


**STANDARD ARTICLE**

# Prevalence, distribution, and clinical characteristics of hemangiosarcoma-associated skeletal muscle metastases in 61 dogs: A whole body computed tomographic study

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**Background:** Skeletal muscle metastases (SMMs) have been described sporadically in canine oncology.

**Hypothesis/Objectives:** To determine the prevalence, localization, and clinical signs of SMMs associated with hemangiosarcoma (HSA) in a population of dogs presented for whole body computed tomography (CT).

**Animals:** Dogs with a histologically confirmed HSA and a tissue core specimen or fine needle aspirate of suspected metastatic lesions were included in the study.

**Methods:** Retrospective study. Dogs with a final diagnosis of visceral or muscular HSA that underwent whole body CT scan were enrolled in the study. Final diagnosis of primary tumor and SMMs was reached by histology, cytology, or both. Signalment, clinical signs, localization of the primary lesion, and metastases characteristics were reviewed.

**Results:** Sixty-one dogs met the inclusion criteria. Skeletal muscle metastases were detected in 15 dogs (24.6%) and all of these dogs had also metastases in  $\geq 1$  sites. Presence of SMMs was significantly higher in males but was not significantly related to age, neuter status, breed, localization, and dimensions of the primary tumor. Nine of 15 (60.0%) dogs with SMMs showed lameness or reluctance to move whereas these signs were not recorded in any of the 42 dogs without SMMs ( $P < .001$ ).

**Conclusion and Clinical Importance:** Prevalence of SMMs in our population of dogs with HSA was higher in comparison to previous studies in the human and veterinary medical literature. Whole body CT is recommended for staging of dogs with HSA, because SMMs could be missed by clinical examination and traditional diagnostic imaging modalities.

**KEYWORDS**

dogs, imaging, lameness, oncology

**Abbreviations:** <sup>18</sup>F-FDG, <sup>18</sup>F-fluoro-2-deoxyglucose; CECT, contrast-enhanced computed tomography; CI, confidence intervals; CT, computed tomography; HSA, hemangiosarcoma; MDCT, multidetector computed tomography; ORs, odds ratios; PET, positron emission tomography; SMMs, skeletal muscle metastases; SPSS, statistical package for social science.

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## 1 | INTRODUCTION

Hemangiosarcoma (HSA) represents approximately 5% of all non-cutaneous primary malignant neoplasms and 12% to 21% of all mesenchymal neoplasms in the dog.<sup>1</sup> Hemangiosarcoma is a neoplasm of vascular endothelial origin that potentially can affect any anatomic site either as a primary or metastatic tumor.<sup>2</sup> It is characterized by aggressive biological behavior because of its high metastatic potential, which leads to a poor prognosis.<sup>3</sup> Hemangiosarcoma affects most every breeds, but, German Shepherd Dogs, Golden Retrievers, Labrador Retrievers, and Schnauzers are predisposed.<sup>4</sup> Males seem to have a higher risk of developing HSA than do females.<sup>5</sup> In the dog, the most common primary site is the spleen, and the most frequent metastatic sites are the liver, omentum, mesentery, and lungs.<sup>1</sup> The presence of primary HSA in other tissues such as liver, right atrium, mesentery, kidney, muscle, skin, subcutaneous tissue, conjunctiva, as well as intrathoracic, retroperitoneal, and epidural spaces has been described.<sup>4,6-12</sup>

Skeletal muscular metastases (SMMs), although uncommon, previously have been described in dogs and cats and have been mainly reported in the limbs.<sup>10,13-16</sup> Skeletal muscular metastases have been considered rare in humans, typically occurring late in the disease course and representing <5% of all cases of systemic metastasis.<sup>17</sup> In humans, the most common malignancy metastasizing to the skeletal musculature is lung cancer, followed by gastrointestinal cancer and renal cell carcinoma with the most commonly reported metastatic sites being the paraspinal muscles and skeletal muscles of the lower extremities.<sup>17,18</sup> The rare occurrence of metastasis to skeletal muscle suggests that this organ may be in fact a hostile environment for tumor emboli.<sup>17</sup> As a consequence, SMMs may progress more slowly than tumor deposits elsewhere in the body or present later in the disease course.<sup>19</sup> Presence of SMMs supports a poor prognosis because their detection indicates widespread metastatic disease (stage III).<sup>1</sup>

In veterinary medicine, the use of ultrasound to detect SMMs in a dog with splenic and cardiac HSA has been described previously.<sup>20</sup> Another study described the use of whole body computed tomography (CT) to detect muscular metastatic lesions from a range of primary malignant neoplasms and to guide tissue sampling.<sup>16</sup> Our aims were to describe the prevalence, distribution, and clinical characteristics of SMMs in dogs with HSA.

