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Bone Tumours in Dogs, Focused on the Canine Osteosarcoma. A Retrospective Study

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Contents

1. Introduction

The main motivation for my research was the unexpected diagnosis of osteosarcoma in Frida, our beloved family dog, who we had to let go of just eight days before her fourth birthday.

This thesis focuses on the prevalent issue of bone tumours in dogs, with a specific emphasis on canine osteosarcoma, a malignant and aggressive form of cancer that poses significant challenges in veterinary oncology. Bone tumours represent an important area of study due to their impact on the health and well-being of affected dogs, and understanding the histological characteristics of these tumours is crucial. Histopathology, the study of the microscopic structure of tissues, is essential for accurately distinguishing between different types of bone tumours, including the Osteosarcoma. The precision in diagnosis that histology provides is vital for determining the most effective treatment strategies and for predicting disease prognosis. Notably, canine osteosarcoma shares many similarities with its counterpart in human patients, making it not only a major concern within veterinary medicine but also a valuable model for studying the disease in humans. These similarities extend across clinical presentation, tumour behaviour, and response to treatment, highlighting the potential for cross-species insights that could advance therapeutic approaches for both dogs and humans alike.

My research hypothesises that certain demographic and clinical characteristics, including age, breed, sex, neuter status, and weight, have a significant impact on the occurrence and prognosis of osteosarcoma in dogs. Furthermore, by analysing retrospective data from two veterinary practices, this study expects to reveal patterns in the aforementioned characteristics, as well as in diagnoses, outcomes, and survival rates of dogs with suspected bone tumours, highlighting the Osteosarcoma. Thus, the aim is to offer valuable insights that either support or differ from current literature on the subject.

2. Literature review

2.1. Bone Tumours: Definition and Origin

Bones are made up of different mesenchymal tissue types, each with the capacity to turn into tumours. Primary bone tumours can thus originate from the initial stages of bone, cartilage, connective, adipose, or blood vessel tissues. The most prevalent tumours are those that come from cells which generate bone and cartilage. Tumours originating from the bone matrix (=osteoid) embrace osteosarcomas, osteomas, multi-lobular tumours, and giant cell tumours [43, 71]. The osteosarcoma and its aggressive behaviour leads to vigorous bone damage and has a malignancy rate of up to 85-90% [27, 48]. The aggressive behaviour of malignant bone neoplasia differs due to its location and the different subtypes. In high-grade cases (III), the osteoblastic subtype is more frequent than the fibroblastic osteosarcomas. Dogs of a younger age (<4y) diseased with osteosarcoma show more aggressive behaviour in grading systems than older patients. In a tumour grading system (Table 1) for osteosarcomas parameters such as the level of nuclear pleomorphism, mitosis stage, production of the matrix, tumour cell density and the level of tumour necrosis may show a correlation to the survival time of the patient [30, 40, 67].

Table 1. Classification for tumour grade determination using predetermined histologic scores for canine osteosarcoma [30]

Tumour Grade	Pleomorphism	Mitoses	Tumour Matrix	Tumour Cells	Necrosis
I	0-1 (<25%)	<10	1 (>50%)	1 (<25%)	0-1 (<25%)
II	2 (25-50%)	10-20	2 (25-50%)	2 (25-50%)	2 (25-50%)
III	3-4 (>50%)	>21	3 (<25%)	3-4 (>50%)	3-4 (>50%)

2.2. Classification and Tumour Characteristics

2.2.1. Specific Features of Bone Forming Tumours

The benign osteoma is a rarely occurring tumour characterized by its lamellar, well-differentiated, mature bone tissue structure. It predominantly occurs in the skull and mandible. Whereas osteoid osteoma and osteoblastoma have a more cellular structure and are highly vascularized, featuring immature bone and osteoid tissue [47]. These tumours are typically very small and induce a reaction in the surrounding bone. In contrast, Osteosarcoma, the most common malignant primary bone tumour, is composed of bone or osteoid tissue directly formed by tumour cells. This tumour exists in a “pure form” as well as in a “combined form”, which may also contain neoplastic cartilage, fibrous tissue, or myxoid tissue. Juxtacortical osteosarcoma, also known as parosteal osteosarcoma, originates in the periosteum. In this very rare form, the cortical bone remains intact, as demonstrated on radiographs. Histological diagnosis can be challenging, as it often presents with well-defined cartilage and fibrous tissue that can probably lead to false negative results (e.g. chondroma, osteoma, or reactive bone) [27, 47].

2.2.2. Specific Features of Cartilage Forming Tumours

In dogs, the benign form of a cartilage tumour, known as a Chondroma, is less frequent than in humans and can manifest as either solitary or multicentric lesions (enchondromatosis). It is composed of mature cartilage. The Osteochondroma is characterized by a cartilage-covered bony outgrowth on the bone’s surface, affecting the ribs, scapulae, vertebrae, and the long bone’s metaphases. In dogs, have shown instances of malignant transformation [47, 53].

Chondrosarcoma, originating from cartilage-producing cells, is the second most common malignant bone tumour in dogs. Histopathologically it is typical to find a high number of cells with altered nuclei, like larger, plump, or double nuclei with cartilaginous or mucinous content in the intercellular space. Compared to Osteosarcoma, Chondrosarcoma has a lower rate of metastasis, which varies depending on the location of the primary

tumour [27, 47]. Table 2 describes the various characteristics of the most significant tumours, including predispositions, preferred sites, and radiographic signs.

2.2.3. Hemangiosarcoma

Hemangiosarcoma, a type of malignant haemangioendothelioma, is highly aggressive and demonstrates a significant tendency to metastasize to the lungs. In dogs, bone-related hemangiosarcoma occurs in less than 2% of all canine hemangiosarcomas [27, 47].

2.2.4. Fibrosarcoma

Less than 5% of all primary bone tumours in dogs are fibrosarcomas, deriving from the connective tissue cells of the bone marrow. They are predominantly found in the axial skeleton, displaying characteristic osteolytic lesions. Distinguishing between a fibrosarcoma and an osteosarcoma with fibrosarcomatosus features can often be challenging. The prognosis for this tumour is better than that of osteosarcoma [27, 47].

2.2.5. Additional Bone Tumours

Other tumours worth mentioning include liposarcoma, giant cell tumour (osteoclastoma), and myeloma. In cases of metastatic tumours, the primary neoplasia may be located in the mammary gland, lungs, or prostate, and radiographically may exhibit similarities to osteosarcoma or other malignant bone tumours [47].

2.2.6. Tumour-like Lesions

Tumour-like lesions such as exuberant fracture callus, multiple cartilage exostosis, and fibrodysplasias, are discussed. Various kinds of bone cysts, including solitary, aneurysmal, or subchondral cysts, can also be noted. These tumour-like lesions, as well as benign bone tumours, display very similar radiographic features, requiring thorough diagnostics to differentiate accurately [27, 43].

Table 2. Differential diagnostic overview of predispositions, frequent primary locations, and radiographic characteristics of the most important tumours with bone involvement in dogs [27]

Type of tumour	Predispositions	Predilection site	Radiographic characteristics
Osteosarcoma at the limbs	Large and giant breeds	Metaphysis of long bones	Mixed osteolytic and osteoproliferative, sunburst-like periostal spiculae
Osteosarcoma of flat and short bones	Small and mid-sized breeds	Jaw, Skull, Ribs, Vertebrae	Mixed osteolytic and osteoproliferative, rarely purely lytic or proliferative
Chondrosarcoma	Large breeds, Shepherd, Boxer, Retriever	Nasal cavity, ribs, skull, rarely long bones	Primary osteolysis, occasionally periostal reaction, clowdy calcification zones
Fibrosarcoma	Large breeds	Jaw, rarely appendicular skeleton	Osteolysis, ulceration (oral mucous membranes), appendicular: mainly osteolytic
Hemangiosarcoma	Large breeds, potentially Great Danes	Appendicular and axial skeleton, potentially proximal humerus	Almost exclusively lytic
Multiple myeloma	Shepherd	Spine, pelvis	Multiple lytic lesions, “moth-eaten” similar, as punched
Synovial cell tumour	Large breeds	Joint proximity, especially Knee, Elbow, Tarsus	Joint near soft tissue mass with osteolysis and periostal reaction in all joint involving bones

2.3. Epidemiology of Bone Tumours in Dogs

In dogs, the prevalence of primary bone tumours is much higher than in human patients. An estimated frequency of 13.9 out of 100.000 in canine domestic animals and a much lower incidence of human patients of 1.02 out of 100.000 shows the marked difference [45, 61]. In Norway for example the incidences of diseased large and giant breed dogs were between 0.2 and 8.9%, depending on the breed [2].

