


Use of C-reactive protein concentration in evaluation of diskospondylitis in dogs

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Abstract

Background: C-reactive protein (CRP) is a positive acute phase protein that increases in many inflammatory conditions of dogs. Serum CRP concentration has important diagnostic and prognostic utility in humans with vertebral osteomyelitis.

Hypothesis/objectives: To determine if a correlation exists between serum CRP concentration and clinical and magnetic resonance imaging (MRI) findings in dogs with diskospondylitis, and if CRP predicts prognosis.

Animals: Eighteen client-owned dogs with MRI diagnosis of diskospondylitis.

Methods: Retrospective study evaluating signalment, clinical signs, neurologic examination findings, white blood cell count, neutrophil count, serum globulin concentration, serum CRP concentration, radiographic findings, MRI findings, bacterial culture results, and outcome in dogs with diskospondylitis.

Results: Serum CRP concentration was significantly more sensitive than were fever and leukocytosis for predicting the presence of diskospondylitis. Serum CRP concentration was more sensitive than neutrophilia and hyperglobulinemia. No difference in serum CRP concentration was found between dogs with single or multiple lesions, nor between dogs with or without empyema, muscular involvement or spinal cord compression. No association was found between serum CRP concentration and positive bacterial culture.

Conclusions and Clinical Importance: C-reactive protein is a sensitive, but non-specific biomarker for diskospondylitis which may prove useful as an adjunctive diagnostic test in patients with suspicious clinical signs and may help predict prognosis.

KEYWORDS

acute phase protein, biomarkers, neurology, vertebral osteomyelitis

1 | INTRODUCTION

Diskospondylitis refers to infection of the vertebral endplates and intervertebral disk. Infection may occur by hematogenous spread from another site (eg, urogenital tract, respiratory tract, oral cavity, traumatic injury), foreign body migration (eg, grass awn), or iatrogenic

Abbreviations: CRP, C-reactive protein; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drug; SRMA, steroid-responsive meningitis-arthritis.

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causes (eg, surgical site infection). Large, purebred, male dogs appear to be predisposed.¹⁻³ Clinical presentation is variable and may include signs of spinal pain, fever, lethargy, decreased appetite, and neurologic signs attributable to myelopathy. Late recognition of the disease is common because of nonspecific clinical signs, delayed appearance of radiographic lesions, difficulty differentiating chronic diskospondylitis lesions from healing or degenerative lesions, and delay in obtaining advanced tests. In humans, magnetic resonance imaging (MRI) is a sensitive and specific diagnostic test for this disease (96% and 95%, respectively)^{4,5} and MRI features of diskospondylitis have been well described in dogs.^{2,6-9}

In humans, diskospondylitis is classified as either diskitis (infection of the intervertebral disk) or vertebral osteomyelitis (infection of the vertebral body).^{10,11} Commonly, fever, leukocytosis, neutrophilia, and hyperglobulinemia are utilized by clinicians as markers of inflammation, which in the presence of spinal pain may increase clinical suspicion for vertebral osteomyelitis.¹⁰ Similar clinical and laboratory findings have been reported in dogs, but no data are available on the frequency of these changes.

C-reactive protein (CRP) is a positive acute phase protein that is produced in many inflammatory conditions in dogs including infection (eg, pyometra,^{12,13} sepsis,¹⁴ bacterial pneumonia^{15,16}), immune-mediated diseases (eg, immune-mediated polyarthritis,^{13,17-19} and steroid-responsive meningitis-arteritis [SRMA]^{20,21}) neoplasia (eg, hemangiosarcoma, lymphoma, malignant histiocytosis).^{13,22,23} Monitoring serum CRP concentrations over time is helpful in guiding duration of treatment in bacterial pneumonia¹⁶ and predicting relapse in SRMA and immune-mediated polyarthritis.^{18,21,24}

