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Elevated platelet-to-albumin ratio may predict worsened prognosis in dogs with appendicular osteosarcoma: a preliminary study

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Objective
To evaluate the associations between the platelet-to-albumin ratio (PAR), platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, neutrophil-to-lymphocyte ratio, and progression-free interval (PFI) and median survival time (MST) in dogs with osteosarcoma. The secondary objective was to evaluate the prognostic value of serum cholesterol in the same population.

Methods
This was a preliminary retrospective study on dogs with appendicular osteosarcoma. Records from 2010 to 2024 were searched for dogs undergoing treatment for osteosarcoma. Data collected included serochemical and hematological values (platelet, monocyte, lymphocyte, neutrophil, albumin, ALP, and cholesterol levels). Variables were assessed for association with PFI and survival time via Kaplan-Meier and Cox proportional hazards analyses.

Results
60 dogs met the inclusion criteria. 50 of 60 dogs were included for survival analysis, and 42 of 60 were included for disease progression. The PAR was significantly associated with decreased PFI, being elevated in 13 dogs (median PFI, 115 days; 95% CI, 73 to 171) and low in 29 dogs (median PFI, 138 days; 95% CI, 95 to 272). Serum cholesterol had no association with PFI (median, 147 days; 95% CI, 95 to 272) or MST (median, 219; 95% CI, 138 to 292).

Conclusions
Elevated PAR was significantly associated with decreased PFI. There was no association between elevated serum cholesterol and MST or PFI.

Clinical Relevance
These results suggest that in dogs with osteosarcoma, an elevated PAR may be associated with a decreased PFI and therefore may have prognostic significance.

Keywords: serum cholesterol, osteosarcoma, platelet-to-albumin ratio, inflammatory ratio, prognostic indicator

Osteosarcoma (OSA) is a locally destructive, highly metastatic mesenchymal bone tumor.[1,2] Osteosarcoma is the most common primary bone tumor in humans and dogs, with interspecies similarities in clinical and biological behavior being well described.[3,4] Osteosarcoma is the cause of up to 85% of malignant bone neoplasms in dogs.[5] Micrometastasis is estimated to be present in up to 90% of dogs with appendicular OSA at the time of initial diagnosis, with 15% of that population having radiographic evidence of metastatic disease.[4,6] Prognosis with surgery alone is poor due to metastatic disease, and survival is improved by adjuvant chemotherapy. Due to the highly metastatic behavior of OSA, standard-of-care treatment includes local treatment via limb amputation, limb-sparing surgery, or stereotactic radiation therapy followed by chemotherapy to control metastasis.[7–9] The progression-free interval (PFI), or the time from local treatment to progression of metastatic disease, and median survival time (MST) in animals undergoing standard-of-care treatment range from a PFI of 73 to 257 days and a MST of 104 to 413 days.[10–12] With such relatively wide ranges in the PFI and MST, having a toolbox of prognosticators can be clinically

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useful in predicting where on the spectrum an individual patient may fall.

Prognostic indicators are essential tools for identifying animals at risk for less favorable prognoses even with treatment, allowing veterinarians to better educate pet owners regarding expected outcomes. While several prognosticators have been identified in dogs with OSA, these indicators have been evaluated as independent factors, and few are clinically applicable. The most clinically applicable prognosticator is elevated serum ALP (SAP), which is associated with rapid bone turnover. Proximal humeral tumor location has been associated with a worse prognosis. Other inconsistently reported and less established poor prognostic indicators include low circulating neutrophils and elevated circulating monocyte and lymphocyte levels.[13–19] Because not one prognosticator is entirely predictive, new prognosticators may be explored and combined with historical prognosticators to provide a more complete clinical picture.