In general, osteosarcoma occurs in middle-aged to older dogs with a mean age of around 7 years [27]. A lower mean age (5.4 years) was detected in dogs with osteosarcomas located in the rib region [26]. Between the age of 18 and 24 months, the probability of osteosarcoma occurring is also described, as a dual-peak [46]. Height, more so than weight, plays a significant role as a risk factor, as discovered by [62]. The metaphyseal part of the bone appears to be the site of preference for osteogenic sarcoma. When comparing the incidence of the tumour across the limbs, it is observed that the forelimbs exhibit a higher frequency of cases, around twice more often than the hindlimbs. Within these, the proximal humerus and the distal radius are the regions most commonly affected. Osteosarcoma is infrequently present close to the elbow and as a central diaphyseal lesion in the bone. In cases where osteosarcoma occurs in the hindlimbs, it is most commonly found in the distal femur, proximal tibia, and distal tibia. The proximal femur is also affected, albeit less frequently [48, 49, 63, 71]. There is a different behaviour observed between osteosarcomas occurring at the axial and the appendicular skeleton. Lower metastasis risk is seen in the case of axial skeleton bone neoplasia [24, 55, 57]. Taking all breeds into consideration, 75% of osteosarcomas affects the appendicular skeleton and 25% affects the axial skeleton which includes the bones of the skull, the mandible, and the maxilla, as well as the spine, rib, sternum, or pelvis. In 95% of instances for giant breed dogs, bone neoplasia is found in the appendicular skeleton. Whereas in dogs with a weight lower than 15 kg osteogenic neoplasia is diagnosed in the axial skeleton in 60% of cases [26, 27]. A retrospective study of 1462 animals described the distribution of appendicular occurring tumours in larger and heavier dogs and the axial occurring neoplasia in lightweight animals [32].

In general, the rate of sex distribution in the case of Osteosarcoma is marginally higher in males than in females. Notably, it is nearly balanced in human patients, too [27, 54, 71]. In

the case of axial skeleton osteosarcomas of a retrospective study with 116 dogs, female dogs exceeded males in a ratio of 2.1:1 which differed due to the site of the tumour. Neoplasia affecting the spine or the rib was more frequent in males [26]. Breeds known as predisposed are Rottweiler, German Shepherd, Great Dane, Boxer, Saint Bernard, Dobermann, Irish Setter, and Golden Retriever [46]. In Sweden, studies of 764 diseased dogs showed the highest incidence in Irish Wolfhounds, Saint Bernard, and Leonberger [14]. A case-control study in the United Kingdom identified a previously unknown predisposed breed, the Rhodesian Ridgeback. Again, Rottweilers and Great Danes were conspicuous risk breeds, as well as Greyhounds. The study showed higher incidences of Osteosarcomas in purebred dogs than in crossbreeds. It is worth noting that a genetic predisposition is evident, particularly among breeds with large body mass and tall shoulder height. Important to mention that the breed population is changing, which automatically influences the ranking of at-risk breeds [13, 27, 62].

2.4. Aetiology and Risk Factors

In general, the aetiology of bone tumours, especially osteosarcoma in dogs and humans is not known. It is believed that various factors interact with the appearance of the osteosarcoma. These factors include the environment through physical and chemical influences, hereditary predisposition, and acquired genetic mutations [17, 27, 71]. For a long time, it was assumed that numerous microtraumas and injuries to the growth plates in large dogs were possible causes of osteosarcoma. It must be said that this tumour occurs more frequently in the weight-bearing limbs and near the late-closing growth plates. Nowadays, however, it is reported that there are no conspicuous micro-injuries and osseous remodelling signs in the affected osteal zone. This factor can therefore be discounted as a possible reason. The aetiology described traumatic- or fracture-related bone tumours. Also ionizing radiation might be a physical factor for the development [20, 27, 71].

Exposure to ionizing radiation has been implicated in the onset of osteosarcoma in canines, observed in various therapeutic and experimental contexts. Cases have been documented where beagles, after exposure to aerosolized plutonium dioxide, exhibited Osteosarcomas in the respiratory system, skeleton, and hepatic tissue. Similar developments have been reported after intravenous administration of Plutonium citrate or Americium [38, 39, 51]. In the case of radiation therapy, one instance involved a vertebral Osteosarcoma five years

post-treatment with Cobalt for a spinal cord tumour. Additionally, a study revealed that 21% of dogs treated with intraoperative radiation therapy (of over 25 gray [Gy]) to the spine, occasionally complemented by external radiation, were found to develop OSA within four to five years after the therapy [9, 59].

The body may react to metallic agents with an inflammatory or foreign body response. In addition to potential complications such as infections, allergic reactions, and, significantly for my thesis, described carcinogenic effects. A case study of 7 dogs and 1 cat described bone neoplasia occurrence after fracture treatment with implants for orthopaedic surgery. The most suspicious implant was the 'Jonas intramedullary splint', which was utilized in 5 out of 8 cases. The in-place period varied from 6 months to 6 years and all tumours were located in the diaphysis of the bone. The other used implants include a 'Steinmann pin' with hemicerclage and an Arbeitsgemeinschaft für Osteosynthesefragen (AO) Plate [64]. Studies described the transformation of the surroundings close to metallic implants or earlier fractures. Proposed explanations for these changes include the direct influence of the metal implants, the risk of infection, instability of the implant, and corrosion. [19, 66] Nevertheless, due to the frequent use of orthopaedic surgical implants and no firm conclusions regarding the impact on sarcoma development, the appearance of cancerous growths in the same location may simply be a coincidence [52].

Regarding this topic, it is noteworthy that three of the animals in my study exhibited abnormalities suggestive of a potential link between implants and the development of bone tumours. Figure 1 displays the tibial bone of a Kangal-Crossbreed dog in 2021. This radiograph was taken after the removal of an implant, which was indicated by signs of lameness, and a painful, weakened bone. The osteosynthesis plate had been utilized for fracture treatment 8.2 years prior (in 2013). The second figure demonstrates the leg post-amputation, with the diagnosis confirmed to be osteosarcoma.

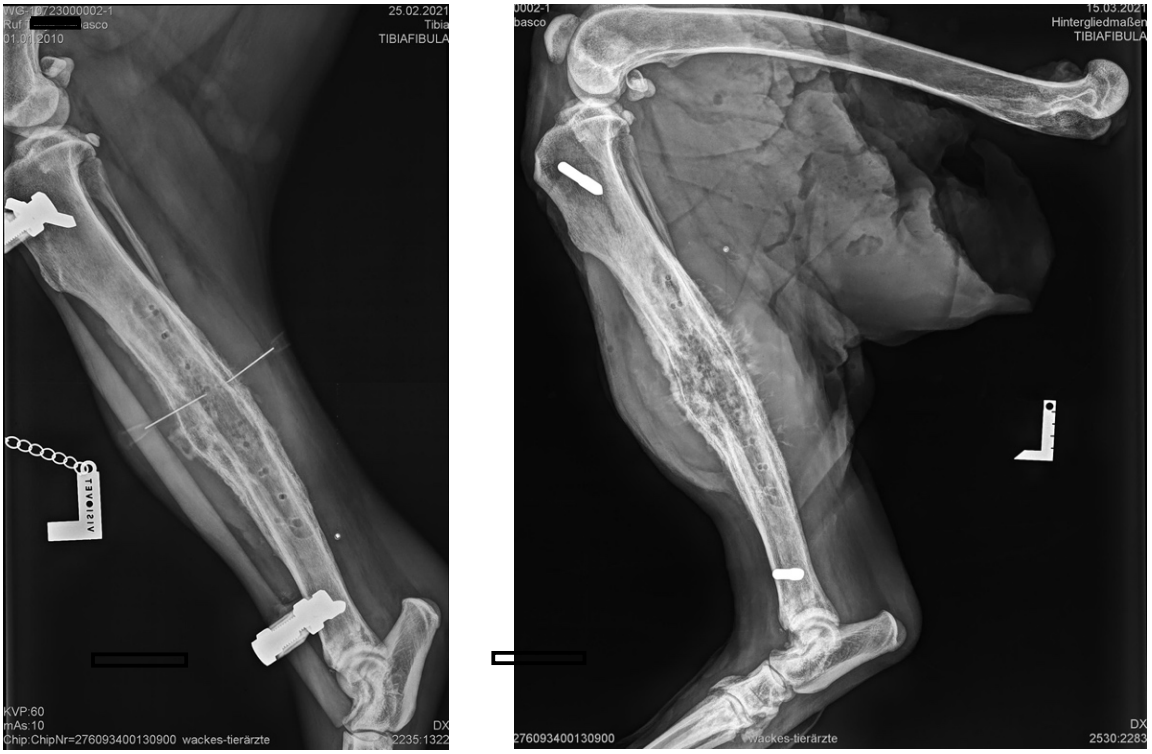

Figure 1 & 2. Radiographs of a confirmed osteosarcoma case after implant removal of fracture treatment seven years earlier (2.) same leg post-amputation, one month later (Data pool of Veterinary practice Wackes-Tierärzte).

In the field of human medicine, occasionally there have been instances where sarcomas have developed within scarred tissue resulting from surgical procedures that were performed to address traumas or burns caused by thermal or chemical agents. Similar observations have been made regarding fractures, particularly those in proximity to synthetic, metal, or assorted biomaterial implants. Usually, such sarcomas manifest after a multi-year latency period [1, 29, 56]. Skeletal disorders that include alterations in bone structure as a result of bone infarcts or chronic osteomyelitis represent risk factors for osteosarcoma emergence in both canines and humans. Cells that proliferate quickly might have a higher vulnerability to cancer-causing agents and mistakes during cell division that can result in transformation [54]. Paget's disease, a skeletal disorder associated with Osteosarcoma in humans, is worth noting. In this disease increased osteoproliferation is seen and it is recorded in more than 20 percent of Osteosarcoma patients over the age of 40. In dogs, this disease has not been described, but the occurrence of osteosarcoma in bone-infarct diseased dogs can be considered similarly [17, 42, 54].

