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A multimodal approach to Canine Osteoarthritis management: A state-of-the-art

Hithem Bougherara*, Saïd Boukhechem and Amira Leila Dib

Gestion de la Santé et Productions Animales Research Laboratory, Institut des Sciences Vétérinaires El-Khroub, Université de Constantine 1 Frères Mentouri, Constantine, Algeria

ABSTRACT
Canine osteoarthritis (OA) is a prevalent, progressive, and debilitating joint disorder characterized by cartilage degradation, synovial inflammation, and subchondral bone remodeling. This multifactorial disease leads to chronic pain and significant impairment of quality of life. As OA remains incurable, therapeutic strategies have shifted toward comprehensive multimodal management aimed at addressing the disease's complex pathophysiology. This review presents an evidence-based overview of current approaches, including weight management, rehabilitation, pharmacologic therapies (Non-Steroidal Anti-Inflammatory Drugs, anti-Nerve Growth Factor monoclonal antibodies), disease-modifying osteoarthritis drugs, regenerative treatments, and nutraceuticals. This study also highlights practical challenges and future directions, emphasizing individualized treatment plans to optimize outcomes in canine OA.
Keywords: Canine osteoarthritis, NSAIDs, Rehabilitation, Nutraceuticals, Regenerative medicine.

Introduction

Osteoarthritis (OA) is one of the most common causes of chronic pain and reduced mobility in dogs, affecting an estimated 25% of the adult canine population (Johnston, 1997; Anderson *et al.*, 2020). The following section provides a detailed overview of the underlying mechanisms of the disease.

Etiology and pathophysiology of canine osteoarthritis

No longer considered a mere "wear-and-tear" disease, OA is now recognized as a complex disorder involving the entire joint. Its etiology is multifactorial, stemming from primary causes such as genetic predisposition (e.g., hip dysplasia) or secondary insults such as trauma, joint instability (e.g., cranial cruciate ligament rupture), or obesity. Regardless of the trigger, pathophysiology involves a cascade of pathological changes. The process is driven by an imbalance between anabolic and catabolic processes within the joint. Pro-inflammatory cytokines, particularly Interleukin-1β and tumor necrosis factor-α, are key mediators that stimulate chondrocytes and synoviocytes to produce matrix-degrading enzymes, such as matrix metalloproteinases and aggrecanases. These enzymes degrade the articular cartilage matrix, resulting in its progressive loss. Concurrently, synovial inflammation (synovitis) perpetuates the inflammatory cycle, and pathological remodeling of the subchondral bone contributes to joint pain and dysfunction. This creates a vicious cycle of cartilage degradation, inflammation, and pain, which underscores the need for multimodal therapies that target these distinct pathways (Brandt *et al.*, 2009; Goldring and Otero, 2011; Wang and He, 2018).

Clinically, OA manifests as lameness, stiffness, and decreased activity. Effective management requires a multimodal, individualized strategy focusing on pain relief, functional preservation, and quality of life enhancement (Brown *et al.*, 2007; Sanderson *et al.*, 2009; Glyn-Jones *et al.*, 2015).

This state-of-the-art review aims to synthesize and critically evaluate the current evidence for various management modalities for canine OA. A comprehensive literature search was conducted using PubMed, Scopus, and Google Scholar databases for articles published between 1995 and 2024, using keywords such as "canine osteoarthritis," "dog," "pain," "multimodal management," "NSAIDs," "bedinvetmab," and "rehabilitation." This review aims to provide veterinary practitioners with a clear, evidence-based framework for developing individualized, multimodal treatment plans.

Foundational management: Non-pharmacological strategies

Weight management

Weight control is critical in the treatment of OA Obesity contributes to disease progression both mechanically, through increased joint loading, and biologically, via proinflammatory adipokines. Body weight should

***Corresponding Author:** Hithem Bougherara. Gestion de la Santé et Productions Animales Research Laboratory, Institut des Sciences Vétérinaires El-Khroub, Université de Constantine 1 Frères Mentouri, Constantine, Algeria.
Email: *Hithem.bougherara@umc.edu.dz*

Table 1. Staged multimodal management plan for Canine Osteoarthritis. A framework for tailoring therapeutic intensity based on OA severity following the COAST guidelines.

