Epidemiology of vascular tumors in the canine population of the Canary Islands during the period from 2003 to 2023

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Academic year:
2023-2024

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0. ABSTRACT

To evaluate the relevance of HA and HSA in dogs, a retrospective study was conducted analysing 1,155 cases of canine vascular tumours in 984 dogs over a study period of 20 years (2003-2023).

Vascular tumours accounted for nearly 6% of all tumours diagnosed in the Canary Islands, with cutaneous locations having the highest incidence at 84% compared to 14.5% in viscera.

Of these tumours, 60% were hemangiosarcomas and 40% were hemangiomas.

The animals in the study, both with hemangiomas and Hemangiosarcomas, had an average age of 9 years; however, it was observed that dogs with hemangiosarcoma in the liver and pancreas were diagnosed at significantly older ages.

Regarding anatomical location, cutaneous vascular tumours were mostly located in the lumbar region (24.8%), where most multiple tumours (25%) were also found, while non-cutaneous tumours were more commonly located in the spleen (48.5%).

In terms of breed, the most frequent were Crossreeds (35.29%), Boxers (10.02%), German Shepherds (5.34%), English Pointers (4.47%), and French Bulldogs (4.25%).

Concerning geographical location, municipalities in Gran Canaria with higher annual solar irradiance were associated with a greater proportion of cases, as well as municipalities with a high population of susceptible dog breeds according to the literature.

The sex variable was analysed, revealing a significant difference between males and females, showing an overrepresentation in male dogs.

Regarding neutering status, we observed that most dogs with vascular tumours were neutered; however, further analysis could not be performed as the Zoocan database is not reliable for that record.

Keywords: Dog, hemangioma, hemangiosarcoma, vascular tumours, cancer

1. INTRODUCTION

Hemangiomas (HA) and hemangiosarcomas (HSA) are vascular tumours that arise from the cells of the vascular endothelium and affect a wide variety of species, with dogs being the domestic animal with the highest prevalence of this disease. It has also been rarely observed in cats and humans (Hendrick, M.J., 2016, Karaba et al., 2011).

HSA is classified according to its anatomical location into visceral and non-visceral types. The non-visceral type can affect the skin, subcutaneous, and muscular tissue, while the visceral type can appear in the spleen, liver, heart (right atrium), lungs, kidneys, oral cavity and tongue, bones, bladder, uterus, and retroperitoneum. Concerning its benign counterpart, its most common location is cutaneous, although both can affect any vascularized tissue (De Nardi et al., 2023). The non-visceral form of HSA with the highest incidence in dogs is the one affecting skin tissue, while the spleen accounts for almost half of visceral HSA cases (Griffin et al., 2021).

HSA has a poor prognosis, with a high incidence of metastasis primarily in the lungs, liver, omentum, and central nervous system, as well as a survival time of only a few months. In general, the cutaneous form has a better prognosis than the visceral form, with a survival time after surgery exceeding 2 years, although it has a higher rate of recurrence (Nóbrega et al., 2019).

In contrast, hemangiomas are usually resolve with complete surgical excision of the mass, although they tend to recur (Schultheiss, 2004).

A definitive diagnosis requires histopathological examination of tissue obtained by biopsy (De Nardi et al., 2023).

The treatment for hemangiosarcoma is based on tumour excision through surgery and administration of adjuvant chemotherapy, with doxorubicin being the drug of choice either alone or in combination with cyclophosphamide or vincristine. Other treatments have been proposed but require more extensive studies on their response since most have not shown improvements in patient prognosis (Mullin and Clifford, 2019).

2. OBJECTIVES

To provide veterinarians and the rest of the scientific community with useful information about hemangiomas and hemangiosarcomas in dogs, the main objective was to conduct a retrospective study on dogs with vascular tumours on the Canarian Archipelago. For this purpose, the objectives were as follows:

1. To evaluate the relative frequency of vascular tumours in dogs compared to other canine tumours in our study population.

2. To analyse the anatomical location of vascular tumours in dogs.

3. To assess the age distribution of vascular tumours in dogs.

4. To analyse the sex distribution of dogs with vascular tumours compared to the canine population registered in the Zoocan database.

5. To analyse the breed distribution of dogs with vascular tumours compared to the general dog population registered in the Zoocan database.

6. To evaluate the relationship between neutered status and diagnosis in dogs with vascular tumours.

7. To analyse the geographical distribution of cases of vascular tumours across different municipalities in Gran Canaria and compare them with other oncological diagnoses, considering the possible risk factor of higher annual solar radiation incidence in certain municipalities and the relationship of predisposed breeds recorded in those municipalities.

3. BIBLIOGRAPHIC REVIEW

3.1. HEMANGIOMA

3.1.1. Epidemiology and etiology

Hemangiomas are benign tumours of the vascular endothelium that appear in subcutaneous or dermal tissue anywhere on the body. They are common in dogs but rare in other domestic animals (Hendrick, M.J., 2016).

The breeds with the highest prevalence of these tumours are Labrador Retrievers, Boxers, Argentine Dogo, German Shepherds, Pitbulls, and Golden Retrievers, as well as mixed-breed dogs (Martins et al., 2022).

In the skin, hemangiomas are more frequent than hemangiosarcomas (Schultheiss, 2004). They are also more common than visceral hemangiosarcomas (Soares et al., 2017).

The incidence of hemangiomas in Switzerland is estimated to be 3.09% of all tumours, while for hemangiosarcoma it is 1.04% (Graf et al., 2018). In Portugal, it is estimated that 5.74% of skin neoplasms are hemangiomas (Martins et al., 2022).

Prolonged exposure to solar radiation is considered a risk factor for the development of hemangiomas, similar to cutaneous HSA (Hargis et al., 1992; Hassan et al., 2021). There is evidence that dog breeds with lightly pigmented skin and short hair that have been exposed to prolonged sunlight show a higher incidence of this tumour (Tostes et al., 2017; Martins et al., 2022). Individuals with sun-induced neoplasia may have multiple tumours of hemangioma, hemangiosarcoma, or intermediate forms occurring simultaneously or sequentially. Likewise, there is no indication that a thick and pigmented coat prevents their development (Hendrick, M.J., 2016; Hargis, 1992).

The most common anatomical locations for sun-induced HA are the limbs and abdominal region, while non-sun-induced HA typically occurs in the dorsal region (Hargis, 1992; Martins et al., 2022).

The age of presentation is usually around 8 years old, within a range of 3 to 14 years. They generally occur before than hemangiosarcomas (Schultheiss, 2004).

No relationship has been detected between the incidence of HA and the sex of individuals (Hargis, 1992).

3.1.2. Clinical signs and lesions

They are well-defined masses that vary in colour from red to dark brown. They can appear anywhere on the body, although they are uncommon in the ventral area (Schultheiss, 2004). They often present as multicentric (Martins et al., 2022).

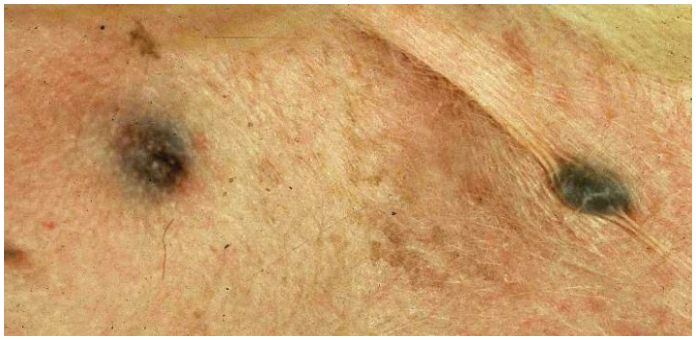


Image 1: Cutaneous HA (Hendrick. M. J., 2016)

The cut surface typically reveals a honeycomb or fibrous trabecular pattern separating blood-filled cavities (Hendrick, M.J., 2016).

Histologically, the tumours are well-circumscribed, either encapsulated or not, and composed of vascular spaces of varying sizes filled with erythrocytes and lined with a single layer of uniform, flattened, well-differentiated endothelial cells, although in some cases they may be ovoid or round. Thrombi are often observed, where fibroblasts and collagen are present, as well as foci of hemosiderosis (Hargis et al., 1992).

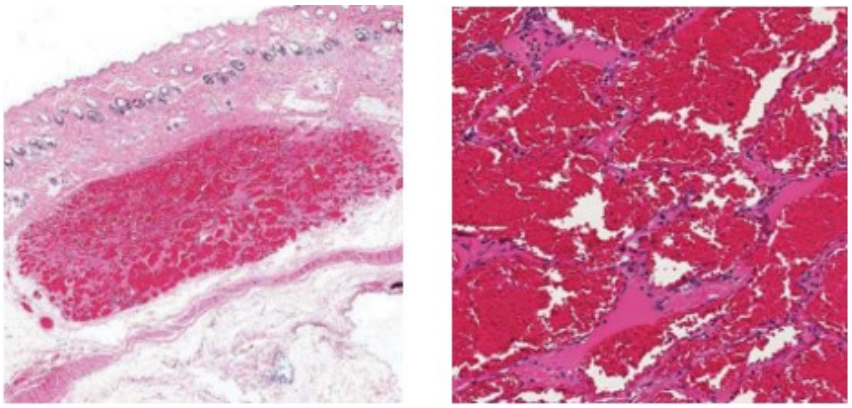


Image 2: Histological images of cutaneous HA (Hendrick. M.J., 2016)

Depending on the size of the vascular channels, the tumours are classified as cavernous or capillary, although both types can appear in the same tumour. In the cavernous type, the channels are larger and separated by fibrous connective tissue that may contain lymphocytes, plasma cells, macrophages with hemosiderin, and focal mast cells. The capillary variant has a small stroma with a more cellular appearance. Mitotic figures are rare (Hargis et al., 1992; Hendrick, M.J., 2016).

