Evaluation of the effects of dietary supplementation with fish oil omega-3 fatty acids on weight bearing in dogs with osteoarthritis

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Objective—To evaluate the effects of a food supplemented with fish oil omega-3 fatty acids on weight bearing in dogs with osteoarthritis.

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

Animals—38 client-owned dogs with osteoarthritis examined at 2 university veterinary clinics.

Procedures—Dogs were randomly assigned to receive a typical commercial food (n = 16) or a test food (22) containing 3.5% fish oil omega-3 fatty acids. On day 0 (before the trial began) and days 45 and 90 after the trial began, investigators conducted orthopedic evaluations and force-plate analyses of the most severely affected limb of each dog, and owners completed questionnaires to characterize their dogs’ arthritis signs.

Results—The change in mean peak vertical force between days 90 and 0 was significant for the test-food group (5.6%) but not for the control-food group (0.4%). Improvement in peak vertical force values was evident in 82% of the dogs in the test-food group, compared with 38% of the dogs in the control-food group. In addition, according to investigators’ subjective evaluations, dogs fed the test food had significant improvements in lameness and weight bearing on day 90, compared with measurements obtained on day 0.


Osteoarthritis has been estimated to affect up to 20% of dogs > 1 year of age.1 Studies2–8 have revealed that omega-3 fatty acids have beneficial effects in the treatment of rheumatoid arthritis. Furthermore, dietary supplementation with omega-3 fatty acids can enhance concentrations of omega-3 fatty acids in tissues and cell membranes, resulting in a corresponding decrease in omega-6 fatty acid concentrations, particularly that of arachidonic acid. When eicosanoids are generated from omega-3 fatty acids, they appear to be less potent inducers of inflammation than those generated from arachidonic acid.9 Ingestion of omega-3 fatty acids may also reduce the serum concentrations and activities of proteoglycan-degrading enzymes, cyclooxygenase-2, and inflammation-inducible cytokines.10 Furthermore, ingestion of fish oil, which is rich in omega-3 fatty acids (particularly EPA and DHA), results in a decrease in serum concentrations of inflammatory factors in mice with rheumatoid arthritis,11 and oral administration of EPA and DHA reduces streptococcal cell wall arthritis in Lew/SsN rats.12

In a preliminary study,13 we found that dietary supplementation with fish oil omega-3 fatty acids increases blood concentrations of these fatty acids and has an ameliorative effect on osteoarthritis in pet dogs according to owners’ assessments. The purpose of the study reported here was to evaluate the effects of a food supplemented with fish oil omega-3 fatty acids on weight bearing in dogs with osteoarthritis on the basis of other types of measurements. Specifically, we used force platform gait analysis and investigator subjective assessments of osteoarthritis severity to further investigate the effects of fish oil omega-3 fatty acids in client-owned dogs with lameness attributable to naturally developing osteoarthritis.

Materials and Methods

Dogs—Dogs were recruited from among the patients of the teaching hospitals of the Colleges of Veterinary Sciences.

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Abbreviations

DHA	Docosahexaenoic acid
EPA	Eicosapentaenoic acid
Study foods—Foods used were as described for another similar study. The control food consisted of typical adult commercial dry and canned foods, and the test food consisted of dry and canned formulations. Identical packaging was used to mask the identity of the foods from all individuals directly involved with evaluating each dog.

Study conduct—This investigation was conducted as a 3-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. 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 study start (baseline; day 0) and on days 45 and 90, investigators (veterinarians) performed clinical evaluations, performed force plate analyses, and collected blood samples for CBCs and serum biochemical analyses. Results of serum biochemical analyses and CBCs were used to screen dogs for study eligibility and to monitor dogs for adverse events. Clinical evaluations were performed as described. Briefly, evaluations consisted of an examination of each dog’s physical condition, wherein a score from 1 through 5 (least to most severe) was assigned 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.