## 2 | MATERIALS AND METHODS

### 2.1 | Experimental design

The study was a multicenter retrospective study. The archives of 3 Italian referral veterinary clinics (Pet Care Veterinary Association, Bologna; I Portoni Rossi Veterinary Hospital, Zola Predosa, Bologna; and Blucenter Veterinary Clinic, Rovigo) were reviewed for dogs with histologic diagnosis of HSA. At these centers, all of the patients included in the study were referred for whole body CT for suspected or diagnosed HSA.

Inclusion criteria were a whole body CT scan and histologically confirmed primary HSA. A tissue core biopsy specimen or fine needle

aspirate of suspected metastatic lesions was performed in each patient under CT or ultrasound guidance. Cases in which HSAs were limited to cutaneous tissues were excluded, because of their less aggressive biological behavior.<sup>21</sup>

Signalment and clinical (eg, anorexia, lethargy, respiratory signs, lameness, and reluctance to move) were retrieved from the clinical records.

### 2.2 | Imaging

Studies were performed with 3 different multidetector CTs (MDCT): (1) a 16-slice MDCT unit (Aquilion, Toshiba Medical Systems Corporation; Tokyo, Japan, at I Portoni Rossi Veterinary Hospital, Zola Predosa, Bologna; n = 11, 18.0%); (2) an 8-slice MDCT unit (BrightSpeed, General Electric Co., Milwaukee, Wisconsin, at Pet Care Veterinary Association, Bologna; n = 40, 65.6%); and (3) a 4-slice MDCT unit (Pronto, Hitachi Ltd., Tokyo, Japan, at Blucenter Veterinary Clinic, Rovigo; n = 10, 16.4%). Animals were anesthetized using different protocols and positioned in sternal recumbency. At I Portoni Rossi Veterinary Hospital, all the patients were ventilated, whereas at Pet Care Veterinary Association and Blucenter Veterinary Clinic, the animals were maintained on spontaneous ventilation.

All of the studies were acquired in helical scan mode and with slice thickness of 1 mm. Contrast-enhanced images were obtained using 600 mg I/kg of nonionic water soluble iodinated contrast medium injected into a cephalic vein with a power injector at 3 mL/s through an IV catheter. Iopamidol (Iopamiro, Bracco Imaging S.p.A., Milan, Italy) was used at the I Portoni Rossi Veterinary Hospital, whereas, Ioversol (Optiray, Mallinckrodt Italia S.p.A., Milan, Italy) at the Pet Care Veterinary Association and Blucenter Veterinary Clinic. The post-contrast CT study was acquired 35-40 seconds after the start of contrast medium administration. All patients received IV fluids during anesthesia.

All images were retrospectively reviewed by 2 radiologists (MP and MV). Localization and diameter of the presumed primary HSA lesions were recorded. Post-contrast CT characteristics of SMMs included size, margination, shape, and pattern of contrast enhancement. On the basis of the localization, the SMMs were divided into 4 groups: "epaxial/paraspinal muscles," "thoracic/abdominal wall muscles," "appendicular skeletal muscles," and "other muscles." If SMMs were present in only 1 group, they were considered as a "single site" metastasis, whereas if SMMs were present >1 group, they were considered as "multiple site" metastases. Presence and localization of other metastatic lesions also were evaluated.

In the event of disparity in any of these characteristics, a consensus was reached by review of the images by both radiologists.