The histological appearance of dermal HA is more varied than that of subcutaneous ones and may be elevated, plaque-like, or polypoid (Hargis et al., 1992).

Generally, sun-induced HA tend to be located more superficially in the dermis and are less circumscribed. There are often regions of early malignant transformation characterized by localized nuclear enlargement and hyperchromasia (Hargis et al., 1992).

3.1.3. Diagnosis

For the diagnosis of HA, a physical examination must be performed since the macroscopic appearance of the lesions is characteristic of vascular tumours. Imaging tests can be used to rule out involvement of other organs (Hargis et al., 1992).

Histopathological examination of the lesions is the only definitive diagnostic method to differentiate it from HSA. The histological appearance is similar to that found in cases of HSA, except for the endothelial cells forming the channels; in HA they do not exhibit cellular atypia characteristic of HSA malignancy (Schultheiss, 2004).

3.1.4. Treatment and Prognosis

HA generally grow slowly and usually heal with complete excision of the tumour but tend to recur, especially sun-induced variants (Schultheiss, 2004; Hendrick, M.J., 2016).

3.2. HEMANGIOSARCOMA

3.2.1. Epidemiology and Etiology

HSA is a mesenchymal neoplasm originating from the endothelial cells of blood vessels, also known as hemangioendothelioma, angiosarcoma, or visceral vascular tumour. The latter term includes hemangiosarcomas and hemangiomas, with hemangioma being the benign counterpart of hemangiosarcoma (Karaba et al., 2011).

Vascular tumours are relatively common in dogs and are the most prevalent sarcomas in this species. They are less common in cats and generally occur in the skin. They are also rare in other animal species, including humans (Schultheiss, 2004).

According to Griffin et al. (2021), HSA accounts for approximately 5% of all primary malignant tumours that are not dermal, less than 5% of all dermal tumours, and about 50% of all splenic tumours. In contrast, Brazilian epidemiological data show a higher prevalence of cutaneous hemangiosarcoma, representing up to 80% of all canine hemangiosarcomas and nearly 14% of all neoplasms diagnosed in dogs; this may be related to a higher incidence of solar radiation in countries with tropical climates (Flores et al., 2012; Soares et al., 2017). On the other hand, a retrospective study conducted by Graf et al. (2018) examining records of dogs with neoplasms in Switzerland found an incidence percentage of hemangiosarcoma at 1.04%. Specifically, regarding splenic HSA, Johnson et al. (1989) proposed the so-called "two-thirds rule," defining that two-thirds of splenic neoplasms are malignant and that two-thirds of these are HSA. Concerning cardiac HSA, it is considered the most common primary cardiac tumour in dogs (Smith, 2003).

It can arise in any organ or vascularized tissue (Nóbrega et al., 2019). It is categorized into two types based on its location or tissue of origin: visceral and non-visceral. The non-visceral type can affect the skin, subcutaneous tissue, and muscle tissue. In contrast, the visceral type can affect the spleen, liver, heart, lungs, kidneys, oral cavity, bones, urinary bladder, uterus, tongue, and retroperitoneum. Cutaneous presentation is the most common in dogs (De Nardi et al., 2023).

It has a high metastatic potential, occurring early in the course of the disease via hematogenous or intracavitary spread due to tumour rupture. The most frequent sites of metastasis are the liver, omentum, lungs, and central nervous system, with secondary

intracranial tumours being the most common in dogs (Mullin and Clifford, 2019; Griffin et al., 2021).

There are two hypotheses regarding the oncogenesis of HSA. The first suggests that HSA originates from differentiated cells of the endothelial lining of blood vessels that undergo mutations granting them malignant potential (angioblasts). The second hypothesis states that HSA arises from multipotential stem cells derived from bone marrow that are incompletely differentiated and close to or at the stage of endothelial commitment (i.e., hemangioblasts) (Lamerato-Kozicki et al., 2006; Griffin et al., 2021).

There is little information on the biological behaviour of non-visceral hemangiosarcoma and its triggering factors; however, overexposure to solar radiation seems to be one such factor along with age, breed, weight, and reproductive status (Schultheiss, 2004; Carnio et al., 2020). Other sources of radiation such as intraoperative radiotherapy can lead to sarcoma formation (Smith, 2003). Visceral HSA as well as subcutaneous and muscular HSA are not associated with solar radiation (De Nardi et al., 2023).

Hargins et al. (1992) observed evidence that hemangiosarcoma may arise from pre-existing hemangiomas caused by solar exposure which suggests there may be progression from a benign dermal tumour to a malignant vascular tumour.

Recent studies such as those conducted by Lashnits et al. (2020) suggest that infections by Bartonella spp. may be correlated with the development of visceral HSA because chronic infection by these agents induces angiogenesis and chronic inflammation—both fundamental factors in the proliferation and development of vascular tumours.

It primarily affects geriatric dogs between ages 8 and 15 years old; cutaneous HSA develops earlier with cases appearing from age 6 (Hillman et al., 2023). Rafalko et al. (2023) found that purebreed dogs develop cancer significantly earlier than crossbreed dogs as well as large and giant breeds compared to smaller ones.

Females present HSA later than males (Pinello et al., 2022). Goldschmidt and Shofer (1992) indicate that less than 49% of hemangiosarcomas develop in females while Sharif et al. (2006) mentions a certain predilection for visceral hemangiosarcomas in male German Shepherds.

Dogs with low pigmentation and areas of hairless skin have a higher risk of developing cutaneous HSA. The most predisposed breeds include Pitbulls, Whippets, Greyhounds, Boxers, Beagles, and Dalmatians (Nóbrega et al., 2019). This higher prevalence is related to their fur providing little protection against solar radiation along with low skin pigmentation and lack of hair exposing them to greater solar radiation than other breeds (Szivek et al., 2012). No specific breed appears to be associated with a particular cutaneous location (Schultheiss, 2004).

On the other hand, subcutaneous and muscular subtypes appear more frequently in Golden Retrievers, Labrador Retrievers, and crossbreeds (De Nardi et al., 2023).

Breeds showing a high proportion of cases of visceral HSA include German Shepherds, Golden Retrievers, Labrador Retrievers, Pointers, Great Danes, Boxers, and Cocker Spaniels among others which suggests possible genetic etiologies although no specific genetic mutations associated with HSA have been discovered so far (Smiths ,2003). Generally speaking, medium to large sized dogs show higher incidence rates with dogs weighing over 17.8 kg being significantly more likely to be diagnosed with HSA (Carnio et al., 2020).

Neutering is associated with an increased risk for developing HSA particularly for splenic and cardiac types across both sexes although it seems to affect females more significantly. Neutered females have five times greater risk for developing cardiac HSA compared to intact females while they have a risk increase factor of 2.2 for splenic HSA suggesting hormones may play a role in disease etiology (Robinson et al., 2020). In a study on estrogen cycles neutering and development of HSA in Golden Retrievers conducted by Torres de la Riva et al. (2013), it was found that the percentage of cases for neutered females after one year was four times greater than intact females or those neutered before twelve months old. Torres de la Riva et al. (2013) suggest that neutering before first estrus prevents potential neoplastic cells from being exposed to estrogen thus minimizing chances for developing neoplasia while females whose cells have already been exposed remain intact protecting them from such neoplasia.

Conversely for males neutering seems to favor neoplasm formation regardless of when performed possibly due loss androgen receptors (Robinson et al., 2020).

3.2.2. Clinical Signs and Lesions

Dermal HSA

Lesions are most frequently found in the ventroabdominal area, prepuce, and pelvic limb regions (Ward, 1994).

The lesions are characterized by being firm due to the presence of hyperkeratosis and acanthosis, elevated, in the form of papules or nodules that are dark red to purple in colour, and commonly associated with dermal ulceration (Griffin et al., 2021).

The clinical manifestations are usually local and limited to mild and intermittent bleeding from the tumour region (De Nardi et al., 2023).

Subcutaneous and Muscular HSA

The lesions present in subcutaneous and muscular HSA subtypes are larger than those in the dermal subtype; they may be adhered or mobile and can have a firm or soft consistency. They may also be associated with ulcerations (De Nardi et al., 2023).