In addition, on days 45 and 90, owners completed a questionnaire to score the change in osteoarthritis severity from the previous to the present visit (1 = better; 2 = about the same; and 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 degree of activity. Investigators reviewed all owner-submitted questionnaires for completeness.

Force plate analysis—Dogs were evaluated by use of biomechanical force platforms at the University of Florida and Kansas State University. The plates were mounted centrally and flush with the surface of a 10-m walkway. The force-plate systems were calibrated for mass (with an 11.4-kg weight) and velocity (with a freely mobile pendulum). A handler trotted dogs across the force plate, and an observer evaluated each pass across the plate to confirm foot strikes and gait. A trial was considered valid when there were distinct ipsilateral forefoot and hind foot strikes while the dog was trotted across the force plate at a velocity of 1.7 to 2.0 m/s and an acceleration-deceleration variation of ± 0.5 m/s². During each trial, each dog's forward velocity was measured with a millisecond timer and 2 photoelectric switches. Each trial was videotaped for review and confirmation of valid foot strikes. Care was taken to ensure that each dog triggered the timer and that a consistent speed was maintained across the force plate during each trial. Five valid trials/test period were obtained for each dog.

Peak vertical force, vertical impulse, braking and propulsive peak forces, and braking and propulsive impulses were measured and recorded by use of force plate analysis software at laboratories of the University
Adverse events—During the study, all adverse events were reported to the investigators, who recorded the nature of the event including severity, whether the event was new, any potential association with the study food or concomitant medication, and other relevant details of the reaction.

Statistical analysis—For force plate results, only data from the most severely affected limb were included in the analysis. Commercially available statistical software was used to perform comparisons between test- and control-food groups, which were analyzed by means of repeated-measures ANOVA for ground reaction–force data as a percentage change of ground reaction–force data for the lame limb between days 0 and 90. In addition, frequency distributions for percentage change on peak vertical force were compared with Mantel-Haenszel χ² analysis.

Analysis of changes in osteoarthritis assessments over time was performed through repeated-measures ANCOVA. Scores from owner and investigator assessments at the start of the study (day 0) were used as covariates, and a first-order autoregressive covariance structure was fit to the data. In addition, net change in scores between the start and end of the study was calculated by subtracting scores at day 0 from scores at day 90 for each dog. The differences were analyzed with 1-way ANOVA to compare mean change attributable to treatment (control vs test food). An assessment of significant change attributable to treatment was also made by testing whether the difference in scores for each treatment were significantly different from 0 with a 1-sample t test. For all data, assumptions of normality and homogeneity of variance were evaluated. All results are reported as mean ± SE. Differences were considered significant at P < 0.05.

Results

Dogs—Eighty-eight client-owned dogs with clinical lameness attributable to naturally developing arthritis were screened at the 2 veterinary teaching hospitals. Of those, 44 were considered eligible for the study and were randomly assigned to receive test (n = 26) or control (18) food for 90 days. Four dogs in the test group and 2 in the control group were dismissed from the study for the following reasons: deterioration of the condition (2 test-food dogs), concurrent medical condition (1 test-food dog), owner noncompliance (1 control-food dog), owner relocation (1 test-food dog), and surgery to repair the anterior cruciate ligament (1 control-food dog). Thus, a total of 38 dogs completed the study, including 22 from the test group and 16 from the control group. Only data from dogs that completed the study were included in the analysis.

