

A Comprehensive review on canine osteosarcoma and treatments

Author list: Grace Lee

Abstract

Cancer is a diverse group of diseases characterized by uncontrolled cell growth, tissue invasion, and tumor formation. It can affect a wide range of organisms, including dogs. In the canine population, cancer represents a significant health burden. Approximately one in four dogs develops cancer during their lifetime, and nearly 50% of dogs over the age of ten are affected, accounting for up to 27% of canine deaths. Common canine cancers include lymphoma, bone tumors, and skin tumors, among which bone cancer is particularly aggressive. Osteosarcoma accounts for approximately 85% of primary bone tumors in dogs, while the remaining cases include chondrosarcoma, fibrosarcoma, and hemangiosarcoma. The development of osteosarcoma is strongly associated with genetic predisposition, especially in large and giant breeds such as Scottish Deerhounds, Rottweilers, Greyhounds, and Irish Wolfhounds, as well as with prior bone trauma, radiation exposure, healed fractures, and chronic osteomyelitis. Current treatment strategies primarily involve surgical intervention combined with chemotherapy, with immunotherapy and palliative care as additional options in selected cases; however, long-term prognosis remains poor due to the aggressive metastatic nature of osteosarcoma, particularly to the lungs. This review provides a broad overview of canine bone cancer with a specific focus on osteosarcoma, emphasizing its prevalence, risk factors, and current treatment approaches.

1. Introduction

Cancer is a large group of diseases that can start in almost any organ or tissue of the body when abnormal cells grow uncontrollably, go beyond their usual boundaries, and form a neoplasia or tumor. When an uncontrollably growing tumor forms distinct masses in organs such as the breast or lung, it is called a solid tumor. Whereas liquid tumors include leukemia or lymphoma that circulate in the blood or bone marrow. These abnormal cells may invade surrounding tissues and, in malignant cases, spread to distant organs through a process known as metastasis. Cancer affects a wide spectrum of living organisms, including molluscs, fish, reptiles, birds, and mammals. This broad biological occurrence highlights cancer as a fundamental disease process rather than a species-specific condition. For example, common cancer types in humans, such as skin cancer, lung cancer, and breast cancer, are also commonly seen in dogs, often sharing similar biological behavior and disease progression.

Approximately one in four dogs has been reported to develop cancer at some point during their lifetime. As veterinary care and nutrition have improved, dogs are living longer, which has contributed to an increased incidence of age-related diseases such as cancer. The risk of developing cancer increases to nearly 50% in dogs aged ten years or older, and canine cancer accounts for up to 27% of deaths in dogs. These statistics underscore cancer as one of the leading causes of morbidity and mortality in the canine population. The most common canine cancers include lymphoma (~24%), bone tumors (5%), and skin tumors (~35%). Although bone tumors occur less frequently than some other cancer types, they are often highly aggressive and associated with poor clinical outcomes.

Bone cancer is a relatively common and clinically significant cancer in dogs. Approximately 85% of canine bone tumors are osteosarcomas, while the remaining 15% include other

malignancies such as chondrosarcoma, fibrosarcoma, and hemangiosarcoma. Among these, osteosarcoma is the most aggressive and carries the highest risk of early metastasis (2). Canine osteosarcoma frequently metastasizes, especially to the lungs, and has a poor long-term prognosis. The median survival is commonly less than 1 year from the diagnosis. The development of osteosarcoma is strongly influenced by genetic factors, with large and giant breeds such as Scottish Deerhounds, Rottweilers, Greyhounds, and Irish Wolfhounds showing a markedly increased risk. This breed predisposition suggests an important role for inherited genetic susceptibility in disease pathogenesis.

In addition to genetic risk factors, osteosarcoma can develop at sites of previous bone trauma, including prior radiation therapy sites, previously healed fractures, and areas of chronic osteomyelitis (bone infection). These associations suggest that chronic inflammation and bone remodeling may contribute to tumor development. Current treatment options for canine osteosarcoma typically include surgical management, most commonly limb amputation or limb-sparing procedures, often combined with chemotherapy. More recently, immunotherapy and other targeted treatment approaches have emerged as areas of active research. Palliative options may be considered for dogs that are unable to undergo surgery or chemotherapy due to advanced disease or concurrent health conditions. However, the long-term prognosis for canine osteosarcoma remains poor, as the cancer tends to spread aggressively and rapidly to the lungs, making complete cure difficult.