Serum CRP concentration has been shown to be of diagnostic and prognostic utility for vertebral osteomyelitis in humans.²⁵⁻²⁷ Serum CRP concentrations increase in many human patients with vertebral osteomyelitis and has a sensitivity of 84% compared to 13% to 60% sensitivity for leukocytosis.²⁵ Patients with higher CRP concentrations on admission are more likely to have shorter duration of symptoms, positive blood, tissue or biopsy culture results, and higher mortality.²⁵⁻²⁷ Pathogen isolation is unlikely in patients with normal serum CRP concentrations.²⁶ A persistent increase in serum CRP concentration at 4 weeks is predictive of treatment failure.²⁵ Furthermore, a 50% decrement in serum CRP concentration each week indicates good response.²⁸

Serum CRP concentration is an adjunctive diagnostic test that may influence clinical decision making in patients diagnosed with diskospondylitis and have utility as a screening tool in suspected cases. The purpose of our study was to evaluate the sensitivity of serum CRP concentration for diskospondylitis in dogs compared to fever, leukocytosis, neutrophilia, and hyperglobulinemia. Secondary aims were to investigate whether serum CRP concentration was associated with bacterial culture results, multifocal disease, empyema, muscular involvement, or spinal cord compression. A tertiary aim was to investigate whether serum CRP concentration was predictive of outcome. We hypothesized that serum CRP concentration would be more sensitive than other laboratory test results for predicting diskospondylitis and that increased concentrations would be more likely in dogs with positive bacterial culture, multifocal disease, empyema, muscular involvement, spinal cord compression, and poor outcome.

2 | MATERIALS AND METHODS

A retrospective review of the medical records and imaging findings of dogs with a diagnosis of diskospondylitis at Bush Veterinary Neurology Service (Leesburg, Virginia, Springfield, Virginia, Richmond, Virginia, and Rockville, Maryland) between 2011 and 2016 was performed. Inclusion criteria for the study included a complete history, physical and neurologic examinations, CBC, serum biochemistry profile, MRI of the vertebral column with findings supportive of diskospondylitis and serum CRP concentration performed at time of diagnosis. Serum CRP concentrations were measured by an outside laboratory (Texas A&M Veterinary Medical Diagnostic Laboratory) using a previously validated commercially available ELISA. An increased serum CRP concentration was defined as a concentration above the reference interval previously established by the laboratory (0-7.6 mg/L). The upper detection limit of the assay was 60 mg/L. If available, results of survey radiographs, bacteriologic culture results (urine, blood, cerebrospinal fluid [CSF], synovial fluid, or biopsied tissues), fungal serology, *Brucella* serology, follow-up MRI, and follow-up serum CRP concentration also were evaluated. Treatment provided (antibiotics and surgery) and patient outcome at the last known examination or phone follow-up were assessed. A good outcome was defined as improved or resolved clinical signs and a poor outcome was defined as static or worsening clinical signs or death or euthanasia because of progression of disease at the time of last follow-up. Any known comorbidities thought to predispose to systemic infection also were documented.

All MRI studies were reviewed and interpreted by a board-certified radiologist. An MRI evaluation of the entire spinal column (C1-S1) was not a requirement for inclusion in the study. The MRI findings used to make an imaging diagnosis of diskospondylitis included T2w and short tau inversion recovery (STIR) hyperintensity with contrast enhancement of affected vertebral endplates and intervertebral disks, and either STIR hyperintensity or contrast enhancement of paravertebral soft tissues.² Imaging findings were correlated with clinical signs to make the clinical diagnosis of diskospondylitis. Documented imaging characteristics included number and location of affected intervertebral disk spaces, and the presence or absence of empyema, muscular involvement, and spinal cord compression. If spinal radiographs also were performed, the interpretation was noted but the images were not reviewed for the purposes of our study because not all radiographs were still available to the investigators. For follow-up imaging studies, criteria used to judge improvement in diskospondylitis lesions included resolution of STIR hyperintensity or contrast enhancement, improvement in measured area affected, or improvement or resolution in number of sites affected.

