to indicate a significant difference between dogs that consumed the control food and those that consumed the test food.

decrease in appetite (3), deterioration of arthritic condition (2), need for surgical repair of a ruptured cranial cruciate ligament (2), and euthanasia for nonarthritic conditions (1). The 24 dogs in the control-food group were lost to follow-up because of owner noncompliance (n = 7), euthanasia for nonarthritic conditions (5), nonarthritic conditions (5), decrease in appetite (3), deterioration in arthritic condition (2), need for surgical repair of a ruptured cranial cruciate ligament (1), and owner relocation (1).

There were 35 mixed-breed dogs in the study, 21 Labrador Retrievers, 18 Golden Retrievers, 7 Kuvasz, 6 German Shepherd Dogs, 6 Rottweilers, 4 Cocker Spaniels, 4 Great Danes, 2 English Springer Spaniels, 2 Irish Setters, 2 Shetland Sheepdogs, and 1 each of the following breeds: Australian Cattle Dog, Alaskan Malamute, Australian Shepherd, Border Collie, Brittany, Dalmatian, English Bulldog, English Labrador Retriever, Flat-coated Retriever, French Bulldog, German Shorthaired Pointer, German Wirehaired Pointer, Greyhound, Mas-

Table 2—Nutrient content of foods used in a study conducted to evaluate the effects of omega-3 fatty acids on osteoarthritis in dogs.

	Control food			Test food		
Nutrient	Dry	Canned	Estimated combined*	Dry	Canned	Estimated combined*
Total protein (%)	23.21	45.76	30.73	19.94	20.76	20.21
Crude fat (%)	13.88	24.38	17.38	13.55	14.97	14.02
Carbohydrates (calculated; %)	54.68	18.76	42.71	53.35	47.81	51.50
Crude fiber (%)	1.97	0.81	1.58	8.97	11.34	9.76
Ash (%)	6.25	10.31	7.60	4.19	5.12	4.50
Calcium (%)	1.28	1.77	1.44	0.66	0.75	0.69
Magnesium (%)	0.12	0.08	0.11	0.13	0.16	0.14
Phosphorus (%)	1.00	1.45	1.15	0.58	0.56	0.57
Potassium (%)	0.69	0.93	0.77	0.61	0.78	0.67
Sodium (%)	0.32	1.35	0.66	0.18	0.31	0.22
Chloride-soluble (%)	0.67	1.83	1.06	0.40	0.59	0.46
C18:3 (α-linolenic acid; %)	0.12	0.16	0.13	2.84	2.23	2.64
C20:4 (AA; %)	0.03	0.26	0.11	0.06	0.10	0.07
C20:5 (EPA; %)	< 0.01	< 0.01	< 0.01	0.38	0.48	0.41
C22:6 (DHA; %)	< 0.01	< 0.01	< 0.01	0.31	0.59	0.40
Sum omega-3 fatty acid (calculated; %)	0.09	0.16	0.11	3.48	3.45	3.47
Sum omega-6 fatty acid (calculated; %)	1.99	4.36	2.78	2.53	2.33	2.46
Omega-6:omega-3 fatty acid ratio	22.75	27.50	24.33	0.73	0.68	0.71
Chondroitin sulfate (%)	0.01	0.22	0.08	0.02	0.05	0.03
Glucosamine (%)	< 0.01	< 0.01	< 0.01	0.04	0.01	0.03
Metabolizable energy (kcal/kg)	3,742	811	NA	3,357	867	NA

All percentages are expressed on a dry matter basis.
*Combined content was estimated on the basis of a 2:1 dry-to-canned food feeding ratio.
NA = Not applicable.

Table 3—Mean ± SE serum fatty acid concentrations before (week 0) and 6, 12, and 24 weeks after initiation of a clinical trial in which dogs with osteoarthritis were fed a control food (n = 56) or food supplemented with omega-3 fatty acids (71).

