Epidemiology

Giant breed and large breed dogs are more likely to develop osteosarcoma than dogs that weigh less than 10 kg. Rapid early growth and increase in stress on weight-bearing limbs may explain why the risk is particularly associated with limb length.\(^1\) Osteosarcoma can affect dogs of any age, although most are middle-aged to old animals with a median age of 8 years. Osteosarcoma most commonly affects the metaphysis of the appendicular skeleton; the most common sites are the distal radius and the proximal humerus (“away from the elbow”) and the proximal tibia and distal femur (“toward the knee”). Previous fractures and/or the use of metal implants have been associated with the occurrence of osteosarcoma years later. A large, recent study showed there was no evidence for such an association.\(^2\)

Staging and Diagnosis

Dogs with a suspected primary bone tumour should have high-detail radiographs of the lesion. In addition, routine blood work and urinalysis should be performed. Although pulmonary metastases are rarely detectable at the time of diagnosis, three-view thoracic radiographs still should be taken; right and left lateral views and a dorsoventral view should be obtained because occasionally lateralizing metastases are seen on only one lateral view but not the other. Dogs with clinically detectable pulmonary metastases have a poor prognosis, with or without treatment. Osteosarcomas frequently include areas of cartilage and fibrous tissue as well as osteoid and are often surrounded by new bone. For these reasons, a biopsy diagnosis of chondrosarcoma, fibrosarcoma, or “reactive” bone should be considered suspect and further samples obtained at definitive surgery should be submitted for histopathologic examination.

Treatment

Surgery

Amputation is the single best pain relief measure for dogs with appendicular osteosarcoma. The surgery eliminates the primary tumour with little to no reduction in mobility and quality of life for most dogs. While surgical treatment of osteosarcoma by amputation is palliative, it rarely increases survival significantly, chemotherapy should be strongly considered (below). The median survival for dogs treated by amputation alone is about 4 months, and only 10% of dogs are alive one year after surgery. Limb-sparing surgery is important in human patients, for whom cosmetic appearance and function are impaired by amputation. In dogs, limb-sparing surgery may be an option for relatively small lesion of the distal radius. Function is poor when tumours of the hindlimb or proximal humerus are treated by limb salvage,\(^3\) and limb salvage is not an option for large lesions that involve more than 50% of the bone, or tumours that invade adjacent soft tissue,
as these are not easily resectable. Limb-sparing surgery is a technically demanding procedure that should be performed only by specially trained surgeons. Another form of limb salvage surgery which combines surgery to resect local tumour and limb salvage using bone transport osteogenesis has been recently reported. 

**Palliative radiation therapy**

If an animal is not considered an eligible candidate for amputation or limb sparing, consideration may be given to palliation with radiation therapy. Coarse fractionation of radiation to be delivered in weekly fractions of 8 to 10 Gy has been reported to palliate pain for dogs with osteosarcoma. Improved limb function was seen in approximately 75% of the dogs treated with either 10 Gy on days 0, 7 and 21 of a 3-week protocol, or 8 Gy on days 0 and 7. Improvement lasted for a median of 2 months regardless of the protocol and toxicities were rare. A potential risk of pain relief is increased use of the limb leading to a stress-induced pathologic fracture.

**Chemotherapy**

Survival of dogs with osteosarcoma can be significantly prolonged by adjuvant chemotherapy. Cisplatin markedly improves median survival times to between 180 and 400 days and 1-year survival rates to between 30% and 62%; 2-year survival rates are between 7% and 21%. Doxorubicin prolonged survival in dogs treated by amputation and five bi-weekly doses with similar results to those achieved with cisplatin. If chemotherapy with doxorubicin is being considered, a baseline echocardiogram should be obtained. Decreased cardiac contractility, even in a dog without clinical signs of heart disease, should prompt the clinician to avoid doxorubicin. Cardiac screening is particularly important in breeds of dogs that are prone to congenital cardiomypathy (e.g. Doberman pinschers, boxers). Combinations of cisplatin and doxorubicin, alternating every 21 days for two cycles, gave a median survival comparable to cisplatin chemotherapy alone. 47% of 102 dogs treated with cisplatin and doxorubicin given on the same day survived 1 year after surgery, 28% were alive 2 years after surgery, and 16% were alive 3 years after amputation and chemotherapy.

Carboplatin given adjunctively after amputation gave a median survival of about 11 months; 35.4% of the dogs were alive one year after surgery. Carboplatin seems to be as effective as cisplatin in treating canine appendicular osteosarcoma, but this drug is not renal toxic and therefore does not require fluid diuresis, which makes carboplatin an easier drug to administer for many private practitioners. The best time after surgery to start chemotherapy is a compromise between allowing time for surgical recovery and not allowing time for micrometastases to grow. In one study, chemotherapy was delayed for either 2 days or 10 days after amputation. No difference in survival was seen regardless of the delay, but increased toxicity was seen in the dogs treated 2 days after surgery. Most oncologists agree a delay of two weeks between surgery and starting chemotherapy is acceptable.

**Prognostic Factors**

**Serum ALP**

Multiple studies have shown an association between elevated serum alkaline phosphatase levels at diagnosis and poor survival after amputation for osteosarcoma. Total alkaline phosphatase (ALP) levels greater than the upper limit of normal range were associated with shorter survival times; 5.5 months versus 12.5 months for dogs with normal serum ALP. Bone ALP levels may be even more powerful in their ability to predict survival in dogs with osteosarcoma.
**Tumour grade**
Multiple recent studies suggest that histologically high-grade tumours are associated with a worse prognosis. 10

**Age**
In one study, age at time of diagnosis was important for determining survival in dogs treated with amputation alone. Dogs between the ages of 7 and 10 years had the longest survival times; both old and young dogs fared less well.

**Monocyte and lymphocyte counts**
A recent study found that higher numbers of circulating monocytes (>0.4 x 10^9/L) and lymphocytes (>1.0 x 10^9/L) before treatment were significantly associated with shorter disease-free interval. 12

**Summary**
Combinations of surgery and chemotherapy make osteosarcoma one of the most treatable cancers in dogs. Advances in the last 15 years have led to approximately 500% improvement in survival rates one year after amputation, and more than 1000% for 2-year survival rates, when compared to amputation alone. Amputation or limb salvage is palliative for pain but should be combined with chemotherapy for improvement in survival. Cisplatin, carboplatin and doxorubicin are the most active chemotherapy agents. Radiation therapy offers palliative pain relief if amputation is not an option.

**References**