Genetic alterations have also been shown to be risk factors for the occurrence of osteosarcomas [49, 71]. The first study in dogs evaluates the prognostic relevance of *TP53* gene mutations in a sizable group of patients with sufficient follow-up information. In total 27 dogs with an alteration of the *TP53* tumour suppressor gene showed a decreased survival time compared to those without mutation [31]. Other studies also showed relations between the *TP53* alteration and tumour behaviour, as higher aggressiveness, and higher tumour grade. Other correlations such as Phosphatase and tensin homolog (PTEN) tumour suppressor gene alterations, as well as various growth factors, have been observed in Osteosarcoma samples [41, 49]. Due to the presence of around 80% ezrin, a membrane cytoskeleton linker, a shorter median disease-free period was observed. It is implicated to be part of the metastasis process [28]. The Activation of transcription 3 (STAT3) and signal transducer has been described to be apparent in canine osteosarcoma samples, but not usual in osteoblasts [18].

In Humans, factors for the development of osteosarcomas include the faster growth rate of bone in adolescence [15], cytogenic abnormalities, chemical exposure, mutations in the *TP53* gene and the retinoblastoma gene, as well as some syndromes for instance the Bloom Syndrome. Additional associations with higher risk are dysregulation of cell signalling and kinase pathways for example vascular endothelial growth factor or platelet-derived growth factor and more [49].

2.5. Natural Behaviour

The formation of a tumour happens due to dynamic changes in the genetic makeup of healthy cells, resulting in shifts in cellular functioning. Six crucial changes in cell physiology together determine the malignant progression. These are self-sufficiency in growth signals, evasion of programmed cell death (apoptosis), limitless replicative potential, sustained angiogenesis, and tissue invasion and metastasis [23].

Due to the highly aggressive behaviour of the osteosarcoma, which I already mentioned above, signs of osteolysis, proliferation of the bone or even both of these effects are represented [71]. The invasion and degradation of spongy bone lead to gradual cortical bone destruction, which may result in a pathological fracture. With sclerotic bone thickening in the medullary cavity and periosteal bone formation, the bone tries to counteract this and build up stability. These processes are considered to be typical radiographic signs of this type of neoplasia [27]. Although the frequent location of osteosarcomas is at the metaphysis, they infrequently spread beyond a joint surface. This limitation within the bone might be due to collagenase inhibitors that restrict its passage through the synovium [4, 34]. Exceptionally, extension into the pelvis through the ligament proprium is possible if the tumour is located in the proximal femur [27].
Nearly 90 per cent of dogs diagnosed with osteosarcoma have a metastatic condition at the first time of diagnosis, but only about 10 per cent exhibit clinical signs of metastasis in this early stage [7]. The frequent metastasis occurs mostly sub-clinically and through the hematogenous route, rarely to the regional lymph nodes. The most prone organ for metastasis is the lungs but there is also the possibility of occurrence in other osseous tissue, visceral organs, the brain, subcutaneous tissue, and the skin [22, 71]. A 6-year-old Rottweiler with osteosarcoma on the distal radius reported cutaneous metastases 4 weeks after initial diagnosis, an occurrence rarely described. A similar case is a 3-year-old Rottweiler with several cutaneous metastases after diagnosis of osteosarcoma of the distal femur [8, 22]. Regarding a study of 116 axial skeletal osteosarcoma cases described a higher incidence of pulmonary metastasis with the tumour located within the skull and the lowest located in the maxilla, rib, and nasal cavity [26]. The frequency of bone metastasis is on the rise. This trend may be attributed to alterations in the tumour's behaviour

following chemotherapy. Research indicates that approximately one-third of dogs previously treated with Doxorubicin exhibited bone metastasis upon euthanasia [27, 71].

2.6. Clinical Signs

Typically, in dogs with Osteosarcoma in the appendicular skeleton, progressive lameness and swelling of the leg are seen. If a mass adjacent to the bone tissue is palpable, it is firm-to-soft and it tends to be painful. An initially mild, later intermittent, and with time chronic and severe lameness can be seen. An acute non-weight-bearing lameness is usually related to a pathological fracture [70, 71]. One of the first ideas for the diagnosis, when a large to giant-breed dog with lameness and/or a mass adjacent to the metaphysis of the bone is presented, would be bone neoplasia and especially Osteosarcoma.

If osseous tumour development occurs in the axial skeleton, the clinical signs differ from those of neoplasia affecting the limbs. If the tumours occur in the ribs, it can involve the pleura, leading to effusion that can result in breathing difficulties. Portions of the tumour can also be located within the thoracic cavity [16].
Depending on the site of the neoplasia, it is possible that signs such as exophthalmos, chewing and/or swallowing difficulties, and deformities can be seen. If the tumour invades nasal cavities or sinuses, a typical sign would be unilateral, bloody discharge. Disorders of the central nervous system can occur if the tumour affects the patient's spinal sites. Systemically symptoms are described, due to alterations in protein synthesis, carbohydrate flux, and other metabolic pathways. Also, muscle atrophy and cachexia can occur [43, 71].

In making a differential diagnosis, consideration should also be given to other primary bone tumours like chondrosarcoma, fibrosarcoma, and hemangiosarcoma. Should these neoplasias be ruled out, the possibility of bone metastases, primary extra-skeletal, and benign tumours should also be considered. Additionally, infectious conditions such as bacterial, fungal osteomyelitis, and Leishmaniasis involving the bone could be a possibility with similar symptoms. A degenerative, reparative, or autoimmune bone lesion must also be mentioned [27].

2.7. Diagnostic Methods

2.7.1. Diagnostic Imaging

Advanced imaging techniques such as CT and MRI are increasingly utilized, often providing initial diagnostic guidance, and influencing treatment plans. However, a definitive diagnosis typically requires a biopsy and a histopathological analysis. Radiography and CT can comprehensively visualize lesion extent and affected bone, offering more aggressive bone neoplasia indications compared to histopathology [10, 43]. Some useful morphologic characteristics to show malignancy and non-malignancy encompass signs of bone destruction, calcification of the tumour or periosteal response, as well as cortical signs, such as erosion, expansion, or penetration of the cortex [43].

By using radiographic examination, we may check:

- whether the lesion is solitary or involves more than one bone;
- the specific location and scope of the lesion within a bone (epiphyseal, metaphyseal, or diaphyseal) and whether it is intramedullary or not;
- the type of bony alterations occurring (including osteolysis and/or sclerosis);
- the opacity of the tumour tissue; the bones' reaction to the tumour;
- the kind of changes in the bone surface can include the destruction of the cortical and formation of periosteal bone;
- the impact of the surrounding tissues, and if a joint is involved [43].

Characteristics of an osteosarcoma radiograph are osteolytic and osteoproliferative signs. Frequently seen is a soft tissue extension with soft tissue swelling, and new bone formation. It has to be distinguished whether it is tumour-new-bone or reactive-new-bone [12]. These regions are in an aligned arrangement, either perpendicularly or spreading outwards from the centre of the cortex, resembling the pattern of a so-called "sunburst" [71]. Tumour infiltration into the cortex leads to the lifting of the periosteum and new bone formation by the inner layer of the periosteum (cambium). This process results in a triangular-shaped accumulation of dense new bone along the edges of the lesion on the cortex. It is called "Codman's triangle". It is not indicative of osteosarcoma, but it is

commonly associated with it [60, 71]. In comparison to reactive-new-bone, tumour-new bone is not that organized and looks more like nests, or numerous spots of dense bone [12]. For bone destruction, there are three typical patterns described: the geographic pattern which shows clear margins from the normal bone. Sclerosis and extended cortex may be present. The geographic pattern is mainly seen in benign tumours but can be present in a few malignant tumours as well. Further intense bone destruction, described as a motheaten pattern, suggests a more gradual transformation of normal to abnormal bone, which indicates a more aggressive pattern of destruction. This pattern is found in malignant bone neoplasia and osteomyelitis. Also, it may be detected in some benign cases. A highly malignant tumour such as osteosarcoma, can present challenges in distinguishing affected and unaffected bone. This is due to the rapid growth and invasion, resulting in diffuse margins, known as the permeative pattern [43, 71]. For the diagnostic imaging of the suspected lesion, a cranio-caudal and latero-medial projection should be taken. The joint near the suspected lesion must be projected as well, to see if there is joint involvement [49, 71]. To screen for metastasis, which typically occurs in the lungs, thoracic radiographs are required in different projections. For this, three views are necessary, a right and left lateral, and a dorsoventral x-ray [35, 58]. In a study of 171 dogs diagnosed with osteosarcoma, 11 dogs exhibited extra-thoracic metastases, while 7 dogs demonstrated lung metastases. Scintigraphy enables the detection of very small metastases and lesions, making it a valuable diagnostic tool for staging and preoperative identification of bone metastases [27]. An image-guided biopsy sampling, as in Figure 3, can be favourable for the sample quality and, consequently, cytological and histopathological results [10]. CT and MRI allow for whole-body bone scans to be performed, which are commonly used for human patients. To check for metastatic spread, CT scans are utilized, and for humans, PET-CT scans of the lung are conducted in specific cases [50].