This type does not seem to have an anatomical predilection and can appear in various locations such as limbs, flanks, trunk, scapula, and cervical area, among others (Bulakowski et al., 2008).

Clinical signs that affected dogs may present include localized pain, weakness, functional deterioration of the affected structures, anorexia, as well as hemorrhages in cases of advanced HSA, which in turn causes anemia. Other laboratory alterations that may be present include neutrophilia and thrombocytopenia (Shiu et al., 2011).

The subcutaneous and muscular forms of HSA are more aggressive than the dermal subtype due to greater infiltrative growth affecting deeper tissues, which increases their metastatic potential (De Nardi et al., 2023).

Visceral HSA

Most cases of visceral HSA occur in the spleen (Schultheiss, 2004). Furthermore, splenic HSA is considered the leading cause of non-traumatic hemoperitoneum in dogs (Hendrick, M.J., 2016; De Nardi et al., 2023).

Macroscopically, tumours appear as nodules that are generally multifocal, non-encapsulated, poorly circumscribed, white, red or purple in colour with a soft, gelatinous, and friable consistency; they are commonly filled with blood and areas of necrosis and may present omental adhesions due to possible ruptures (Griffin et al., 2021).

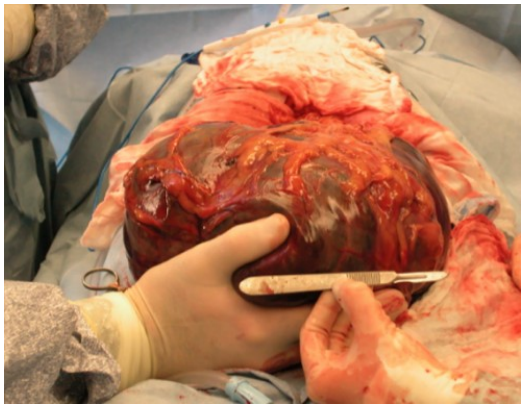


Image 3: Intraoperative image of a splenic HSA (Griffin et al., 2021)

The most frequent clinical signs include weakness and acute collapse associated with rupture of the visceral mass. Related to hypovolemia due to hemorrhage, tachycardia, tachypnea, pale mucous membranes, abdominal distension, a palpable abdominal mass, anorexia, and cachexia may be observed (Griffin et al., 2021).

If the neoplasm is located in the heart, signs of right heart failure may also be observed including abdominal distension, jugular pulse, muffled heart sounds, cough and dyspnea as well as syncope, ataxia and cyanosis along with severe arrhythmias (Smith, 2003). In cases where metastasis occurs in the brain seizures may appear (Mullin and Clifford, 2020).

Histologically all subtypes of HSA are similar and consist of pleomorphic endothelial cells that are oval or spindle shaped. Notable features include channels of varying sizes filled with erythrocytes along with ovoid to elongated vesicular nuclei. Cytoplasmic borders are indistinct with numerous mitoses both typical and atypical as well as thrombi and areas of necrosis. Solar elastosis is also frequently found in cutaneous HSA (Hargins et al., 1992). Infiltration by inflammatory cells is common (Karaba et al., 2011). Tumors involving the subcutis—with or without muscle infiltration—tend to be poorly circumscribed and infiltrative with markedly anaplastic endothelial cells (Ward

et al., 1994). Channels differentiate according to their size into capillary or cavernous types; both can be present within the same tumour (Kim et al., 2015).

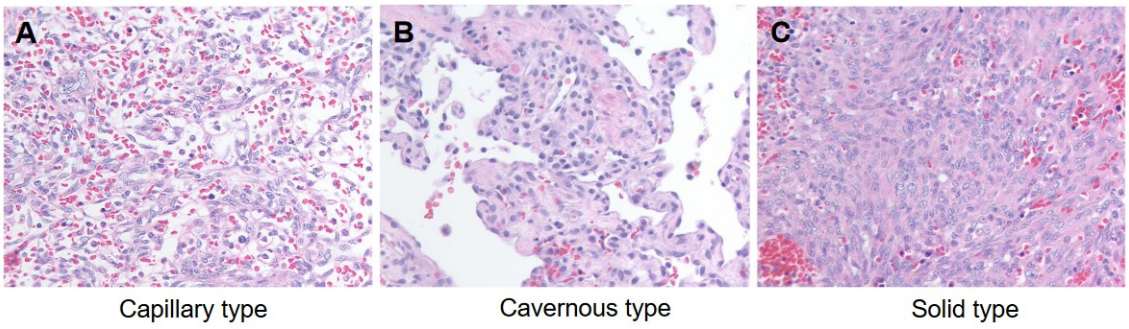


Image 4: Histological findings of canine HSA according to the type of channels (Kim et al., 2015)

3.2.3. Diagnosis

The clinical tests necessary to establish a diagnosis of HSA include a complete blood count, serological panel, urinalysis, complete coagulation profile, thoracic radiographs in three projections, abdominal ultrasound, echocardiogram, and electrocardiogram (Smith, 2003).

Some abnormalities commonly found in blood tests for dogs include regenerative anemia, anisocytosis, polychromasia, and reticulocytosis, as well as neutrophilic leukocytosis, thrombocytopenia, hypoproteinemia, and disseminated intravascular coagulation (DIC) (Smith, 2003; Shiu et al., 2011).

Abdominal and thoracic radiographs may show pleural or peritoneal effusion secondary to hemorrhage or right heart failure due to cardiac tamponade, as well as a multifocal to coalescent miliary to nodular pulmonary pattern characteristic of pulmonary metastasis. In cardiac tumours, an abnormal cardiac silhouette is typically observed, usually globoid in shape. In the abdomen, splenomegaly, hepatomegaly, or another abdominal mass consistent with primary or metastatic HSA may be seen (Mullin and Clifford, 2019; De Nardi et al., 2023).

The echocardiogram and electrocardiogram have limited capacity for detecting HSA but can be used to assess cardiac function before initiating chemotherapy or surgical treatment (Mullin and Clifford, 2019).

The use of CT scans, PET-CTs, and MRIs allows for precise determination of the anatomical origin and tumour invasion, greatly aiding in the planning of surgery or

radiotherapy. Additionally, both modalities have high sensitivity and specificity in distinguishing between benign and malignant tumours (Armbrust et al., 2012; Clifford et al., 2004).

Some biomarkers that may allow for early detection of the disease include cardiac troponin I, serum collagen peptide XXVII, and thymidine kinase (Griffin et al., 2021). Definitive diagnosis is only obtained through histopathological analysis of excisional biopsies. Staining with hematoxylin-eosin should be performed and in some cases immunohistochemistry with von Willebrand factor FVIII, CD31, and CD34 is necessary as they are useful markers for differentiating HSA from other sarcomas (De Nardi et al., 2023).

At least five fragments of the tumour should be sent to obtain a representative sample; it is recommended to send the entire spleen in cases of splenic HSA (Herman et al., 2019).

Other options include evaluating serum VEGF. Frenz et al. (2014) observed significantly higher circulating levels of this serum in animals with splenic lesions but found no difference between levels presented in benign and malignant lesions; therefore, it cannot be taken as a standalone diagnostic test. Cytology is contraindicated due to a high risk of blood contamination and hemodilution of the sample which can lead to confusion with HA or mast cell tumour. Additionally, this process can cause rupture of the mass and "seeding" of neoplastic cells (De Nardi et al., 2023; Griffin et al., 2021).

For staging the clinical staging model indicated in table 1, adapted from Mullin and Clifford's study (2020), is used.

Primary tumour (T)
T0: no tumour evidence
T1: tumour < 5 cm in diameter, confined to organ, and does not invade beyond tissue
T2: tumour > 5 cm, ruptured or invasive into subcutaneous tissues
T3: tumour invades adjacent structures
Regional lymph nodes (N)
N0: no regional node involvement
N1: regional node involvement

N2: distant node involvement
Distant metastasis (M)
M0: no distant metastasis found
M1: distant metastasis confirmed
Staging
I T0 or T1; N0; M0
II T2; N0, N1 or N2; M0
III T1, T2 or T3; N0, N1 or N2; M1

Table 1: Proposed clinical staging system for canine HAS (Mulling and Clifford, 2020)

3.2.4. Treatment

Surgical excision of the tumour with wide margins of 1 to 2 cm and a deep facial plane is the treatment of choice for HSA limited to dermal tissue (Ward, 1994). In the case of subcutaneous and intramuscular types, margins should be at least 3 cm; radical resection such as amputation may be necessary if the neoplasm is advanced and has infiltrated deeply (Mullin and Clifford, 2019). Due to the strong metastatic capacity exhibited by HSA few cutaneous tumours are limited to the skin; therefore, in cases where it has spread to other locations adjuvant treatments are recommended (Hargins et al., 1994).

There are few reports describing surgical excision for cardiac HSA since it is rarely feasible. Generally, a pericardiectomy is performed which is considered palliative treatment to prevent recurrence of cardiac tamponade (Case et al., 2013).

