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Stereotactic Radiotherapy with Internal Fixation as An Amputation-Sparing Strategy for Canine Osteosarcoma: Safety, Local Control, and Functional Recovery

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A B S T R A C T

Canine appendicular osteosarcoma (OSA) is the most common primary malignant bone tumor in dogs and is characterized by aggressive local growth and early metastatic spread. Prognosis remains poor, largely due to the presence of micrometastatic disease at the time of diagnosis. This review summarizes current knowledge on the epidemiology, diagnostic approaches, and treatment strategies for canine appendicular osteosarcoma. A literature review was conducted using PubMed, Scopus, and Google Scholar, focusing on studies published between 2000 and 2025, with an emphasis on the most recent findings. Amputation with adjuvant chemotherapy is still the best way to treat cancer, and it does improve survival, but it doesn't stop the cancer from spreading. Limb-sparing surgery and stereotactic body radiation therapy (SBRT) may be considered in selected cases to preserve limb function, but they do not appear to offer a survival advantage compared to amputation. Palliative treatments, including radiotherapy and analgesic management, play an important role in maintaining quality of life. Novel approaches such as immunotherapy and targeted therapy have shown promising early results. However, these approaches are largely still in the research phase. Overall, canine appendicular osteosarcoma should be considered a systemic disease. Better control of metastatic disease in the future will improve outcomes through the integration of novel systemic therapies.

Keywords: canine osteosarcoma, primary bone tumor, diagnostic staging, limb sparing surgery, adjuvant chemotherapy

INTRODUCTION

Canine appendicular osteosarcoma (OSA) is the most common malignant primary bone tumor of dogs and continues to be a prominent clinical challenge because of its aggressive local behavior, coupled with a high metastatic potential. Osteosarcoma disproportionately affects large and giant breed dogs with epidemiological studies consistently showing strong associations with risk of developing OSA including factors such as body size, breed conformation and purebred genetic background (**1–3**). In addition to key OSA influencing regulators cited in the multifactorial etiology of OSA (**4,5**), additional age-related parameters such as reproductive status and biomechanical stresses from rapid skeletal growth have been shown to further enhance disease susceptibility.

Clinically, appendicular OSA is characterized by progressively destructive bone lesions commonly presenting as severe pain and lameness often resulting in an initial veterinary visit. Diagnosis is usually made by

using some imaging and an evaluation of the tissue. Radiographic evidence of aggressive bone lesions, such as cortical lysis and periosteal reaction, is suggestive, but a definitive diagnosis would require cytology or histopathology (**6,7**). Staging procedures usually involve thoracic imaging to identify pulmonary metastases, as well as advanced imaging modalities like computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography/computed tomography (PET/CT) to enhance detection of metastatic and multifocal disease (**8-9**).

Management of canine OSA remains a challenge, however, even with advances in the diagnostic approach, with increased focus on local tumor control and systemic disease management. Amputation of the limb remains the standard for local control and prompt analgesia. Median survival durations are usually increased to approximately 9–12 months alongside adjuvant chemotherapy containing platinum-based protocols, like carboplatin (**10,11**). Local control strategies including limb-salvage surgery and stereotactic body radiation therapy (SBRT) have been explored to develop ways to preserve function of the affected limb in selected patients as these are shown to improve quality of life. However, none of these approaches have evident survival benefits as compared to amputation with similar systemic therapies (**12,13**).

At diagnosis, micrometastatic (MM) disease poses a major challenge in canine OSA management. Despite these successful local tumor control efforts, metastatic disease manifests in most dogs (typically in the lungs) and remains a leading cause of death (**10,14**). Such complexity impacts the systemic biology of OSA and underpins a model for metastatic niches that extends beyond the scope of existing therapeutic paradigms designed to impact primary tumor.