		Week 0		Week 6		Week 12		Week 24	
Fatty acid	Food	Mean ± SE	*P* value	Mean ± SE	*P* value	Mean ± SE	*P* value	Mean ± SE	*P* value
Omega-6 (mg/mL)									
C18:2 (linolenic acid)	Control	55.9 ± 3.0	0.30	57.1 ± 2.6	0.47	56.9 ± 2.8	0.25	56.6 ± 2.5	0.56
	Test	51.6 ± 2.7		54.6 ± 2.4		61.3 ± 2.5		58.7 ± 2.3	
C20:4 (AA)	Control	72.0 ± 3.4	0.08	67.3 ± 2.4	< 0.001	68.6 ± 2.8	< 0.001	69.1 ± 2.7	< 0.001
	Test	63.9 ± 3.1		45.5 ± 2.2		45.9 ± 2.4		42.1 ± 2.4	
Total omega-6	Control	141.9 ± 7.4	0.26	140.1 ± 5.9	0.03	138.3 ± 6.6	0.31	142.0 ± 6.2	0.12
	Test	130.2 ± 7.3		116.9 ± 8.3		127.9 ± 7.7		121.8 ± 8.3	
Omega-3 (mg/mL)									
C18:3 (α-linolenic acid)	Control	1.1 ± 0.1	0.76	0.9 ± 0.3	< 0.001	0.5 ± 0.4	< 0.001	0.5 ± 0.4	< 0.001
	Test	1.0 ± 0.1		5.6 ± 0.3		6.5 ± 0.3		7.1 ± 0.4	
C20:5 (EPA)	Control	1.1 ± 0.2	0.63	0.9 ± 0.9	< 0.001	0.7 ± 1.0	< 0.001	0.9 ± 1.0	< 0.001
	Test	1.3 ± 0.2		16.4 ± 0.8		18.7 ± 0.9		20.1 ± 0.9	
C22:6 (DHA)	Control	2.7 ± 0.3	0.50	2.0 ± 0.4	< 0.001	1.7 ± 0.5	< 0.001	2.0 ± 0.5	< 0.001
	Test	2.9 ± 0.3		11.3 ± 0.4		12.2 ± 0.4		12.2 ± 0.4	
Total omega-3	Control	5.0 ± 0.5	0.57	3.8 ± 1.5	< 0.001	2.9 ± 1.7	< 0.001	3.5 ± 1.8	< 0.001
	Test	5.4 ± 0.5		33.5 ± 1.4		37.6 ± 1.5		37.6 ± 1.7	

Values of $P < 0.05$ indicate a significant difference between dogs that consumed the control food and those that consumed the test food.

tiff, English Setter, Pembroke Welsh Corgi, pit bull–type dog, Saint Bernard, Chinese Shar-Pei, and Soft Coated Wheaten Terrier.

Baseline (week 0) values did not differ significantly between the two treatment groups (control food and food supplemented with omega-3 fatty acids) with respect to body condition score, location of the arthritis, use of concurrent therapies, sex, or reproductive status (**Table 1**). In addition, there were no significant differences in the investigator-assessed clinical signs between groups at study start. At study end (week 24), the body weight and body condition scores were not significantly different between the groups or compared with values at the study start ($P = 0.05$ and $P = 0.83$ for control and test groups, respectively).

Study foods—Nutritional analysis revealed that the total fat, total protein, total carbohydrates, and metabolizable energy values were similar in the 2 types of food, but formulation constraints resulted in differences in crude fiber to attain the desired concentrations of omega-3 fatty acids in the test food (**Table 2**). In addition, the percentage of chondroitin sulfate was lower in the test food than in the control food. The amount of glucosamine was less than the detectable range in the control food and represented < 0.05% of total dry weight in both the dry and canned test foods. Taking into account the dry-to-canned food feeding ratio of 2:1 determined from the total quantities of foods consumed during the study, dogs fed the test food received an estimated 31-fold higher amount of total omega-3 fatty

Table 4—Mean ± SE scores assigned by owners to characterize apparent severity of osteoarthritis in dogs with osteoarthritis fed a control food (n = 56) or food supplemented with omega-3 fatty acids (71) for 24 weeks.

