



## UNIVERSITY OF CALGARY FACULTY OF VETERINARY MEDICINE

*This review accompanies the relevant episode of the Cutting Edge veterinary podcast. In each episode of this podcast, 3rd year students in the University of Calgary's veterinary medicine program fill you in on the most up-to-date literature and evidence-based practices on topics that matter to you, the practising veterinarian.*

# What Is the Efficacy of Omega-3 Fatty Acids for Management of Canine Osteoarthritis Pain?

STUDENTS: Jamie Cole and Rayne-Joy Dack

FACULTY MENTOR: Dr. Marina McConkey

### Introduction to Canine Osteoarthritis

Osteoarthritis (OA) is a progressive, degenerative and inflammatory condition, and is the most diagnosed arthropathy of small animal patients.<sup>1,2</sup> Current data suggests that prevalence ranges from upwards of 20-30% of the canine population over 1 year of age, and >90% of the canine population over 5 years of age in the UK and USA.<sup>3,4,5</sup> OA may occur secondary to developmental disease or orthopedic injury, but many factors determine disease onset and progression.<sup>6</sup> Risk factors for the development of OA include size and breed of dog, where purebred dogs have inherited genetic predisposition, and large breeds are more affected than small breeds.<sup>4,2,6,7</sup> Age, sex, and desexing play a role, as risk progresses with age and desexed males carry a high risk.<sup>4</sup> Obesity increases risk, as overweight dogs are >2.3x more likely to develop OA.<sup>4,6,7</sup> Clinical signs of OA include lameness, painful joints, joint effusion and swelling, decreased range of motion, muscle atrophy, behavioral changes, decreased activity, and difficulty rising.<sup>4</sup> OA treatment aims to prevent, slow the progression, provide pain control and reduce clinical signs.<sup>8,9</sup> As no singular treatment is superior alone, a multimodal approach to therapy is key for management of OA.<sup>4,6,10,11</sup> This approach includes oral and injectable anti-inflammatory and analgesic pharmaceuticals, weight management, physical rehabilitation and controlled exercise, nutrition, and disease-modifying agents.<sup>8,4,6,10,9</sup>

### Veterinary Nutraceuticals

Nutraceuticals are becoming more commonly implemented in this multimodal approach, but many are lacking scientifically valid studies.<sup>1</sup> Nutraceuticals can be defined as non-pharmaceutical substances that provide medicinal benefits improving the health and well-being of animals.<sup>12,13</sup> Veterinary nutraceuticals are not subject to any regulation, and assessments typically focus on safety but do not require therapeutic efficacy.<sup>14</sup> Systematic reviews are generally uncommon in veterinary medicine, making the efficacy of these compounds challenging to assess.<sup>6</sup>

### Omega 3 Fatty Acids and Osteoarthritis

As the pathophysiology of canine OA is becoming better understood, nutritional supplements that provide anti-inflammatory and/or disease-modifying compounds could be beneficial.<sup>15,5</sup> Amongst the numerous nutraceuticals available, omega-3 fatty acids (O3FA) have been proposed as an adjunctive treatment for OA. O3FAs have been investigated as a pain relieving, disease-modifying treatment for rheumatoid arthritis in humans.<sup>15,16,17,18</sup> Use of O3FAs have since emerged in veterinary medicine. It is proposed that O3FAs, specifically eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), reduce activity of cartilage degrading enzymes and inflammatory cytokines which contribute to the pain and clinical signs of OA.<sup>5,9</sup>

### **Efficacy of Omega 3 Fatty Acids in Canine OA: Subjective Measures**

Due to the limited objective measures used to evaluate OA, many studies rely on subjective scores to assess the effect of O3FAs. These include owner questionnaires and subjective veterinarian assessments regarding severity of clinical signs, activity, and quality of life. Studies found that subjective scores of pain decreased<sup>19,2</sup> and quality of life indexes were better for dogs supplemented with O3FAs.<sup>5,16</sup> One study found that dogs fed a diet high in O3FAs had less OA progression and lower subjective osteoarthritis scores compared to a control diet.<sup>20</sup> Similarly, another study found a significant decrease in arthritis score, joint swelling and pain when treated with a green lipped mussel powder high in O3FAs.<sup>21</sup>