Characteristics of participating dogs were summarized (Table 1). There were no significant differences

### Table 1
Mean ± SD (range) 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 = 16) or a test food supplemented with omega-3 fatty acids (22) in a 90-day clinical trial to evaluate the effect of ingestion of omega-3 fatty acids on weight bearing.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control food</th>
<th>Test food</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at study start (y)</td>
<td>8.0 ± 4.8</td>
<td>7.0 ± 6.9</td>
<td>0.60</td>
</tr>
<tr>
<td></td>
<td>(1 to 12)</td>
<td>(1 to 18)</td>
<td></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>30.9 ± 6.2</td>
<td>32.7 ± 7.4</td>
<td>0.44</td>
</tr>
<tr>
<td>Start of study</td>
<td>(19.3 to 44.0)</td>
<td>(20.4 to 52.9)</td>
<td></td>
</tr>
<tr>
<td>Day 90</td>
<td>31.5 ± 6.7</td>
<td>31.9 ± 7.8</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>(19.4 to 46.7)</td>
<td>(20.5 to 54.0)</td>
<td></td>
</tr>
<tr>
<td>Change in body weight over time</td>
<td>0.63 ± 1.04</td>
<td>−0.62 ± 1.81</td>
<td>0.004</td>
</tr>
<tr>
<td></td>
<td>(−0.8 to 2.7)</td>
<td>(−4.1 to 3.0)</td>
<td></td>
</tr>
<tr>
<td>Body condition score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Start of study</td>
<td>3.19 ± 0.54</td>
<td>3.14 ± 0.64</td>
<td>0.79</td>
</tr>
<tr>
<td></td>
<td>(2 to 4)</td>
<td>(2 to 4)</td>
<td></td>
</tr>
<tr>
<td>Day 90</td>
<td>3.19 ± 0.54</td>
<td>3.19 ± 0.66</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td>(2 to 4)</td>
<td>(2 to 4)</td>
<td></td>
</tr>
<tr>
<td>Change in score over time</td>
<td>0.00 ± 0.00</td>
<td>0.05 ± 0.21</td>
<td>0.39</td>
</tr>
<tr>
<td></td>
<td>(0)</td>
<td>(0 to 1)</td>
<td></td>
</tr>
<tr>
<td>Reproductive status</td>
<td></td>
<td></td>
<td>0.65</td>
</tr>
<tr>
<td>Spayed female</td>
<td>8 (50)</td>
<td>9 (41)</td>
<td></td>
</tr>
<tr>
<td>Sexually intact female</td>
<td>0 (0)</td>
<td>2 (9)</td>
<td></td>
</tr>
<tr>
<td>Neutered male</td>
<td>8 (50)</td>
<td>11 (50)</td>
<td></td>
</tr>
<tr>
<td>Primary affected joint at study start</td>
<td></td>
<td></td>
<td>0.41</td>
</tr>
<tr>
<td>Carpus</td>
<td>3 (19)</td>
<td>1 (5)</td>
<td></td>
</tr>
<tr>
<td>Elbow</td>
<td>1 (6)</td>
<td>4 (18)</td>
<td></td>
</tr>
<tr>
<td>Stifle</td>
<td>4 (25)</td>
<td>3 (14)</td>
<td></td>
</tr>
<tr>
<td>Hip</td>
<td>4 (25)</td>
<td>9 (41)</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td>4 (25)</td>
<td>5 (23)</td>
<td></td>
</tr>
</tbody>
</table>

A value of P < 0.05 was considered significant.
between control and test groups at enrollment (day 0) or study completion (day 90) in mean age, body weight, and body condition score; primary affected joint (location of most severe arthritis); distribution of reproductive status; or reasons for dismissal. Also, body weights and body condition scores within the groups did not vary significantly during the study period. Among dogs completing the study, the following breeds were represented: mixed breed (n = 14), German Shepherd Dog (4), Greyhound (4), Golden Retriever (3), Rottweiler (3), Australian Cattle Dog (2), and 1 each of Boxer, Dobermann Pinscher, Dogue de Bordeaux, German Shorthaired Pointer, Giant Schnauzer, Labrador Retriever, pit bull-type dog, and Siberian Husky.