	Weeks 0 to 6			Weeks 6 to 12			Weeks 12 to 24		
Clinical sign	**No. of dogs**	**Score**	***P* value**	**No. of dogs**	**Score**	***P* value**	**No. of dogs**	**Score**	***P* value**
Rising from rest			0.03			0.49			0.99
Control	54	1.74 ± 0.08		54	1.76 ± 0.08		54	1.93 ± 0.08	
Test	66	1.53 ± 0.07		66	1.83 ± 0.07		66	1.92 ± 0.08	
Limping			0.64			0.20			0.80
Control	52	1.65 ± 0.08		52	1.85 ± 0.09		52	1.90 ± 0.09	
Test	63	1.60 ± 0.07		63	1.70 ± 0.08		62	1.94 ± 0.08	
Stiffness			0.70			0.77			0.49
Control	53	1.68 ± 0.08		53	1.77 ± 0.08		53	1.91 ± 0.08	
Test	66	1.64 ± 0.07		66	1.74 ± 0.07		65	1.98 ± 0.08	
Soreness			0.60			0.78			0.66
Control	30	1.63 ± 0.09		30	1.73 ± 0.08		30	1.93 ± 0.09	
Test	33	1.70 ± 0.08		34	1.76 ± 0.08		34	1.88 ± 0.08	
Vocalizing in pain			0.64			0.37			0.97
Control	20	1.55 ± 0.12		20	1.95 ± 0.12		20	1.90 ± 0.10	
Test	19	1.47 ± 0.12		20	1.80 ± 0.11		19	1.90 ± 0.10	
Aggression			0.18			0.05			0.78
Control	7	1.43 ± 0.20		7	1.86 ± 0.20		7	1.86 ± 0.15	
Test	11	1.82 ± 0.18		11	1.36 ± 0.13		10	1.80 ± 0.13	
Lagging behind on walks			0.95			0.60			0.19
Control	32	1.59 ± 0.10		32	1.72 ± 0.09		32	1.97 ± 0.09	
Test	41	1.59 ± 0.09		41	1.78 ± 0.08		41	1.80 ± 0.08	
Running			0.26			0.29			0.94
Control	33	1.73 ± 0.10		33	1.82 ± 0.09		33	1.94 ± 0.10	
Test	43	1.58 ± 0.08		43	1.70 ± 0.07		42	1.93 ± 0.09	
Walking			0.65			0.02			0.003
Control	19	1.63 ± 0.12		19	2.00 ± 0.10		19	2.21 ± 0.12	
Test	27	1.70 ± 0.10		27	1.70 ± 0.08		27	1.78 ± 0.09	
Jumping			0.18			0.96			0.78
Control	42	1.86 ± 0.09		42	1.83 ± 0.08		42	1.95 ± 0.08	
Test	62	1.72 ± 0.07		62	1.84 ± 0.06		60	1.98 ± 0.07	
Stair climbing			0.81			0.50			0.13
Control	31	1.77 ± 0.10		32	1.78 ± 0.10		31	2.10 ± 0.11	
Test	47	1.74 ± 0.08		46	1.87 ± 0.08		48	1.90 ± 0.08	
Playing			0.01			0.50			0.47
Control	31	1.84 ± 0.10		31	1.87 ± 0.08		31	2.06 ± 0.09	
Test	33	1.48 ± 0.09		34	1.79 ± 0.08		34	1.97 ± 0.09	
Activity level			0.21			0.77			0.88
Control	56	1.66 ± 0.08		56	1.66 ± 0.08		56	1.84 ± 0.08	
Test	71	1.54 ± 0.06		71	1.69 ± 0.07		69	1.86 ± 0.07	

Scores represent owner-assessed change in osteoarthritis severity (1 = better; 2 = about the same; 3 = worse) for indicated period.
Week 0 was the week in which dogs were enrolled in the study.
See Table 3 for remainder of key.

Table 5—Mean ± SE scores assigned by veterinarians to characterize apparent severity of osteoarthritis in dogs with osteoarthritis fed a control food (n= 56) or food supplemented with omega-3 fatty acids (71) for 24 weeks.