Veterinarian assessed lameness and weight bearing scores were found to be significantly improved in a number of studies.<sup>22,9</sup>, but others found no change in lameness scores.<sup>23,19</sup> While some studies found no measurable difference in lameness, owners anecdotally report improved mobility, decreased pain and increased physical activity.<sup>8,23</sup> Overall owners were happier with the treatment of their dog when treated with O3FAs compared to controls.<sup>5</sup>

### **Efficacy of Omega 3 Fatty Acids in Canine OA: Objective Measures**

Peak vertical force (PVF) is used as the only objective measure of OA and therefore is evaluated in many studies. An increase in PVF indicates that more weight is being placed on the limb meaning lameness and pain are decreased. Moreau<sup>19</sup> evaluated PVF measurements in dogs fed a therapeutic diet high in O3FAs compared to a control diet. Dogs fed the therapeutic diet had a significantly higher PVF after 2 months of supplementation and this was maintained thereafter.<sup>19</sup> Baltzer<sup>23</sup> compared a test diet high in O3FAs to a control diet. Dogs fed the test diet had significant increases in PVF and vertical impulse, a measure of how fast the animal is stepping, compared to those fed a control diet.<sup>23</sup> A study by Hielm-Björkman<sup>5</sup> fed dogs a fish oil supplement and found similar results of a significantly increased PVF in the supplemented dogs, indicating improved weight bearing. These studies reveal that both supplementation and therapeutic diets decrease pain and lameness in dogs.

Another study by Roush<sup>22</sup> comparing dogs fed a test food high in O3FAs to a control diet found that PVF increased in both groups, however the test group had 40% more dogs with increased PVF than the control. Roush's<sup>22</sup> work using PVF analysis also indicates that supplementation with O3FAs results in greater improvements in weight bearing and clinical signs than treatment with NSAIDs. Here, the test group had a significantly increased level of weight bearing compared to that which other studies found with NSAID treatment only.<sup>24</sup> Roush's<sup>22</sup> study found that dogs fed O3FAs were 7 times more likely to have an improvement in

lameness while other studies found that carprofen treatment only provided an improvement likelihood of 3 times<sup>25</sup>. Roush's study provides evidence that O3FAs have a therapeutic effect that may be on par with NSAIDs.<sup>25</sup>

### **Efficacy of Omega 3 Fatty Acids in Canine OA: Effects on NSAID Use**

O3FAs were observed to influence concurrent NSAID treatment. NSAIDs are typically used for pain management in canine OA, but use does carry a higher risk of adverse effects such as gastrointestinal ulceration, renal failure, hepatic failure, and death.<sup>4,26</sup> NSAIDs also have deleterious effects on cartilage and may accelerate cartilage degeneration associated with OA.<sup>4,8,5</sup> Additionally, tolerance may develop leading to increased NSAID doses and further risks of adverse systemic effects.<sup>27</sup> It would be desirable to titrate the dose of NSAIDs used to limit side effects but provide effective analgesia. This is where a synergistic, multimodal approach to OA becomes important.

A study by Fritsch<sup>16</sup> found that combining NSAID therapy (carprofen) with an O3FA-enriched diet led to 25% decrease in NSAID requirements over a 12-week period compared to patients on an adult maintenance diet. Mean dose, frequency of dosing, and use of rescue NSAID therapy was observed during the study.<sup>16,10</sup> A significant interaction between the diet and dosage of NSAIDs was observed, as feeding the enriched diets led to a significant rapid tapering of carprofen dosage for dogs in the test group vs the placebo group. There was also a significant decrease in the mean carprofen dose in those dogs treated with O3FA over the study period. The distribution of changes in carprofen doses also significantly changed. Dogs in the test group initially needed larger doses, but this decreased to lower than the control group throughout the remainder of the study.<sup>16</sup> Fritsch<sup>16</sup> also found that although O3FA supplementation led to reduced consumption of NSAIDs and better quality of life, there was not a significant difference in pain between groups. Overall, results support that in dogs with chronic OA receiving NSAIDs, such as carprofen to alleviate pain, feeding an O3FA-enriched diet may allow for a more rapid reduction of NSAID dosage and decreased consumption over time.