The prognostic value of inflammatory ratios for both people and animals with neoplasia is an area of emerging interest, with inflammation being an accepted component of tumorigenesis and progression.[19–23] Grading schemes using inflammatory indices have been used in both human and veterinary medicine for evaluating prognosis for OSA.[19,20,22]

Historically, a high neutrophil-to-lymphocyte ratio (NLR) has been associated with a worse prognosis in both humans and dogs with OSA. In a veterinary study[19] evaluating 59 dogs with OSA, a high NLR was significantly associated with decreased progression-free survival. Analyses of human patients with OSA have shown a high NLR, high platelet-to-lymphocyte ratio (PLR), and low lymphocyte-to-monocyte ratio (LMR) to be significantly associated with both the presence of metastatic disease and with decreased overall survival.[21,22,24]

In juvenile and adolescent humans with OSA, patients with a high platelet-to-albumin ratio (PAR) experienced significantly shorter survival times when compared to patients with a low PAR, with the overall 5-year survival rates in individuals with an elevated and low PAR being 37.9% and 71.6%, respectively.[20] This is the first veterinary-based study evaluating the PAR as a prognosticator in canine OSA.

Serum cholesterol is another readily available serochemical value that has shown prognostic potential. Elevated or decreased cholesterol has been proposed as a prognostic indicator in both humans and dogs for a variety of neoplasms.[25–27] Leeper et al[27] demonstrated that in a population of dogs undergoing standard-of-care treatment for OSA, 45.3% were found to have elevated total serum cholesterol levels, whereas hypercholesterolemia was demonstrated in 10% of a control population. In this study, hypercholesterolemia was significantly associated with a reduced hazard ratio (HR) for overall mortality in dogs with OSA.[27] To the authors' knowledge, this finding has not been reproduced in veterinary medicine.

The primary objective of this study was to evaluate the inflammatory ratios PAR, PLR, LMR, and NLR and their association with PFI and MST in dogs with OSA. A secondary objective was to further evaluate the prognostic value of elevated serum cholesterol in the same patient population.

The authors hypothesized that high PAR, high NLR, low LMR, and high PLR would be associated with shorter PFI and MST and that animals with fasted hypercholesterolemia would have increased PFI and MST.

Methods

Record review

The medical records of client-owned dogs diagnosed with OSA between 2010 and 2024 were retrospectively evaluated. Records were obtained from a single institution's database. Follow-up information was obtained from institutional hospital records and/or referring veterinary records and telephone contact with owners.

Inclusion

Dogs were included if a diagnosis of appendicular OSA was confirmed via histopathology. A minimum of 30 days follow-up was required for inclusion, with animals that died or were lost to follow-up in the perioperative period being excluded. All dogs received standard-of-care treatment (amputation or surgical excision) followed by single-agent carboplatin, doxorubicin chemotherapy, or toceranib phosphate protocols. Animals with evidence of pulmonary metastasis at presentation that received toceranib phosphate were also included. Animals that were enrolled in an initial proof-of-concept study involving a single histotripsy tumor ablation treatment[28] performed within 1 to 5 days of amputation were included. Fasted chemistry and CBC panels were obtained preoperatively and were performed through the diagnostic laboratory at the primary or satellite clinic. Preoperative imaging (radiographs or CT) of the primary lesion and the thorax was performed and reviewed by a boarded veterinary radiologist at the institution. Disease progression was monitored with radiographs and CT. Dogs diagnosed with pulmonary metastasis at presentation receiving toceranib phosphate as a single agent were included for MST analysis.

Exclusion

The following animals were excluded from this study: dogs with nonappendicular osteosarcoma, dogs that did not receive standard-of-care treatment, dogs for which there was no preoperative serum chemistry or CBC available, dogs enrolled in clinical trials at other institutions, dogs that had concurrent disease conditions, or dogs without preoperative thoracic imaging.

Data collection

Clinical data recorded included age, sex, reproductive status, breed, body weight, tumor location, evidence of metastasis at presentation, imaging modality, the presence of endocrinopathies, and method and date of local treatment via amputation. Lab work parameters included preoperative fasted serum cholesterol (reference interval [RI], 110 to 320 mg/dL), SAP (RI, 23 to 212 U/L, 8 to 70 U/L), segmented neutrophil count (RI, 2.95 to 11.64 K/µL), absolute monocyte count (0.16 to 1.12 K/µL), absolute lymphocyte count (RI, 1.05 to 5.10 K/µL), platelet count (RI, 148 to 484 K/µL), and serum albumin levels (2.3 to 4.0 g/dL). Data gathered following surgical excision included histopathological diagnosis, tumor subtype, chemotherapy agent(s), number or duration of treatments, date of distant metastasis, imaging modality used to detect metastasis, date and cause of death, and necropsy findings.