2.1 | Statistical analysis

Normal probability plots showed that age and weight followed a normal distribution whereas duration of signs and serum CRP concentrations were skewed. Normally distributed variables were summarized as means (SD) whereas skewed variables were summarized as medians (range). Categorical variables including sex, breed, fever, anti-

inflammatory treatment, antibiotic treatment, leukocytosis, neutrophilia, hyperglobulinemia, location (multifocal vs single intervertebral disk), empyema (present vs absent), bacterial culture (positive vs negative), increased serum CRP concentration, and improved outcome were summarized using 1-way contingency tables. Associations between increased serum CRP concentration and each of bacterial culture, empyema, earlier treatment (anti-inflammatory or antibiotics), location of diskospondylitis, muscular involvement, and spinal cord compression were assessed using Fisher's exact tests. Association between an increased follow-up serum CRP concentration and poor outcome also was assessed using Fisher's exact test. Diagnostic sensitivity for increased serum CRP concentration for diagnosis of diskospondylitis was compared to the diagnostic sensitivity for each of fever, leukocytosis, neutrophilia, and hyperglobulinemia using McNemar's Chi-square test. Association between duration of clinical signs and increased CRP concentration was assessed using the Wilcoxon rank sum test. Associations between serum CRP concentration and each of bacterial culture, improved outcome, location of diskospondylitis, empyema, muscular involvement, and spinal cord compression also were assessed using the Wilcoxon rank sum test. A complete set of diagnostic properties (sensitivity, specificity, positive predictive value, and negative predictive value) were generated to evaluate increased serum CRP concentration as a predictive guide for positive bacterial culture and poor outcome. Statistical significance was set at $P < .05$. Post hoc power analysis was performed to reach a power of 80%. Analyses were performed using SAS version 9.4 (Cary, North Carolina) and MedCalc (Ostend, Belgium).

3 | RESULTS

3.1 | Population

Eighteen dogs were included in the study. There were 9 males (2 intact, 7 neutered) and 9 females (2 intact, 7 spayed). Mean age was 5.3 years (range, 1-12). Mean weight was 34.75 kg (range, 4.7-79.0) with affected breeds including 2 Labrador Retrievers, 2 Rhodesian Ridgebacks, 2 German Shepherds, 2 Boxers, 1 Mastiff, 1 Newfoundland, 1 Doberman, 1 English Bulldog, 1 German Shorthair Pointer, 1 Saint Bernard, 1 Beagle, and 3 mixed breed dogs. Normal probability plots showed that age and weight followed a normal distribution.

3.2 | Clinical presentation

The most common clinical sign was spinal pain, present in 100% (18/18) of dogs evaluated. Fifty percent (9/18) of dogs had variable degrees of limb paresis. Body temperature was evaluated in all 18 dogs, and 27.8% (5/18) were found to be hyperthermic ($T > 102.5$ F) on presentation. Sensitivity of increased serum CRP concentration for diagnosing diskospondylitis was significantly higher ($>2\times$) than that of fever ($P = .01$; Table 1). Duration of signs before presentation ranged from 6 to 299 days with a median of 90 days. Duration of clinical signs was

significantly shorter in dogs with increased serum CRP concentration than in those with normal serum CRP concentration ($P = .05$).

3.3 | Clinicopathologic findings

Total white blood cell counts were performed in all patients, with 1 dog having leukocytosis (6%). Differential cell counts were performed in 17/18 patients and neutrophilia was identified in 6/17 (35%) dogs. Serum globulin concentration was measured in all patients and 6/18 (33%) were hyperglobulinemic. The CRP assay was performed using serum at the time of diagnosis in all 18 dogs and concentrations were increased in 11 (61.1%) dogs (Figure 1). Diagnostic sensitivity of increased serum CRP concentration for diagnosing diskospondylitis was significantly higher (10 \times) than the sensitivity of leukocytosis ($P = .002$; Table 1). Although sensitivity for increased serum CRP concentration was approximately twice the sensitivity of neutrophilia and hyperglobulinemia, these changes did not reach statistical significance ($P = .06$, $P = .10$, respectively; Table 1).