### 2.3 | Ethics

All animals included in the study were client-owned and for each case an informed consent was signed by the owner. All animals received humane care according to the principles outlined in the "Good Clinical Practice (VICH GL9)" proposed by the US Department of Health and Human

**TABLE 1** Additional metastatic sites according to primary tumor localization

Additional metastatic sites	Overall	Presumed primary tumor localization				
		Spleen (n = 40)	Liver (n = 9)	Muscles (n = 5)	Peritoneum (n = 4)	Others (n = 3)
Spleen	17 (27.9%)	9 (22.5%)	4 (44.4%)	2 (40.0%)	0	2 (66.7%)
Liver	21 (34.4%)	12 (30.0%)	5 (55.6%)	1 (20.0%)	2 (50.0%)	1 (33.3%)
Right atrium	3 (4.9%)	2 (5.0%)	1 (11.1%)	0	0	0
Kidney	7 (11.5%)	6 (15.0%)	0	0	0	1 (11.5%)
Bone	3 (4.9%)	2 (5.0%)	0	0	1 (25.0%)	0
Lungs	20 (32.8%)	11 (27.5%)	4 (44.4%)	2 (40.0%)	1 (25.0%)	2 (66.7%)
Lymph nodes	11 (18.0%)	6 (15.0%)	3 (33.3%)	0	2 (50.0%)	0
Abdominal effusion	10 (16.4%)	7 (17.5%)	2 (22.2%)	0	1 (25.0%)	0
Other sites	11 (18.0%)	5 (12.5%)	2 (22.2%)	0	1 (25.0%)	3 (100%)

Services, Food and Drug Administration, Center for Veterinary Medicine (2001).

## 2.4 | Statistics

Mean, SD, range, and frequencies were used as descriptive statistics. Logistic regression was applied to identify factors significantly associated with SMMs and odds ratios (ORs) and their 95% confidence intervals (95% CI) were computed. Age, sex, neuter status, breed, primary tumor location and dimension, and additional metastatic sites were the putative factors considered for logistic regression analysis. The Fisher exact test was used instead of logistic regression when null frequency occurred and no OR could be determined. Data were analyzed using the SPSS Statistics package (IBM Co., Armonk, New York; Version 23) and 2-tailed *P* values <.05 were considered significant.

## 3 | RESULTS

Sixty-one dogs of 21 different breeds met the inclusion criteria. The mean age was 10.3 ± 2.2 years (range, 4–15 years), 39 (63.9%) were males (6/39, 15.4% neutered) and 22 (36.1%) were females (9/22, 40.9% spayed) with a total of 15 (24.6%) animals that were sterilized. Crossbreed (n = 20, 32.8%), Golden/Labrador Retriever (n = 10, 16.4%), German Shepherd (n = 6, 9.8%), and Boxer (n = 6, 9.8%) were most commonly affected. The presumed primary tumor was located in spleen (n = 40, 65.6%), liver (n = 9, 14.8%), muscles (n = 5, 8.2%), and peritoneum (n = 4, 6.6%), as well as in right atrium, kidney, and mediastinum (n = 1, 1.6% each). The diameter of the primary lesion (mean, 8.3 ± 4.5 cm) was recorded in 53 (86.9%) of the 61 dogs with HSA because in the remaining 7 cases the dogs had undergone whole body CT after the primary tumor had been removed in 6 (5 in the spleen and 1 in the mesentery), and 1 in the right auricle was not well defined and impossible to measure.

Diagnosis of HSA metastasis was achieved by cytology in 24 (39.3%) dogs and by histopathology in 44 (72.1%), thus in 7 (11.5%) dogs both cytology and histopathology were available. Forty-six out of the 61 dogs (75.4%) had from 1 to 6 additional metastatic sites for

a total of 107 metastases in multiple organs. Spleen, liver, and lungs were the most frequent sites (Table 1).