For other types of visceral HSA excisional surgery is the treatment of choice performed via laparotomy. It is important to examine the rest of the cavity and obtain biopsies from other organs such as the liver to rule out possible metastases. In cases of splenic HSA total splenectomy is recommended along with removal of any present omental adhesions (Griffin et al., 2021).

Radiotherapy has not been extensively studied as a treatment for this neoplasm since it is considered more systemic than localized disease; in cases where it has been applied results have been poor because although an initial positive response may be observed it does not increase survival time. Its use has been suggested for controlling HSA with incomplete surgical resection and as a palliative method (Shiu et al., 2011; Bulakowski

et al., 2008), as well as preventing cardiac tamponade requiring pericardiocentesis in cardiac HSA (Nolan et al., 2017).

On the subject of chemotherapy its use is recommended as adjuvant treatment in all cases of HSA except for cutaneous ones without metastasis, although no study has demonstrated a statistically significant increase in survival time for dogs with HSA treated with chemotherapy and surgery compared to those treated solely with surgery (Griffin et al., 2021; Shiu et al., 2011). In advanced infiltrative lesions chemotherapy is recommended as neoadjuvant therapy prior to surgery to reduce tumour size before surgical excision or as palliative care to improve patient quality of life (De Nardi et al., 2023). The most effective drug against canine HSA is doxorubicin either alone or in combination with cyclophosphamide or vincristine. It should always be used as an adjuvant to surgery. The use of a combination of all three drugs (VAC protocol) frequently causes toxicity in patients requiring hospitalization due to neutropenia or gastrointestinal toxicity. The doxorubicin-cyclophosphamide protocol (AC) presents fewer cases of secondary toxicity (Mullin and Clifford, 2019). One study showed an older average age at which metastases developed along with longer survival times in dogs treated with doxorubicin and decarbazine compared to those treated with doxorubicin and cyclophosphamide although the study sample was small, consisting only of 27 dogs, thus requiring further research on this topic (Finotello et al., 2017).

Other drugs that have been evaluated for use in HSA include epirubicin, ifosfamide, metronomic cyclophosphamide, thalidomide, metronomic chlorambucil, along with COX-2 inhibitors, and toceranib some showing promising results (Griffin et al., 2021; Nóbrega et al., 2019; Gardner et al., 2015).

Immunotherapy while not regularly used has shown potential as treatment for HSA. Brown and Reetz (2021) suggest that administration of a single polysaccharopeptide agent delays progression of metastasis while prolonging survival times in dogs with HSA.

Finally, electrochemotherapy has emerged as an alternative therapy for various types of cutaneous and subcutaneous neoplasms primarily using bleomycin and cisplatin administered intravenously or intratumorally (Ragel et al., 2019). Several studies have shown promising results in canine sarcomas but its potential in cutaneous HSA has yet

to be thoroughly studied having been administered almost exclusively as an adjunctive treatment following surgery (Spugnini et al., 2019).

3.2.5. Prognosis

HSA is associated with aggressive biological behaviour and poor prognosis. All subtypes except cutaneous are associated with rapid metastasis formation and short survival times (Shiu et al., 2011). Death usually results from metastatic disease or rupture of masses (Smith, 2003).

In a descriptive analysis conducted by Hillman in 2023 it was found that 93.1% of dogs diagnosed with hemangiosarcoma died. Regarding cutaneous cases, two out of thirteen died due to HSA. The probability of surviving more than one year with cutaneous HSA was found to be 84.6%. It should be noted that this study only included Golden Retrievers. In Szivek et al.'s study (2011), 44% survived three years after diagnosis. Although cutaneous HSA has lower mortality compared to other forms it has a high rate of recurrence (Griffin et al.,2021).

In the study conducted by Shiu et al. in 2011, which examined the prognosis of dogs with subcutaneous or intramuscular HSA, it was found that factors significantly associated with shorter survival time included age, larger tumour size, presence of clinical signs and anemia at the time of diagnosis, presence of metastasis at the time of diagnosis, incomplete surgical removal of the neoplasm, and not receiving surgical treatment. In contrast, weight, presence of thrombocytopenia or neutrophilia at the time of diagnosis, intramuscular infiltration, local tumour recurrence, and the use of chemotherapy or radiotherapy did not significantly affect survival time. In this study, the median survival time was 172 days, with a one-year post-treatment survival rate of only 25%, suggesting that subcutaneous and intramuscular HSA have a poor prognosis and long-term survival chances are low. For splenic HSA, median survival following surgical treatment and administration of doxorubicin ranges from 5 to 8 months. The same treatment for cardiac HSA has a median survival of 4 months (Sorenmo et al., 2004).

Only stage I superficial dermal HSA treated with surgery shows a survival time greater than 1 year (Smith, 2003). The probability of surviving 12 months with visceral HSA is less than 10% (Griffin et al., 2021).

3.2.6. Hemangiosarcoma in Dogs as a Potential Animal Model for Human Angiosarcoma

Human angiosarcoma (AS) and canine HSA are both sarcomas originating from vascular endothelium and are examples of diseases shared between humans and dogs, as they exhibit very similar characteristics and biological behaviours, such as highly aggressive nature, limited treatment options, and high mortality rates, as well as molecular profiles and treatment responses (Heishima et al., 2023).

AS is a rare neoplasm, occurring in less than 0.01% of all neoplasms in adult humans. Most cases affect the skin, although there are also some cases in viscera, primarily in the liver, right atrium of the heart, and spleen (Heishima et al., 2023).

So far, the first-line treatment for AS has been surgery with complete resection; however, due to the invasive nature of the neoplasm, achieving a resection with clear margins is complicated, which often leads to the use of neoadjuvant chemotherapy that has not demonstrated benefits in survival. This is also true for canine HSA (Heishima et al., 2023).

Wang et al. (2020) identified several molecular subtypes within canine HSA that showed significant similarities with the molecular profiles observed in human AS cases, such as CD31, VEGF, and CD34, as well as shared genetic alterations in genes like TP53.

Dogs develop HSA naturally, providing a relevant clinical context to study the disease; unlike rodent models, they have genetic heterogeneity and an intact immune system, including the complexity of the tumour microenvironment, which may facilitate the translation of preclinical findings into effective treatments for humans. The use of canine HSA could accelerate the process of discovering useful drugs for AS and improve understanding of metastasis processes, drug resistance, and interactions between tumours and the patient's immune system (Heishima et al., 2023).

Despite significant advantages, there are also ethical challenges and barriers to using domestic animals; it is difficult to evaluate them while meeting the necessary standards for conducting an effective study (Heishima et al., 2023).

Therefore, canine HSA represents a promising and valuable model for research on human AS, both to advance understanding of the neoplasm and to discover potential treatments. However, further research is still required to establish standardized protocols that allow this model to be used effectively in future clinical trials (Heishima et al., 2023).

3.3. GEOGRAPHICAL AND CLIMATOLOGICAL SITUATION OF THE CANARY ISLANDS

The Canary Islands are located in the Atlantic Ocean, northwest of the African continent, in a subtropical situation. They are small islands but have significant elevation (Pulido et al., 2007).

The climate of the islands is influenced by a high subtropical pressure system known as the Azores High from which trade winds originate; these winds have a northeast-southwest direction in the archipelago. This anticyclone persists throughout the year and causes the characteristic "seasonal swing" of the islands. The structure of the trade winds creates a lower layer that is humid and cool and an upper layer that is warm and dry, producing thermal inversion that forms stratocumulus-type cloud banks known as sea of clouds. This phenomenon is characterized by low clouds that divide the island vertically and produce significant changes in climate and solar irradiance according to altitude (Pulido et al., 2007).

Specifically in Gran Canaria, its northwest orientation allows trade winds to directly impact it, creating a mass of low clouds commonly referred to as "donkey belly," which filters and attenuates solar radiation, especially in summer (Pulido et al., 2007).

The Technological Institute of Canarias has established a network of twenty stations that continuously measure solar irradiance and has created solar maps encompassing areas with similar radiation levels. In image 3, the red zone corresponding to the southwest is where cloud formation is least frequent; therefore, it has the highest radiation levels with an annual average of 5.7 kWh/m²/day; while the blue zone in mid-altitude areas has an average value of 3.6 kWh/m²/day (Pulido et al., 2007).

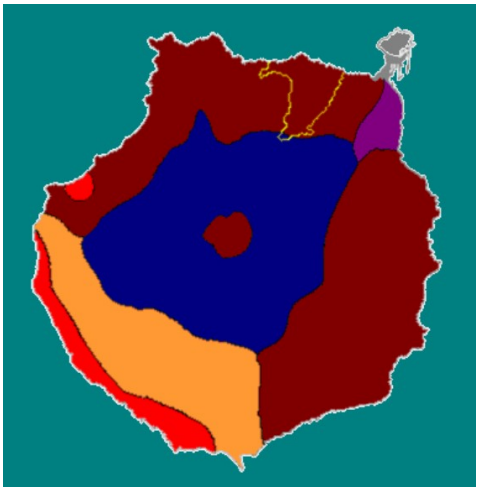


Image 3: Map of Gran Canaria according to annual solar radiation (Pulido et al., 2007).