Modality	Mild-to-moderate OA (stages 1–2)	Moderate to severe OA (stages 3–4)
Foundational	Weight optimization and controlled exercise	Strict weight control and formal rehabilitation
Pharmacologic	NSAIDs/Grapiprant, anti-NGF mAb	NSAIDs + anti-NGF mAb, adjunctive analgesics
Nutraceuticals	Omega-3 fatty acids	Omega-3 fatty acids
DMOADs	Adjunctive: Pentosan polysulfate sodium	Adjunctive: Pentosan polysulfate sodium
Interventional	Consider HA injections	Corticosteroids, PRP, and MSCs
Surgical	Not indicated	Joint replacement or arthrodesis

Table 2. Summary of key pharmacologic interventions for canine OA. An overview of primary drug classes, their mechanisms, and important clinical considerations for safe and effective use of these drugs.

Drug class	Examples and (Dosage)	Mechanism of action	Key clinical considerations
NSAIDs (Cyclooxygenase-2 Selective)	Carprofen (2.2 mg/kg BID), Meloxicam, and Firocoxib	Inhibit cyclooxygenase (COX) enzymes, reducing prostaglandin synthesis involved in pain and inflammation	• Efficacy: Good analgesic and anti-inflammatory effects. • Contraindications: Pre-existing renal, hepatic, or gastrointestinal disease. • Monitoring: Requires baseline and periodic bloodwork for long-term use.
EP4 receptor antagonist	Grapiprant (2 mg/kg SID)	Specifically, it blocks the EP4 prostaglandin receptor, a key mediator of OA pain and inflammation, while sparing homeostatic prostaglandins.	• Efficacy: Effective for controlling pain and inflammation. • Advantages: Favorable safety profile compared with traditional nonsteroidal anti-inflammatory drugs, with lower risk of GI and renal side effects.
Anti-NGF monoclonal antibody	Bedinvetmab (0.5–1.0 mg/kg SC monthly)	A canine-specific antibody that binds to and neutralizes nerve growth factor (NGF), a key driver of chronic osteoarthritic pain.	• Efficacy: High efficacy for chronic OA pain, mobility, and quality of life. • Advantages: Highly targeted mechanism with an excellent safety profile; ideal for dogs with NSAID contraindications.
DMOADs	Pentosan polysulfate sodium (3 mg/kg SC, weekly for 4 weeks)	Exerts chondroprotective and mild anti-inflammatory effects, potentially stimulating HA and inhibiting catabolic enzymes.	• Efficacy: It is considered an adjunctive therapy, not a primary analgesic. • Use case: Best used in early-to-moderate OA as part of a multimodal plan.

be objectively assessed using a standardized Body Condition Score system, such as the 9-point scale, with a target score of 4 or 5. Therapeutic diets designed for weight loss are often formulated with reduced calories and increased fiber, and may be supplemented with L-carnitine to promote fat metabolism. Clinical studies have demonstrated that even a modest weight loss (6%–8% of body weight) can significantly reduce lameness and analgesic reliance (Marshall *et al.*, 2010; Impellizeri *et al.*, 2000).

Therapeutic exercise and rehabilitation

Controlled, low-impact exercise (e.g., leash walking and swimming) maintains joint mobility and periarticular muscle mass, providing dynamic support to affected joints. A formal rehabilitation plan should be tailored to the individual patient, avoiding activities that

cause pain exacerbation. Contraindications for certain exercises include acute inflammatory flares, where rest and pharmacological management take precedence. Rehabilitation techniques, such as hydrotherapy, manual therapy, and photobiomodulation, further enhance function and alleviate pain (Marcellin-Little *et al.*, 2005; Dycus *et al.*, 2017).

Pharmacologic interventions

Pharmacologic interventions are aimed at directly mitigating the pain and inflammation associated with the OA pathophysiological cascade. Table 2 provides a summary of key options.