Hjelm-Björkman<sup>5</sup> yielded similar results. Both the test and placebo groups were fed one of two commercially available maintenance diets with similar nutritional values and low O3FA content. The test group received a purified O3FA supplement, while the placebo group received a corn oil supplement containing no O3FAs. Results obtained suggest that inclusion of O3FAs at therapeutic levels led to a decrease in the use of rescue NSAID doses in the test population. Overall, dogs administered the O3FAs during the 16-week study had reduced consumption of NSAIDs over time. This ideal is also relevant in human medicine, where studies such as Lau<sup>28</sup> show that patients with rheumatoid arthritis were able to reduce their NSAID requirement without any decrease in analgesia or further disease progression when taking an O3FA supplement daily.

Finally, Sastravaha<sup>29</sup> also assessed the analgesic effects of O3FA supplementation in dogs with coxofemoral OA. Dogs were fed a maintenance diet and were supplemented with O3FAs at a high dose. Subjective pain scores associated with walking/trotting, joint manipulation, and range of motion were assessed progressively for 4 weeks. Results of the study suggest that O3FA led to significantly lower pain scores associated with walking/trotting, range of motion, and joint manipulation compared to baseline measures, even in the absence of NSAID

treatment. These findings suggest that in some cases, especially in patients where NSAIDs are contraindicated, O3FAs alone could provide some benefit to analgesia and quality of life.

### **Omega 3 Fatty Acids - Approach to Treatment and Recommended Dosing**

Owner compliance with treatment for OA may be an issue, especially for owners of large or giant breed dogs which require large doses of O3FAs.<sup>4</sup> Fortunately, there are many approaches to omega 3 supplementation which can be easily implemented, allowing for both patient and client success. There are several complete and balanced diets on the market containing adequate levels of O3FAs in the desired ratios which are labeled for canine OA.<sup>30</sup> These therapeutic diets eliminate the need for multiple pill administration, and supply the recommended amounts of O3FAs when fed according to the label.<sup>4</sup> These products have good palatability and eliminated the need to deliver large quantities of liquid to the pet,<sup>31</sup> but enrichment with fatty acids in therapeutic amounts will shorten the shelf life of the food, which may have financial implications.<sup>31</sup>

In situations where owners are reluctant to change the diet or have financial constraints, administration of fish oil supplements in liquid or capsule form containing adequate levels of EPA and DHA should be considered.<sup>4</sup> A large amount of these products must be administered to achieve therapeutic levels which can affect palatability causing the patient to not eat, and may have negative impacts on the gastrointestinal system.<sup>31</sup> Severe side effects have not been documented with omega 3 fatty acids short-term, although long-term studies are not prevalent in the current literature. Side effects such as diarrhea and vomiting may occur.<sup>31</sup> These can be given in addition to a maintenance diet, but owners and veterinarians alike should be aware that not all products are equal! Products containing concentrated ethyl ester oil which are purified and have the highest levels of DHA and EPA are desirable.<sup>32</sup>

Overall, current literature supports the belief that dietary supplementation of O3FAs is safe and effective.<sup>9,29</sup> Current dose recommendations is a combined dosage of EPA and DHA that is between 230-370 mg/kg BW<sup>0.75</sup>/day.<sup>20,4,23,33,29</sup>

### **Limitations and Bias of Current Literature**

There are many limitations to the O3FA studies present in the literature currently and studies discussed have some degree of inherent bias. There is a lack of objective measures to assess clinical sign improvement and pain scores in animals. Currently the most utilized objective measure for the clinical effectiveness of O3FA is mechanical force plate analysis. There is difficulty in recruiting patients due to lack of owner compliance, inability to adhere to study protocols, and concurrent diseases which led to many dogs being excluded from studies. In addition, low sample sizes were a common finding and likely impacted the power of the study. In addition, significant results in a small sample population will not always indicate clinical success. As well, methodological variations exist between studies. Differences in product, diet, and dose of product introduces variables which make comparison across studies difficult. Many studies rely on subjective measurements that are insensitive and may introduce bias. Overall, using clinical signs and subjective measures to evaluate these treatments may be biased by the caregiver placebo effect and natural fluctuations in OA signs.<sup>6</sup> Similar to this idea, having owners or veterinarians who were aware of treatments may also introduce bias.