## 3.1 | Prevalence of skeletal muscle metastasis

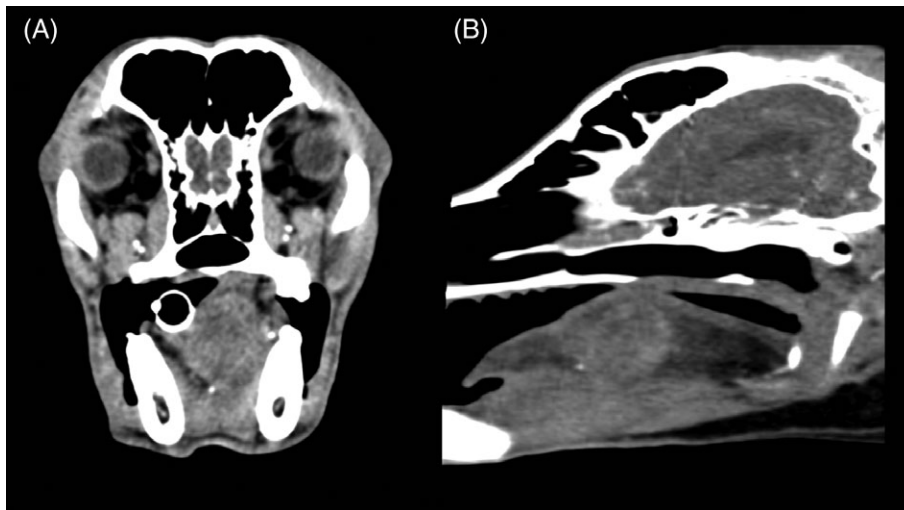
Skeletal muscle metastases were detected in 15 of 61 dogs (24.6%). On pre-contrast CT studies, SMMs were not identifiable. Post-contrast CT findings of SMMs consisted of multiple, well demarcated, oval-to-round lesions. Enhancement patterns varied from hypodense with ring enhancement to heterogeneously or homogeneously hyperdense. In each dog with SMMs, different lesions had different patterns of enhancement.

Of these 15 dogs, 11 (73.3%) had single lesions and 4 (26.7%) had multiple lesions identified. Ten dogs had metastases localized in the epaxial/paraspinal muscles (66.7%), 4 dogs in the thoracic/abdominal wall muscles (26.7%), 6 dogs in muscles of appendicular skeleton (40.0%), and 1 dog in the tongue muscles (6.7%; Figures 1 and 2).

Table 2 shows the prevalence of metastases according to the characteristics of the 61 HSA dogs. Presence of SMMs was significantly higher in males (35.9% versus 4.5%; OR, 11.8; *P* = .02) whereas age (*P* = .16), neuter status (*P* = .64), breed (*P* = .55) as well as localization (*P* = .82) and dimension of the presumed primary tumor (*P* = .69) were not significantly different between dogs with and without SMMs. All 15 dogs with SMMs also had additional metastatic lesions as compared to 31 of the 46 dogs without SMMs (*P* = .01). The presence of SMMs was positively related to the presence of additional metastases in kidney (OR, 11.0; *P* = .008), bone (*P* = .01), and lungs (OR, 7.20; *P* = .003), whereas the presence of SMMs in dogs with neoplastic cells in abdominal effusion failed to reach significance (*P* = .05). No statistical correlation has been found between the presence of SMMs and metastases in the liver, spleen, and lymph nodes.

## 3.2 | Clinical signs

Clinical signs were recorded in 57 of the 61 animals included in the study. Nine (60.0%) of the 15 dogs with SMMs showed signs of lameness or were reluctant to move whereas none of the 42 dogs without SMMs showed musculoskeletal signs (*P* < .001; Table 3). In these 9 dogs,



**FIGURE 1** A, Transverse and B, sagittal contrast-enhanced computed tomographic images of an 11-years-old neutered male cross-breed dog with a hemangiosarcoma metastasis in the tongue muscle. The lesion appears round, heterogeneous, and with mild ring enhancement

no other signs were recorded and, consequently, these 9 dogs initially were considered to have primary orthopedic or neurologic disease. No significant relationship was found between presence of SMMs and both lethargy and respiratory signs, whereas a higher frequency of SMMs was found in dogs with anorexia (20.0% versus 2.4%; OR, 10.3), although this difference was not statistically significant ( $P = .05$ ).