This explains why recent studies have increasingly concentrated on developing strategies for systemic regulation through designing new therapeutic approaches. These therapeutic approaches consist of immunotherapy (**19**) and oncolytic virotherapy (**20**), targeted molecular therapies (**10**) as well as modulation of the microenvironmental signals toward tumor dormancy, in order to delay or prevent metastatic progression and improve long-term patient outcomes(**16-18**). Some of these approaches have yielded promising early results, but the strategies are still largely experimental and have not supplanted traditional chemotherapy as standard clinical practice.

In addition to survival outcomes, quality of life (QoL) has become a salient end-point in clinical decision-making. When curative intent is not achievable, our selection of an effective treatment plan should balance the need for adequate tumor control against preserving ambulation, managing pain and contributing to overall welfare in this particular patient population (**13,19**). This highlights the importance of developing a personalized treatment plan based on clinical and owner-related factors.

Therefore, the goal of this review is to provide a comprehensive summary of current literature on canine appendicular osteosarcoma epidemiology, diagnostic algorithms and treatment modalities with an emphasis on systemic therapy and implementation of multimodal therapy aimed at improving survival and quality of life.

MATERIALS AND METHODS

Study Design

This study was conducted as a narrative review to summarize current knowledge on canine appendicular osteosarcoma (OSA), with emphasis on epidemiology, diagnosis, and treatment. Findings from clinical studies, retrospective analyses, and recent developments in veterinary oncology were used to provide a clinically relevant overview.

Literature Search Strategy

A literature search was carried out on PubMed, Scopus and Google Scholar databases. Searches were limited to the years 2000-2025, although given this time frame, studies from the latter half of 2021–2025 would be most likely to provide recent evidence.

Search terms were any combinations of the following keywords: “canine osteosarcoma”, “appendicular osteosarcoma dog”, “limb-sparing surgery”, “chemotherapy”, “radiotherapy” and/or “stereotactic body radiation therapy” and/or “immunotherapy. The search strategy was optimized and the relevance of retrieved articles improved by using Boolean operators (AND, OR). For example, a search string employed would be: (“canine osteosarcoma” OR “appendicular ostesarcoma dog”) AND (“chemotherapy “OR” radiotherapy *OR* “limb-sparing surgery”).

Study Selection Criteria

Articles were selected based on their relevance to the aims of this review. Priority was given to peer-reviewed studies on canine appendicular osteosarcoma, especially those related to diagnosis, treatment, prognosis, and survival. Eligible studies included clinical trials, cohort and retrospective studies, as well as review articles. Studies focusing only on non-canine species, single case reports, or those without accessible full text were excluded.

Data Extraction and Thematic Analysis

Information from the selected studies was extracted and organized into several key topics, including epidemiology and risk factors, diagnostic and staging methods, treatment strategies (both surgical and non-surgical), chemotherapy protocols, radiotherapy, emerging therapies, and quality of life considerations. After the findings were gathered, they were reviewed and compared across the studies to find common patterns and clinically relevant results. Due to differences in study design and reported results, a qualitative approach was used rather than a quantitative analysis.

Quality Consideration

In interpreting the findings, greater attention was given to studies with stronger clinical relevance, such as

randomized trials, large cohort studies, and consensus guidelines. Additional consideration was given to methodological clarity, sample size, and the applicability of results to clinical practice.

Literature Selection Process

The preliminary search yielded approximately 120 articles from the chosen databases. Following the elimination of duplicates, 95 articles underwent screening based on their titles and abstracts 40 were subsequently deemed irrelevant and excluded. A full-text evaluation was then performed on the remaining 55 articles, resulting in the inclusion of 35 that satisfied the established inclusion criteria in the final analysis. Studies characterized by transparent methodologies, clinical significance, and more recent publication dates were prioritized. The overall selection process is summarized in **Figure 1**.