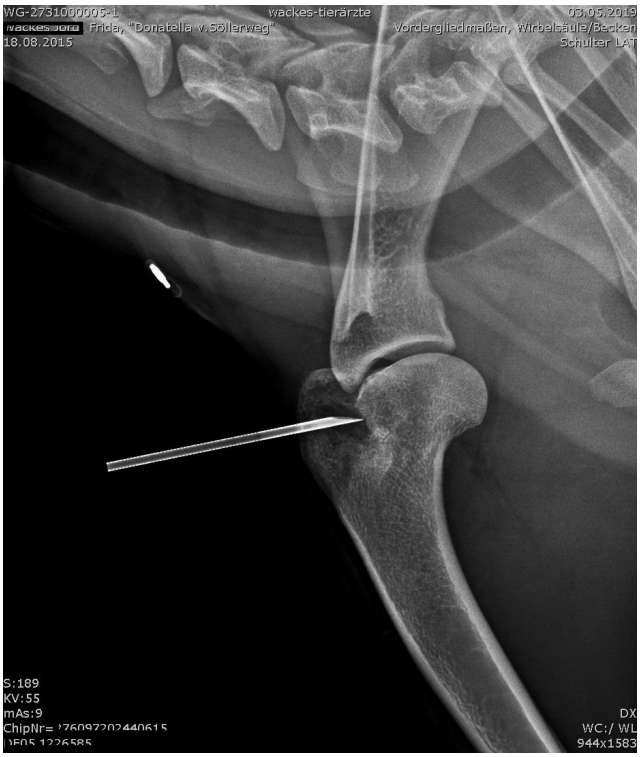

Figure 3. Radiographically guided biopsy sampling of an osteosarcoma of a 3,9 years old, female, Lagotto Romagnolo (Data pool Wackes-Tierärzte).

2.7.2. Cytology

Fine needle aspiration (FNA) of the suspected lesion can assist in initial diagnosis. When clinical signs, medical history, physical examination, and digital diagnostic imaging collectively indicate a bone tumour, cytology can effectively contribute to the diagnosis. Furthermore, using alkaline phosphatase (ALP) staining on the samples can facilitate the differentiation of sarcoma cells from other primary bone tumour cells. Cytology offers benefits such as the requirement for less anaesthesia and a reduced risk of complications such as infections, bleeding, and tumour implantation along the biopsy tract [43, 49, 71]. A study utilizing sonography for fine needle aspiration of bone tumours showed that cytopathology had a sensitivity of 97% and a specificity of 100% for the diagnosis of bone sarcoma [5].

2.7.3. Histopathology

If suspicion of a tumour or uncertainty about a tumour's characteristics and severity persists following non-invasive diagnostics, it is advisable to conduct a histopathological examination of a tissue sample. The sampling is important in the case of taking biopsies for histopathological diagnosis. Usually, for the best result, two full-core samples are needed. One of them should be taken from the centre of the lesion, and the other one should be taken from the margin of the transition area [60]. There are different possibilities for getting samples of the suspected region of the bone. Performing an open incisional or a closed technique, with Jamshidi needle or Michelle's trephine. An open incisional biopsy is beneficial for achieving a precise histologic diagnosis, as it allows for a larger tissue sample [49, 71].

If the biopsies of the bone are small it can be difficult to distinguish between osteosarcoma and other types of bone tumours, due to no osteoid or only a small amount is present. However, the main issue for differentiation is the lack of osteoid. In the case the main matrix demonstrated is of cartilaginous character, it might correspond to a chondrosarcoma or chondroblastic osteosarcoma. Correspondingly, it could be said, that if the main cells of detection are of pleomorphic spindle cells and collagen, it may align with a fibrosarcoma or a fibroblastic osteosarcoma [10]. Reaching a definitive diagnosis can be complex, particularly in distinguishing between reactive bone and cancerous disease processes, and among different forms of bone sarcomas. Nevertheless, employing a comprehensive approach involving an assessment of the signalment, medical history, clinical presentation, radiographic findings, and microscopic characteristics may lead to a preliminary diagnosis. The pathologist benefits from interpreting bone samples by utilizing the imaging results. It is recommended for pathologists always to request imaging results if not provided by referring veterinarians [10].

2.7.4. Labor diagnostics

Hematologic parameters, like alkaline phosphatase (ALP), may show an increase in both total and bone-specific ALP levels, which can be associated with a shorter survival time and therefore poorer prognosis [43, 49]. N- Telopeptid acts as a marker of bone resorption. Increased levels of N-Telopeptid in both serum and urine can serve as a diagnostic indicator for osteosarcoma [27].

2.8. Treatment

For achieving the longest median survival times, chemotherapy and surgery combined do give the most favourable outcomes. In human patients, it is common to administer neoadjuvant chemotherapy prior to surgery followed by postsurgical adjuvant chemotherapy. For the systemic chemotherapy in canine patients' platinum- or doxorubicin-related protocols are frequently utilized, typically delivered in 3-6 cycles post-surgery [50]. To reach constant local disease control, surgery is essential [69].

2.8.1. Surgery methods

The local staging extent is influenced by the intended treatment choice, whether it involves amputation or limb-sparing techniques. Radiography is typically sufficient for assessing margins in most of the tumours affecting the appendicular skeleton or mandible. When dealing with sites in the axial skeleton, more comprehensive preoperative imaging like computed tomography (CT) or magnetic resonance imaging (MRI) is often beneficial [69]. If the medical history, physical examination, and diagnostic imaging lead to the suspicion of a primary tumour, surgery can be done without a prior biopsy. However, the excised tumour ought to undergo histological analysis after the surgery. This procedure confirms the successful removal for prognosis assessment and reinforces the initial diagnosis as needed [25]. For the survival time after surgery, there are no statistical differences described between amputation and limb-sparing technique, if sufficient systemic chemotherapy is administered [68]. Preoperative, using a combination of cisplatin chemotherapy and radiation has demonstrated positive outcomes in reducing the

advancement of osteosarcoma [69]. The average survival time post-surgery, which on its own is described as a palliative treatment, ranges from 103 to 175 days [49].

2.8.1.1. Amputation

Limb amputation is the conventional local therapy for dogs with appendicular osteosarcoma. Despite the assumption that large dogs might struggle on three legs, the reality proves otherwise. Dogs with three limbs quickly adapt, often exhibiting similar mobility and life quality as those with four legs. This approach is not recommended for severely obese animals or those with known orthopaedic or neurological conditions. Therefore, a thorough examination before surgery is crucial [49]. Complete hind-leg amputation, a coxofemoral disarticulation, is required for most femoral osteosarcoma. If the neoplasia is located in the proximal part of the femur, the en-bloc acetabulectomy is advised to reach wide enough margins. In the case of tibial location, an amputation is necessary as well [69, 71]. Amputation without chemotherapy should be regarded as a palliative measure, due to the occurrence of micrometastasis prior to surgery [65].

2.8.1.2. Limb-Sparing-Surgery

If the neoplasm is relatively small and does not extensively affect soft tissue, limb-salvage surgery can be an effective option. The distal radius is the preferred site for this surgery, due to favourable outcomes in limb function. Defecting the bone by removing the tumour, reconstruction with an allograft or prosthesis becomes necessary, along with arthrodesis of the adjacent joint [58]. The option of preoperative treatment encompasses primary or neoadjuvant intra-arterial, or intravenous cisplatin, radiation therapy, or a combination of both. These preoperative methods are associated with reduced vascularization and increased tumour necrosis [17].

A careful procedure is necessary when taking samples prior to a limb-sparing surgery. Focus on asepsis, bleeding control, and proper wound closure [71]. To assess a tumour's spread within the bone's medulla, MRI is the most detailed and thus the preferred method prior to planning limb-sparing surgery [49]. Several methods can be employed as

alternatives to amputation for limb preservation. The bony defect resulting from tumour resection can be filled by using a frozen cortical allograft, an endoprosthesis, or with the excised tumorous bone treated by pasteurization, irradiation, or autoclaving. Fixation is achieved with a plate and screws. Frequent issues linked with these methods consist of tumour recurrence (15-28%), failure or loosening of the implant (11-40%), and infection (31-60%) [49]. In a study, the majority of dogs undergoing limb-sparing surgery experienced wound infections. Interestingly, this outcome positively correlated with longer survival times and delayed metastasis. The average survival time following limb-sparing surgery with wound infection is reported to be 685 days, whereas, without infection, it is 289 days [36, 37].

2.8.2. Adjuvant Chemotherapy

The adjuvant setting is the time immediately after resection of the primary tumour. A certain form of chemotherapy, adjuvant chemotherapy allows decreasing the rate of relapse from micrometastatic disease. Evidence described that a certain form of chemotherapy gives a better result with microscopic tumours than with macroscopic tumours. Common agents used for adjuvant treatment to control micrometastasis are cisplatin, carboplatin, and doxorubicin. Research indicates an average survival rate of 12 months for dogs treated surgically followed by chemotherapy [21, 69].

2.8.3. Palliative Treatment

Palliative treatment is an option, if the tumour is inoperable, the owners do not want surgery or chemotherapy, or it has already metastasized. In that case, it is possible to manage symptoms like pain and lameness with NSAIDs and other analgesics, which can as well enhance the quality of life. In addition to that, radiation therapy can be used as well as palliation. It helps reduce the inflammation and leads to necrosis of the tumour cells. It comes to replacement due to fibrous tissue, as well as formation, and calcification of the bone [50].