3.4 | Radiographic findings

Spinal radiographs were evaluated in 10 patients. Diskospondylitic lesions were evident in 2 of these cases (20%). Of dogs without radiographic evidence of disease ($n = 8$), duration of clinical signs ranged from 6 to 270 days with a median of 21 days. Of the 2 dogs with radiographic lesions, the duration of clinical signs was 10 and 195 days, respectively.

3.5 | MRI findings

Forty-five sites of diskospondylitis were identified among the 18 patients (3 cervical, 21 thoracic, 21 lumbar). The L7-S1 intervertebral disk space was the most commonly affected site (11/18 [61.1%] dogs; 11/45 [24.4%] lesions). Nine patients had single lesions and 9 had multiple lesions, ranging from 2 to 10 affected

TABLE 1 Sensitivity of different diagnostic criteria for diagnosing diskospondylitis and the level of significance when compared to serum C-reactive protein concentration. Each P -value is for comparison between that diagnostic criterion and increased serum CRP concentration. Asterisk (*) indicates statistical significance

Diagnostic criteria	Sensitivity		P value
	Proportion	% (95% CI)	
Fever	5/18	27.8 (4.9-50.7)	.01*
Leukocytosis	1/18	5.6 (0.0-17.3)	.002*
Neutrophilia	6/17	35.3 (10.0-60.6)	.06
Hyperglobulinemia	6/18	33.3 (9.2-57.5)	.09
Increased CRP	11/18	61.1 (36.2-86.1)	

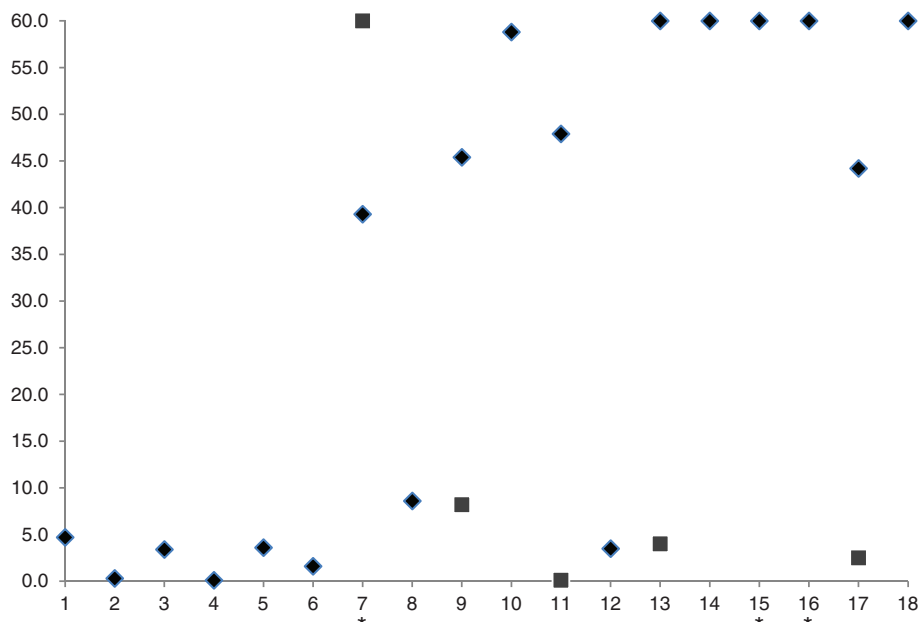


FIGURE 1 Serum C-reactive protein (CRP) concentrations in 18 dogs with diskospondylitis. The CRP measurements are represented on the y-axis and patient number on the x-axis. CRPi (black diamond) represents initial CRP concentration and was measured in all dogs. CRPf (gray square) represents follow-up CRP concentration and was measured in 5 dogs. Dogs with poor outcome are denoted with an asterisk (*)