Given the prevalence, aggressive nature, and poor long-term survival associated with canine osteosarcoma, a comprehensive understanding of this disease is essential for improving clinical outcomes. In this review, we aim to provide a broad overview of canine bone cancer, with a specific focus on osteosarcoma, including its epidemiology, risk factors, biological behavior, current treatment strategies, emerging therapeutic approaches, and future research directions.

2. Main body

2.1. Epidemiology and Clinical presentations of canine osteosarcoma

Osteosarcoma is a highly aggressive and clinically significant bone tumor in dogs. It is one of the more common primary skeletal malignancies in the canine population. With cancer affecting approximately one in four dogs developing cancer during their lifetime, osteosarcoma represents a significant health concern worldwide, particularly in large and giant breeds with inherited genetic susceptibility. Although genetic factors play a major role, especially in large breeds with a strong familial history of cancer, environmental and physical factors such as prior bone trauma, chronic inflammation, radiation exposure, or previous fractures may also contribute to disease development. While no single definitive cause has been identified, research continues to highlight osteosarcoma as a disease influenced by both hereditary and acquired factors.

Clinically, osteosarcoma is characterized by rapid local bone destruction and a high likelihood of early metastasis, most commonly to the lungs. Because of its aggressive biological behavior, treatment typically requires different approaches. Surgical intervention, most often limb amputation, remains the primary method for achieving local tumor control and relieving pain. Limb-sparing procedures may be considered in select cases. However, since microscopic metastatic disease is often present at the time of diagnosis, chemotherapy is routinely

administered following surgery to delay metastatic progression and improve survival outcomes. While these treatments can extend median survival to approximately one year in many cases, long-term prognosis remains guarded due to the high metastatic rate.

2.2 An overview of the treatment options for dogs.

In this section of the manuscript, we will review the major treatment options for osteosarcoma and provide an update on the latest advances in osteosarcoma care. Generally, patients receive different treatment options depending on their treatment goals. Treatment goals can range from achieving the local control of the primary tumor, addressing metastatic disease to improve survival and quality of life, to managing pain and improving quality of life. The standard of care treatment of canine osteosarcoma typically involves a multimodal approach including surgical intervention and/or chemotherapy.

Surgical interventions include amputation of the affected limb, often with adjuvant chemotherapy therapy and limb-sparing treatment. Surgical amputation followed by several rounds of chemotherapy has been shown to have the longest disease control and overall survival time. Palliative treatment aims to alleviate pain and improve the quality of life for dogs that have advanced osteosarcoma and are not suitable for definitive surgical intervention.

2.2.1 Surgical intervention

Surgical intervention is the primary treatment option for treating canine osteosarcoma, with the main goal of removing the primary tumor, alleviating pain, and improving the quality of life. Several surgical approaches are available, and the choice of the procedure type depends on the tumor location, severity, and the patient's overall health.

The most common surgical treatment for canine osteosarcoma is complete limb amputation. Amputation removes the entire affected limb and eliminates the primary source of pain associated with the tumor. This procedure is overall well-tolerated. Dogs with lower body weights tend to adapt more easily to full limb amputation, whereas overweight dogs may experience greater difficulty adjusting and recovery. Additionally, amputation of a hind limb typically has less functional impact than amputation of a forelimb, as dogs bear a greater proportion of their body weight on the front limbs. Although amputation provides effective local tumor control, it does not prevent metastatic spread, and recurrence most often occurs in the form of distant metastases, particularly to the lungs.

Partial removal of the affected part of the limb is common for treating primary tumours that are limited in size and location. The benefit of this procedure is the possibility of preserving some limb function and a quick recovery time. Furthermore, it prevents the development of a chronic fracture in the future from untreated bone that weakens over time.