2.8.4. Prognosis

Due to the utilization of a well-established multidrug adjuvant protocol, a notable advancement in the survival rates in humans has been observed. Typically, older age, tumour location in the axial skeleton, a larger affected area, and reduced necrosis after neoadjuvant therapy tend to have an unfavourable effect on the prognosis. Limb-sparing options are increasing, and many individuals retain fully functional, pain-free limbs, but the need for effective systemic treatments to improve survival is of particular significance [71]. The location of the tumour is an important factor in the prognosis. It can be said that the proximal humeral location is a noteworthy negative prognostic factor for humans and dogs. Additional factors related to the survival of an osteosarcoma patient are the presence of metastasis, the use of adjuvant and/or neoadjuvant chemotherapy, and postoperative infection at surgical sites after limb-sparing surgery or amputation [3, 17].

2.9. Human vs. Domestic Animals: Main Differences

The highly malignant bone tumours in dogs have the highest incidence of being primary tumours among domestic animals. The canine osteosarcoma has an incidence of around 8000 to 10 000 per year. Whereas in humans the incidence amounts 600 to 1000 per year [17, 49]. The incidence of osseous neoplasia in dogs is significantly higher compared to humans, with rates reported to be around 10 times greater in the United States and 27 times higher in Sweden. In contrast to humans, where benign and secondary tumours are more common, metastasis in the skeletal system of domestic animals, including dogs, is less commonly observed [11, 14, 43]. Although the physical characteristics and biological traits of canine osteosarcomas resemble those of human osteosarcomas, the age and location of occurrence differ. In the case of canines, this disease is more frequently observed in middle-aged to older patients (7-9 years), sometimes in the age of 18 to 24 months. Whereas in humans, it is most commonly associated with adolescents between 10-20 years of age [17, 49, 54]. In both species, there is an association between developing osteosarcoma and large dogs, and more frequently, taller humans [13, 44]. The metaphyseal zones of the weight-bearing bones are the main sites of occurrence in dogs and in humans, including the distal femur, proximal tibia, and proximal humerus. In dogs, the forelimbs are more susceptible to osteosarcoma due to the plantigrade locomotion and

distribution of weight in their anatomy. The distal radius and proximal humerus are more frequently affected. Conversely, in humans, these tumours typically occur nearer to the knee [21, 33]. Without chemotherapy, canine osteosarcoma shows a higher metastasis rate, with approximately 90% occurring within a year or less. In humans, the likelihood is around 85-90% within two years or less. Another key difference lies in the survival rates; with chemotherapy, it is around 60% at 1 year for dogs, while in humans, the survival rate reaches 70% at 5 years [17, 49]. In therapy, the proportion of amputation to limb-preserving surgeries varies; dogs more frequently undergo amputation, while limb-preserving techniques are preferred in human patients.

3. Material and Methods

The objective of my study was to survey cases of dogs affected by suspected bone neoplasia and analyse potential association with age, breed, gender, neuter status, and weight parameters. However, due to difficulties in collecting trauma-related data, which was my first intention to analyse, I chose to focus on the other parameters and searched for any conspicuous features in contrast to the literature I found.

3.1. Study Design

The objective of this retrospective study was initially to investigate potential correlations between juvenile traumas and the subsequent development of bone tumours in dogs. However, the difficulty in obtaining reliable data on past traumas within the available data pool necessitated a shift in focus. Consequently, the study expanded to include a wider range of parameters, sidestepping the trauma-neoplasia correlation due to the insufficiency of relevant data. All instances selected for the study involved dogs with any indication or suspicion of bone neoplasia, recorded over a 12-year period, from November 4, 2010, to November 4, 2022. The study analysed cases from two veterinary institutions in Southwest Germany: The Veterinary Surgery ‘Wackes-Tierärzte’ in Gundelfingen and ‘Kleintierklinik Frank’ in Freiburg im Breisgau.

3.2. Data Collection

All relevant data were collected from the medical records of the Vetinf software at ‘Wackes-Tierärzte’ and the Vetera software at ‘Kleintierklink Frank’. The inherent challenge encountered during the data collection phase was the limited willingness among pet owners to pursue beyond a preliminary diagnosis, leading to only 18 cases being confirmed via histopathology as osteosarcoma. Reasons for the low number of histopathologically confirmed diagnoses include the costs and the cautious to poor prognosis. Despite this, both confirmed and unconfirmed cases were included in this study

to widen the study's scope. However, the importance of histopathology for a better prognosis and treatment must be noted. Many of the documented cases involved previously examined animals by other veterinarians which had been sent for further diagnostics or for a second opinion. Information was diligently organized and prepared for analysis in Microsoft Excel, with all relevant details provided by the participating veterinary surgeries. The parameters included in the study were weight, age, gender, neutering status, age at first suspicion of neoplasia, date of death if recorded, diagnostic methods performed, location of the tumour, detection of macrometastasis, and occurrence of a pathologic fracture. The procedure for collecting the data in the respective systems of the providing surgeries proceeded as follows. In the Vetinf software, it was only possible to search for a diagnosis. Such as osteosarcoma, chondrosarcoma, bone tumour, pathologic fracture, implant reaction, bone metastasis, osteomyelitis, osteofibrosarcoma, … additional in the Vetera software I had to look up for every word which could possibly have been written in the patient file, in combination with the diagnosis of bone tumour. I collected for the same as in the other software, plus all the prefixes, like 'osteo' or 'osteosar', 'osteochondr', 'osteofibro'.

Additionally, it is important to mention that only a minority of the cases were confirmed via histopathological examination to differentiate bone tumours. This discrepancy is largely attributed to the reluctance of many pet owners to pursue further diagnostics, often deterred by the associated costs and the guarded to poor prognosis generally associated with bone cancer. This limitation underscores the challenges faced in the definitive diagnosis of canine bone tumours.

3.3. Statistical Analysis

The collected data were entered into a table using the program Numbers (spreadsheet). Afterwards, the data cleaning and formatting were performed in the Microsoft Excel Program. Also, for the statistical analysing, the program Microsoft Excel 365 MSO Version 16.82 was used.

4. Results Overview

4.1. Descriptive Statistics

In this retrospective study, a descriptive analysis of 176 dogs has been performed. Out of these, 104 (59.1%) were female of which 55 (52.9%) were neutered. Whereas 72 out of 176 dogs (40.9%) were male, and 31 out of these 72 (43.1%) were neutered (Figure 4). Out of 176 dogs, a limitation of 13 cases without recorded weight, the mean±SD weight (n=163) was 35.74 ± 13.76 kg, the minimum weight was 3 kg, and the maximum weight of a dog was 75 kg.

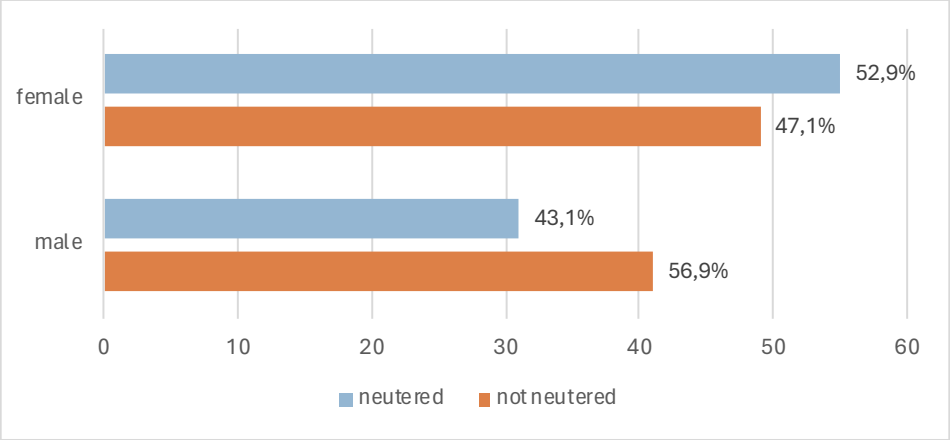

Figure 4 Gender and neutering status (n=176)

The mean±SD age of the animals at the time of first suspicion was 9.23 ± 3.04 years. The youngest animal was 1 year old, and the oldest was 15 years old. It can be said that most dogs with 16.5% (29/176) were around 10 years of age. Interestingly 3/176 (1.7%) were not older than one year (Figure 5.).

