Cerebrospinal fluid myelin basic protein as a prognostic biomarker in dogs with thoracolumbar intervertebral disk herniation.

Gwendolyn J. Levine, DVM; Jonathan M. Levine, DVM, DACVIM (Neurology); Tige H. Witsberger, DVM; Sharon C. Kerwin, DVM, MS, DACVS; Karen E. Russell, DVM, PhD, DACVP; Jan Suchodolski, Dr.med.vet., PhD; Jörg Steiner, Dr.med.vet., PhD, DACVIM, DECVIM-CA; Geoffrey T. Fosgate, DVM, PhD, DACVPM

From the Departments of Veterinary Pathobiology (G. J. Levine, Russell) and Veterinary Small Animal Clinical Sciences (J. M. Levine, Witsberger, Kerwin, Suchodolski, Steiner) College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX 77843 and the Department of Production Animal Studies (Fosgate), University of Pretoria, Onderstepoort, South Africa

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Abbreviations: Cerebrospinal fluid (CSF), Confidence Interval (CI), Intervertebral disk herniation (IVDH), Magnetic resonance imaging (MRI), Modified Frankel Score (MFS), Myelin Basic Protein (MBP), Receiver-operating Characteristics Curve (ROC), Spinal Cord Injury (SCI), T2-weighted (T2W).

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Address correspondence to Dr. Gwendolyn J. Levine; Department of Veterinary Pathobiology, Texas A&M University, 4467 TAMU, College Station, TX 77843 USA. e-mail: gjlevine@cvm.tamu.edu; phone: (979)845-9180

Abstract:

Background: Release of myelin basic protein (MBP) into the cerebrospinal fluid (CSF) is associated with active demyelination and correlates with outcome in various neurological diseases.

Hypothesis/Objectives: To describe associations between CSF MBP concentration, initial neurological dysfunction, and long-term ambulatory outcome in dogs with acute thoracolumbar intervertebral disk herniation (IVDH).

Animals: 574 dogs with acute thoracolumbar IVDH and 16 clinically normal dogs.

Methods: Prospective case seriesclinical study. Signalment, initial neurological dysfunction as determined by a modified Frankel score (MFS), and ambulatory outcome at > 3 month follow-up were recorded. Cisternal CSF MBP concentration was determined using an enzyme-linked immunosorbent assay (ELISA). Associations were estimated between CSF MBP concentration and various clinical parameters.

Results: Dogs with thoracolumbar IVDH that did not ambulate at follow-up had a higher CSF MBP concentration (median, 3.56 ng/ml; range, 0.59-51.2 ng/ml) compared to control dogs (median, 2.22 ng/ml; range, 0-3.82 ng/ml) (P = 0.032). A CSF MBP concentration of ≥ 3 ng/ml had a sensitivity of 78% and specificity of 76% to predict an unsuccessful outcome based on receiver-operating characteristics curve analysis (area under the curve = 0.688, P=0.079). Affected dogs with a CSF MBP concentration ≥ 3 ng/ml had 0.09 times the odds of ambulation at follow-up compared to affected dogs with CSF MBP concentration <3 ng/ml when adjusted for initial MFS (95% CI 0.01-0.66, P = 0.018).

Conclusions and Clinical Importance: These results would suggest that CSF MBP concentration may be useful as an independent prognostic indicator in dogs with thoracolumbar IVDH.

Intervertebral disk herniation (IVDH) is a common cause of acute spinal cord injury (SCI) in dogs, representing 2.3% of all admissions to 13 veterinary teaching hospitals.[1] Disk herniation leads to SCI via a combination of primary and secondary mechanisms, which can result in spinal cord edema, demyelination, necrosis, and intraparenchymal hemorrhage.[2-4] Currently, only the absence of pelvic limb deep nociception and the presence of intramedullary T2-weighted (T2W) hyperintensity on magnetic resonance imaging (MRI) are known to be strongly associated with functional outcome in dogs with thoracolumbar IVDH.[5-9]

Myelin basic protein (MBP) is found only in the nervous system and accounts for 30% of all myelin proteins.[10,11] Various central nervous system diseases that cause demyelination can lead to release of MBP and MBP-like peptides into disrupted parenchyma and surrounding cerebrospinal fluid (CSF).[11,12] For example, MBP has been detected in the CSF of humans with multiple sclerosis,[13,14] traumatic brain injury,[15] and optic neuritis.[16] Dogs with demyelinating canine distemper[17] and degenerative myelopathy[18] have MBP detectable in CSF.