4. MATERIALS AND METHODS

4.1. Materials

A retrospective study of vascular tumours was conducted based on a statistical and epidemiological analysis of a sample of 1,155 vascular tumours in 984 dogs, diagnosed by the Pathological Anatomy Diagnostic Service (PADS) of the Faculty of Veterinary Sciences of the University of Las Palmas de Gran Canaria (ULPGC) through biopsy during the study period from 2003 to 2023.

Information was collected and analysed regarding breed, sex, sterilization status, age, anatomical location of the identified neoplasms, geographical distribution of the veterinary clinics on the Canary Archipelago that provided the respective cases, description of biopsy protocols, and the histopathological diagnosis described in pathology reports. Cases from the Veterinary Clinical Hospital of ULPGC were excluded since, being a referral centre, the origins of the patients are not representative. Only dogs with histologically confirmed diagnoses were included.

Information on average annual radiation was obtained from Cartográfica de Canarias S.A. (GRAFCAN).

For statistical analysis, the distribution of sex and breed among animals in the study sample was compared with a control group consisting of 328,265 dogs registered in the Canary Registry of Animal Identification (Zoocan) to observe if there were significant differences between both groups.

Regarding the variable of castration status, Zoocan's registry has certain limitations since animals are typically registered during their first visit to the veterinarian and it is not common for this data to be updated in subsequent visits; therefore, sterilized patients are underrepresented in this database and were not considered a sufficiently reliable value for comparison in this study.

The evaluated histopathological reports were written by professors of Veterinary Pathology at the University of Las Palmas de Gran Canaria. Dogs were individually classified according to breed, sex, castration status, diagnosis, age, year of diagnosis, anatomical location, and distribution across different localities in the Canary Islands in an Excel spreadsheet with each sample recorded in each row. Some dogs had more than

one neoplasm or non-neoplastic skin lesion; in these cases, each diagnosis was classified individually.

4.2. Methods

Initial data exploration was performed using MS Excel. The variables breed, sex and neutered status were homogenized by means of "key-value" dictionaries and the function SEARCHV was used to map the dictionary data to the database.

Subsequent statistical analysis was performed using R statistical software.

For the analysis of the sex variable, the Zoocan dogs were used as a control group. The analysis compared the distribution of male and female animals with vascular tumours.

For the analysis of the breed variable, the distribution of breeds with HA and HSA animals (including only breeds with at least 5 vascular tumours diagnosed) was compared with the distribution of breeds in the control group (Zoocan).

For the neutered status variable, animals diagnosed with any other lesion (tumour or not) were used as a control group versus the group of neutered and unneutered animals that presented vascular tumours. This is because, as far as the Zoocan database is concerned, dogs are usually recorded in the system at their first visit to the veterinarian, but follow-up information (e.g., changes in spay/neuter status) is usually not recorded.

For the geographical analysis, we compared the distribution of diagnoses HA and HSA in the municipalities of Gran Canaria with the distribution of other diagnoses, whether tumorous or not, in the different municipalities, to observe whether there was a higher relative proportion of diagnoses of vascular tumours in those municipalities with a higher annual radiation rate.

Categorical variables (sex, neutered status and breed) were compared by performing a chi-square test. Age was analysed by calculating the median and standard deviation of dogs with vascular tumours, and nonparametric tests (Wilcoxon test) were used for comparison between groups.

In all cases, p-values less than 0.05 were considered statistically significant.

5. RESULTS

984 dogs with histopathologically confirmed hemangioma or hemangiosarcoma were included in the study. The total number of vascular tumours diagnosed during the study period (2003-2023) was 1,155, as some dogs had more than one compatible lesion. The relation of vascular tumours diagnosed per year is shown in table 2.

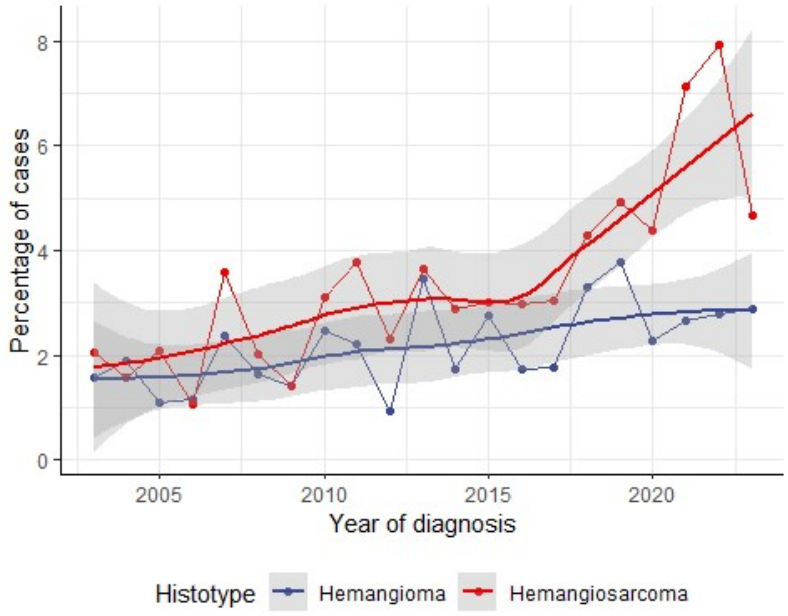
Year	Hemangioma	Hemangiosarcoma	Total vascular tumours
2003	13	17	30
2004	17	14	31
2005	9	17	26
2006	12	11	23
2007	26	39	65
2008	16	20	36
2009	14	14	28
2010	26	33	59
2011	24	41	65
2012	9	22	31
2013	34	36	70
2014	18	30	48
2015	23	25	48
2016	18	31	49
2017	19	33	52
2018	41	53	94
2019	39	51	90
2020	25	48	73
2021	22	59	81
2022	25	71	96
2023	23	37	60
Total	453	702	1,155

Table 2: Vascular tumours diagnosed per year

Of the 984 affected dogs, 387 were diagnosed with hemangioma and 597 with hemangiosarcoma, resulting in a ratio of 1.16 and 1.17 hemangiomas and hemangiosarcomas per dog, respectively.

5.1. Vascular neoplasm vs other diagnosed tumours over the study period

The proportion of vascular neoplasms was studied in relation to other tumours diagnosed during the study period, where an upward trend was observed over the years. As can be seen in graphic 1, in the first year (2003), malignant vascular neoplasms represented 2% of all diagnosed neoplasms, while benign ones accounted for 1.8%. In the case of HA, the increase in cases was gradual and constant throughout the study, reaching 3.9% by the end of that period. HSA showed a similar upward trend to HA until 2016, when the number of diagnosed cases began to increase more rapidly, reaching a percentage of 6.5% of HSA in relation to other tumours by the end of the study period (2023).



Graphic 1: Longitudinal analysis between 2003 and 2023 years comparing vascular neoplastic lesion versus other diagnosed tumours.

During the study period, 20,353 neoplasms of all etiologies were diagnosed. Of these cases, 1,155 were vascular, representing 5.67% of the total number of neoplasms.

5.2. Analyses of the distribution of the different vascular lesions diagnosed

On the other hand, more HSA than HA were diagnosed during the study period. Of the 1155 cases of vascular tumours, 40% (n = 453) were diagnosed as HA and 60% (n = 702) as HSA.

5.3. Cutaneous vs non-cutaneous vascular tumours

The proportion of cutaneous and non-cutaneous vascular tumours of both neoplasms was calculated, where a higher proportion of cutaneous neoplasms was obtained in both types, like is shown in table 3.

Vascular tumour	n	Cutaneous	Non-cutaneous
Hemangioma	453	94.5%	3.9%
Hemangiosarcoma	702	77.6%	20.9%
Total	1155	84.6%	13.8%

Table 3: Comparison of cutaneous and non-cutaneous vascular tumours in dogs according to the type of neoplasia

5.4. Anatomic location of cutaneous vascular tumours

Of the 453 diagnosed HA, the most common locations were the thorax, lumbar region, hind limbs, head and face, neck, and trunk. In 9.5% of cases, the anatomical location of the skin was not specified.

On the other hand, regarding HSA, the most common locations were the lumbar region, skin of the penis and scrotum, hind limbs, thorax, abdominal region, trunk, mammary glands, and forelimbs. In 9.6% of cases, the anatomical location is unknown.

The distribution of anatomical location of both neoplasms is expressed in Table 4.

Cutaneous location	Hemangioma (%)	Hemangiosarcoma (%)
Abdominal region	2.1%	6.6%
Auditory system	0.2%	0.4%
Eye and adnexa	0.5%	1.1%

Cutaneous location	Hemangioma (%)	Hemangiosarcoma (%)
Forelimb	5.4%	2.9%
Head and face	7.7%	2.4%
Hindlimb	14.6%	9.9%
Limb	0.0%	0.2%
Lumbar region	16.4%	29.4%
Mammary gland (skin)	0.7%	3.1%
Neck	6.3%	1.7%
Paws	0.5%	0.2%
Pelvic region	1.9%	0.7%
Perianal region	2.6%	1.3%
Scrotum and penis (skin)	5.4%	18.2%
Skin NOS*	9.4%	9.4%
Tail	2.6%	0.4%
Thorax	17.6%	8.1%
Trunk	6.1%	4.0%

Note: 'NOS stands for Not otherwise specified.