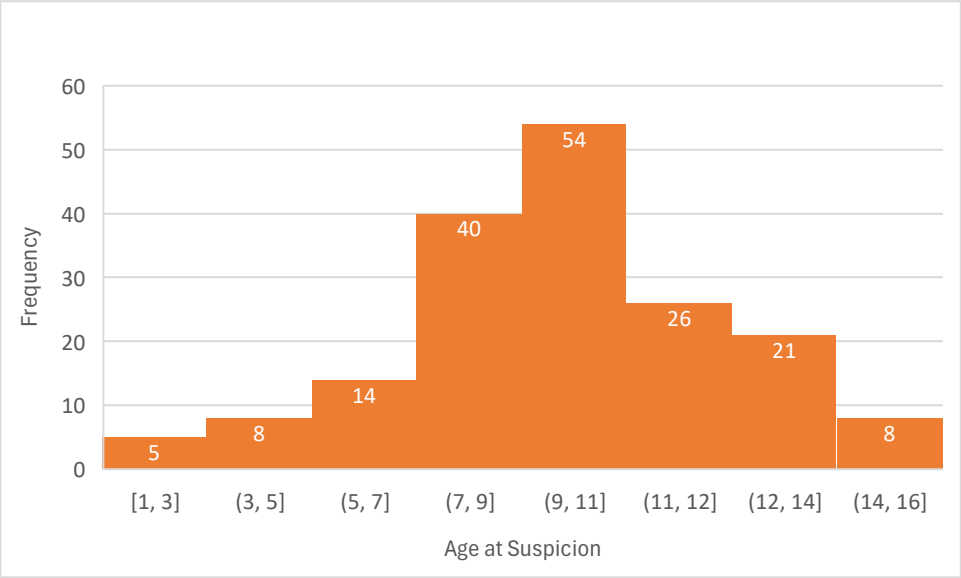

Figure 5. Distribution of the age at suspicion (n=176)

4.1.1. Breed Analysis

For clearer organization, I classified the various breeds into 41 groups, encompassing 5 major 5 subgroups: 'Dane', which included the German Dane, Great Dane, Bordeaux Dane, and Antique Dane. Among these groups, the 'Mountain Dog' subgroup stood out, comprising the Bavarian, Bernese, Swiss, and Pyrenean Mountain dogs, as well as the Swiss Appenzeller and Berger des Pyrénées. The 'Greyhound' subgroup encompassed Afghan, Chart Polski, Greyhounds, and Galgo breeds. Combining the small, medium, and giant Schnauzers, the 'Schnauzer' group was formed. The largest group, 'Crossbreed', encompassed all types of crossbreed dogs, representing also the largest affected group among the 176 dogs in my research (Figure 6.).

In terms of statistical analysis, breeds occurring three times, or more were presented individually. Additionally, I grouped together breeds that each had a frequency of ≤ 2 times under the category 'Further Breeds'. As mentioned earlier, crossbreed dogs were the most commonly affected in the study, with 59 out of 176 (33.5%). Following this, the 'Further Breeds' group accounted for 31 out of 176 (17.6%). Rottweilers were the second most frequently affected breed with 20 out of 176 (11.4%), followed by Labradors with 13 out of 176 (7.4%). The Golden Retrievers were present in 7 out of 176 (4%). Mountain dogs were represented by 10 out of 176, equivalent to 5.7% of the total. Both Danes and

Greyhounds totalled 6 out of 176 (3.4%), while Leonbergers and Rhodesian Ridgebacks comprised 5 out of 176 (2.8%) and 4 out of 176 (2.3%), respectively. Breeds like Schnauzers, Shepherds, Hovawarts, Irish Wolfhounds, and Newfoundlands each accounted for 3 out of 176 (1.7%).

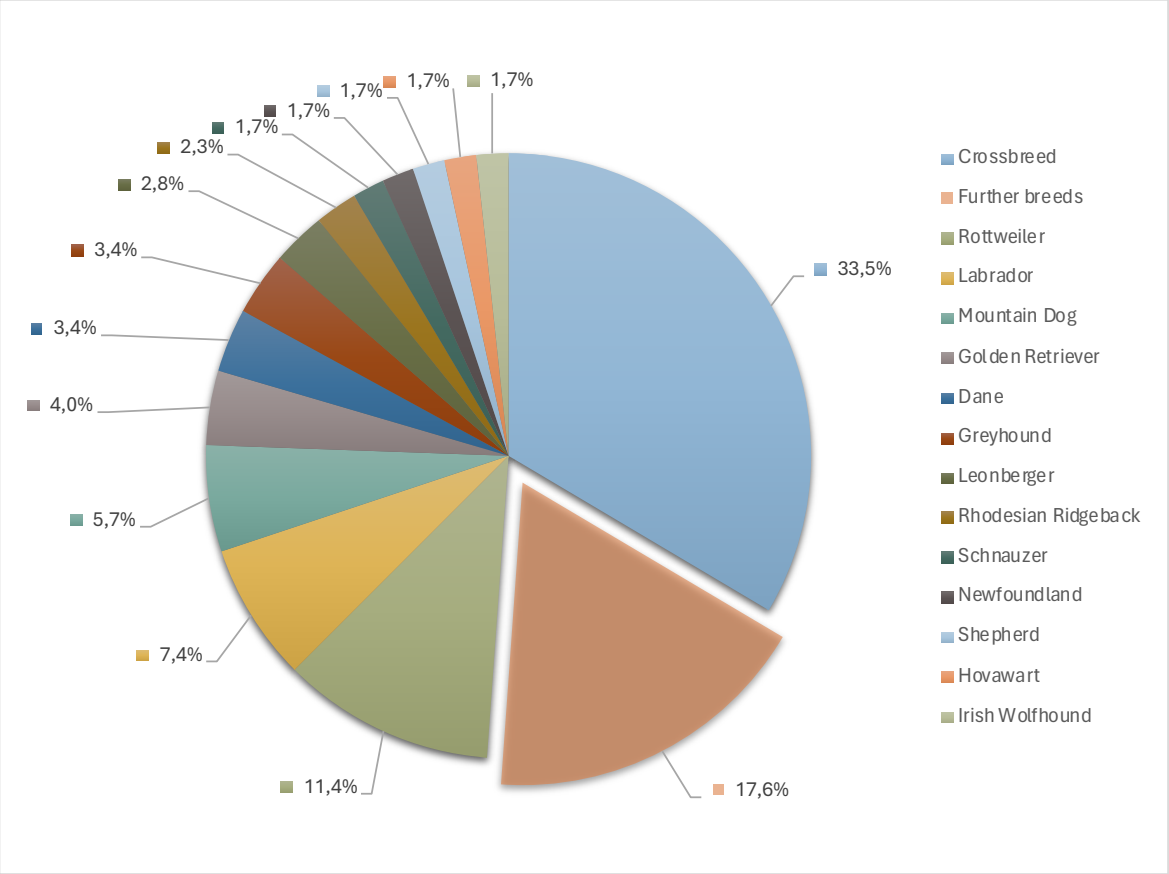

Figure 6. Breed Distribution (n=176)

4.1.2. Survival Analysis

It is important to note that there is very little data on the death of the animals. This may be attributed to the fact that the two clinics providing the data did not receive any re-presentations or follow-ups from the patients. One reason may be that the pet owners returned to the veterinarian they first visited, another is that the animals may have passed away at home without any subsequent sharing of data. Data on the date of death were recorded for 77 out of the 176 dogs. The mean±SD survival time was 4.87 ± 15.42 months, with the shortest being 0 months, often due to frequent euthanasia at the time of diagnosis. The longest reported survival time among these 77 patients can be reported as 119 months.

4.1.3. Diagnostic analysis

For diagnostic imaging (Figure 7.), the majority, 140 out of 176 (79.5%) of the cases in my study underwent Radiography, while 14 out of 173 (8%) received a Computer Tomography (CT) scan. For 10 out of 176 cases (5.7%), both Radiography and Computer Tomography were utilized. Sonography was used for one out of 176 cases (0.6%).

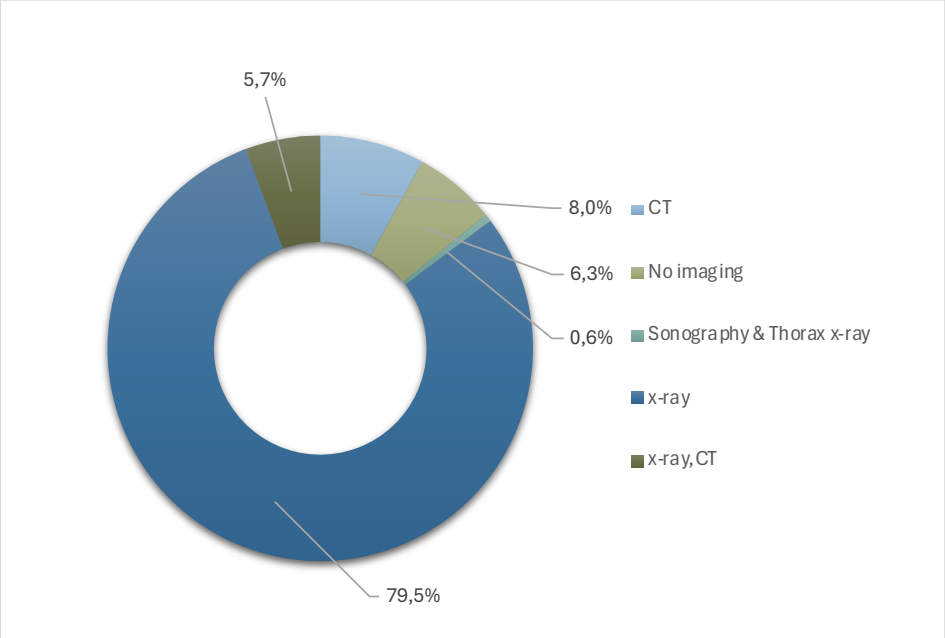

Figure 7. Diagnostic imaging (n=176)

Histopathology is one of the most important methods, to get the specific distinguishing between various bone tumours. It is necessary to mention, that the sampling for this procedure has to be taken from the specific regions and has to be performed carefully. In my research, out of the provided cases from the veterinarians, a limited number of patients underwent specific diagnostic methods (Figure 8.). Histopathology was performed on 29 out of 176 patients (16.5%), while 17 patients (9.7%) were examined via cytopathology. Only 3 patients (1.7%) underwent examination using both diagnostic methods. Among the cases that underwent both histopathological and cytopathological examination, 26 out of 176 (14.8%) exhibited cytological signs, with 7 out of these 26 (26.9%) showing positive results. Among these cases, 18 out of 26 patients (69.2%), were confirmed to have osteosarcoma, while one patient (3.8%) was diagnosed with chondrosarcoma.