intervertebral disk spaces. No significant difference was found in median serum CRP concentrations ($P = .21$) or in frequency of increased serum CRP concentration ($P = .60$) between dogs with single vs multiple lesions. Fifteen patients had lesions involving a single neuroanatomic location (1 cervical, 3 thoracic, 11 lumbar) and 6 patients had lesions involving >1 neuroanatomic location. Empyema was present in 6 cases (33.3%), muscular involvement in 14 cases (77.8%) and spinal cord compression in 11 cases (61.1%). No significant relationship was found between increased serum CRP concentration and presence of empyema ($P = 1.00$), muscular involvement ($P = 1.00$) or spinal cord compression ($P = .64$), nor was any difference found in median serum CRP concentration between dogs with or without empyema ($P = .38$), muscular involvement ($P = .79$), or spinal cord compression ($P = .59$).

3.6 | Causative agents

Diagnostic tests to identify a causative agent were performed in 18 dogs and included cerebrospinal fluid (CSF) analysis (6/18), CSF culture (5/18), blood culture (4/18), urine culture (17/18), synovial fluid culture (1/18), fungal serology (13/18), *Brucella* serology (13/18), and culture of surgically biopsied intervertebral disk material (3/18). An infectious organism was identified in 6/18 (33.3%) cases with positive culture present in 4/17 (23.5%) cases. Identified organisms included *Staphylococcus pseudintermedius* ($n = 1$, urine and synovial fluid culture), methicillin-resistant *S. pseudintermedius* ($n = 1$, blood culture), *Staphylococcus aureus* ($n = 1$, blood culture), *Enterobacter cloacae* ($n = 1$, CSF culture), *Sphingomonas pauci* ($n = 1$, CSF culture), *Corynebacterium spp.* ($n = 1$, blood culture), *Aspergillus* ($n = 1$, serology), and *Brucella* ($n = 2$, serology). Two dogs had multiple infectious agents identified. Among dogs with increased serum CRP concentration, 3/10 (30.0%) had positive

bacterial culture, whereas 1/7 (14.3%) dogs with normal serum CRP concentrations had positive bacterial culture; these 2 proportions were not significantly different ($P = .60$). Also, no significant difference was found in median serum CRP concentration between dogs with positive vs negative cultures (59.4 and 8.6 mg/L, respectively, $P = .25$). Increased serum CRP concentration was 75% sensitive (95% confidence interval [CI], 19.4-99.4) and 46.2% specific (CI, 19.2-74.9) in predicting positive bacterial culture. When receiver operator characteristic curve analysis was performed, a serum CRP concentration >47.9 mg/L was found to be 75% sensitive and 84.6% specific for predicting positive bacterial culture, but this result did not achieve significance (area under the curve [AUC] = 0.712; $P = .28$).

3.7 | Concurrent disease conditions

Comorbidities potentially causing a predilection to infection included chronic pododermatitis (1), recent orthopedic surgical site incision infection (1), renal hematuria (1), hypothyroidism (1), recent parturition (1), recent exploratory laparotomy for foreign body (1), cardiac arrhythmia (1), and polyarthropathy (1).

3.8 | Treatment

At the time of presentation, 12/18 (66.7%) dogs were receiving either a nonsteroidal anti-inflammatory drug (NSAID) or corticosteroid. Four (33.3%) of these had normal serum CRP concentrations compared to 3/6 (50.0%) of those not treated with either drug; these 2 proportions were not significantly different ($P = .63$). A post hoc power analysis showed that a difference between proportions of 54% would be needed to reach a power of 80%. Antibiotic treatment had been

initiated in 3/18 (16.7%) patients at the time of presentation. One (33.3%) of these dogs had a normal serum CRP concentration compared to 6/15 (40.0%) of those not receiving antibiotics. These 2 proportions were not significantly different ($P = 1.00$). A post hoc power analysis showed that a difference between proportions of 39% would be needed to reach a power of 80%. One dog (5.6%) received an antifungal agent before presentation. After diagnosis, all patients received antibiotics and 3/18 (16.7%) also were managed surgically.