The PAR was calculated by dividing platelet count (K/µL) by serum albumin (g/dL).[29] The NLR was calculated by dividing the segmented neutrophil count (K/µL) by absolute lymphocyte count (K/µL), the PLR was calculated by dividing platelet count (K/µL) by absolute lymphocyte count (K/µL),[30] and the LMR was calculated by dividing the absolute lymphocyte (K/µL) count by the absolute monocyte count (K/µL).[22,24] The median of each ratio was calculated, and all values above the median were considered high, and all values below the median were considered low.

The development of distant metastasis or local recurrence following treatment was documented with diagnostic imaging (radiographs, CT, and abdominal ultrasound) or palpation with cytological confirmation. The PFI was calculated from the date of local treatment to the date of documented recurrence or distant metastasis. The MST was calculated from the date of local treatment to the date of death from disease.

Statistical analysis

Continuous variables were summarized as medians (range), while categorical variables were summarized as counts and percentages. Bivariable associations between CBC and serochemical parameters and PFI and survival time were assessed using Kaplan-Meier log-rank tests. Significant variables on bivariable analysis were included in a multivariable proportional hazards model and subjected to stepwise variable reduction procedures. Hazard ratios and their 95% CIs were computed variables retained in the final models. Statistical significance was set to $P < .05$. All analyses were performed using SAS, version 9.4.

Censored data

Dogs were censored from PFI analysis if distant metastasis was not documented with imaging (radiographs or CT) and/or histology or cytology. Dogs were censored from MST analysis if they died from known causes unrelated to disease or were alive at the conclusion of data collection. Animals diagnosed with distant metastasis at presentation were excluded from PFI analysis but included for MST. Dogs with documented platelet count abnormalities but manual platelet count were excluded from PAR analysis.

Results

Patient population

Following an initial data search of 267 dogs with bone tumors, a total of 74 dogs were considered for inclusion. All dogs had histologically confirmed OSA. Five dogs had axial osteosarcoma, and 1 had parosteal osteosarcoma; they were therefore excluded. Four dogs were excluded because postoperative information regarding chemotherapy administration was unavailable. One dog was excluded due to death from vehicular trauma 2 weeks postoperatively. One dog was excluded due to being enrolled in a clinical trial at another institution. One dog was excluded due to a lack of recorded preoperative chemistry and CBC. Finally, 1 dog was excluded due to euthanasia following the development of a diaphragmatic hernia 30 days postoperatively. Sixty dogs were therefore included for descriptive and statistical analysis.

Patient factors

The median age was 8 years (range, 2 to 16). Twenty-nine of 60 dogs were spayed females, 28 of 66 were neutered males, 1 of 60 was an intact female, and 2 of 60 were intact males. The median weight was 31.2 kg (range, 4.3 to 65.1 kg). Twenty breeds were represented, with the majority being mixed-breed canines (15 of 60), followed by Golden Retrievers (7 of 60), Labrador Retrievers (6 of 60), Greyhounds (5 of 66), German Shepherd Dogs (5 of 66), Rottweilers (4 of 66), Doberman Pinchers (2 of 66), Great Pyrenees (2 of 66), and English Bulldogs (2 of 66) and 1 of each of the following breeds: Akita, German Shorthaired Pointer, Saint Bernard, Great Dane, Newfoundland, Cane Corso, Standard Poodle, Pointer, Siberian Husky, Scottish Terrier, Boston Terrier, and Chihuahua.

Follow-up

The minimum follow-up for the entire population was 30 days (range, 32 to 1,195).

Endocrinopathies

One dog was being managed for hypothyroidism, and 1 dog was being treated for diabetes mellitus at presentation.

Tumor location

All dogs had appendicular OSA, with the distal radius being the most common primary tumor site (16 of 60 [26.7%]), followed by the proximal humerus (11 of 60 [18.3%]), the distal femur (12 of 60 [20%]), the distal tibia (7 of 60 [11.7%]), the proximal tibia (6 of 60 [10%]), the proximal femur (3 of 60 [5%]), the scapula (2 of 60 [3.3%]), the digits (2 of 60 [3.3%]), and the distal ulna (1 of 60 [1.7%]).