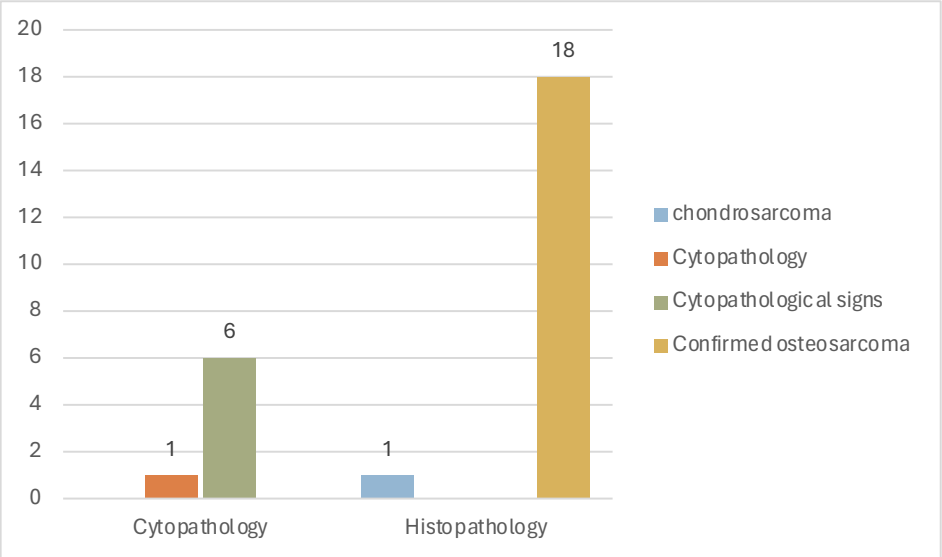

Figure 8. Confirmation with Cytopathology and Histopathology (n=26)

4.1.4. Localisation and Macrometastasis

For the subsequent analysis of metastasis occurrence concerning neoplasia location, the case number had to be reduced to n=174 due to missing data. In the evaluation, 156 out of 174 (89.7%) displayed no signs of macrometastasis, while it was positively detected at the initial diagnosis in 18 out of 174 (10.3%), based on diagnostic imaging of the thorax.

When examining tumour localisation in appendicular and axial regions, we observed that 138 out of 174 lesions (79.3%) were in the appendicular region, with 36 out of 174 (20.7%) occurring in the axial region (Figure 9.). It can be said that 124 out of 138 patients (89.9%) showed no signs of macrometastasis, whereas 14 (10.1%) out of 138 dogs with appendicular suspected tumours were diagnosed with macrometastasis at first presentation. In the case of axial occurrence of the neoplastic lesion, 4 out of 36 dogs (11.1%) were positive for metastasis, and 32 out of 36 (88.9%) had no metastatic signs.

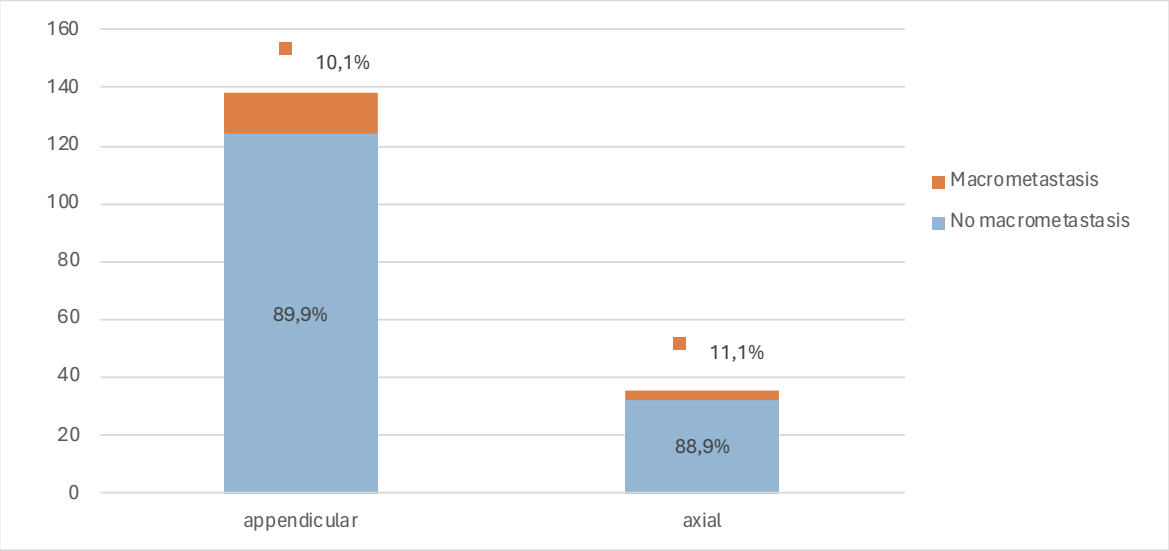

Figure 9. Occurrence of macrometastasis concerning the distribution (n=173)

Among 18 out of 176 (10.2%) patients were reported to have macrometastasis at the initial diagnosis (Figure 10.). Half of them, 9 out of 18 (50%) had a hindlimb location of the tumour. Despite a higher number of front limb lesions 75 out of 176 (42.6%) as compared to hindlimb lesions 61 out of 176 (34.7%), the occurrence of macrometastasis was lower in dogs with suspected neoplasia in the front limbs 5 out of 18, (27.8%). Additionally, 2 out of 18 patients (11.1%) showed signs of further metastasis with rib-affected lesions, 1 out of 18 (5.6%) had an alteration located in the maxilla, and one dog had a tumour in the sternum.

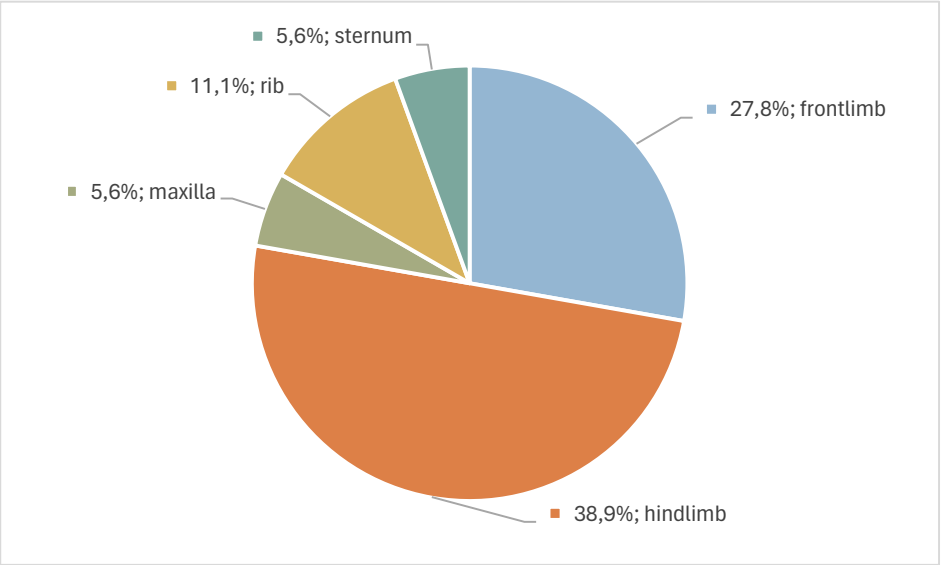

Figure 10. Macrometastasis related to the Location of Tumour (n=18)

4.1.5. Tumour Distribution Analysis

For the distribution of the tumour, I separated the axially located ones from the appendicular located ones. In the group of neoplasia occurring in the appendicular skeleton, I separated them into proximal and distal. Proximal included in the forelimb bones proximally of the elbow, such as the shoulder and humerus, and in the hindlimb, only the proximal and mid part of the femur were included. So, for distal located neoplasia in the hindlimb, all bony parts distally from the mid femur were considered as distal. In the forelimb, all bones distally the humerus were regarded as distal.

The average body weight for distally occurring tumours was 41.15 kg, 32.65 kg for those with proximal tumours, and 30.39 kg for cases of axially located cancerous alterations. As I mentioned above the majority of neoplasia in my data affected the appendicular skeleton with 79.3%, while 20.7% were affecting the axial skeleton. For further analysis of the distribution of the appendicular affecting tumours (Figure 11.), it can be mentioned, that 66 out of 137 (48.2%) were proximally, and 71 (51.8%) distally diagnosed. The most frequently occurring location for a suspected lesion was the front limb with 75 out of 176 (42.6%), following the hindlimb with 61 out of 176 cases (34.7%). Third place was the

pelvis recorded with 7 out of 176 (4%), followed by the spine with a frequency of 6 out of 176 (3.4%). Neoplastic alterations in the skull, rib, and mandible could be analysed with an amount of 5 out of 176 (2.8%). Near to that, the maxilla with 4 out of 176 (2.3%) has to be mentioned. Of 3 out of 176 cases (1.7%) the definite location could not be described. One (0.6%) case out of 176 was reported as located in the front-, as well as, in the hindlimb. Another case was presented in the sternum of a dog. Three (1.7%) patients out of 176 had been demonstrated to have an extraskeletal neoplastic lesion, which includes one histopathologically confirmed osteosarcoma in the jejunum of a 10-year-old, female Yorkshire Terrier. Also, one located in the ventral abdominal wall which was recorded with cytological signs for an osteo- or chondrosarcoma. This patient was a female 12-year-old Labrador, that showed an intraoral fast-growing mass, without further diagnostics or data, only 12 months later.