**Force plate analysis**—Analysis of force plate results was performed with only data for the most severely affected limb for each dog (Table 2). None of the values were significantly different between control-food and test-food groups at study start (day 0) or study end (day 90). However, the mean change in peak vertical force for the most severely affected limb between day 90 and 0 was significant for the test-food group (+5.6%; \(P = 0.01\)) but not for the control-food group (+0.4%; \(P = 0.85\)). Additionally, at day 90, 82% of dogs in the test-food group but only 38% of the dogs in the control-food group had a significant (\(P = 0.01\)) improvement in peak vertical force (Figure 1). This corresponds to an odds ratio of 7.0, indicating dogs fed the test food were 7 times as likely to have an improvement in lameness after 90 days, compared with those fed the control food. There were no significant differences in braking and propulsive peak forces or in braking and propulsion impulses between test- and control-food groups or between the day 90 and day 0 values for these variables, and the changes in these values were not significant for either group (data not shown).

**Investigator scores for clinical signs**—Mean scores for investigators’ subjective assessments of osteoarthritis signs on days 90 and 0 were summarized (Table 3). Between day 0 and 90, there were significant improvements in lameness (\(P = 0.02\)) and weight bearing (\(P = 0.001\)) for dogs in the test-food group. Differences for the other categories between day 0 and 90 and between control- and test-food groups were not significant.

**Owner scores for clinical signs**—On days 45 and 90, dog owners assessed changes in the severity of their dogs’ osteoarthritis signs, compared with signs in the previous visit (ie, day 45 vs 0 and day 90 vs 45). There were no significant differences for any of the scores at day 45 or 90 (data not shown).

**Adverse events**—Six adverse events were reported during the feeding trial. Four of these were in dogs fed the test food, including 2 dogs with moderate inappetence likely related to the study food, 1 dog with mild joint swelling unlikely to be related to the study food, and 1 dog with mild vomiting and possible pancreatitis that was probably related to the study food, although laboratory test results did not support a diagnosis of pancreatitis. The 2 adverse events in dogs on the control food included an acute onset of hind limb lameness unlikely related to the study food and a ruptured cranial cruciate ligament of the right hind limb considered mild and also unrelated to the study food.

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### Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Day 0</th>
<th>Day 90</th>
<th>Mean change</th>
<th>Percentage change</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Value</td>
<td>Value</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak vertical force</td>
<td>72.2 ± 4.8</td>
<td>76.6 ± 5.2</td>
<td>+4 ± 1.6</td>
<td>+2 ± 9.4</td>
<td>0.85</td>
</tr>
<tr>
<td>Control</td>
<td>69.7 ± 4.1</td>
<td>73.6 ± 4.5</td>
<td>3.9 ± 1.3</td>
<td>+5.6 ± 18.8</td>
<td>0.01</td>
</tr>
<tr>
<td>Test</td>
<td>10.4 ± 0.76</td>
<td>10.4 ± 0.75</td>
<td>0.0 ± 0.3</td>
<td>−0.1 ± 2.5</td>
<td>0.97</td>
</tr>
<tr>
<td>Test</td>
<td>10.1 ± 0.65</td>
<td>10.2 ± 0.64</td>
<td>0.1 ± 0.2</td>
<td>+2.3 ± 2.1</td>
<td>0.28</td>
</tr>
</tbody>
</table>

A value of \(P < 0.05\) was considered significant for all analyses.

*P value obtained from a 1-sided t test in which the observed percentage change was compared to 0%.
The study also revealed that ingested EPA and DHA fatty acids (22) for 90 days.