	Week 6			Week 12			Week 24		
Clinical sign	**No. of dogs**	**Score**	***P* value**	**No. of dogs**	**Score**	***P* value**	**No. of dogs**	**Score**	***P* value**
Lameness			0.29			0.80			0.32
Control	40	1.88 ± 0.12		38	1.81 ± 0.14		40	1.82 ± 0.16	
Test	51	2.04 ± 0.12		50	1.86 ± 0.14		52	2.06 ± 0.17	
Reluctance to bear weight			0.33			0.40			0.76
Control	35	1.90 ± 0.12		33	1.95 ± 0.16		35	1.84 ± 0.19	
Test	40	2.03 ± 0.10		39	1.76 ± 0.14		41	1.77 ± 0.17	
Reduction in joint range of motion			0.48			0.93			0.92
Control	41	2.09 ± 0.11		40	2.11 ± 0.13		41	2.13 ± 0.16	
Test	53	2.21 ± 0.11		52	2.13 ± 0.12		54	2.11 ± 0.15	
Reluctance to hold up contralateral limb			0.33			0.63			0.31
Control	34	1.83 ± 0.13		32	1.82 ± 0.14		35	1.65 ± 0.17	
Test	40	1.99 ± 0.12		39	1.72 ± 0.12		42	1.86 ± 0.16	
Pain on palpation of the affected joint			0.16			0.76			0.94
Control	41	1.78 ± 0.14		39	1.79 ± 0.13		41	1.78 ± 0.13	
Test	45	2.05 ± 0.15		44	1.84 ± 0.12		46	1.76 ± 0.13	

See Appendix 2 for scoring system. *See* Table 3 for remainder of key.

acids (3.47% on a dry-matter basis) than those fed the control food (0.11%).

Serum fatty acid concentrations—Serum fatty acid concentrations were analyzed at 0, 6, 12, and 24 weeks of feeding the control and test foods (**Table 3**). Dogs fed the test food had significantly ($P < 0.001$) higher concentrations of total omega-3 fatty acids, including EPA and DHA, and significantly ($P < 0.001$) lower concentrations of AA at weeks 6, 12, and 24 than did dogs fed the control food. The largest magnitude of change in serum concentrations compared with baseline values was a 15-fold increase in mean EPA concentration for dogs fed the test food. There were no significant changes in serum fatty acid concentrations for dogs fed the control food throughout the study and no significant differences in serum fatty acid concentrations between test and control groups at the beginning of the study.

Changes in the severity of osteoarthritis—At weeks 6, 12, and 24, owners assessed the change in severity of arthritic signs relative to those of the previous veterinary visit (**Table 4**). According to owners, between weeks 0 and 6, dogs fed the test food had significant improvements in ability to rise from a resting position ($P = 0.033$) and play ($P = 0.011$), compared with dogs fed the control food. In addition, owners reported that between weeks 6 and 12 and weeks 12 and 24, dogs fed the test food had a significant ($P = 0.024$ and $P = 0.003$, respectively) improvement in ability to walk. In contrast, dogs fed the control food did not have any improvement in the owner-assessed signs, compared with dogs fed the test food. Finally, there were no significant differences in investigator assessments of clinical signs of osteoarthritis at any of the assessment points (**Table 5**).

Because a reduction in body weight alone can improve lameness in dogs with osteoarthritis,[20] we investigated the impact of weight loss and gain on owner- and investigator-assessed clinical signs of disease. However, there were no significant differences between dogs losing and gaining weight for any of the measures (data not shown).

Discussion

In the study reported here, the effects of a standard control food on the serum fatty acid concentrations and disease severity were compared with those of a food supplemented with fish oil omega-3 fatty acids in dogs with osteoarthritis. This study included investigator-assessed clinical signs and owner-assessed signs because results of previous studies on chronic pain in dogs suggested that a combination of the 2 is more sensitive than investigator-assessed clinical signs alone.[21,22] At the time the present study was performed, however, there were no validated scoring systems for severity of osteoarthritis by use of subjective or objective measures. Therefore, we used our own nonvalidated questionnaires to assess osteoarthritis in dogs.