Initial imaging and metastasis

Seven of 60 (11.7%) of dogs had evidence of pulmonary metastasis at initial presentation. Twenty-four animals (40%) were evaluated using CT at presentation, and 36 (60%) were evaluated radiographically. Four of 6 (66.7%) of the dogs diagnosed with pulmonary gross metastasis at presentation were evaluated via CT, with pulmonary lesions ranging from 4 to 17 mm.

Local treatment

Treatment for OSA included 32 forequarter amputations, 26 amputations via coxofemoral disarticulation, 1 amputation with hemipelvectomy, and 1 partial foot amputation.

Tumor subtype

The tumor subtype was unspecified on histopathology in 19 of 60 (31.7%) of dogs. Thirty-three of 60 (55%) were subclassified as osteoblastic, 3 of 60 (5%) were chondroblastic, 4 of 60 (6.6%) were telangiectatic, and 1 of 60 (1.6%) was anaplastic.

Histotripsy tumor ablation

Twenty-two of 60 (36.7%) dogs received a single histotripsy treatment within 1 to 5 days of amputation, 6 of which were alive at the time of data collection.

Chemotherapy

Fifty-four of 60 (90%) dogs received carboplatin as part of a single-agent protocol, averaging a total of 4.4 treatments. Four of 60 (6.7%) dogs received doxorubicin as part of a single-agent protocol, averaging 2.6 treatments. Two of 60 (3.3%) received carboplatin and rapamycin, 4 of 60 (6.7%) received toceranib phosphate as an adjunctive treatment following carboplatin, and 2 of 60 (3.3%) dogs received toceranib phosphate as a single agent.

Serochemical and CBC parameters

Serum cholesterol was elevated in 5 of 60 (8.3%) animals before local treatment. No animals had a serum cholesterol below RI. Thirteen of 60 (21.7%) dogs had elevated SAP, 2 of 60 (3.3%) animals had neutropenia, 3 of 60 (5%) had segmented neutrophilia, and 5 of 60 (8.3%) dogs had elevated circulating monocyte levels. Fifteen of 60 (25%) dogs had abnormalities in lymphocyte counts, with 14 of these dogs having a lymphopenia and 1 having a lymphocytosis. One of 66 (1.7%) dogs had a thrombocytopenia, and 6 of 60 (10%) had a thrombocytosis. The median PAR across all included dogs was 86.45 (range, 42.5 to 196.7), the median NLR was 5.54 (range, 0.97 to 16.23), the median LMR was 2.59 (range, 0.33 to 14.5), and the median PLR was 203.7 (range, 12.97 to 927.1).

Development of distant metastasis

Forty-two of 60 (70%) dogs developed documented distant metastasis and were included for PFI analysis. The most common site for metastasis was pulmonary (39 of 42 [92.8%]). Three of 42 (7%) dogs developed metastatic bone lesions. One dog developed SC metastatic lesions, and 1 dog developed hepatic metastasis, both of which also developed pulmonary metastasis. The median PFI for all noncensored dogs was 200.9 days (range, 32 to 1,442).

Survival

50 of 60 (83.3%) dogs were included in survival analysis. Six of 60 (10%) dogs were alive at the completion of data collection, and the follow-up on these patients ranged from 681 to 1,185 days. One dog was excluded from survival analysis due to the development of a second neoplasia, and 3 dogs were lost to follow-up. The MST for included dogs was 189 days (49 to 1,442).

Statistical results and prognostic significance

Elevated PAR was significantly associated with decreased PFI (*P* = .0375) but not survival (*P* = .238) using the log-rank test **(Figure 1)**. Animals that received a single histotripsy treatment had a