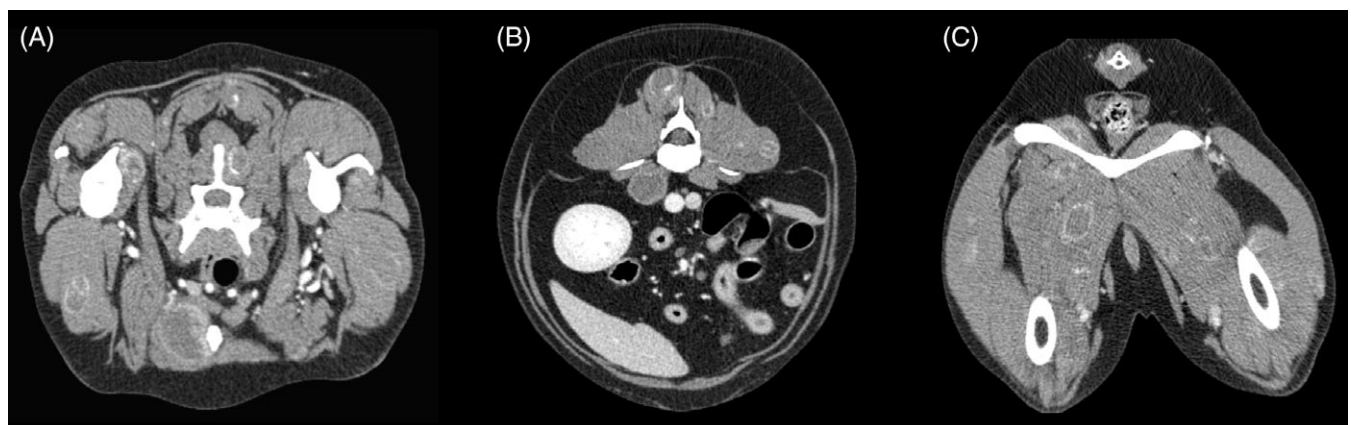
#### 4 | DISCUSSION

In dogs, HSA may be solitary, multifocal within an organ, or widely disseminated at presentation and because of its intimate association with the vasculature, facilitating extravasation and angiogenesis of metastatic clones, it is typified by very aggressive biologic behavior, with rapid and widespread metastasis occurring frequently.<sup>1</sup> In our study population, we found that the prevalence of SMMs in dogs with HSA was higher in comparison with previously published studies in the human and veterinary medical literature.<sup>16,17,22</sup> The higher prevalence of SMM in our cohort may reflect some selection bias and may be higher than that seen in all dogs with HSA. Clients may have opted for euthanasia of patients with radiologically overt metastasis, inoperable primary lesions, or clinically relevant comorbidities.

We found that 46 of 61 dogs with HSA had additional metastatic sites with spleen, liver, and lungs being most common, consistent with previous reports in the veterinary literature.<sup>1,7,23</sup>

As previously observed,<sup>10,23-25</sup> no statistical correlation was found in our study between the dimension of the primary tumor and the presence of metastasis, meaning that the size of the primary tumor alone cannot be used to estimate biological behavior, and even small tumors could result in widespread metastatic disease.

In humans, SMMs can be observed on CT with 5 types of lesion: intramuscular mass (type I), abscess-like intramuscular lesion (type II), diffuse metastatic muscle infiltration (type III), multiple muscle calcification (type IV), and intramuscular bleeding (type V).<sup>26</sup> The tomographic features of SMMs in our study were variable, as has been reported with SMMs from several primary tumor types. Metastases can appear as ring-enhancing lesions with a hypodense necrotic center, heterogeneous nodules, hyperdense nodules, and as areas of multifocal intramuscular mineralization.<sup>16</sup> The radiological patterns of SMMs in our population had multiple features in common with the enhancement characteristics described in nonparenchymal HSA such as ring enhancement or heterogeneous contrast enhancement.<sup>12</sup> These 2 patterns most often were observed in our population whereas intraleisional mineralization was less common. Because of the retrospective