3.9 | Outcome

Follow-up periods ranged from 12 to 870 days (mean, 216.67 days; median, 120 days). Fifteen (83.3%) dogs had good outcomes with follow-up periods ranging from 12 to 870 days (median, 147 days) and 3/18 (16.7%) had poor outcome with follow-up periods of 66 to 120 days (median, 119 days). Median serum CRP concentration for dogs with good outcome was 8.6 mg/L (range, 0.1-60 mg/L). Median serum CRP concentration for dogs with poor outcome was 60 mg/L (range, 39.3-60 mg/L). All dogs with poor outcome had increased initial serum CRP concentrations; 1 of these patients died because of complications associated with *Aspergillus* infection. No significant difference was found in median serum CRP concentrations between patients with good vs poor outcome ($P = .17$). A post hoc simulation power analysis showed that a mean difference of 48 would be needed to reach a power of 80.5%. The observed mean difference was 26.3. Table 2 summarizes the diagnostic properties of increased serum CRP concentration for predicting poor outcome.

Follow-up CRP assays were performed in 5 patients and serum CRP concentration was increased in 1 patient. The mean time to follow-up CRP assay was 112.6 days (range, 37-215). No significant difference in follow-up serum CRP concentration was found between patients with good vs poor outcome ($P = .17$), but only 5 dogs had follow-up CRP assays performed with 4 having normal serum CRP concentration and good outcome and 1 having increased serum CRP concentration and poor outcome. Median follow-up serum CRP concentration for dogs with good outcome was 3.25 mg/L (range, 0.1-8.2 mg/L). The follow-up serum CRP concentration for the dog with poor outcome was 60 mg/L. Figure 1 summarizes initial and follow-up serum CRP concentrations for all dogs included in the study. Follow-up MRI was performed in 4 patients (range, 90-428 days postdiagnosis; median, 139 days) and lesions were improved in 2 of these

patients. Only 1 dog had both MRI and follow-up CRP assay performed and that dog had a persistently increased serum CRP concentration.

4 | DISCUSSION

C-reactive protein is a valuable biomarker for inflammation in many diseases in both human and veterinary medicine, but the utility of this biomarker in dogs with diskospondylitis has not been investigated. In our study, increased serum CRP concentration was the most frequent clinicopathologic finding in patients with diskospondylitis. Serum biochemistry and CBC changes suggestive of infection (eg, leukocytosis, neutrophilia, hyperglobulinemia) were unreliably present. This discrepancy partially could be a consequence of differences in the duration of clinical signs together with concurrent anti-inflammatory treatments, but it is also possible that these indicators of inflammation could be less frequent than commonly presumed. Increased serum CRP concentration was significantly more sensitive than leukocytosis for predicting presence of diskospondylitis. This finding is consistent with previous studies investigating SRMA²¹ and vertebral osteomyelitis in humans.²⁵ The sensitivity of leukocytosis in predicting diskospondylitis was lower in our study compared to what has been described in humans (5.6% vs 13%-60%).²⁵ In our study, CRP also was found to be significantly more sensitive than fever for predicting the presence of diskospondylitis. Fever was an infrequent clinical sign, present in only 27.8% of patients. The frequency of fever in dogs with diskospondylitis previously has been reported as 37%.³

Serum CRP concentration was not affected by earlier treatment with corticosteroids or NSAID, which is similar to findings in other studies.^{21,29-31} Antibiotic treatment before diagnosis was not correlated with serum CRP concentration in our study. This finding is likely because of the relatively short course of treatment before diagnosis of diskospondylitis, as well as the potential for these patients to have not received an effective antibiotic for the infection present. Both of these factors would have resulted in inadequate treatment so that a decrement in the inflammatory response was not observed.