For dogs in the control-food group, the change in mean peak vertical force over 90 days, compared with dogs in the control foods in dogs with osteoarthritis. In particular, we focused on the peak vertical force because that variable reflects weight bearing and is considered most relevant for assessing the effects of drug treatments on osteoarthritis.14–17 For dogs in the control-food group, the change in mean peak vertical force throughout the 90-day trial (+0.4%) was not significant. In contrast, the change in peak vertical force (+5.6%) was significant for dogs in the test-food group. Also, dogs in the test-food group were 7 times as likely to have an improvement in weight bearing over 90 days, compared with dogs in the control-food group. The magnitude of change in peak vertical force was at least as large as that reported in other studies in which drugs were used to treat osteoarthritis. For example, 28-day treatment with licofelone (a dual cyclooxygenase-lipoxygenase inhibitor) reportedly results in a 1.7% increase in peak vertical force (vs a 0.3% decrease for placebo treatment).17 Also, dogs treated for 2 weeks with the NSAID carprofen are 3.3 times as likely to have an improvement in peak vertical force, compared with dogs treated with a placebo.18 Thus, the magnitude of our results suggested that dietary supplementation with fish oil omega-3 fatty acids can result in a clinically meaningful improvement in weight bearing in dogs with osteoarthritis.

Although radiography was used to confirm a diagnosis of osteoarthritis, we did not radiographically evaluate dogs at study end because we did not expect to detect meaningful changes in such a short period. Also, another study19 revealed that radiographic signs do not correspond to clinical function in dogs with osteoarthritis. Accordingly, the results of the present study support the use of peak vertical force as the more appropriate objective measure for short-term studies of osteoarthritis.

Subjective assessment of osteoarthritis signs by investigators provided additional evidence that consumption of the test food can improve clinical performance. Despite the improvement in lameness scores detected in dogs in the test-food group, we considered objective assessment of weight bearing by force platform gait analysis to be more sensitive than investigator-assessed signs for measuring changes in clinical performance. Indeed, results of previous studies20,21 suggest that subjective assessment of limb function lacks repeatability as an outcome measure and is inferior to objective data obtained from force platform gait analysis. The fact that significant changes were not detected in investigator-assessed signs in our other study13 but were detected here was not unexpected because the other study involved 18 primary care
veterinarians without calibration of scoring, whereas the present study involved only 3 certified veterinary surgeons with extensive experience in treating osteoarthritis. In general, we consider objective measures to be preferable for measuring clinical performance in osteoarthritis but maintain that when subjective measures must be used, then a composite score or a more refined scoring system will be more effective than individual scores for clinical signs. However, such scoring systems remain to be developed.

We did not detect significant differences in the owner-assessed signs of osteoarthritis between days 45 and 0 or between days 90 and 45. This contrasts with the results of our other study,13 in which the same questionnaire was used, wherein owners reported some improvements in their dog’s signs, namely the ability to rise from rest and to play at week 6 and the ability to walk at weeks 12 and 24. The inability to detect any significant differences in the present study is likely attributable to the low number of dogs that completed the trial (38 vs 127 in the other study). Indeed, power calculations using data from our other study indicated it would be unlikely to detect differences in dog-owner assessments of the clinical signs in the present study. Results from the other study indicated that with 56 dogs fed the control food and 71 fed the test food, the power values were 0.55 for difficulty rising from rest, 0.97 for difficulty walking, and 0.99 for difficulty playing. When the same treatment differences and SDs as detected in that study were used to calculate power, the present study with only 22 dogs fed the control food and 16 fed the test food would have yielded power values of 0.20 for difficulty rising from rest, 0.54 for difficulty walking, and 0.65 for difficulty playing. A larger study, combined with a more refined scoring scale and possibly a validated composite score, may be needed to more consistently detect differences in owners’ assessments of their dog’s arthritic condition.

One limitation of the present study is that not only the fatty acid content but also some other ingredients differed between the 2 foods. Therefore, it is possible that ingredients other than the fish oil omega-3 fatty acids accounted for the detected effects of food. We consider this unlikely because nutritional analysis revealed that the 2 foods had similar total amounts of fat, protein, metabolizable energy, and other nutrients.13 Although the amounts of glucosamine and chondroitin sulfate differed between the foods, systematic reviews of the literature revealed there is a lack of clinical evidence to support an effect of either agent in dogs22 or humans.23,24 Consequently, it is likely that the detected effects of the test food were indeed attributable to supplementation with fish oil omega-3 fatty acids.