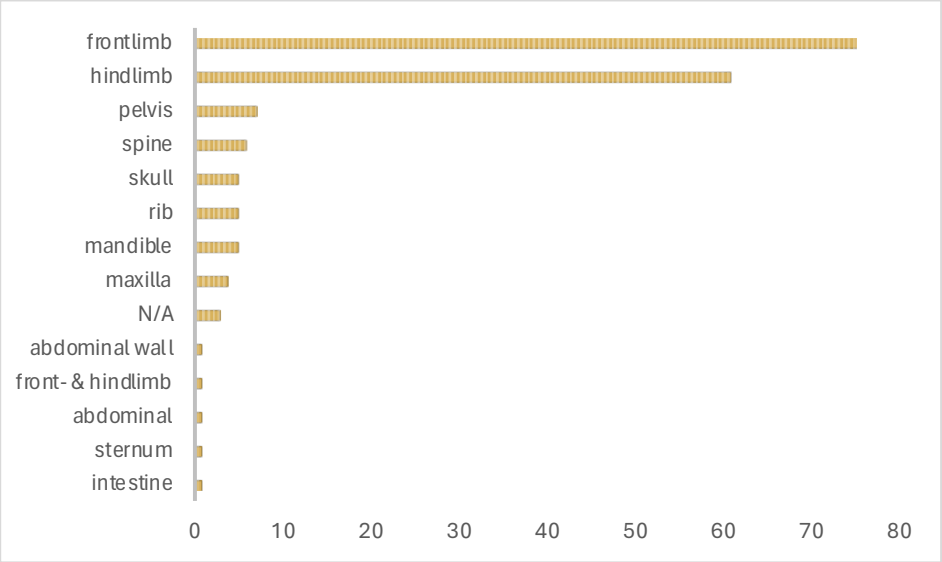

Figure 11. Location Distribution (n=176)

4.1.6. Pathologic Fracture Analysis and More

Due to the alteration of bone structure, the possibility of pathologic fracturing is given. For the occurrence of that condition, the number of positives was 20 out of 176 (11.4%) and 156 out of 176 cases (88.6%) showed no signs of pathological fracturing.

In relation to the sex of the animals, it can be observed that out of the 176 patients, 104 were female (59.1%). Among these female patients, 13 (7.4%) were diagnosed with a pathologic fracture. The males which represented 72 dogs (40.9%) out of 176, a total of 7 (4%) had pathologically fractured bones.

Regarding surgical treatment of cancerous alteration in the limbs, like amputation, a number of 9 out of 176 cases (5%) had received such a surgery. The last topic I analysed was the cases which had any kind of earlier fracture treatment or for instance a cruciate ligament rupture surgery. Both conditions may be treated by implant using which means foreign body material, like Tibia Plateau Leveling Osteotomy (TPLO) plates and screws. Out of all 176 dogs, a total of 5 (3%) had data as described above

5. Discussion

The present study aimed to investigate cases of dogs suspected of having bone neoplasia by analysing various factors like age, breed, gender, neuter status, and weight parameters. The study encompassed a range of parameters over a 12-year period.

In this discussion section, I will put my major findings into discussion with existing literature. The first finding I want to present is the sex distribution, which in my study highlights a female:male ratio of 13:9. This suggests that in the cases of my research, females might have a higher risk compared to males of being affected by bone neoplasia. On the contrary, the literature describes a higher male:female ratio of patients in a reference study [62].

Due to some limitations of bodyweight data, the mean weight could only be analysed for 163 instead of 176 dogs, to be 35.74 kg. This finding shows similarities to existing literature, which describes a higher risk for animals with increased body mass compared to dogs weighing under 10 kg [13].
Furthermore, I would like to address the occurrence of pathological fractures. This can also be a reason for visiting the veterinarian with acute non-weight bearing lameness as a result of the neoplastic alteration of the bone. In such, instances, the diagnosis often involves radiography, which may lead to considering euthanasia. In the statistical analysis of my cases, I found that a total of 20 out of 176 (11.4%) dogs suffered a pathological fracture. The existing literature describes the occurrence of pathological fractures at the time of diagnosis, as well as later on [6].

Another topic to discuss the findings of the descriptive statistic is the age of the dogs. As already described in the existing literature, the results of my study show the same age group [6]. My findings showed that the mean age of the dogs at the time of first suspicion was 9.23 years. The youngest dog was one year old, which is consistent with the literature that indicates there can be a small peak at the age of 18-24 months. Thus, my results confirm the current knowledge and findings.

Regarding the survival time, my limited cases and results demonstrate that it is not very significant compared to the existing literature. This is because the majority of patients did not return to the veterinarians who provided me with the data after the diagnosis. Therefore, there was a low number of follow-ups. Due to this the limited amount of data on survival time or death is better understood. Of the 77 patients for whom information exists, the mean survival time was 4.87 months, approximately 148 days. This outcome can be confirmed by existing literature, which states that animals that underwent surgery without adjuvant chemotherapy could have an average survival time of 103-175 days [49].

As there were barely any cases with adjuvant therapy or surgery, I decided to exclude this interesting analysis, as it would hardly have had a statement due to too little data.

Regarding breed analysis, various breeds were categorised into 41 groups, with crossbreed dogs forming the largest group at 33.5%. Other large dog breeds, including Rottweilers, Labradors, and Golden Retrievers, also showed significant frequencies. Breeds encompassing both giant and small dog breeds appeared less frequently and were collectively referred to as ‘Further Breeds’. These statistical results, along with other findings from my study, largely align with existing literature, except for the observation that crossbreed dogs were more commonly affected than purebred dogs which contrasts with previously reported data [13, 17, 27].

Other findings that I could confirm were that the majority of the tumours were diagnosed in the appendicular skeleton in the forelimb and also the rarely occurring metastasis at the time of tumour suspicion, which aligns with the existing study situation [46]. In my current research, the proportion of dogs diagnosed positive for metastases was 10.3 %, matching the statements [27, 71], which also report that fewer than 15% of patients show macrometastases at the initial presentation.

In the last discussion section, I will put my findings about the specific diagnostics into discussion with the existing literature. Regarding diagnostic methods, it is once again to emphasise that histopathology can provide the decisive differentiation between the different types of bone tumours. In all the cases that I was able to include in my statistics, indeed only 29 out of 176 patients (16.5%) utilized this specific diagnostic method. There were also patients, 17 (9.7%), who were further diagnosed using cytology. Of the total 26

dogs that received one of the specific diagnostic methods, 18 (69.2%) were diagnosed with osteosarcoma, and one patient was classified as chondrosarcoma. Seven others showed cytological signs that were highly likely to indicate osteosarcoma. To conclude this section, it can be added that in all the cases I collected, the majority of dog owners decided against further diagnostic procedures, and thus also against therapy. This can be confirmed by the topic that the prognosis in most, especially already advanced bone alterations, is guarded to poor classified. The existing research highlights the importance of using specific diagnostic methods with high-quality samples to differentiate the tumour. It also shows that if the clinical signs and medical history strongly suggest a diagnosis, and include characteristic signs, on a radiograph, further diagnostics may not be necessary, which can be seen in a great number of patients in my study [10, 71].

6. Summary

A comprehensive literature review provided a foundation by outlining the origins, classifications, and characteristics of bone tumours. Special focus was placed on osteosarcomas, including their aggressive nature and treatment challenges. Motivated by the early personal loss of Frida, my 3.9-year-old dog, who died due to osteosarcoma, the research underscores the relevance of comprehensive histopathological evaluations in distinguishing bone tumours and formulates treatment strategies. The study also ventured into etiological discussions, highlighting genetic factors and the potential impact of implants on sarcoma development. Moreover, it provided a critical comparison between canine and human osteosarcomas, emphasizing the potential for cross-species learning.
The research methodology involved a retrospective design, gathering data over a 12-year span to examine potential associations with various clinical parameters. Despite constraints, such as the collection of trauma-related information, the study succeeded in analysing a significant number of dogs across a wide array of breeds.
Descriptive statistics offered a panoramic view of the study population, revealing a notable prevalence of crossbreeds among the affected dogs. Survival analysis, diagnostic approaches, and tumour localization further enriched the dataset, offering insights into the complexity of bone neoplasia in dogs. Particularly, the research underscored the predominance of appendicular skeleton tumours and the diagnostic utility of radiography and histopathology. Discussion of the findings highlighted several key takeaways, including the correlation between specific breeds and the incidence of osteosarcoma, the influencing role of demographic factors, and the challenges faced in obtaining comprehensive diagnostic data.

Conclusively, while aligning with a significant portion of existing literature, this thesis uniquely unveiled the higher susceptibility of crossbreeds to osteosarcoma, a higher female:male ratio, and challenging predominant views. Additionally, it emphasized the necessity of advanced diagnostic methods in strengthening the accuracy of osteosarcoma diagnoses. To summarize, the relation of demographic and clinical aspects plays a crucial role in the development and prognosis of osteosarcoma in dogs. This study underlines the need for further research in veterinary and human medicine to expand and improve the diagnostic possibilities and optimise the subsequent treatment options. Ultimately, this should ultimately lead to better survival chances for the diseased animals.

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