Table 4: Anatomical distribution of cutaneous vascular tumours.

5.5. Anatomic location of non-cutaneous hemangiosarcoma

Regarding non-cutaneous hemangiosarcomas (n = 155), the most common location is the spleen, accounting for more than half of the cases. This is followed by the oral cavity, liver and pancreas, lymph nodes, female reproductive system, urinary system, eyes and appendages, and heart.

Non-cutaneous location	Hemangiosarcoma (%)
Spleen	58.5%
Oral cavity	10.2%
Liver and pancreas	8.2%
Lymph node	8.2%
Female reproductive system	4.1%
Urinary system	3.4%
Eye and adnexa	2.7%
Heart	2.7%
Abdominal cavity	0.7%
Respiratory tract	0.7%
Retroperitoneum and peritoneum	0.7%

Note: 'NOS stands for Not otherwise specified.

Table 5: Anatomical distribution of non-cutaneous HSA.

5.5.1. Anatomic location of non-cutaneous hemangiosarcoma by sex

The same analysis was conducted, separating the cases by sex.

In females, it was observed that more than half of the tumours developed in the spleen, followed by the liver and pancreas, oral cavity, female reproductive system, eyes and appendages, lymph nodes, urinary system, heart, abdominal cavity, and respiratory tract. No cases were observed in females in the peritoneum and retroperitoneum.

In males, a higher proportion was observed in the spleen compared to females. The next most common locations were lymph nodes, oral cavity, heart, urinary system, and peritoneum and retroperitoneum. No cases were found in males for the respiratory tract, abdominal cavity, or eyes and appendages.

Non-cutaneous location	Female (%)	Male (%)
Abdominal cavity	1.4%	0.0%
Eye and adnexa	4.2%	0.0%
Female reproductive system	8.3%	0.0%
Heart	2.8%	2.7%
Liver and pancreas	11.1%	5.4%
Lymph node	4.2%	12.2%
Oral cavity	11.1%	9.5%
Respiratory tract	1.4%	0.0%
Retroperitoneum and peritoneum	0.0%	1.4%
Spleen	51.4%	66.2%
Urinary system	4.2%	2.7%

Note: 'NOS stands for Not otherwise specified.

Table 6: Anatomical distribution of non-cutaneous HAS by sex.

5.6. Anatomic location of multiple vascular tumours

In the case of HA, out of the 387 diagnosed dogs, a total of 27 dogs presented with more than one vascular tumour at the time of diagnosis. Of these, 25% (n = 7) had more than one skin lesion with unspecified location in the report. Another 25% had skin tumours in the lumbar region, and 10.7% (n = 3) were in the trunk. Other locations included the forelimb, hind limb, thorax, abdominal region, mammary glands, neck, spleen, penis, and testicles.

Regarding HSA, out of 597 dogs, 45 presented with multiple neoplasms, with the most common location being the lumbar region, which had a prevalence of 41.7% (n = 20). In the skin of the penis and scrotum, it appeared in 12.5% of cases (n = 6). Additionally, 12.5% of cases had nonspecific skin tumours and 8.3% (n = 4) were found in the forelimb. Other locations included lymph nodes, abdominal region and thorax, female reproductive system, neck, spleen, trunk, and testicles and penis.

The distribution of multiple tumours according to whether HA, HSA or both were present is shown in Table 7.

Multiplicity	Dogs (n)	Proportion (%)
Multiple hemangiosarcoma	45	60.0%
Multiple hemangioma	27	36.0%
Hemangioma and Hemangiosarcoma	3	4.0%
Total	75	-

Table 7: Proportion of multiple vascular tumours

5.7. Age at diagnosis

The median age at diagnosis of dogs with HA and HSA respectively was calculated, represented in table 8, giving a median age of 9 years in both cases, with a non-significant p-value (Graphic 2).

The age range analysed was from 1 to 18 years. Most cases were diagnosed between 7 and 12 years of age, although about 40 cases were diagnosed before 3 years of age.

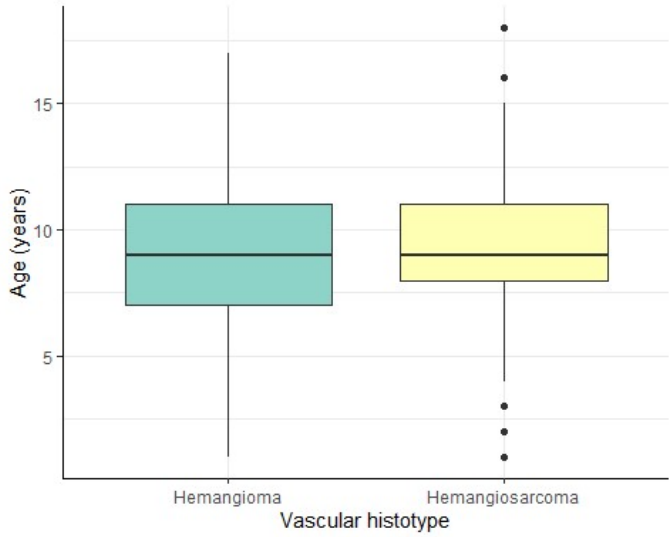
Variable	Overall N =1155	Diagnosis		P-value
		Hemangioma N =453	Hemangiosarcoma N =702	
Age	9.00 (7.00; 11.00)	9.00 (7.00; 11.00)	9.00 (7.25; 11.00)	0.8186

Table 8: Age range of HA and HSA, using non-parametric tests (Wilcoxon test).

On the other hand, when performing the variable differentiating the anatomical location of the neoplasms, we observe that there are important variations, contemplated in the table 9. In this case, a significant difference is observed, with the age of presentation being noticeably higher in the case of the liver and pancreas.

Variable	Overall N =636	Location				P-value
		Heart N =4	Liver and pancreas N =12	Skin N =534	Spleen N =86	
Age	9.00 (7.00; 11.00)	9.50 (7.25; 11.75)	12.00 (10.00; 13.25)	9.00 (7.00; 11.00)	10.00 (8.00; 12.00)	0.0002

Table 9: Age range of HA and HSA according to the location, using non-parametric tests (Wilcoxon test).



Graphic 2: Representation of the mean age at diagnosis of vascular neoplasms in this research

5.8. Breed distribution of dogs diagnosed with vascular tumours

Breed distribution of dogs with diagnosis of hemangioma (only breeds with at least 5 diagnosis) was calculated and it was found that the breeds with the most cases of HA were the Crossbreed, Boxer, German Shepherd, French Bulldog and Labrador Retriever. Next, we compared this distribution with the distribution of breeds registered in Zoocan (used as reference) and found that some breeds were overrepresented. For example, the proportion of Boxers in the Zoocan database was 0.7% while, on the hemangioma dataset, proportion of Boxers were 10.7% (Table 10). Other breeds overrepresented were German Shepherd, Cocker Spaniel, Golden Retriever, Poodle and French Bulldog. Conversely, some breeds were underrepresented as the Canarian Warren Hound represented with a lower proportion on the hemangioma dataset (1.8%) than on the Zoocan database (15.9%).

Breed	Dogs from Zoocan (%)	Dogs with hemangiomas (%)	Difference (%) HA dataset and Zoocan dataset
Crossbreed	35.5%	35.7%	0.2
Canarian Warren Hound	15.9%	1.8%	-14.1
Yorkshire Terrier	6.5%	3.6%	-2.9
English Pointer	2.7%	2.1%	-0.6
French Bulldog	2.5%	3.9%	1.4
Labrador Retriever	2.4%	3.3%	0.9
Canarian Mastiff	2.4%	1.8%	-0.6
German Shepherd Dog	2.1%	7.4%	5.3
Pit Bull Terrier	1.7%	2.4%	0.7
Poodle	0.9%	2.7%	1.8
Golden Retriever	0.9%	2.1%	1.2
Cocker Spaniel	0.8%	2.1%	1.3
Boxer	0.7%	10.7%	10

Table 10: Comparison of breeds between the control group consisting of dogs registered in the Canary Islands Animal Identification Registry (Zoocan) (n=328265) and dogs with HA.

Regarding hemangiosarcoma, the distribution of breeds with the most cases of HSA were Crossbreeds, Boxers, English pointers, German shepherds, Pitbull terriers, and French bulldogs. In this case, when comparing the distribution of dogs with HSA with the distribution of breeds registered in Zoocan, the overrepresented breeds were Boxers, English pointers, Pitbulls Terrier, French Bulldog, Beagle and German Shepherds, as

shown in the table 11. As in the HA, the Canarian Warren Hound is underrepresented, representing only 3.6% of HSA cases.