**FIGURE 2** Same dog as in Figure 1. Diffuse SMMs with varied enhancement patterns are visible

**TABLE 2** Frequency of skeletal muscle metastases (SMMs) in 61 dogs with hemangiosarcoma

Characteristics	Prevalence of SMMs	OR (95% CI) <sup>a</sup>	P value <sup>a</sup>
<b>Age</b>			
Up to 10 years	10/31 (32.3%)	2.38 (0.70-8.07)	.16
More than 10 years	5/30 (16.7%)	Reference	-
<b>Sex</b>			
Males	14/39 (35.9%)	11.8 (1.43-97.0)	.02
Females	1/22 (4.5%)	Reference	-
<b>Sterilized</b>			
Intact	12/46 (26.1%)	1.41 (0.34-5.88)	.64
Sterilized	3/15 (20.0%)	Reference	-
<b>Breed</b>			
Crossbreed	3/20 (15.0%)	Reference	-
German Shepherd	1/6 (16.7%)	1.13 (0.10-13.4)	.92
Retriever/Labrador	4/10 (40.0%)	3.78 (0.65-22.0)	.14
Boxer	1/6 (16.7%)	1.13 (0.10-13.4)	.92
Others	6/19 (31.6%)	2.62 (0.55-12.5)	.23
<b>Primary tumor localization</b>			
Spleen	10/40 (25.0%)	Reference	-
Liver	1/9 (11.1%)	0.38 (0.04-3.38)	.38
Muscles	2/5 (40.0%)	2.00 (0.29-13.7)	.48
Peritoneum	1/4 (25.0%)	1.00 (0.09-10.7)	1.00
Others	1/3 (33.3%)	1.50 (0.12-18.4)	.75
<b>Dimension of primary tumor (cm)</b>			
No metastases	8.41 ± 4.77 (n = 40)	Reference	-
Presence of metastases	7.84 ± 3.76 (n = 13)	0.97 (0.84-1.13)	-
<b>Additional metastatic sites</b>			
Spleen	4/17 (23.5%) versus 11/44 (25.0%) <sup>c</sup>	0.92 (0.25-3.43)	.91
Liver	6/21 (28.5%) versus 9/40 (22.5%) <sup>c</sup>	1.38 (0.41-4.59)	.60
Right atrium	0/3 (0%) versus 15/58 (25.9%) <sup>c</sup>	N/a	.57 <sup>b</sup>
Kidney	5/7 (71.4%) versus 10/54 (18.5%) <sup>c</sup>	11.0 (1.86-65.1)	.008
Bone	3/3 (100%) versus 12/58 (20.7%) <sup>c</sup>	N/a	.01 <sup>b</sup>
Lungs	10/20 (50.0%) versus 5/41 (12.2%) <sup>c</sup>	7.20 (2.00-25.9)	.003
Lymph nodes	3/11 (27.3%) versus 12/50 (24.0%) <sup>c</sup>	1.19 (0.27-5.20)	.82
Abdominal effusion	0/10 (0%) versus 15/51 (29.4%) <sup>c</sup>	N/a	.05 <sup>b</sup>
Other sites	3/11 (27.3%) versus 12/50 (24.0%) <sup>c</sup>	1.19 (0.27-5.20)	.82

Abbreviation: N/a, not available because a null frequency was found.

<sup>a</sup>Logistic regression.

<sup>b</sup>Fisher exact test.

<sup>c</sup>Frequency of SMMs in dogs with additional metastases in the specific site versus frequency of SMMs in dogs without additional metastases.

nature of our study, it was not possible to obtain the exact percentage of each pattern, and further prospective studies are warranted.

Muscular metastases in veterinary patients have been described in cases of carcinoma, sarcoma, lymphoma, and mast cell tumor.<sup>13-16,27,28</sup>

In 1 study, sarcomas were highly represented with HSA being the most common subtype.<sup>16</sup>

In our study, the presence of SMMs associated with HSA was significantly higher in males. This finding may reflect that males are slightly

predisposed to HSA.<sup>1,5,7,25,29</sup> Males may be predisposed to SMMs, but a larger group of patients would be necessary to assess any possible differences in the rate of SMMs between sexes. No correlation was found between SMMs and age of the dogs included in our study even though HSA is mostly described in middle-aged to older animals.<sup>1,7,25</sup> This finding may be a consequence of the limited number of dogs with SMMs in our study. We did not find any correlation between the presence of SMMs and breed, although German Shepherds,

**TABLE 3** Frequency of signs of 57 dogs with hemangiosarcoma stratified according to presence or absence of skeletal muscle metastases

Signs	Overall (n = 57)	Metastases		OR (95% CI) <sup>a</sup>	P value <sup>a</sup>
		Presence (n = 15)	Absence (n = 42)		
Lameness	9 (15.8%)	9 (60.0%)	0	N/a	<.001 <sup>b</sup>
Lethargy	20 (35.1%)	7 (46.7%)	13 (31.0%)	1.95 (0.58-6.52)	.28
Respiratory signs	5 (8.8%)	0	5 (11.9%)	N/a	.31 <sup>b</sup>
Anorexia	4 (7.0%)	3 (20.0%)	1 (2.4%)	10.3 (0.98-108)	.05

Abbreviation: N/a, not available because a null frequency was found.