Although there were no significant differences in investigator-assessed clinical signs between dog groups, owners of dogs fed the supplemented food reported some improvements in their dogs' clinical signs, namely the ability to rise from rest and play at week 6 and the ability to walk at weeks 12 and 24 after the feeding trial began. The fact that there were few significant changes may have been attributable to insensitivity of the 3-point scale used for owner assessments. Regardless, our results suggested an ameliorative effect of omega-3 fatty acid supplementation in arthritic dogs and indicated that more detailed studies that involve objective measures and perhaps more refined scales or composite scores are warranted.

Notwithstanding the possibility that dietary omega-3 fatty acid supplementation had no effect on investigator-assessed clinical signs of osteoarthritis, the lack of significant differences between dietary groups may have been attributable to several factors. First, the

unfamiliar environment of a veterinary hospital may alter the usual behavior of a dog.[23] Second, veterinarians have a limited opportunity to evaluate the arthritic condition of dogs during an orthopedic examination, whereas owners routinely observe overt signs of arthritis in their dogs and are also more likely to be aware of any day-to-day variation in those signs. Third, 18 veterinary practitioners performed the evaluations, and the assessment system was not standardized, which would have resulted in substantial inter-rater variability.

In overweight dogs with osteoarthritis, a reduction in body weight alone reportedly can improve signs of lameness.[20] However, investigator- or owner-assessed scores did not differ between dogs that gained or lost weight in the present study.

Our study also revealed that the dietary supplementation with omega-3 fatty acids resulted in an increase in serum concentrations of the same fatty acids. For example, by week 24, the serum EPA concentration in dogs fed the test food increased 15-fold, compared with the baseline value, whereas the concentration in dogs fed the control food did not change. This indicated that the omega-3 fatty acids in the test food were bioavailable. Indeed, dietary supplementation with omega-3 fatty acids, which cannot be synthesized in mammals, causes an increase in concentrations of these fatty acids in inflammatory cells.[24] When in the cell membrane, omega-3 fatty acids can compete with omega-6 fatty acids in the production of eicosanoids, resulting in fewer inflammatory forms of eicosanoids. Moreover, dietary supplementation with fish oil omega-3 fatty acids, namely EPA and DHA, yields anti-inflammatory effects. Thus, any effects of the test foods on the severity of osteoarthritis were likely attributable to the increase in serum omega-3 fatty acids concentrations.

One potential limitation to the interpretation of the results of the present study is that the test food also contained added glucosamine and chondroitin sulfate, both of which may be beneficial in the treatment of osteoarthritis. Specifically, there was a higher concentration of glucosamine but a lower concentration of chondroitin sulfate in the test food than in the control food. Recent systematic reviews of the literature, however, revealed that there is a lack of clinical evidence to support an ameliorative effect of these components in the treatment of osteoarthritis in dogs[25] or humans.[26,27] Thus, we suspect that beneficial effects of the test food detected in the present study were mostly attributable to the fish oil omega-3 fatty acids.

a. Purina Dog Chow, Nestlé Purina PetCare Co, St Louis, Mo.
b. Pedigree Choice Cuts, Mars Petcare US, Brentwood, Tenn.
c. Prescription Diet Canine j/d, Hill's Pet Nutrition Inc, Topeka, Kan.
d. Eurofins, Des Moines, Iowa.
e. Agilent 6890 gas chromatography system, Agilent Technologies, Wilmington, Del.
f. SP2380, Sufelco, Bellefonte, Pa.
g. ChemStation, Agilent Technologies, Wilmington, Del.
h. PROC GLIMMIX, SAS, version 8, SAS Institute, Cary, NC.
i. PROC MIXED, SAS, version 8, SAS Institute, Cary, NC.

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Appendix 1

Composition of foods in a study conducted to evaluate the effects of omega-3 fatty acids on osteoarthritis in dogs.