## **Conclusion**

In conclusion, there are a limited number of veterinary-centered randomized controlled trials with adequate sample sizes involving O3FA efficacy in OA. In general, standardization of reporting, larger sample sizes, and more objective methods of measurements are needed.<sup>6</sup> However, there is scientific support to use of O3FAs for management of canine OA.<sup>5,8,16,19,20,22,23</sup> Analgesic and NSAID potentiating effects of O3FAs have been observed, resulting in clinical improvement.<sup>16,5,28, 29</sup> When considering which nutraceutical to add to the multimodal therapy for canine OA, you can be confident that the literature currently supports the positive impacts of O3FAs.

## References

1. Vandeweerd JM, Coisson C, Clegg P, Cambier C, Pierson A, Hontoir F, Saegerman C, Gustin P, Buczinski S. Systematic review of efficacy of nutraceuticals to alleviate clinical signs of osteoarthritis [Internet]. *Journal of veterinary internal medicine*. U.S. National Library of Medicine; 2012 [cited 2023Feb15]. Available from: <https://pubmed.ncbi.nlm.nih.gov/22404506/>
2. Alves JC, Santos AM, Jorge PI. Effect of an oral joint supplement when compared to Carprofen in the management of hip osteoarthritis in working dogs. *Topics in Companion Animal Medicine*. 2017;32(4):126–9. Available from: <https://doi.org/10.1053/j.tcam.2017.10.003>
3. Johnston SA. Osteoarthritis: Joint Anatomy, physiology, and Pathobiology [Internet]. *The Veterinary clinics of North America. Small animal practice*. U.S. National Library of Medicine; 1997 [cited 2023Feb15]. Available from: <https://pubmed.ncbi.nlm.nih.gov/9243777/>
4. Johnson KA, Lee AH, Swanson KS. Nutrition and nutraceuticals in the changing management of osteoarthritis for dogs and cats. *Journal of the American Veterinary Medical Association*. 2020;256(12):1335–41. Available from: <https://doi.org/10.2460/javma.256.12.1335>
5. Hielm-Björkman A, Roine J, Elo K, Lappalainen A, Junnila J, Laitinen-Vapaavuori O. An un-commissioned randomized, placebo-controlled double-blind study to test the effect of deep sea fish oil as a pain reliever for dogs suffering from canine OA. *BMC Veterinary Research*. 2012;8(1):157. Available from: <https://bmcvetres.biomedcentral.com/articles/10.1186/1746-6148-8-157>
6. Williams P, Pettitt R. Nutraceutical use in osteoarthritic canines: A Review. *Companion Animal*. 2021;26(7):1–5. Available from: <https://blog.adoresbeast.com/wp-content/uploads/2022/02/Williams-and-Pettitt-2021-OA-review-canine.pdf>
7. Pye C, Bruniges N, Peffers M, Comerford E. Advances in the pharmaceutical treatment options for canine osteoarthritis. *Journal of Small Animal Practice*. 2022;63(10):721–38. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9790257/>
8. Roush JK, Dodd CE, Fritsch DA, Allen TA, Jewell DE, Schoenherr WD, et al. Multicenter Veterinary Practice Assessment of the effects of omega-3 fatty acids on osteoarthritis in dogs. *Journal of the American Veterinary Medical Association*. 2010;236(1):59–66. Available from: <https://doi.org/10.2460/javma.236.1.59>
9. Fritsch DA, Allen TA, Dodd CE, Jewell DE, Sixby KA, Leventhal PS, et al. Dose-titration effects of fish oil in osteoarthritic dogs. *Journal of Veterinary Internal Medicine*. 2010;24(5):1020–6. Available from: <https://doi.org/10.1111/j.1939-1676.2010.0572.x>
10. Gaynor JS. Recommending nutraceuticals for joint health [Internet]. *Clinician's Brief*. 2010 [cited 2023Feb15]. Available from: <https://www.cliniciansbrief.com/article/recommending-nutraceuticals-joint-health>