Although imaging changes are often useful in assessing the extent of disease, no association was found between serum CRP concentration and number of lesions, presence of empyema, muscular involvement, or spinal cord compression on MRI. This observation was contrary to our hypothesis and seems to indicate that the severity of pathology cannot be predicted based on serum CRP concentration. The frequency of single vs multiple lesions was similar to what has been reported in previous studies^{1,2} and the lumbosacral intervertebral disk space was the most common site affected, which is also consistent with previous reports.^{1,6,32,33}

Radiographs have been utilized commonly in the diagnosis of diskospondylitis because of ease of access and relatively low cost as compared with MRI. Previous reports have described a 2 to 6 week lag time for the appearance of radiographic lesions.^{34,40}

In our study, only 20% of radiographs available from the primary care clinicians showed lesions consistent with diskospondylitis, which was surprising. By excluding patients in which the diagnosis was made by radiographs alone, we were unable to draw further conclusions

TABLE 2 Diagnostic properties of increased serum C-reactive protein (CRP) concentration (ie, above the reference interval previously established by the laboratory (0-7.6 mg/L) for poor outcome

Operating characteristic	Proportion	% (95% CI)
Sensitivity	3/3	100.0 (29.2-100.0)
Specificity	7/15	46.7 (21.3-73.4)
Positive predictive value	3/11	27.3 (6.0-61.0)
Negative predictive value	7/7	100.0 (59.0-100.0)

regarding the diagnostic sensitivity of radiographs compared to MRI. In a previous study, radiographic lesions were observed in all dogs in which they were performed, with excellent correlation to MRI findings.² Fifty-seven percent of the total population in that study had clinical signs lasting >30 days before presentation.² In our study, only 40% of the dogs with radiographs performed had clinical signs lasting >30 days. Magnetic resonance imaging has the advantages of detecting lesions earlier, differentiating active lesions from chronic lesions or degenerative changes and identifying spinal cord compression that could necessitate surgical intervention. Because early diagnosis has been shown to improve outcome in humans, it is reasonable to assume this may also be the case in dogs.³⁵ Magnetic resonance imaging should be considered for any patient with spinal pain, neurologic signs, or both, especially if serum CRP concentration is increased. Future studies are needed to elucidate the relationship between delay in treatment and outcome.

Because CRP concentrations were more likely to be increased in patients with shorter duration of signs (similar to what has been reported previously in humans), this test may be useful in the early stages of disease in dogs presented for spinal pain, mild neurologic deficits or both. Serum CRP concentration does not increase in patients with intervertebral disk disease, thus increased serum CRP concentration may help exclude intervertebral disk disease as a cause of clinical signs.¹³ Advanced imaging may help differentiate other diseases in which increased serum CRP concentration is expected (eg, diskospondylitis, SRMA, neoplasia). The poor reliability of evidence of systemic involvement on both routine examination and clinicopathologic testing (eg, fever, leukocytosis, neutrophilia, hyperglobulinemia) and of radiographic lesions highlights the importance of advanced imaging techniques to ensure proper diagnosis. Also, it is more difficult to evaluate whether or not a lesion is active on radiographs, and soft tissue changes cannot be evaluated.

Serum CRP concentration is utilized in humans with vertebral osteomyelitis as a way to monitor response to treatment.²⁵ In humans with vertebral osteomyelitis, persistent increases in serum CRP concentration after 4 weeks of treatment are predictive of treatment failure.²⁵ We did not find an association between serum CRP concentration at time of follow-up and outcome in our study, but our study lacked the power to draw definite conclusions. Only 3 animals had poor outcome and follow-up serum CRP concentrations were both infrequently performed and evaluated at different time points (5 dogs, 4 with good outcomes, and 1 with poor outcome). The dog with persistently increased serum CRP concentration and poor outcome had follow-up MRI performed, which showed progressive disease. The remaining dogs with follow-up CRP assays performed had good outcomes and serum CRP concentrations either within the reference range (3 dogs) or just outside of the reference range (1 dog). Unfortunately, the other 2 dogs with poor outcome had neither follow-up CRP assay nor imaging performed. Although conclusions cannot be made based on this data, it may be useful to follow serum CRP concentrations to assess progression of disease.