An additional potential limitation is that the present study involved enrollment of generally nonsevere cases of osteoarthritis.13 Indeed, most of the dogs received a disease severity rating of moderate, mild, or none by investigators at the study start, although we did not have a score for the overall severity of osteoarthritis because a validated scoring system did not exist when the study was conducted. Regardless, the dogs that participated in the present study had severe enough osteoarthritis to be referred by their primary care veterinarians to a specialist at 1 of the 2 universities for additional treatment. Dogs with more severe osteoarthritis would probably have been treated with drugs or surgery and would therefore have been excluded from the present trial. A larger study including a validated scoring system for overall severity of osteoarthritis would be needed to determine whether the effectiveness of supplementation with fish oil omega-3 fatty acids differs according to disease severity.

Overall, the study food appeared safe for ingestion, with 2 dogs developing mild inappetence believed associated with the food. In addition, 1 dog in the test-food group had both a substantial loss of body weight (> 10%) and a reduction in peak vertical force (> 25%). It appeared that this dog lost weight because the owner restricted the quantity of food, but the reason for the large reduction in peak vertical force was not clear because there were no adverse events reported for the dog.

Together with the findings of our other study,13 findings of the study reported here supported the hypothesis that ingestion of fish oil omega-3 fatty acids improves clinical signs in dogs with osteoarthritis. These effects may be attributable to the ability of omega-3 fatty acids to alter the eicosanoids produced to less inflammatory forms.9 Additional studies are needed to assess the long-term effects of supplementation with fish oil omega-3 fatty acids on osteoarthritis, confirm the results in larger study samples, make use of composite and objective scores for clinical signs, and examine the effect of confounding factors such as home treatments, severity of osteoarthritis at study start, and the number of limbs and joints affected on outcomes.

References


b. Pedigree Choice Cuts, Mars Petcare US, Brentwood, Tenn.


d. Model OR6-6-1000, Advanced Mechanical Technology Inc, Newton, Mass.

e. Model 9281B11, Kistler Instrument Corp, Amherst, NY.


h. SAS, version 8, SAS Institute Inc, Cary, NC.

i. PROC MIXED, SAS, version 8, SAS Institute Inc, Cary, NC.


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**From this month’s AJVR**

**Evaluation of a behavioral method for objective vision testing and identification of achromatopsia in dogs**

Monique M. Garcia et al

**Objective**—To develop a quantifiable behavioral test for identification of achromatopsic dogs based on visual performance.

**Animals**—14 dogs.

**Procedures**—A 3.6-m-long obstacle-avoidance course with 6 obstacle panels was developed from a preliminary 2.4-m course. Achromatopsic and visually normal control dogs were run through the course at 4 ambient light intensities (from dim to brightest: 0.2, 25, 65, and 646 lux). Completion of 4 runs ranging from dimmest to brightest light intensity constituted 1 complete trial. Each dog underwent 3 trials. Transit times were measured and compared between dog groups and between light intensities by use of a generalized linear model and ANOVA.

**Results**—At the 3 highest light intensities, the achromatopsic dogs needed significantly more time to pass through the obstacle course than the control animals. Compared with the mean transit time at the lowest light intensity, mean transit times were 2.6 times as long at 25 lux, 3.2 times as long at 65 lux, and 5.7 times as long at 646 lux. The achromatopsic dogs had signs of increasing difficulty navigating around the obstacle panels with increasing light intensities; this was not the situation for the control dogs.

**Conclusions and Clinical Relevance**—A 3.6-m obstacle-avoidance course with 6 movable obstacle panels allowed identification of achromatopsic dogs at ambient light intensities ≥ 25 lux based on transit times. This test could be helpful in the evaluation of new cone photoreceptor–specific treatments. (*Am J Vet Res* 2010;71:97–102)