<sup>a</sup>Logistic regression.

<sup>b</sup>Fisher exact test.

Labrador Retrievers, and Boxers were most common, as they are in most veterinary studies on HSA.<sup>1,7,25,30</sup>

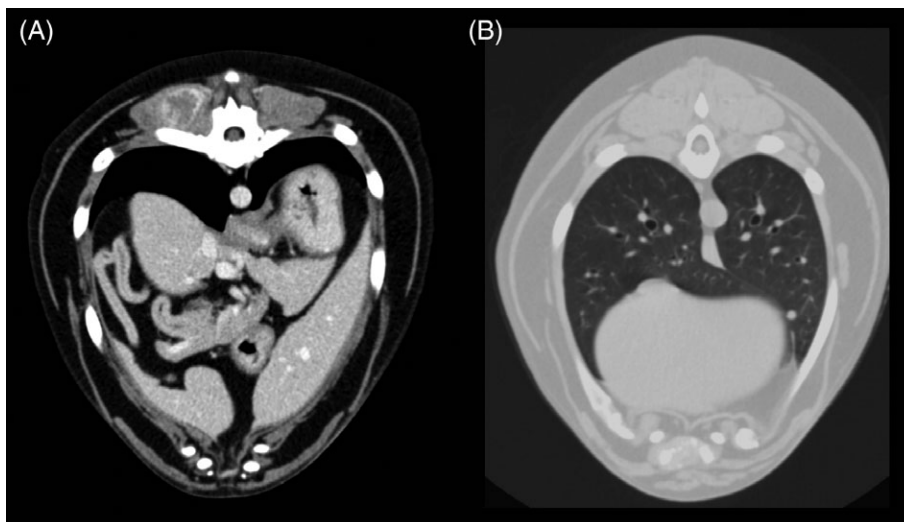
In our cohort of 61 dogs with HSA, all of the patients with SMMs (15/15, 100%) also had additional metastases in  $\geq 1$  site, representing an advanced stage of the disease and this data was found to be statistically significant. Because SMMs are considered distant metastases, their presence places these patients in a higher stage of disease (stage III), according to the "Clinical Staging System for Canine Hemangiosarcoma."<sup>1</sup> This is consistent with previous reports in human medicine that describe the presence of muscle metastasis as a late event in the clinical progression of the disease.<sup>17,19</sup> In fact, SMMs may progress more slowly than tumor deposits elsewhere in the body or present later in the course of the disease because of different mechanisms such as contractile activity, local alteration in pH, intramuscular blood pressure, accumulation of metabolites, and local temperature.<sup>19</sup> On the other hand, in dogs, the presence of SMMs may be a reflection of an aggressive neoplasm with early metastasis rather than late or chronic disease.

We found a significant correlation between SMMs and metastatic lesions in bone, lungs, and kidneys. We hypothesize this findings could be related to the fact that metastases in these sites remain subclinical for a longer time than do metastases, to other sites, such as liver or spleen, which can be associated with rupture and hemorrhage, usually

leading to euthanasia early in the disease course.<sup>31</sup> In addition, we did not find a statistical correlation between the presence of SMMs and the presence of neoplastic cells within abdominal effusion.