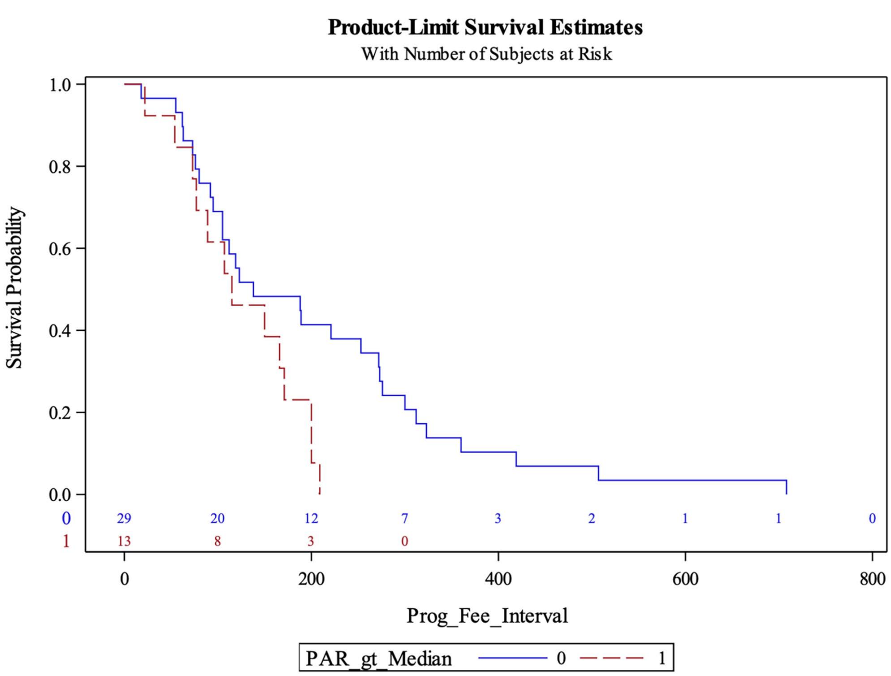

Figure 1—Kaplan-Meier analysis of the relationship between progression-free interval and elevated platelet-to-albumin ratio (PAR) in dogs with osteosarcoma. A PAR elevated above the median before treatment was significantly associated with decreased progression-free interval (*P* = .038) when compared to dogs with a PAR below the median.

significantly longer MST (P = .002) but not PFI (P = .254) using the log-rank test. Animals with elevated monocytes had a significantly shorter MST (P = .0256) but not PFI (P = .707) using the log-rank test. Dogs with elevated SAP had a significantly shorter MST (P = .0111), but there was no association with PFI (P value = 0.229) using the log-rank test. There was no association between PLR and PFI or MST (P = .873 and .662), LMR and PFI or MST (P = .887 and .873), and NLR and PFI or MST (P = .476 and .552) using the log-rank test. Elevated serum cholesterol was not found to be significantly associated with PFI or MST (P = .415 and .776).

Using the Cox proportional hazard model, dogs with an elevated PAR were 2.1 times more likely to have distant metastasis when compared to dogs with a low PAR (HR, 2.1; CI, 1.0 to 4.4; P = .00429). A stepwise variable reduction method was utilized to create a parsimonious Cox proportional hazard model for survival time. Survival time was modeled using the single histotripsy treatment and elevated SAP covariates. Single histotripsy treatment was associated with a 60% reduction in risk of mortality (HR, 0.40; CI, 0.21 to 0.76; P = .005). Elevated SAP was associated with an increase in risk of death (HR, 2.2; CI, 1.1 to 4.4; P = .030) when controlling for single histotripsy treatment.

Discussion

Despite the high incidence of OSA in dogs, reliable prognostic indicators are limited; therefore, emerging prognosticators must be evaluated. Ideal prognosticators should be minimally invasive, cost effective, and readily gleaned from routine diagnostics. The primary goal of this study was to evaluate associations between inflammatory ratios such as PAR, NLR, PLR, LMR, and PFI and MST. The secondary goal was to further evaluate the prognostic significance of elevated serum cholesterol for dogs with OSA.

Our results suggest that the PAR has value as a prognosticator for dogs with OSA, as dogs with an elevated PAR had significantly shorter PFI compared to dogs with a low PAR. The combined evaluation of platelet and albumin levels serves as an accessible inflammation-based prognostic model. A high PAR has also been significantly associated with poor overall survival and shortened PFI for humans undergoing treatment for esophageal squamous cell carcinoma,[31] nasopharyngeal carcinoma,[32] and large B-cell lymphoma.[33]