Surprisingly, serum CRP concentrations were not associated with bacterial culture results in our study. This observation contrasts with

findings in humans with vertebral osteomyelitis.²⁵⁻²⁷ Bacterial cultures were positive in only 23.5% of patients in our study, which is far fewer compared to other reports (78%² and 46.3%¹). Blood cultures were more commonly positive than were urine cultures in other reports; blood cultures were performed infrequently in our study.^{1,2} The relationship between serum CRP concentration and culture results has been based largely on blood cultures in previous reports.²⁵⁻²⁷ In our study, only 4 patients had blood cultures performed, and 3/4 were positive. This proportion is similar to that reported previously (82%).² Rate of positive blood culture has ranged from 33.9% to 82% in other studies.^{1,2,36} Urine cultures were performed in 17 dogs with only 1 yielding positive results. The proportion of positive urine cultures in our study is lower than previously reported (25%-45%).^{1,2,34,37} A causative agent could not be identified in 66.7% of dogs in our study. Two dogs were treated with antibiotics before presentation and had cultures performed, both with no growth. Treatment based on culture results is ideal for any infection, and multiple sample types (eg, blood, urine, CSF, surgical biopsy) are helpful to maximize the opportunity for organism isolation.

The population of dogs in our study was similar to that reported in other studies^{1,2} with mostly large breed, purebred, middle-aged dogs. No sex predisposition was observed in our study, similar to a previous report.² Spinal pain was the most reliable clinical sign in our study (100% of dogs) and was much more common than previously reported (13%).² Paresis (50%) was less common in our study population compared to previous reports (87%² and 80%¹).

Our study had several limitations, largely related to its retrospective design. There was a high degree of variation in samples obtained for bacterial culture. This variability could have affected the relationship between serum CRP concentration and culture results. Future studies should focus on obtaining blood cultures routinely at the time of diagnosis. Magnetic resonance imaging of the entire vertebral column was not performed in every patient in our study, and the number of affected sites may have been underestimated (particularly within the cervical spine because it was not routinely evaluated). This limitation could have impacted the statistical comparison between number of affected sites and serum CRP concentration. Also, the variability in follow-up evaluation was a major limitation. It is possible that serum CRP concentration could be more predictive of outcome if a larger population of dogs could be investigated, with more dogs having poor outcomes and with follow-up CRP assays consistently performed at several points in time. For subgroup comparisons, small numbers caused the study to be underpowered and may have contributed to type II error, and thus nonsignificant findings should be interpreted with caution.

Although a control population was not utilized in our study, a previous study evaluating serum CRP concentrations in dogs with SRMA found that serum CRP concentrations were significantly higher in dogs with SRMA than in dogs with a variety of other neurologic diseases, but the study did not include dogs with diskospondylitis.²⁰ Also, a known laboratory-specific reference range in healthy dogs has been established previously. The purpose our study was to evaluate serum CRP concentrations at initial examination in a group of dogs with

diskospondylitis. Our study population was relatively small, with only 18 dogs included. This limitation is at least in part because of the uncommon occurrence of this disease, at least at our referral institution.

It remains challenging in veterinary medicine to know when to discontinue treatment for many infectious and inflammatory diseases, including diskospondylitis. Typically, a combination of clinical signs, culture results, and imaging findings is utilized, but each of these tests is imperfect for guiding treatment duration. Serum CRP concentration has been shown to be useful in guiding treatment duration in dogs with bacterial pneumonia¹⁶ and in humans with neonatal septicemia.^{38,39} Future studies should assess the role of following serum CRP concentrations and MRI findings to determine duration of treatment. Because serum CRP concentration at 4 weeks has been shown to provide important prognostic information in humans with vertebral osteomyelitis,²⁵ we propose that this time point also be investigated in dogs.

C-reactive protein is a sensitive but nonspecific biomarker for diskospondylitis and may prove useful in patients with suspicious clinical signs. Furthermore, measurement of serum CRP concentration at different points in time may have utility in making diagnostic and treatment decisions as well as predicting outcome. Although no single test is conclusive in the evaluation of diskospondylitis, CRP combined with clinical signs, other laboratory tests, and imaging findings is useful in deriving a more complete evaluation in the diagnosis and management of this disease.

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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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