In SCI, MBP has been associated with neurological impairment and exacerbation of secondary mechanisms. In mouse models of contusive SCI, preservation of MBP immunostaining was correlated with functional recovery, reduced impact force, and lower MRI lesion burden.[19] Also, active and passive immunization against MBP following SCI has resulted in increased lesion size and impaired functional recovery due to autoimmune destruction of white matter in a similar model.[20] Transgenic mice with MBP autoreactive CD4+ T-cells have also been found to have impaired locomotion following SCI compared to littermate controls.[21]

The prospective study reported here was designed because of the previous data indicating a relationship between MBP and lesion development following SCI as well as information supporting the release of CSF MBP in animals with naturally occurring neurological disease. We hypothesized that CSF MBP concentration in dogs with thoracolumbar IVDH would be positively associated with initial injury severity and negatively associated with long-term functional outcome.

Materials and Methods

Study dogs

Non-ambulatory dogs admitted to Texas A&M University Veterinary Medical Teaching Hospital with a history of acute-onset thoracolumbar IVDH were prospectively recruited between March 2008 and December 2008 for participation in this study and another investigation.[22] Owner consent was obtained prior to diagnostic imaging and CSF acquisition using standard documents approved by the Clinical Research Review Committee (Protocol 08-08). Dogs had to meet the following additional criteria to be included in the affected study population: ≤7 day duration of neurologic impairment, non-ambulatory paraparesis or paraplegia at initial evaluation, and extra-dural disk-associated spinal cord compression located between the T3-L5 vertebral articulations at surgery or necropsy.

Procedures

Age, sex, breed, duration of clinical signs prior to admission, pre-referral administration of glucocorticoids (yes/no), and pre-referral administration of non-

steroidal anti-inflammatory drugs (NSAIDs; yes/no) were recorded for all dogs. Dogs were classified as chondrodystrophoid (Dachshund [miniature and standard], Pekingese, West Highland White Terrier, Corgi, Japanese Chin, Bassett Hound, Shih Tzu, Cocker Spaniel, Lhasa Apso, Bichon Frise, and Beagle) or non-chondrodystrophoid.[23-26] Neurologic dysfunction was classified at admission according to the modified Frankel score (MFS) as follows: paraspinal hyperesthesia only (grade 5), ambulatory paraparesis and ataxia (grade 4), non-ambulatory paraparesis (grade 3), paraplegia with nociception (grade 2), paraplegia with no superficial nociception (grade 1) and paraplegia with no deep nociception (grade 0).[27]

After premedication, anesthesia was induced in all dogs with propofol[a] (IV) and maintained on inhalant anesthetic (sevoflorane[b] or isofluorane[c]) for CSF sampling from the cerebromedullary cistern and advanced imaging. All dogs with thoracolumbar IVDH underwent advanced imaging consisting of myelography, computed tomography, or MRI. For those dogs that underwent MRI, T2W sagittal images of the vertebral column were reviewed by a board certified neurologist (JML) using a computer workstation with a 19 in. flat panel display[d] and commercially available software[e] to determine if spinal cord T2W hyperintensity was present.

Intervertebral disk herniation was confirmed at surgery (hemilaminectomy or pediculectomy) or necropsy. Routine post-operative care included opioid analgesics, bladder management, passive range of motion and physical rehabilitation and was performed for all dogs as needed until discharge. Owners were instructed to confine their dogs for an additional four to six weeks after discharge and continue post-operative care as needed.

Sample collection and testing

Approximately 1 to 1.5 ml of CSF from the cerebromedullary cistern was submitted for fluid analysis to include cytology, cell counts, and protein determination in a standard red-top tube. In addition, 2-4 additional aliquots (200-300µL) of the CSF were frozen at -80°C immediately after CSF acquisition. Within 1 hour, CSF nucleated cell (NC) count, NC differential, and protein concentration were determined. Dogs in which samples had excessive blood contamination (>13,200 RBCs/µL) were excluded from the study.[28] Pleocytosis was defined as a CSF NC count ≥ 5 cells/µL. Type of pleocytosis was defined by >60% predominance of a particular cell type or >40% of one cell type with no other cell type >33%.[29] The reference interval for CSF protein concentration was <27 mg/dL. Dogs without sufficient CSF for MBP determination were excluded.