It is well established that platelets play a role in the initiation and propagation of the inflammatory cascade via cytokine secretion and are heavily involved in the recruitment of monocytes and neutrophils.[34,35] Platelet-enhanced inflammation has been shown to sustain proliferative signals, promote resistance to cell death, induce angiogenesis, activate invasion and metastasis, and allow tumor cells to evade immune detection.[35] Tumor progression is associated with thrombosis and the activation of the coagulation system,[36] and a 2023 veterinary study[37] demonstrated a high prevalence of microthrombi and concurrent hemostatic dysfunction in dogs with carcinomas and sarcomas. Tumor-activated platelet aggregation aids in tumor proliferation by cloaking circulating neoplastic cells, resulting in protection from host immune surveillance.[30,36] Additionally, thrombocytosis is correlated with a decreased response to platinum-based chemotherapeutic agents, with the proposed mechanism being a platelet-mediated counteraction of cisplatin-induced tumor cell apoptosis.[38] While cisplatin is no longer commonly used, carboplatin is a commonly used single-agent chemotherapeutic agent for dogs with OSA, and these 2 drugs share a mechanism of action.[8,10,11,14]

Cancer-induced systemic inflammation reduces albumin synthesis, and hypoalbuminemia is associated with poor prognosis for a variety of cancers.[29,39] Albumin, a negative acute phase protein, has both anti-inflammatory functions[40] and anticoagulation properties. Albumin has been shown to act as a tumor suppressor, with hypoalbuminemia resulting in reduced host immune response and increased migration and invasion of tumor cells.[41] High levels of albumin have been associated with impaired clot formation[20,42] and the inhibition of tumor cell proliferation.[31] Based on these studies, proposed explanations for the association between an elevated PAR and a decreased PFI for our population include platelet-mediated tumor promotion, platelet-mediated counteraction of platinum-based chemotherapeutic agents, and tumor-related inflammation with subsequent decreased serum albumin levels.

Few dogs in our study had elevated serum cholesterol levels. While there is a correlation between some cancers and cholesterol, the mechanism behind the association remains unknown. Cholesterol's role in immune cell function may play a role in improved prognosis.[43] Lipodomics in animals with cancer is limited, although there are human-based studies[44,45] suggesting that the primary metabolite of cholesterol may decrease osteoblast differentiation, enhancing bone resorption through increased osteoclastogenesis. In humans, low levels of high-density lipoprotein-cholesterol have been significantly associated with decreased survival in patients with renal cell carcinoma[25] and breast cancer.[26] The findings in our study contrast a previous study[27] in which 45.3% (14 of 31) of a population of dogs with OSA had elevated serum cholesterol levels. In that study, 30 dogs with appendicular fractures that were otherwise systemically healthy served as a control group. Three of 30 (10%) of those animals had elevated total serum cholesterol.[27] The percentage of patients with elevated total cholesterol levels in our population was 10%, which is comparable to the control group of the aforementioned study; therefore, the results of this study do not support the prognostic value of serum cholesterol for dogs with OSA.

Elevated SAP has been established as a reliable prognosticator for dogs with OSA[15,17,18] and was significantly associated with increased risk for death in this study **(Table 1)**. A previous study[15] identified elevated circulating monocytes as a poor prognostic indicator for PFI; however, survival analysis was not performed. For the current study, elevated

Table 1—Results of bivariable log-rank analysis of survival for 60 dogs with appendicular osteosarcoma.

Variable	Comparison	Median survival time (d)	95% CI	*P* value
Platelet-to-albumin ratio	Elevated vs low	115	73–171	.038
Histotripsy recipient	Yes/no	194	76–276	.253
Monocytes	Elevated vs normal	149	89–189	.707
Serum ALP	Elevated vs normal	144	95–221	.229
Platelet-to-lymphocyte ratio	Elevated vs high	150	77–200	.662
Lymphocyte-to-monocyte ratio	Elevated vs low	138	76–221	.887
Neutrophil-to-lymphocyte ratio	Elevated vs high	130	80–200	.477
Serum cholesterol levels	Elevated vs normal	138	105–209	.415

monocytes were associated with a shortened MST but not PFI (Table 1 and **Table 2**). Further investigation evaluating the role of monocytosis for both PFI and MST is warranted. Contrary to reports from human medical literature, no associations were found between NLR, PLR, and LMR and PFI or MST in dogs with OSA.[21,22,24]

Interestingly, dogs that were enrolled in an initial proof of concept that underwent histotripsy tumor ablation to a small portion of their tumors within a week of surgical tumor resection demonstrated a significant increase in MST and reduction in risk of death when compared to dogs that did not undergo a partial histotripsy tumor ablation (Table 1). The role of histotripsy ablation in prognosis for dogs with OSA is unknown and is an area of future investigation.