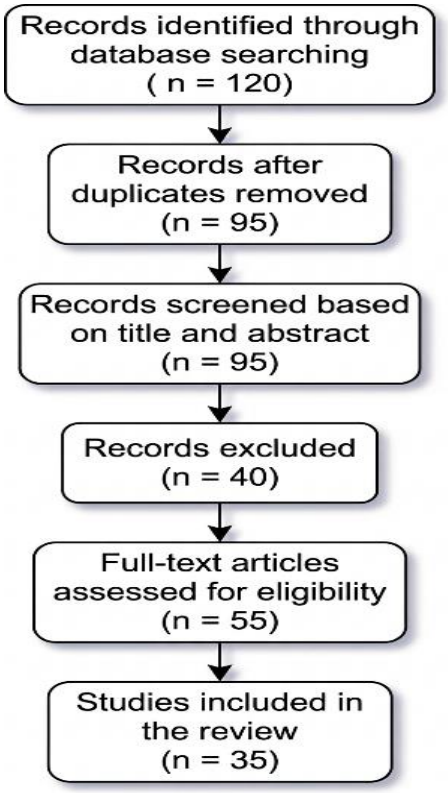

Figure 1. Flow diagram of literature search and study selection process

RESULTS AND DISCUSSION

Epidemiology and Risk Factors

Canine appendicular osteosarcoma (OSA) is an aggressive cancer that largely occurs in large and giant breed dogs, where body size, conformation of the breed, and genetic predisposition have been identified as primary risk factors (**1–3**). Epidemiological studies consistently show an increased incidence in breeds including Rottweilers and Irish Wolfhounds, suggesting a strong hereditary component (23). Various age-related factors and rapid skeletal growth also playa role in the susceptibility to disease, hence confirming their multifactorial etiology for OSA (**4,5,32**).

Diagnosis and Staging

An accurate diagnosis and staging of malignant tumors are critical for appropriate treatment planning and prognostic assessment. Radiography is still the main imaging modality, which usually shows aggressive bone lesions with features of cortical lysis, periosteal reaction and loss of normal bone architecture (**6**). However, cytological or histopathological confirmation is necessary for a definitive diagnosis (**7,22**). The use of advanced imaging modalities such as CT, MRI and PET/CT imaging has dramatically increased staging accuracy (**2,5,35**). CT remains valuable in the detection of pulmonary metastases, whereas MRI is superior in assessment of extension into soft tissue and marrow involvement (**35**). Compared with conventional imaging techniques, PET/CT provides higher sensitivity in the detection of early metastatic disease (**2**). A summary of the commonly used diagnostic and staging modalities is presented in **Table 1**.

As shown in Table 1, each modality offers distinct advantages, and their combined use enables a more comprehensive assessment of disease extent. This multimodal approach reflects the increasing recognition

that accurate staging is essential, given the high likelihood of micrometastatic disease at the time of diagnosis.

Treatment Strategies

The mainstay of local tumor control remains surgery in canine OSA. Limb amputation is a gold standard treatment that has been well accepted globally; it provides immediate efficient pain control and excises the foremost tumor. More importantly, the majority of dogs behaviorally adapt to normal function after amputation (**26**), particularly when there is no concurrent orthopedic or neurologic disease.

Alternatives to amputation such as limb-sparing techniques have been developed for a select group of patients, particularly when an amputation is not accepted or is contraindicated. The goal of these procedures are to maintain limb function and local tumor control. However, to date, all evidence suggests that limb-sparing surgery results in no improved survival compared to amputation with adjunctive equivalent systemic therapy (13,26). In addition, increased episodes of complications such as infection, implant failure and local recurrence have to be taken into account.