Cerebrospinal fluid MBP was measured using a commercial enzyme-linked immunosorbent assay (ELISA) kit[f] for measurement of human MBP. This assay is intended for the measurement of human MBP in CSF, and contains a goat antihuman MBP antibody. Previously published data[18] have supported the detection of canine MBP by the goat antihuman MBP antibody. In-house validation of the assay in the study reported here consisted of intra- and interassay variability, dilutional parallelism, and spiking recovery. Intra-assay variability was determined using 5 replicates of 3 CSF samples, and the coefficient of variation ranged from 2.3-5.5%. Inter-assay variability was determined using 3 CSF samples, and the high and low controls provided with the assay. The interassay coefficient of variation for MBP ranged from 8 to 19.5%. The

observed-to-expected ratio for CSF serial dilutions for 4 CSF samples ranged from 78.9 to 124.4% of expected. CSF containing low, medium, and high MBP concentration were obtained. The observed-to-expected ratios for combined low+medium, medium+high, and low+high pooled MBP CSF were 105.6, 91.7, and 113.7%, respectively.

Long-term follow-up

All dogs with thoracolumbar IVDH that were alive were assessed for voluntary ambulation > 3 months after discharge. Ambulatory status was determined via in-hospital examination or through a brief questionnaire sent to owners via electronic or regular mail. Owners that did not respond were subsequently contacted by telephone. Functional outcome was considered a success if a dog regained the ability to walk voluntarily at any point during the study. Dogs that did not recover ambulation during the follow-up period or were euthanized due to non-ambulatory status were classified as unsuccessful outcomes.

Control dogs

Normal research colony dogs (n = 16) were used as a control population after obtaining approval from the Institutional Animal Care and Use Committee (AUP 08-115). Control dogs were required to have normal physical and neurological examinations, complete blood count, and serum biochemistry results at the time of enrollment. Cerebrospinal fluid collection, CSF analysis, and MBP measurement were performed in the same manner as for dogs with thoracolumbar IVDH.

Statistical Analysis

Descriptive statistics were calculated for CSF MBP stratified by group (IVDH versus control), long-term success (versus not), signalment, administered treatments, and spinal cord T2W hyperintensity. Continuous variables were dichotomized based on the median and Mann-Whitney U tests were used to compare CSF MBP concentration between groups. The correlation of CSF MBP concentration with MFS at admission, duration of injury at admission, and CSF parameters was assessed using Spearman's rho. Receiver-operating characteristics (ROC) curve analysis was performed to determine the overall effectiveness of CSF MBP concentration to predict an unsuccessful long-term outcome in dogs with confirmed thoracolumbar IVDH. The cutoff that maximized the Youden index (sensitivity + specificity -1) was selected as optimal.

Multivariable logistic regression was used to estimate the ability of CSF MBP concentration to predict a long-term successful outcome while adjusting for disease severity and other potential predictors. Quantitative variables were assessed for the assumption of being linear in the natural logarithm of the odds and those that violated this assumption were modeled as categorical variables. CSF MBP concentration was dichotomized based on the optimal cutoff identified from the ROC analysis. MFS at admission was forced into all models to adjust for disease severity. A backwards stepwise approach based on Wald tests was used to evaluate the ability of signalment and administered treatments to predict a successful outcome. Hosmer and Lemeshow tests were used to assess the fit of multivariable models. The final multivariable model was further assessed excluding non-condrodystrophic dogs to detect qualitative differences.

All analyses were performed with a commercially available software package[g] and evaluated at the 5% level of significance.

Results

There were 57 dogs with thoracolumbar IVDH that met the inclusion criteria, but 3 were subsequently excluded because of insufficient CSF for MBP determination. Median age of the 54 dogs was 5 years (range, 1.5-13 years). There were 6 sexually intact females, 19 spayed females, 8 sexually intact males, and 21 castrated males. Breeds included Dachshund (miniature and standard grouped together; n = 35), mixed breed (4), Pembroke Welsh Corgi (2), Maltese (2), and 11 other breeds with 1 dog each. The majority of dogs were classified as chondrodystrophoid (50/54). The median duration of neurological signs prior to admission was 1 day (range, 1-7 days). The median MFS at admission was 2 (range, 0-3). Thoracolumbar IVDH was identified by MRI in 24 dogs, myelogram in 21 dogs, and CT in 9 dogs. Disk-associated compressive lesions were seen at 8 different articulations, with T13-L1 (n = 16), T12-T13 (14), and T11-T12 (10) being most common. At long-term follow-up, 42/54 dogs were voluntarily ambulatory. Of the 9 dogs with unsuccessful outcomes, 5 were euthanized prior to long-term follow-up with ascending-descending myelomalacia confirmed at necropsy in 3/5. Three dogs were not available for long-term follow-up.