11. Epstein ME, Rodan I, Griffenhagen G, Kadrlik J, Petty MC, Robertson SA, et al. 2015 AAHA/AAFP Pain Management Guidelines for dogs and cats. *Journal of Feline Medicine and Surgery*. 2015;17(3):251–72. Available from: [https://www.aaha.org/globalassets/02-guidelines/pain-management/2015\\_aaha\\_aafp\\_pain\\_management\\_guidelines\\_for\\_dogs\\_and\\_cats.pdf](https://www.aaha.org/globalassets/02-guidelines/pain-management/2015_aaha_aafp_pain_management_guidelines_for_dogs_and_cats.pdf)
12. Finno CJ. Veterinary pet supplements and nutraceuticals. *Nutrition Today*. 2020;55(2):97–101. Available from: [https://journals.lww.com/nutritiontodayonline/Fulltext/2020/03000/Veterinary\\_Pet\\_Supplements\\_and\\_Nutraceuticals.9.aspx](https://journals.lww.com/nutritiontodayonline/Fulltext/2020/03000/Veterinary_Pet_Supplements_and_Nutraceuticals.9.aspx)
13. Robinson NG. Nutraceuticals and dietary supplements in veterinary patients - management and Nutrition [Internet]. *Merck Veterinary Manual*. Merck Veterinary Manual; 2023 [cited 2023Feb15]. Available from: <https://www.merckvetmanual.com/management-and-nutrition/integrative-complementary-and-alternative-veterinary-medicine/nutraceuticals-and-dietary-supplements-in-veterinary-patients>
14. Barbeau-Grégoire M, Otis C, Cournoyer A, Moreau M, Lussier B, Troncy E. A 2022 systematic review and meta-analysis of enriched therapeutic diets and nutraceuticals in canine and feline osteoarthritis. *International Journal of Molecular Sciences*. 2022;23(18):10384. Available from: <https://doi.org/10.3390/ijms231810384>
15. Cordingley DM, Cornish SM. Omega-3 fatty acids for the management of osteoarthritis: A narrative review. *Nutrients*. 2022;14(16):3362. Available from: <https://doi.org/10.3390/nu14163362>
16. Fritsch DA, Allen TA, Dodd CE, Jewell DE, Sixby KA, Leventhal PS, et al. A multicenter study of the effect of dietary supplementation with fish oil omega-3 fatty acids on carprofen dosage in dogs with osteoarthritis. *Journal of the American Veterinary Medical Association*. 2010;236(5):535–9. Available from: <https://pubmed.ncbi.nlm.nih.gov/20187817/>
17. Kremer JM. Effects of modulation of inflammatory and immune parameters in patients with rheumatic and inflammatory disease receiving dietary supplementation of N-3 and N-6 fatty acids. *Lipids*. 1996;31(1). Available from: <https://doi.org/10.1007/BF02637084>
18. Nielsen GL, Faarvang KL, Thomsen BS, Teglbjaerg KL, Jensen LT, Hansen TM, et al. The effects of dietary supplementation with N-3 polyunsaturated fatty acids in patients with rheumatoid arthritis: A randomized, double blind trial. *European Journal of Clinical Investigation*. 1992;22(10):687–91. Available from: <https://doi.org/10.1111/j.1365-2362.1992.tb01431.x>
19. Moreau M, Troncy E, del Castillo JR, Bédard C, Gauvin D, Lussier B. Effects of feeding a high omega-3 fatty acids diet in dogs with naturally occurring osteoarthritis. *Journal of Animal Physiology and Animal Nutrition*. 2012Jul14;97(5). Available from: <https://doi.org/10.1111/j.1439-0396.2012.01325.x>