NSAIDs and grapiprant

NSAIDs, particularly COX-2 selective agents such as carprofen, meloxicam, and firocoxib, remain the cornerstone for managing OA pain and inflammation by inhibiting prostaglandin synthesis. However, long-term use requires careful patient selection and monitoring for potential gastrointestinal, renal, and hepatic adverse effects (Innes *et al.*, 2010; KuKanich *et al.*, 2012; Kirkby Shaw *et al.*, 2016). Grapiprant, an EP4 prostaglandin receptor antagonist, offers an alternative mechanism that spares other prostanoid pathways, providing a favorable safety profile, particularly for dogs with certain comorbidities (Kirkby Shaw *et al.*, 2016).

Anti-NGF monoclonal antibodies

Bedinvetmab (Librela™), a canine-specific monoclonal antibody against nerve growth factor (NGF), represents a paradigm shift in OA management. NGF is a key mediator in pain signaling, and by neutralizing it, bedinvetmab provides potent analgesia and improved quality of life, as demonstrated in randomized controlled trials (Enomoto *et al.*, 2019; Krautmann *et al.*, 2021; Corral *et al.*, 2021). This option, administered as a monthly subcutaneous injection, is particularly valuable for dogs with NSAID contraindications, such as those with renal or gastrointestinal disease (Monteiro *et al.*, 2024).

Disease-modifying Osteoarthritis drugs

Pentosan Polysulfate *demonstrates* chondroprotective and anti-inflammatory effects, supporting its adjunctive use in OA management (Read *et al.*, 1996).

Interventional and regenerative therapies

Intra-articular injections

Hyaluronic acid restores synovial fluid viscosity, while corticosteroids offer short-term relief for inflammatory flares. However, the repeated long-term use of corticosteroids is discouraged due to potential chondrotoxicity (Hepper *et al.*, 2009; Budsberg *et al.*, 2018).

Regenerative medicine

Platelet-rich plasma (PRP) and mesenchymal stem cell (MSC) therapies modulate joint inflammation and promote repair. Although promising, further standardization and large-scale studies are necessary to confirm efficacy and safety (Hu and Li, 2019; Upchurch *et al.*, 2022; Franklin and Cook, 2023).

Nutraceuticals and dietary modifications

Therapeutic diets enriched with omega-3 fatty acids (Eicosapentaenoic Acid and Docosahexaenoic Acid) have strong evidence of anti-inflammatory effects. Conversely, the results for glucosamine and Chondroitin Sulfate remain inconclusive. Other supplements, such as green-lipped mussel extract and undenatured type II collagen, have shown potential benefits in some studies (D'Altilio *et al.*, 2007; Roush *et al.*, 2010; Rialland *et al.*, 2013; Comblain *et al.*, 2016; Mehler *et al.*, 2016).

Implementation of a multimodal plan

An individualized, stage-based approach—such as the COAST guidelines—helps to structure therapeutic decisions. Early-stage OA management emphasizes weight control and exercise, whereas advanced cases may require pharmacologic, nutraceutical, and regenerative therapies (Table 1) (Cachon *et al.*, 2018).

Practical challenges and future directions

High costs of novel biologics and regenerative therapies, as well as long-term owner compliance, present significant barriers (Belshaw *et al.*, 2020). In resource-limited settings, it is essential to prioritize affordable strategies like weight control and NSAID use. Future directions include gene therapies, novel small-molecule inhibitors, and precision medicine approaches.

Conclusion

The management of canine OA has evolved into a sophisticated, multimodal discipline that moves beyond treating symptoms to managing the disease as a whole. This modern approach strategically integrates foundational, non-pharmacological strategies, such as weight management and rehabilitation, with advanced pharmacologic agents that target specific pathophysiological pathways, including novel biologics, such as anti-NGF monoclonal antibodies. The success of this comprehensive strategy hinges on the creation of an individualized plan tailored to the patient's specific clinical stage, comorbidities, and needs. As research continues to unveil new therapeutic targets, the future promises even more refined and personalized interventions, including gene therapies and novel small-molecule inhibitors. Ultimately, combining these varied therapeutic modalities under skilled veterinary supervision, with strong owner compliance, provides the best opportunity to effectively alleviate pain, preserve joint function, and significantly improve the quality of life of dogs suffering from this chronic condition.

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Conflict of interest

The authors have no conflicts of interest to declare.

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Authors' contributions

All authors contributed equally to this review.

Data availability

All data were provided in the manuscript.

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