Signs such as anorexia and lethargy are nonspecific and could be related to primary or metastatic HSA or concurrent unrelated illness. In our study, some of the major clinical signs were lameness and reluctance to move and were reported as the primary presenting complaint in 9 of 15 dogs with SMMs. Orthopedic or neurologic clinical examinations or both did not confirm the etiology of the signs. Besides lameness and reluctance to move, these dogs did not show other clinical signs specifically attributable to their metastatic disease. This lack of specific signs associated with SMMs agrees with what has already been described in the veterinary literature.<sup>16</sup> In people, the most frequent clinical sign of muscular metastasis is localized muscle pain, swelling, or both.<sup>17</sup> One dog with diffuse SMMs also had a SMM in tongue muscle. In addition to a SMM in the epaxial muscles, another patient had a single small (4 mm) pulmonary metastasis (Figure 3). These findings support the use of whole body contrast-enhanced computed tomography (CECT) to help with staging oncologic patients, and to better characterize pulmonary or non-pulmonary metastatic lesions.

In 1 study, ultrasound diagnosis of metastasis in the skeletal musculature of the thoracic wall was described in a dog with splenic and cardiac HSA, but deeper muscles were difficult to visualize with



**FIGURE 3** Computed tomographic study in an 8-year-old spayed female Labrador Retriever. The contrast enhanced study shows a ring-enhancing lesion in the right epaxial muscle at the level of T11 (A). In the lungs, there is only 1 soft tissue nodule in the ventral part of the left caudal lung lobe (B). No other metastatic lesions were found in this patient

sufficient resolution because of the reflection or absorption of sound by superficial tissue layers, and ultrasound survey of the skeletal muscles is impractical.<sup>20,32</sup>

In human medicine, positron emission tomography (PET) has been described for detecting SMMs.<sup>33,34</sup> In a recent study in humans, the detection rate of SMMs by PET was 100% (51/51), whereas that of CT was 23.5% (12/51).<sup>35</sup> <sup>18</sup>F-fluoro-2-deoxyglucose (<sup>18</sup>F-FDG)-PET-CT provides information otherwise not obtainable using conventional diagnostic tools, potentially improving the quality of staging and management of dogs with cancer.<sup>36</sup> <sup>18</sup>F-fluoro-2-deoxyglucose is the most commonly used PET radiopharmaceutical in oncology because this isotope maps glucose metabolism in the body,<sup>37,38</sup> and because tumor cells often use more glucose than normal cells, <sup>18</sup>F-FDG is an excellent tool to detect neoplastic tissue.<sup>39</sup> To distinguish between benign inflammatory disease and malignancy, CT and PET images are fused, to determine if areas of noticeably high metabolic activity show morphologic changes on CT.<sup>39,40</sup> <sup>18</sup>F-fluoro-2-deoxyglucose-PET-CT has been described as a promising tool for staging and monitoring of dogs with HSA,<sup>41</sup> but to our knowledge, no studies using PET-CT to detect SMMs in dogs have been reported.

The primary limitation to our study is its retrospective nature. Another limitation is the possibility of missed lesions from lack of sensitivity of CT. In some of the dogs included in the study, it was difficult to distinguish between the primary tumor and metastatic lesions. In those cases, we considered as primary lesions those with consistent epidemiological, clinical, and also radiological findings (eg, common primary sites, presenting signs related to affected organ, disparity in number, and size of lesions). We acknowledge that we cannot know for sure which lesion is the primary lesion in all cases.

Computed tomography is widely available and has been recommended for evaluation of patients with malignant neoplasia with potential for lung metastases.<sup>42-44</sup> We believe that whole body CECT should be considered as a routine staging procedure for dogs with HSA because SMMs may not cause clinical signs and are not readily detected by other diagnostic imaging modalities. Whole body CECT could give more information to help the clinician in the management and monitoring of patients with HSA. We do not yet know the prognostic relevance SMMs in patients with HSA. Further studies are warranted to further evaluate the importance of SMMs in the staging process of dogs with HSA.

## 5 | CONCLUSION

In our study population, HSA had a high prevalence of SMMs. Most of the dogs with SMMs (60%) showed lameness or reluctance to move with an inconclusive neurologic or orthopedic examination. The remaining 40% were clinically silent with no attributable signs. Thus, whole body CECT, with histological or cytological sample collection, may be helpful in staging dogs with HSA and unspecified lameness. Moreover, because HSA is a tumor with a high metastatic rate, we believe CECT is likely the best widely available imaging modality to detect metastasis to lungs, muscle, and other sites.

## ACKNOWLEDGMENT

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## CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

## OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

## INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

## HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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