Median age of the 16 control dogs was 3 years (range, 2-4 years). Three were spayed females and 13 were castrated males. Breeds included Labrador retriever (n = 7), mixed breed (5), Red Bone hound (2), and Blue Tick hound (2). Control dogs did not have CSF pleocytosis or elevated CSF protein.

In dogs with thoracolumbar IVDH, the median CSF NC count was 3 cells/µL (range, 0-245 cells/µL), the median CSF RBC count was 27 cells/µL (range, 0-10780 cells/µL), and the median protein concentration was 28 mg/dl (range, 12-110 mg/dl). Seventeen dogs had CSF pleocytosis which was classified as neutrophilic in 12 dogs, mixed cell in 4 dogs, and large mononuclear in 1 dog. CSF protein concentration was above the reference interval (≥ 27 mg/dl) in 28 dogs.

The CSF MBP concentration did not differ between control dogs and dogs with thoracolumbar IVDH (Table 1). Within dogs with thoracolumbar IVDH, the concentration of CSF MBP did not vary by duration of signs at admission, signalment features, corticosteroid administration, the presence of CSF pleocytosis, or T2W spinal cord hyperintensity. The CSF MBP concentration was higher in dogs with an unsuccessful long-term outcome (median, 3.56 ng/ml) compared to those with a successful outcome (median, 1.53 ng/ml), but this difference was not significant (P = 0.081). The concentration of CSF MBP was higher in dogs with an unsuccessful outcome compared to the healthy controls (P = 0.032). CSF MBP concentration was not significantly correlated with MFS at admission or CSF parameters. CSF MBP concentration did not vary over initial MFS categories within the successful outcome group (Table 2). CSF MBP concentration did not vary with initial MFS categories within the failure group (P=0.548). The ROC curve analysis suggested an optimal CSF MBP cut-off value of 3 ng/ml (Figure 1). The sensitivity and specificity for predicting an unsuccessful outcome at this cut-off were 78% and 76% respectively. Area under the ROC curve was estimated as 0.688 (95% confidence interval, 0.445 – 0.930), but the

overall ability of CSF MBP concentration in this analysis to predict successful long-term outcome was not significant (P = 0.079).

Both CSF MBP concentration and MFS at admission were significant predictors of long-term functional outcome (Table 3). Dogs with a CSF MBP concentration ≥ 3 ng/ml (cut-off identified by the ROC analysis) had 0.09 times the odds (95% CI 0.01-0.66) of long-term voluntary ambulation compared to dogs with CSF MBP concentration < 3 ng/ml when adjusted for the effect of initial MFS (P = 0.018). The final multivariable model was a good fit to the data based on the Hosmer and Lemeshow test (χ^2 = 1.49, df = 4, P = 0.828). The exclusion of non-condrodystrophic dogs did not change qualitative results of the logistic models (data not shown).

Discussion

The results of the present study indicate that in dogs with thoracolumbar IVDH, CSF MBP concentration was associated with long-term functional outcome. A CSF MBP concentration of 3 ng/ml or greater had a sensitivity of 78% and specificity of 76% to predict an unsuccessful outcome based on the ROC analysis. A multivariable logistic regression was utilized to adjust for confounding by variables including MFS. In that model, dogs with CSF MBP ≥ 3 ng/ml had 0.09 times the odds of recovery compared to dogs with CSF MBP < 3 ng/ml (95% CI 0.01-0.66, P = 0.018). Although CSF MBP has not previously been investigated in naturally occurring SCI, data from human traumatic brain injury and rodent models of SCI are consistent with these results.[12,30,31]

In rodent spinal cord contusion models, demyelination is initiated almost immediately following SCI, but can occur for months after injury due to autoimmune

events and Wallerian degeneration.[32] In dogs and humans with naturally occurring SCI, myelin destruction may be severe hours following primary events.[33,34] As the persistence of functional white matter tracts is essential to limb function caudal to a lesion site, relationships between outcome and measures of myelinated axons are expected.[35,36] For example, in histological spinal cord samples from injury models, loss of immunostaining for MBP is associated with contusion severity and physical examination-based determinants of recovery.[19] Not only might high CSF MBP concentrations act as a surrogate measure for active demyelination, but MBP has been shown to exacerbate immunological secondary SCI. Rodents with experimental SCI that have been exposed to MBP exhibit enhanced rubrospinal tract loss, increased intra-lesional T-cell accumulation, and poorer locomotion compared with control animals.[20]