Breed	Dogs from Zoocan (%)	Dogs with hemangiosarcoma (%)	Difference (%) HAS and Zoocan dataset
Crossbreed	35.5%	32.2%	-3.3
Canarian Warren Hound	15.9%	3.6%	-12.3
Yorkshire Terrier	6.5%	1.5%	-5
English Pointer	2.7%	6.1%	3.4
French Bulldog	2.5%	4.2%	1.7
Labrador Retriever	2.4%	3.8%	1.4
Canarian Mastiff	2.4%	1.5%	-0.9
German Shepherd Dog	2.1%	4.9%	2.8
Pit Bull Terrier	1.7%	4.0%	2.3
Poodle	0.9%	1.5%	0.6
Golden Retriever	0.9%	1.3%	0.4
Cocker Spaniel	0.8%	1.1%	0.3
Boxer	0.7%	8.5%	7.8
Beagle	0.6%	3.2%	2.6
Bull terrier	0.5%	1.9%	1.4
Canarian Mastiff	2.4%	1.5%	-0.9

Table 11: Comparison of breeds between the control group consisting of dogs registered in the Canary Islands Animal Identification Registry (Zoocan) (n=328265) and dogs with HSA.

5.9. Sex distribution

The sex distribution between dogs with vascular tumours and the control group consisting of dogs enrolled in Zoocan was compared (Table 12).

The Chi-square statistical test performed on the individuals shown in the table below presented a significant p-value (p-value = 0.04236).

Sex	Dogs with vascular tumours (%)	n	Dogs from ZOOCAN (%)
Female	51.3%	323474	54.7%
Male	48.6%	268424	45.3%

Table 12: Comparison of sexes with vascular tumours of a control group of dogs registered in the Canary Islands Animal Identification Registry (n = 328265)

5.10. Neutered status

The percentage of neutered and entire dogs with vascular tumours by sex was obtained. The record of sterilized and intact dogs from Zoocan was also obtained, but no further analysis was performed because the data obtained from Zoocan is not representative of the population.

Dogs with vascular tumours (%)	Entire	Neutered
Female	59.8%	40.2%
Male	74.1%	25.9%

Neuter_status	Dogs from Zoocan (%)
Entire	89.9%
Neutered	10.1%

Table 13: Comparison of the neutered status in dogs with vascular tumours by sex and the distribution of entire and neutered dogs registered in Zoocan

5.11. Geographical distribution of dogs with cutaneous hemangiosarcoma

Regarding the geographical distribution of the islands of Gran Canaria, Table 14 shows the municipalities where at least 5 cases of dogs with cutaneous vascular tumours were

diagnosed, compared with the dogs registered in Zoocan and the distribution of all neoplastic pathologies that were diagnosed in said municipality.

Municipality	Annual solar irradiance (Wh/m2)	Distribution of dogs per municipality according to Zoocan (%)	Distribution of all tumours per municipality (%)	Distribution cutaneous vascular tumours per municipality (%)
Agüimes	225.9	1.8%	6.7%	9.3%
Arucas	200.4	1.8%	3.5%	3.1%
Las Palmas de Gran Canaria	119.1	10.6%	22.4%	18.7%
San Bartolomé de Tirajana	228.4	2.9%	5.8%	5.3%
Santa Brígida	203.7	1.2%	2.3%	4.9%
Santa Lucía de Tirajana	230.7	2.8%	5.1%	5.3%
Santa María de Guía	202.6	0.8%	2.2%	2.7%
Telde	221.8	4.8%	10.5%	5.3%

Table 14: Table comparing relative proportion of vascular tumours with other kind of tumours per municipality of Gran Canaria

The municipalities of Gran Canaria with the highest annual solar irradiance are Santa Lucía de Tirajana, San Bartolomé de Tirajana, Agüimes and Telde.

The municipalities that present an overrepresentation of vascular tumours with respect to the canine population of the area are Agüimes, Santa Brígida, Las Palmas de Gran Canaria, Santa Lucía de Tirajana and San Bartolomé de Tirajana.

The proportion of breeds registered in each municipality affected by HSA was also analysed to determine whether there is a relationship between the overrepresentation of cases and a higher population of predisposed breeds according to the literature, which are Golden Retriever, Labrador Retriever, Beagle, Boxer and Pitbull Terrier, as mentioned by Nobrega et al. (2019) and De Nardi et al., (2023) in their respective studies.

Breed	Agüimes	Arucas	Las Palmas de Gran Canaria	San Bartolomé de Tirajana	Santa Brígida	Santa Lucía de Tirajana	Santa María de Guía	Telde
Crossbreed	53.1%	47.3%	54.9%	45.5%	46.5%	43.7%	35.3%	47.2%
Beagle	0.4%	1.0%	1.1%	0.6%	1.3%	0.6%	0.7%	0.9%
Boxer	0.7%	0.9%	0.6%	0.7%	1.2%	0.5%	1.3%	0.8%
Bull Terrier	1.2%	0.8%	0.9%	0.7%	0.3%	0.7%	0.8%	0.8%
Bulldog	0.6%	0.9%	1.1%	0.7%	0.6%	0.7%	1.9%	0.8%
Canarian Mastiff	2.4%	3.7%	2.0%	2.4%	2.4%	2.3%	5.9%	3.9%
Canarian Warren Hound	19.0%	14.8%	8.6%	24.7%	21.7%	21.0%	21.5%	19.8%
Cocker Spaniel	0.8%	0.8%	1.0%	0.8%	0.7%	0.9%	0.7%	0.7%
English Pointer	1.8%	1.8%	1.1%	2.6%	4.1%	2.8%	4.3%	2.1%
French Bulldog	3.0%	4.0%	4.3%	3.2%	2.1%	4.7%	4.4%	3.3%
German Shepherd Dog	2.2%	3.3%	2.4%	2.2%	3.4%	1.9%	3.7%	2.5%
Golden	0.4%	0.7%	1.0%	0.7%	1.9%	0.4%	0.4%	0.6%

Breed	Agüimes	Arucas	Las Palmas de Gran Canaria	San Bartolomé de Tirajana	Santa Brígida	Santa Lucía de Tirajana	Santa María de Guía	Telde
Retriever								
Labrador Retriever	3.2%	4.8%	3.5%	3.1%	5.3%	3.4%	4.0%	3.1%
Pit Bull Terrier	2.0%	3.2%	2.9%	1.9%	1.2%	3.1%	2.3%	2.7%
Poodle	0.4%	0.6%	1.1%	1.1%	0.7%	0.7%	0.5%	0.7%
Staffordshire Bull Terrier	0.8%	1.9%	1.4%	1.3%	0.6%	1.3%	4.4%	1.0%
Yorkshire Terrier	8.0%	9.5%	12.2%	7.7%	6.0%	11.2%	8.1%	9.0%

Table 15: Comparison of breeds by municipality

It was found that municipalities with many cases and high annual solar irradiance (Agüimes, Santa Lucía de Tirajana and San Bartolomé de Tirajana) did not show a significant proportion of dogs of predisposed breeds (Golden Retriever, Labrador Retriever, Beagle, Boxer and Pitbull Terrier).

In Las Palmas de Gran Canaria, despite not having high solar irradiance, a high population of dogs of predisposed breeds was not found either.

On the other hand, in the case of Santa Brígida, with overrepresented cutaneous HSA but with low solar irradiance, a higher proportion of dogs of the Beagle, Boxer, Golden Retriever and Labrador Retriever breeds was observed compared to the other municipalities.

6. DISCUSSION

The present study has characterized the nature of vascular tumours in dogs, with a sample of 702 hemangiosarcomas and 453 hemangiomas in 597 and 387 dogs respectively.

More cases of HSA were diagnosed than HA. Additionally, HSA presented more cases of multiple tumours. These data are contrary to what has been previously described regarding vascular tumours, as both Schultheiss (2004) and Soares et al. (2017) state that HA are more frequent than HSA, both cutaneous and visceral, which aligns with the data collected by Graf et al. (2018), where the incidence of HA in Switzerland was higher than that of HSA. We can suspect that the lack of HA cases in our study may be due to the fact that, being a benign disease, the limited extent of lesions and clinical consequences may have led pet owners not to show concern for it and, consequently, many cases went undiagnosed.

A gradual increase in the diagnosis of cases was detected over the study period, which was more significant in the case of HSA. This could be because, over time, dog owners have acquired more knowledge about the importance of veterinary consultations and more check-ups have been carried out. It could also be due to an increase in the density of the canine population in the Canary Islands, as well as the implementation of better diagnostic methods.

When analysing the frequency of vascular tumours in relation to other tumours in dogs, it is observed that these neoplasms represent almost 6% of tumours of all etiologies. These data are consistent with previous studies, which indicate that vascular tumours account for approximately 5-6% of tumours (Griffin et al., 2021, Martins et al., 2022). In addition, it was found that most vascular tumours were located in the cutaneous tissue. These data are consistent with what has been observed in previous studies, which have shown that almost all HA develop in the cutaneous tissue, as do a large part of HSA (Schultheiss, 2004, Flores et al., 2012).