Food	Ingredients
Dry control formula	Whole grain corn, poultry by-product meal, animal fat, corn gluten meal, brewer's rice, soybean meal, malted barley flour, natural flavor, calcium carbonate, salt, calcium phosphate, potassium chloride, L-lysine, choline chloride, zinc oxide, vitamin E, ferrous sulfate, manganese sulfate, niacin, vitamin A, copper sulfate, calcium pantothenate, garlic oil, pyridoxine hydrochloride, vitamin B-12, thiamine mononitrate, vitamin D-3, riboflavin, calcium iodate, menadione sodium bisulfite complex, folic acid, biotin, and sodium selenite.
Canned control formula	Water, poultry, meat by-products, wheat flour, chicken, wheat gluten, salt, sodium tripolyphosphate, natural flavors, guar gum, sodium alginate, vegetable oil, minerals (potassium chloride, zinc sulfate, copper sulfate, and potassium iodide), titanium dioxide, xanthan gum, vitamins (vitamin E, A, and D3; D-calcium pantothenate; thiamine mononitrate; and biotin), onion powder, garlic powder, yellow No. 6, yellow No. 5, and sodium nitrite.
Dry test formula	Whole grain corn, chicken by-product meal, brewer's rice, soybean mill run, peanut hulls, flaxseed, fish oil, flaxseed oil, natural flavor, corn gluten meal, dried egg product, animal fat, potassium chloride, L-carnitine, calcium carbonate, L-lysine, choline chloride, iodized salt, vitamins (vitamin E, ascorbic acid, niacin, thiamine mononitrate, vitamin A, calcium pantothenate, biotin, vitamin B12, pyridoxine hydrochloride, riboflavin, folic acid, and vitamin D3), taurine, soy lecithin, glucosamine hydrochloride, minerals (ferrous sulfate, zinc oxide, copper sulfate, manganous oxide, calcium iodate, and sodium selenite), L-tryptophan, chondroitin sulfate, and β-carotene.
Canned test formula	Water, ground whole grain corn, meat by-products, soybean mill run, liver, flaxseed, corn gluten meal, fish oil, egg product, powdered cellulose, chicken liver flavor, calcium carbonate, iron oxide, dicalcium phosphate, L-lysine, iodized salt, vitamin E, choline chloride, glucosamine hydrochloride, L-tryptophan, taurine, potassium chloride, soy lecithin, ascorbic acid, L-arginine, L-carnitine, zinc oxide, thiamine mononitrate, chondroitin sulfate, copper sulfate, manganous sulfate, niacin, calcium pantothenate, vitamin B12, pyridoxine hydrochloride, biotin, vitamin D3, riboflavin, calcium iodate, folic acid, and sodium selenite.

Appendix 2

Clinical evaluation scoring systems in a study conducted to evaluate the effects of omega-3 fatty acids on osteoarthritis in dogs.

Clinical sign	Score	Description
Lameness	1	Stands and walks normally
	2	Stands normally, with slight lameness at walk
	3	Stands normally, with severe lameness at walk
	4	Abnormal posture when standing, with severe lameness at walk
	5	Reluctant to rise and will not walk > 5 strides
Weight bearing	1	Normal weight bearing on all limbs at rest and when walking
	2	Normal weight bearing at rest but favors affected limb when walking
	3	Partial weight bearing at rest and when walking
	4	Partial weight bearing at rest and non–weight bearing when walking
	5	Non–weight bearing at rest and when walking
Joint range of motion	1	No limitation of joint motion
	2	Mild limitation of joint motion
	3	Moderate limitation of joint motion
	4	Severe limitation of joint motion
	5	Unable to move joint
Willingness to hold up the contralateral limb	1	Readily accepts contralateral limb elevation and bears full weight on affected limb
	2	Offers mild resistance to contralateral limb elevation but bears full weight on affected limb
	3	Offers moderate resistance to contralateral limb elevation
	4	Offers strong resistance to contralateral limb elevation
	5	Refuses to raise contralateral limb at all
Pain	1	No pain response elicited on palpation of affected joint
	2	Mild pain response elicited on palpation of affected joint
	3	Moderate pain response elicited on palpation of affected joint
	4	Severe pain response elicited on palpation of affected joint
	5	Will not allow examiner to palpate affected joint because of pain