Table 1. Summary of diagnostic and staging modalities in canine appendicular

Modality	Primary role	Key findings / advantages	Limitations	Source
Radiography	Initial diagnosis	Identifies aggressive bone lesions (osteolysis, periosteal reaction, cortical destruction) suggestive of OSA	Cannot confirm tumor type; limited sensitivity for metastasis	(**6**)
Cytology (FNA)	Preliminary diagnosis	High sensitivity for detecting malignant bone tumors; minimally invasive	Limited accuracy for tumor subtyping; possible non-diagnostic samples	(**7**)
Histopathology (biopsy)	Definitive diagnosis	Gold standard for diagnosis and tumor classification	Invasive; requires anesthesia and specialized processing	(**6,7**)
Computed Tomography (CT)	Local staging and lung metastasis detection	Superior assessment of cortical destruction, tumor extent, and small pulmonary nodules	Limited soft tissue contrast compared to MRI	(**2,35**)
Magnetic Resonance Imaging (MRI)	Soft tissue and marrow evaluation	Excellent visualization of medullary involvement, soft tissue extension, and neurovascular structures	Less sensitive for pulmonary metastasis; higher cost	(**35**)
Thoracic radiography	Metastatic screening	Widely available and routinely used for detecting pulmonary metastasis	Low sensitivity for small nodules compared to CT	(**8**)
Bone scintigraphy (SPECT)	Detection of skeletal metastasis	More sensitive than radiography for detecting multiple bone lesions	Limited availability; lower specificity	(**8**)
PET/CT (18F-FDG)	Whole-body staging	High sensitivity for detecting skeletal and distant metastases; identifies additional lesions not seen on CT	Limited availability; high cost	(**2,5**)

OSA: osteosarcoma, FNA: fine-needle aspiration, CT: computed tomography, MRI: magnetic resonance imaging, SPECT: single-photon emission computed tomography, 18F-FDG: 18F-fluorodeoxyglucose

Chemotherapy

Systemic chemotherapy represents an important component of OSA management, as micrometastatic disease is presumed at the time of diagnosis for most cases. Adjuvant chemotherapy after surgery has been consistently demonstrated to provide a significant survival benefit when compared with surgery alone. Platinum-based agents, especially carboplatin, are still the most widely utilized protocols in monotherapy or in combination with doxorubicin (**10,34**).

The median survival times for dogs receiving combined surgery with chemotherapy are usually 9–12 months. Nonetheless, despite these advances, long-term survival is still poor, a consequence largely of metastatic progression. In addition, adjunctive therapeutic regimens based on bisphosphonates alone or in combination with other systemic modalities have also been investigated as a way to augment treatment response and clinical outcomes, although the evidence is still sparse (**22**).

Radiotherapy

Radiotherapy is a critical adjunct, especially when surgery cannot be performed. Minimally invasive techniques, such as microwave ablation and focused ultrasound therapy, are gaining traction as alternative options for local tumor control in patients who are not surgical candidates (**30,31**). Stereotactic palliative treatment (as opposed to conventional) radiotherapy has been shown to significantly reduce pain and improve limb function (**27**), however the effect on survival remains marginal.

Stereotactic body radiation therapy (SBRT) represents a more sophisticated treatment, as higher doses of highly focused radiation drastically prolong local tumor control. Although SBRT could be a limb-sparing option in some selected cases, it carries a high risk of pathological fracture and is not a substitution for surgical approaches in curative-intent treatment (**26,18**). This complication has been observed in canines undergoing radiation-based treatments, and its potential impact must be factored into treatment strategies (**28,29**). Furthermore, beyond conventional surgical and radiation interventions, progress in limb reconstruction techniques and combined therapeutic approaches has enhanced local disease management and functional results for specific patient populations (**20,21**). A comparison of major treatment modalities and their clinical outcomes is summarized in **Table 2**.

Indeed, as depicted in Table 2, effectiveness of systemic therapy is the primary determinant of survival outcome compared to local treatment modality alone. This

emphasizes the importance of chemotherapy for improving survival, while local treatments are mainly focused on pain and tumor burden control.

Emerging and Targeted Therapies

Since disease control is often suboptimal with conventional therapies, there has been extensive research in establishing new therapeutic approaches to increase the efficacy of systemic immune responses. These include immunotherapy, oncolytic virotherapy and targeted molecular therapies (**27**). Complementary immunotherapeutic strategies, such as adoptive natural killer (NK) cell therapy and multi-agent immunomodulatory regimens also showed promise in promoting anti-tumor immune responses in canine osteosarcoma (**23,25**).