Dogs with evidence of metastatic disease at initial diagnosis were included for survival analysis but not for disease progression. These animals were included because the relationship between inflammatory ratios and serum cholesterol and MST and PFI was evaluated as independent factors. Future studies investigating the combined relationship between MST, PFI, and these serochemical and hematological changes may be useful in reinforcing clinical relevance.

Major limitations of this study include its retrospective nature, limited case numbers, differing treatment protocols, and a lack of cytologically or histologically confirmed disease progression. Just 42 dogs were included for PAR analysis, and increased case numbers may strengthen or refute the association between an elevated PAR and PFI. A variety of chemotherapeutic agents and protocols were used for this patient population, and this lack of standardization may have influenced both PFI and MST. While the majority of the population received carboplatin or doxorubicin as their primary chemotherapy treatment, two of the dogs received toceranib phosphate as a single agent chemotherapeutic agent. This treatment was administered as recommended by a board-certified medical oncologist. Previous studies[8] evaluating the use of single-agent carboplatin and doxorubicin showed no difference in outcomes between groups. Additionally, another study[10] demonstrated no difference in outcomes for animals undergoing an alternating doxorubicin and carboplatin treatment protocol.

Twenty-two dogs received a single histotripsy ablation treatment to a small volume of their tumors for proof of principle of the efficacy of histotripsy in ablating OSA cells. The effect of histotripsy on OSA survival has not been previously evaluated, but ablation of a small tumor volume for proof of principle is not expected to affect overall survival. Regardless, survival analysis results may be confounded as these animals were found to have significantly increased MST and decreased risk of death when compared to the remainder of the population. Another limitation of this study is owner subjectivity where time of euthanasia is concerned. Because the decision to euthanize an animal was often made due to poor quality of life, the survival time due to natural disease progression was not established.

The primary objective of this study was to determine the prognostic significance of inflammatory ratios in animals with histologically confirmed OSA. The median ratios for the studied population were used to determine low or high values. There are limited veterinary data establishing RIs for inflammatory ratios in systemically healthy dogs, with no RIs for the PAR or LMR being reported. Normal RIs for the NLR have been reported to range from 0.74 to 13.3,[46–48] while the PLR is reported to range from 84.2 to 146.9.[46,48] The population in the current study had higher upper limits for both the NLR and PLR, with median NLR and PLR values being 5.38 and 195.7, respectively. Future areas of research

Table 2—Results of bivariable log-rank analysis of progression-free interval (PFI) for 60 dogs with appendicular osteosarcoma.

Variable	Comparison	Median PFI (d)	95% CI	*P* value
Platelet-to-albumin ratio	Elevated vs low	267	138–314	.493
Histotripsy recipient	Yes/no	309	144–810	.002
Monocytes	Elevated vs normal	221	154–307	.025
Serum ALP	Elevated vs normal	144	91–241	.011
Platelet-to-lymphocyte ratio	Elevated vs high	221	129–375	.873
Lymphocyte-to-monocyte ratio	Elevated vs low	289	123–402	.891
Neutrophil-to-lymphocyte ratio	Elevated vs high	221	111–494	.845
Serum cholesterol levels	Elevated vs normal	219	138–375	.776

may include the continued establishment of normal RIs for inflammatory ratios in healthy dogs, particularly for the PAR and LMR.

In conclusion, we rejected the hypothesis that high PLR, high NLR, low LMR, and high serum cholesterol would be significantly associated with decreased PFI and MST in dogs with OSA. A high PAR was significantly associated with decreased PFI on both bivariable and multivariable analysis. These findings serve as a promising first step in identifying the prognostic value of the PAR in dogs with OSA, suggesting that a high PAR at presentation is indicative of a worse prognosis. To firmly establish this association, prospective studies with standardized treatment protocols and control groups need to be undertaken.

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