The independence of CSF MBP from initial MFS in dogs with thoracolumbar IVDH is important, especially considering the association between MFS and outcome. Physical examination-based SCI scales like the MFS are commonly used to characterize lesion severity, monitor recovery, and determine prognosis following injury. In the study reported here, dogs with an initial MFS of 2 had 13.9 times the odds of long-term ambulation compared to those dogs with an initial MFS of 0-1 (95% CI 1.08-179, P = 0.047). Yet, SCI scores have limitations. For example, scores do not inform observers about the mechanisms underlying a particular SCI and are imperfect at discerning structural versus functional lesions. It appears that regardless of MFS group, elevated CSF MBP concentration is an indicator of poor functional outcome (Tables 2 and 3). This may suggest that either demyelination associated with CSF MBP release or

secondary injury resulting from MBP have negative consequences in dogs with SCI resulting from thoracolumbar IVDH.

CSF MBP concentration was likewise not correlated to MRI-based markers of SCI in the study reported here. The lack of association with spinal cord T2W hyperintensity (Table 1) is not entirely surprising as high T2 signal following SCI may occur as a result of various pathological processes, including edema, necrosis, and hemorrhage.[37,38] Additionally, the relatively low field strength (1.0 T) of the MR in this report may have prohibited the detection of some lesions associated with demyelination on T2W images.[39,40] Finally, only 24/54 dogs with IVDH had MRI performed, which likely limited our ability to detect associations.

In this report, the concentration of CSF MBP did not differ significantly between controls and dogs with thoracolumbar IVDH. Although, dogs with unsuccessful outcomes did have significantly higher CSF MBP concentration compared to unaffected control dogs. In humans with traumatic brain injury, the sensitivity of CSF MBP to detect injury was only 36% which suggests significant overlap between concentrations in cases and controls in that group of patients.[30] Dogs with degenerative myelopathy and control dogs did not have significant differences in cisternal CSF MBP concentration, although dogs with degenerative myelopathy did have higher CSF MBP concentration compared to controls when samples from the lumbar cistern were analyzed.[18] Sample size and the site of CSF collection may have contributed to the lack of statistical significance for some comparisons. Differences in breed distribution and chondrodystrophoid status between the control and affected populations also may have influenced measured associations.

The lack of significance in the comparison of CSF MBP concentration between successful and unsuccessful outcome groups is different than the logistic regression results suggesting that CSF MBP concentration is a significant predictor of outcome. This contradiction is related to the designation of variables as predictors and outcomes in the statistical techniques. The comparison of CSF MBP concentration across outcome groups is beneficial as a descriptive technique, but from an analytic standpoint this comparison treats ambulatory outcome as a predictor of CSF MBP concentration. Logistic regression allows assessment of CSF MBP concentration as a predictor of ambulatory outcome and additionally controls for potential confounding variables. Therefore, it has an advantage over comparison of CSF MBP concentrations when ambulatory outcome prediction is the goal of an analysis. In the present study discordant results were observed because the variability in CSF MBP concentration was high relative to the sample size. A larger sample size might have prevented this situation from occurring.

It is important to note that while CSF MBP is predictive of long-term functional outcome in dogs with thoracolumbar IVDH, cut-off values reported in this study are imperfect for determining outcome. For example, if the CSF MBP cutoff were applied to a population of 100 dogs with 25 unsuccessful outcomes, 6 dogs that ultimately failed to ambulate would be incorrectly assessed as having a good prognosis and 18 dogs that ultimately ambulated would be initially classified as having a poor prognosis. In the author's view, CSF MBP should be thought of as an additional, independent prognostic indicator that can be used in combination with other assessment tools.

The major limitations of this study included the available sample size, single follow-up interval, and single center design. Although our sample size was similar to other biomarker studies on veterinary[41-44] and human[45-47] neurological diseases, a larger population could have enhanced the detection of differences between groups and improved the precision in reported associations. Specifically, the low number of unsuccessful outcomes (9/51) in this study reduced the power of statistical tests to evaluate predictors. The follow-up interval used in this report was based on data suggesting that the majority of dogs that voluntarily ambulate following surgical thoracolumbar IVDH do so within 3 months of SCI.[5,48] Multiple intermediate follow-up intervals could have been utilized to detect differences in functional progression in the sub-acute phases of SCI between CSF MBP groups. Finally, the data in this report were generated at a single institution. A multi-center approach might have helped confirm these single center data, reduce potential confounders, and enhance study population.