Limb-sparing surgery refers to any type of treatment in which the primary tumour is removed without a full limb amputation. Common examples include removing fractions of the ulna or scapula if the tumour is limited to these bones. While limb-sparing surgery can preserve the limb, it is associated with a higher risk of complications, including infection. If the tumour is found in a major long bone that supports the dog's weight, implants could replace the removed bone when detaching the tumour.

2.2.2 Chemotherapy

While primary tumours are often treated with amputation, metastatic secondary tumours are often treated with chemotherapy, which is often considered the best treatment for secondary osteosarcoma, as it significantly increases patients' survival. This treatment is normally performed every 3 weeks for 4 doses. In most veterinary clinics, chemotherapy is well tolerated by patients.

There are mainly 3 chemotherapeutic drugs used in treatment: Cisplatin, Doxorubicin, and Carboplatin. Cisplatin and Doxorubicin can be used separately or together. All three of the drugs have advantages and disadvantages.

Cisplatin works by damaging the DNA of cancer cells so they can't replicate properly, the population of cancer cells decreases over time. The active platinum compound binds to guanine and adenine bases in the nuclear DNA, forming covalent adducts. Lesions induced by cisplatin cause significant distortion of the DNA helix, triggering apoptosis in cancer cells. Following cisplatin treatment, most dogs live 6-13 months, and 33-50% are still alive at 1 year, with a small number reaching 2 years. The downsides of this treatment are that it can cause renal damage since Cisplatin is nephrotoxic, and the patients should receive heavy IV fluids before and after the drug to protect the kidneys. Also, this treatment can cause mild side effects such as vomiting or diarrhea, and decreased appetite for a few days.

Carboplatin damages cancer cell DNA by a mechanism of action similar to that of cisplatin, and is used after amputation for canine osteosarcoma to slow cancer spread. It is not nephrotoxic and does not require dogs to receive intensive intravenous fluid support like you would need for Cisplatin. Carboplatin is given intravenously, about every 3 weeks, for 4-6 doses. It can cause minor side effects like nausea, vomiting or diarrhea. The average 1-year survival after this treatment is up to 35%.

Doxorubicin also works by damaging the cancer cell DNA, stopping the cells from dividing and growing. Doxorubicin inserts itself between DNA base pairs, disrupting the structure and function of the DNA helix. Also, it forms a stable complex with topoisomerase II and DNA, preventing the DNA strands from recombination. This causes irreversible double-strand breaks in DNA, leading to cell death. Fast-growing cancer cells are impacted more than healthy normal cells. This treatment is usually given via intravenous every 2-3 weeks for 4-6 treatments, and hospitalization isn't often required. The main disadvantage of this treatment is the weakening of the heart. Vets always perform a baseline echocardiogram (heart ultrasound) before treatment. Some breeds, such as Dobermans and Boxers, are not suited for this treatment because they are prone to heart disease.

Using both chemicals could either be a method of alternating every 3 weeks or having 2 on the same day, which has a higher risk of side effects as the patient's body has both chemo drugs injected at once.

2.2.3 Novel treatment options

Despite advances in surgery and chemotherapy, long-term outcomes for canine osteosarcoma remain poor. It is largely due to the high rate of metastasis. There is a growing interest in developing novel treatment options. Recent research has shifted towards therapies that

modify the tumor microenvironment and disrupt the processes that enable tumor cells to establish metastases in distant organs. This section focuses on emerging and experimental treatment approaches for canine osteosarcoma.

One emerging area of research in canine osteosarcoma is the prevention of metastatic spread to other organs, including the lungs. A longtime researcher of osteosarcoma in dogs and a member of the University of Colorado Cancer Centre, Dan Regan, DVM, has received a grant from the National Institutes of Health to investigate a new method to prevent bone cancer from spreading to the lungs. Regan's group, in collaboration with Breelyn Wilky, MD, is investigating lung fibroblasts and their role in the spread of osteosarcoma. Fibroblasts normally support organ structure, but cancer can hijack them into an activated state that fuels tumor growth and metastasis. Their team will study this process in dogs with naturally occurring osteosarcoma, combining standard chemotherapy with a drug that targets focal adhesion kinase (FAK), a signaling pathway found to be overactive in both tumor cells and fibroblasts. This overactivation appears to create a tumor-friendly environment in the lungs, attracting immune cells that further promote cancer spread. By blocking FAK, the researchers aim to disrupt this "metastatic niche," preventing or even reversing lung metastases. Although FAK inhibitors have been tested in other cancers, this is their first evaluation in osteosarcoma. Using a comparative oncology approach, the team can study the disease more efficiently in dogs, where osteosarcoma is far more common than in children, and potentially accelerate the development of new treatments for human patients.