The most frequent cutaneous locations in HSA were the lumbar area, the skin of the penis and scrotum, the hind limbs and the thorax; while in HA were the thorax, the lumbar area, the hind limbs and the head and face. According to the literature, the areas frequently affected by HSA are usually the ventral abdomen, inguinal region, the pelvic

limbs and the conjunctiva (Mullin and Clifford, 2019). The lumbar area, where a significant part of the cases collected in the present study were found, is not a preferred location for cutaneous HSA, but it should be noted that, in this study, the tissue of origin of the neoplasms was not assessed, so it cannot be discern whether these cases are of HSA derived from dermal or subcutaneous tissue, and, this last variant is not affected by solar radiation nor does it present preferred locations, as does the dermal variant (Bulakowski et al., 2008). There is also insufficient data to clarify whether the tumours presented lesions typical of sun damage, such as solar steatosis. Regarding HA, the most frequent anatomical locations were the extremities and the abdominal region for sun-induced HA and the dorsal region for non-sun-induced HA (Hargis, 1992, Martins et al., 2022), which is consistent with our results.

Regarding non-cutaneous locations of HSA, we observed than more than half of HSA were found on the spleen in line with other studies like those performed by Hendrick, MJ (2016) and Griffin et al. (2021). In other studies, the most prevalent locations after the spleen are usually the right atrium and liver (Smiths et al., 2003), however, in our results, we obtained few cases affecting the heart, and a significant amount in the female reproductive organ and oral cavity.

Regarding multiple tumours, more than half of the dogs diagnosed were HSA and a small proportion had both. Both types were found more frequently in the lumbar region. Multiple tumours in visceral locations were not studied. According to Hargins et al. (1994), cutaneous vascular tumors are commonly multicentric, especially those induced by sun exposure. In addition, regional and distant metastases are common, both in cutaneous and visceral tumors (Shiu et al., 2011, Griffin et al., 2021).

About the median age, we did not observe differences in age at diagnosis of HA and HSA, However, liver and pancreas HSA were diagnosed at older ages than other locations. As described in previous studies, advanced age is a risk factor for the development of neoplasms (Graf et al., 2018), and HA occurs in younger animals than HSA, as well as cutaneous tumours appear before visceral tumours (Schultheiss, 2004).

Regarding breeds, HA was overrepresented in Boxers, German Shepherds, and Poodles, while the overrepresented breeds for HSA were Boxers, English Pointers, German Shepherds, Pit Bull Terriers, and Beagles. According to Nóbrega et al. (2019), the

breeds with the highest incidence of cutaneous HSA are Pitbulls, Whippets, Greyhounds, Boxers, Beagles, and Dalmatians, while subcutaneous and muscular HSAs develop more frequently in Golden Retrievers, Labrador Retrievers, and crossbreeds (De Nardi et al., 2023). Nevertheless, visceral HSAs are more commonly found in German Shepherds, Golden Retrievers, Labradors, Pointers, Great Danes, and Cocker Spaniels (Smiths, 2003), while HA is associated with Labrador Retrievers, Boxers, Argentine Dogo, German Shepherds, Pitbulls, and Golden Retrievers (Martins et al., 2022). In the data from this study, anatomical location was not taken into account for breed variation; therefore, it could not be determined whether proportions vary. However, it can be confirmed that some breeds presented align with those predisposed to developing this pathology in the previously cited studies. This raises the theory that there may be a genetic predisposition in certain breeds that makes them more susceptible to this pathology. A study conducted by Tonomura et al. (2015) determined that Golden Retrievers in the U.S. show a significantly elevated risk of developing hemangiosarcoma and found two loci associated with chromosome 5 that together contribute 20% to the risk of developing the neoplasm. These data should be taken with caution since this study was conducted on USA dogs which genetic relation with dogs in our study is uncertain. In the cases collected in this study, Golden Retrievers are not among the breeds with a higher predisposition to present vascular tumours as Boxers are; therefore, it is possible that Boxers in the Canary Islands carries genes that increase the risk of developing vascular tumours. However, future studies on this matter need to be conducted. Unlike what happens with the previously mentioned breeds, the Canarian Warren Hound shows a marked underrepresentation, as it is one of the most common breeds in the Canary Islands, yet few cases of HA and HSA were recorded. This may raise the theory that it is a breed resistant to the formation of vascular tumours; however, in this case, a more sociological approach should be taken, as this breed is generally used for hunting. This group typically does not show concern for the health status of their animals, as they are commonly regarded as working animals rather than sentient beings. This may have led to them not being taken to the veterinarian and consequently not having the neoplasia diagnosed before the dog's death. This theory is supported by a study performed by the Affinity Foundation about the abandonment of animals in Spain, which mentions the end of the hunting season as one of the main causes of dog abandonment.

On the other hand, regarding the sex of the animals, the cases in females are slightly higher, but, when compared with the data of the dogs registered in Zoocan, it can be observed that in this registry there are more females than males, so males are overrepresented, with a significant p-value in the presentation in males, being able to reach the conclusion that the male sex has a higher risk of suffering from the disease. In previous studies, a consensus has not been reached on the relationship of sex with a higher incidence of vascular tumours, since in some cases, such as in the study carried out by Sharif et al. (2006) there is a higher incidence in males, while in others, such as the retrospective study by Soares et al. (2017), the variation is null.

Regarding the neutered status, 66.8% of the dogs were intact, while 32.2% had been sterilized. This data could not be compared with the general dog population of the Canary Archipelago because, in the registry of dogs registered in the Canary Islands, the neutered variable is not reliable. This is because, generally, the registration of the animals is carried out at the first veterinary consultation and it is not common to update the data in subsequent consultations, so the neutered status is not representative. This is demonstrated by comparing the proportion of sterilized and intact dogs in the data of dogs with vascular tumours compared to those obtained from the Zoocan registry, since the results vary significantly. However, according to Robinson et al. (2020) and Torres de la Riva et al. (2013), sterilized dogs are at higher risk of suffering from visceral HSA, particularly splenic and cardiac types, and affecting females more significantly.

Regarding the geographical location of the cases on the island of Gran Canaria, the municipalities with an overrepresentation of vascular tumours compared to the canine population in the area were Agüimes, Santa Brígida, Las Palmas de Gran Canaria, Santa Lucía de Tirajana, and San Bartolomé de Tirajana. Additionally, the proportion of theoretically prevalent breeds according to the literature was studied in these municipalities. It was observed that municipalities with high annual solar irradiance, such as Agüimes, Santa Lucía de Tirajana, and San Bartolomé de Tirajana, did not have a significant proportion of these breeds. In contrast, Santa Brígida, which has notably lower solar irradiance than the previously mentioned municipalities, did have a significant population of these breeds. Based on this data, the higher proportion of vascular tumours in these areas appears to align more closely with the prevalence of predisposed breeds (e.g., Golden Retrievers) rather than the impact of solar radiation.

However, we acknowledge that our methodology may not have been sensitive enough to establish a robust link between solar radiation and cutaneous vascular tumours. First, the data from Grafcan represents a single average irradiance value for an entire municipality, which may not reflect variations within specific areas. Second, municipalities with higher incomes may have owners who are more likely to invest in veterinary care, potentially biasing the data. Third, the geographical variable was based on where the animals were diagnosed rather than their place of residence, which could introduce confounding factors.

For instance, in Las Palmas de Gran Canaria, the higher percentage of cases—despite its lower solar irradiance may be attributed to its status as the island's capital, with the largest population (both human and canine) (INE - National Institute of Statistics, n.d.), greater availability of veterinary clinics, and higher average income compared to other areas. Additionally, this trend might reflect greater awareness and concern for pet health among urban pet owners or a preference for seeking veterinary care in the capital, even for residents of more rural areas.

In conclusion, more solid methodologies are needed to contrast the role of solar radiation as risk factor for cutaneous vascular tumours as has been shown in former studies (Soares et al., 2017; Carnio et al., 2020; Hargins et al., 1992).

No follow-up was conducted on the patients, so it was not possible to study the survival time or prognosis of these cases.

7. CONCLUSION

1. Hemangiosarcomas are more common than hemangiomas in dogs in the Canary Islands.

2. Cutaneous vascular tumours occur at a significantly higher percentage than visceral tumours in dogs.

3. The most affected anatomical locations for canine vascular tumours are the lumbar region in cutaneous cases and the spleen in visceral cases. The lumbar region is also the most frequently affected by multiple lesions.

4. The age of presentation for canine vascular tumours is approximately 9 years, appearing earlier in HA and in cutaneous lesions compared to visceral ones for both neoplasms.

5. The most common dog breeds associated with hemangiomas (HA) and hemangiosarcomas (HSA) include Boxers, German Shepherds, and Poodles, with additional predispositions for HSA observed in English Pointers and French Bulldogs.

6. Vascular tumours show a slight predisposition towards male dogs compared to females. However, the potential influence of neutering status on the presentation of these tumours could not be assessed due to insufficient reliable data.

7. More refined methodologies are needed to evaluate the potential role of solar radiation as risk factor for cutaneous vascular tumours, accounting for detailed individual and environmental factors.

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