20. Verpaalen VD, Baltzer WI, Smith-Ostrin S, Warnock JJ, Stang B, Ruaux CG. Assessment of the effects of diet and physical rehabilitation on radiographic findings and markers of synovial inflammation in dogs following tibial plateau leveling osteotomy. *Journal of the American Veterinary Medical Association*. 2018;252(6):701–9. Available from: <https://doi.org/10.2460/javma.252.6.701>
21. Bierer TL, Bui LM. Improvement of arthritic signs in dogs fed green-lipped mussel (*Perna canaliculus*). *The Journal of Nutrition*. 2002Jun1;132(6):1634S–1636S. Available from: <https://doi.org/10.1093/jn/132.6.1634S>
22. Roush JK, Cross AR, Renberg WC, Dodd CE, Sixby KA, Fritsch DA, et al. Evaluation of the effects of dietary supplementation with fish oil omega-3 fatty acids on weight bearing in dogs with osteoarthritis. *Journal of the American Veterinary Medical Association*. 2010;236(1):67–73. Available from: <https://pubmed.ncbi.nlm.nih.gov/20043801/>
23. Baltzer WI, Smith-Ostrin S, Warnock JJ, Ruaux CG. Evaluation of the clinical effects of diet and physical rehabilitation in dogs following tibial plateau leveling osteotomy. *Journal of the American Veterinary Medical Association*. 2018;252(6):686–700. Available from: <https://doi.org/10.2460/javma.252.6.686>
24. Moreau M, Lussier B, Doucet M, Vincent G, Martel-Pelletier J, Pelletier J-P. Efficacy of licofelone in dogs with clinical osteoarthritis. *Veterinary Record*. 2007;160(17):584–8.
25. Vasseur PB, Johnson AL, Budsberg SC, Lincoln JD, Toombs JP, Whitehair JG, et al. Randomized, controlled trial of the efficacy of carprofen, a nonsteroidal anti-inflammatory drug, in the treatment of osteoarthritis in dogs. *J Am Vet Med Association*. 1995Mar15;206(6):807-11. Available from: <https://pubmed.ncbi.nlm.nih.gov/7759332/>
26. Eckert T, Jährling-Butkus M, Louton H, Burg-Roderfeld M, Zhang R, Zhang N, et al. Efficacy of chondroprotective food supplements based on collagen hydrolysate and compounds isolated from marine organisms. *Marine Drugs*. 2021;19(10):542. Available from: <https://www.mdpi.com/1660-3397/19/10/542> ]
27. Innes JF, Clayton J, Lascelles BD. Review of the safety and efficacy of long-term NSAID use in the treatment of canine osteoarthritis. *Veterinary Record*. 2010;166(8):226–30. Available from: <https://bvajournals-onlinelibrary-wiley-com.ezproxy.lib.ucalgary.ca/doi/pdfdirect/10.1136/vr.c97>
28. Lau CS, Morley KD, Belch JJ. Effects of fish oil supplementation on non-steroidal anti-inflammatory drug requirement in patients with mild rheumatoid arthritis—a double-blind placebo controlled study. *Rheumatology*. 1993;32(11):982–9. Available from: <https://doi.org/10.1093/rheumatology/32.11.982>
29. Sastravaha A, Suwanna N, Sinthusingha C, Noosud J, Roongsitthichai A. Ameliorative effects of omega-3 concentrate in managing coxofemoral osteoarthritic pain in dogs [Internet]. *Chula Digital Collections*. 2016 [cited 2023Feb15]. Available from: <https://digital.car.chula.ac.th/tjvm/vol46/iss2/15>



30. Hills Pet Nutrition . Hill's prescription diet J/D dry dog food [Internet]. Hill's Pet Nutrition - Dog Food, Cat Food That Transforms Lives. 2020 [cited 2023Feb14]. Available from: <https://www.hillspet.ca/en-ca/dog-food/pd-jd-canine-dry>
31. Moriello K. Omega-3 therapy in dogs [Internet]. Clinician's Brief. 2013 [cited 2023Feb16]. Available from: <https://www.cliniciansbrief.com/article/omega-3-therapy-dogs>
32. Arford K. Fish Oil for Dogs [Internet]. American Kennel Club. American Kennel Club; 2020 [cited 2023Feb14]. Available from: <https://www.akc.org/expert-advice/nutrition/fish-oil-for-dogs/>
33. Chandler ML. Top 5 therapeutic uses of omega-3 fatty acids [Internet]. Clinician's Brief. 2015 [cited 2023Feb15]. Available from: <https://www.cliniciansbrief.com/article/top-5-therapeutic-uses-omega-3-fatty-acids>