Another focus of emerging therapies in canine osteosarcoma is immunotherapy. The goal is to prevent or delay lung metastases after standard treatment of amputation and chemotherapy. For example, LeBlanc's group completed a large, multicenter prospective clinical trial evaluating an adjuvant vaccine made from *Listeria monocytogenes* engineered to express a HER2-targeting antigen. HER2 is a tumor-associated antigen used in this study. In this study, of dogs with appendicular osteosarcoma treated with standard-of-care therapy received this vaccine. Researchers identified immune-response patterns that differed in dogs with particularly long survival. Even when an immunotherapy does not produce a dramatic across-the-board survival improvement, these trials help define which immune signals might matter and how future therapies could be better targeted to the patients most likely to benefit.

Findings from emerging research areas may not directly improve treatment options for dogs at the moment, but they provide valuable insights for the development of novel therapies. Yet, further clinical studies are required to determine the safety, efficacy, and long-term benefit of these approaches before they can be developed into a standard treatment.

3. Conclusion

Canine osteosarcoma is one of the most common primary bone tumors in dogs. It remains one of the most aggressive malignancies in veterinary oncology. It affects approximately one in four dogs and occurs most frequently in large breeds. Clinically, osteosarcoma is characterized by a rapid local bone destruction, pain, and a high likelihood of early metastasis, particularly to the lungs. The primary cause of mortality is metastasis.

Current treatment strategies rely on a multimodal approach. Surgical intervention, most commonly limb amputation or limb-sparing procedures. It provides effective local tumor control

and significant pain relief. However, because microscopic metastatic disease is often present at diagnosis, chemotherapy using agents such as cisplatin, carboplatin, or doxorubicin is routinely administered to delay disease progression and improve survival time. Although these treatments can extend median survival to approximately one year in many cases, long-term prognosis remains guarded due to the aggressive metastatic nature of the disease.

Recent advances in veterinary oncology focus on developing novel therapeutic strategies, including targeted therapies that disrupt metastatic niche formation and immunotherapies that stimulate anti-tumor immune responses. Although these emerging approaches are still under investigation, they offer promising directions for improving the management of both canine and human osteosarcoma through comparative oncology research.

4. Discussion

A major challenge in the management of canine osteosarcoma is balancing the goal of extending survival with maintaining an acceptable quality of life for the patient. Treatments such as limb amputation followed by chemotherapy can significantly increase median survival time, often extending life to around one year or longer in some cases. However, these treatments are physically demanding and may involve repeated veterinary visits, potential side effects, and recovery periods that can affect a dog's daily comfort and activity. While many dogs adapt remarkably well to limb amputation and tolerate chemotherapy better than humans do, the decision to pursue aggressive treatment must take into account the individual dog's age, overall health, temperament, and the owner's ability to manage ongoing care. For some patients, particularly those with advanced disease or additional health problems, aggressive treatment may not necessarily translate to meaningful improvements in day-to-day well-being.

Because osteosarcoma is highly metastatic and often incurable, veterinarians and pet owners must carefully weigh the benefits of extending life against the importance of preserving comfort and normal behaviour. Palliative treatments, such as pain management, radiation therapy, and supportive care, may be chosen when the goal shifts from prolonging survival to maximizing the dog's quality of life for the time remaining. These approaches focus on reducing pain, maintaining mobility, and allowing the dog to continue engaging in normal activities such as eating, walking, and interacting with owners. Ultimately, treatment decisions are often guided not only by expected survival statistics but also by ethical considerations surrounding animal welfare. A compassionate approach that prioritizes the dog's comfort, dignity, and overall well-being is essential when determining the most appropriate course of action for managing canine osteosarcoma.

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