Table 2. Comparison of major treatment modalities and clinical outcomes in canine appendicular osteosarcoma

Treatment modality	Primary objective	Median survival time	Advantages	Limitations	Source
Amputation alone	Local tumor control	~3–4 months	Rapid pain relief; removes primary tumor effectively	Does not address micrometastasis	(**10,34**)
Amputation + chemotherapy	Local + systemic control	~235–366 days	Standard of care; significantly improves survival	Metastatic progression still common	(**12,33**)
Limb-sparing surgery + chemotherapy	Preserve limb function + systemic control	~235–324 days	Maintains limb function; comparable survival to amputation	High complication rates (infection, implant failure, recurrence)	(**10,14**)
Chemotherapy alone	Systemic disease control	Variable (~6–10 months)	Targets micrometastatic disease	Ineffective for local tumor control	(**18,27**)
Palliative radiotherapy	Pain relief and functional improvement	~3–5 months	Effective analgesia; improves quality of life	Limited impact on survival	(**27,20**)
Stereotactic body radiation therapy (SBRT)	Local control (limb-sparing alternative)	~6–8 months (~233 days)	High local tumor control; preserves limb function	High risk of pathological fracture; not curative	(**21**)
Radiotherapy + adjunctive therapy (e.g., bisphosphonates)	Pain control and bone stabilization	Variable	May reduce skeletal complications	Limited survival benefit	(**10,26**)

Novel immunotherapeutic strategies have shown encouraging efficacy in early-phase clinical trials, including myeloid-targeted therapies, cancer vaccines and adoptive cell therapies which lead to enhanced immune-mediated tumor control and delayed, metastases progression (**30, 28**). Oncolytic virotherapy has also demonstrated promise and in a subset of treated dogs, there have been indications of improved long-term survival (**17**).

Furthermore, new advanced and minimal invasive technologies like focused ultrasound (FU) and thermal ablation have been studied as promising candidates for local tumor control in non-surgical candidates (**31,25**). **Table 3** summarizes recent therapeutic approaches with their current clinical status.

Table 3 shows that although these therapies have shown encouraging biological activity, most are still in early stages of development and are not yet part of standard treatment.

Prognosis and Metastatic Disease

The hallmark feature of canine OSA is aggressive metastatic behavior, which continues to be the major predictor of clinical outcome. Even with effective local treatment of the tumor, most dogs eventually develop metastatic disease; lung metastasis is the most common (**10,17**). This data underlines the point that canine OSA should not only be considered an epithelial neoplasm, but actually a systemic disease from its onset. Current therapies are typically effective in suppressing primary tumor but limited if any effect on metastatic progression. Hence, better control of systemic disease is the most important unmet need in OSA management.

Quality of Life Considerations

With survival, quality of life (QoL) is the other main domain in treatment planning. Patient well-being is ultimately defined by adequate and satisfactory pain control, preservation of functional status, and minimization of therapy-associated comorbidity according to it (**26**). Amputation effectively offers immediate and long-lasting pain relief,while limb-preserving technique combined with SBRT results may improve functional outcome in selected patients. In cases where curative treatment is not an option, QoL can still be greatly improved by radiotherapy, multimodal analgesia and other palliative measures (**27**). In **Table 4** we show the effect of different treatment modalities on QoL and clinical decision making.

Survival outcomes, as well as feasibility of effective pain control and functional mobility should inform treatment selection as demonstrated in Table **4**. This highlights the importance of performing own treatment planning tailored to patient condition and owner expectations. Apart from clinical considerations, the perception and expectations of owners have also been proven to serve as a very important factor in the selection of treatment and decision making while practicing veterinary medicine (**35**).

In conclusion, although advances in imaging diagnosis and local treatment modalities have certainly enhanced the clinical management of canine appendicular osteosarcoma, overall outcomes are still hampered by an inadequate control of metastatic disease. Classically, the standard of

care is multimodality treatment with surgical resection along with chemotherapy and adjunctive therapies.

Prognosis will surely improve in the coming years with translation of novel systemic therapies targeting metastasis progression into clinical practice. In the meantime, optimizing existing treatment algorithms and living well are just as important as clinical decisions.

Table 3. Emerging and targeted therapies in canine appendicular osteosarcoma

Therapy type	Target / mechanism	Key findings	Current status	Source
Myeloid-targeted immunotherapy (losartan + toceranib ± ladarixin)	Modulation of tumor microenvironment (MDSC inhibition, anti-angiogenesis)	Clinical benefit rate up to ~50–70% in metastatic OSA; improved response in combination protocols	Early clinical studies; not standard of care	(**28,16**)
Oncolytic virotherapy (VSV-IFNβ-NIS)	Direct tumor lysis and immune activation	Safe in clinical use; associated with increased long-term survival in a subset of dogs (~35%)	Investigational (clinical trials ongoing)	(**17**)
Cancer vaccines (peptide-based / tumor cell vaccines)	Induction of tumor-specific immune response	Prolonged survival and delayed metastasis in small studies	Experimental; requires further validation	(**30**)
Adoptive cell therapy (NK cells, T cells)	Enhancement of cytotoxic immune response	Evidence of long-term survival in selected cases	Early-stage clinical application	(**12**)
CAR-T cell therapy (B7-H3 target)	Targeted T-cell-mediated tumor destruction	Strong anti-tumor activity in preclinical models	Preclinical / translational stage	(**4,24**)
Radioimmunotherapy (e.g., anti-IGF2R, anti-GD2)	Targeted radiation delivery to tumor cells	Delayed metastasis and tumor control in early studies	Experimental; limited clinical data	(**3,15**)
Targeted therapy (PI3K/mTOR inhibitors, TKI)	Inhibition of tumor growth signaling pathways	Reduced tumor growth and improved survival in preclinical models	Preclinical / early clinical stage	(**19**)

Table 4. Influence of treatment modalities on the quality of life and clinical decision making in canine appendicular osteosarcoma

Treatment modality	Pain control	Functional outcome	Quality of life impact	Clinical considerations	Source
Amputation + chemotherapy	Rapid and effective pain relief	Good adaptation in most dogs; return to normal activity possible	Generally high QoL when no comorbidities present	Preferred standard treatment; requires owner acceptance	(**26, 34**)
Limb-sparing surgery + chemotherapy	Effective if healing successful	Preserves limb function and weight-bearing	Often perceived as improved QoL due to limb preservation	Higher complication risk; requires careful case selection	(**13, 33, 6**)
Palliative radiotherapy	Moderate to good pain relief	Improved gait and limb use in many cases	QoL improved in ~75–90% of patients	Suitable for non-surgical candidates	(**27,9**)
SBRT (stereotactic radiotherapy)	Significant pain reduction	Maintains limb function; improved mobility	Good QoL in selected patients	Risk of pathological fracture; monitoring required	(**18,26**)
Medical palliative management (analgesics ± bisphosphonates)	Variable pain control	Limited improvement in function	QoL may be acceptable depending on response	Requires continuous monitoring and adjustment	(**11**)
Minimally invasive techniques (ablation, cementoplasty)	Rapid pain reduction	Improved short-term function	Promising QoL outcomes in early reports	Experimental; limited clinical data	(**31,25**)

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Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Conceptualization, Methodology, Investigation, Resources: A.H., H.U., O.P.C; Writing – Original Draft: A.H., H.U.; Writing – Review & Editing: A.H., H.U., O.P.C. All authors have read and approved the final version of the manuscript.

Artificial Intelligent Declaration

The authors declare that they are responsible for the accuracy and integrity of all content of the manuscript, including part generated by AI, and it is not used as a co-author.

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