A limited number of outcome determinants are known in dogs with acute thoracolumbar IVDH. These predictors are not absolute and the success proportion may be high even in the most severe injury groups. For example, voluntary ambulation occurs in 43-62% of dogs lacking pelvic limb deep nociception prior to surgery for thoracolumbar IVDH.[5,8,49] Data from the study reported here suggest that sub-stratification of outcome groups might be achieved using CSF MBP as the presence of high CSF MBP concentration was associated with poor long-term outcome regardless of MFS. Group stratification may assist in the early recognition of dogs that are in positive outcome categories based on MRI findings or MFS, but may be at risk for limited functional recovery. Additionally, based on the relationships detected in this report and

experimental data to suggest a role for MBP in secondary SCI, future studies investigating targeted therapies may be warranted.

Footnotes

[a] Rapinovet, Schering-Plough Animal Health Corp, Union, NJ

[b] SevoFlo, Abbott Laboratories, North Chicago, IL

[c] IsoFlo, Abbott Laboratories, North Chicago, IL

[d] Dell 1905 FP, Dell Corporation, Round Rock, TX

[e] eFilm 2.1 Veterinary, MERGE Healthcare, Cleveland, OH

[f] Active MBP ELISA, Diagnostic Systems Laboratories, Inc, Webster, TX

[g] SPSS version 15.0 for Windows, SPSS Inc., Chicago, IL

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Table 1. Myelin basic protein (MBP) concentrations measured in the cerebrospinal fluid (CSF) of 54 dogs with surgically confirmed intervertebral disk herniation (IVDH) and 16 healthy control dogs.

	CSF MBP with Factor		CSF MBP in Comparison Group		
Factor (comparison)	**n**	**Median (range)**	**n**	**Median (range)**	**P value***
Affected (control)	54	1.83 (0.54 - 72.6)	16	2.22 (0 - 3.82)	0.706
Successful outcome (not successful)	42	1.53 (0.64 - 72.6)	9	3.56 (0.54 - 51.2)	0.081
Successful outcome (control)	42	1.53 (0.64 - 72.6)	16	2.22 (0 - 3.82)	0.237
Not successful (control)	9	3.56 (0.54 - 51.2)	16	2.22 (0 - 3.82)	0.032
Female (male)	25	1.75 (0.54 - 24.0)	29	1.85 (0.74 - 72.6)	0.362
Intact (neutered)	14	1.80 (0.74 - 72.6)	40	1.83 (0.54 - 51.2)	0.813
Age < 5 yrs (age ≥ 5 yrs)	23	1.43 (0.54 - 72.6)	31	1.94 (0.64 - 48.8)	0.441
Chondrodystrophic breed (other)	49	1.75 (0.54 - 72.6)	4	6.48 (1.43 - 9.20)	0.071
Corticosteroids administered (not)	15	1.75 (1.14 - 72.6)	39	1.85 (0.54 - 51.2)	0.582
NSAIDs administered (not)	10	1.95 (1.06 - 24.0)	43	1.85 (0.54 - 72.6)	0.682

CSF pleocytosis (not)	17	1.23 (0.54 - 51.2)	37	1.94 (0.74 - 72.6)	0.103
T2W hyperintensity (not)	10	1.82 (0.87 - 24.0)	14	1.77 (0.64 - 51.2)	0.841

NSAID = nonsteroidal anti-inflammatory drugs

*Based on Mann-Whitney U tests

Table 2. Myelin basic protein (MBP) concentration measured in the cerebrospinal fluid (CSF) of 51 dogs with surgically confirmed intervertebral disk herniation (IVDH) by initial modified Frankel score (MFS) and successful outcome from a single referral hospital in Texas during 2008.

	Success		Failure		
Initial MFS	**n**	**Median (range)**	**n**	**Median (range)**	**P value***
0	3	1.39 (1.04, 5.92)	5	3.56 (0.54, 51.2)	0.571
1	3	1.94 (1.43, 7.71)	1	0.91	1.0
2	14	1.51 (0.87, 72.6)	1	5.25	1.0
3	22	1.59 (0.64, 9.74)	2	26.1 (3.49, 48.8)	0.087
P value†		0.539		0.548	

*Based on Mann-Whitney U tests comparing MBP between success and failure groups within MFS categories.

†Based on Mann-Whitney U tests comparing MBP between success and failure groups within MFS categories (0-1 versus 2-3).

Table 3. Utility of myelin basic protein (MBP) in the cerebrospinal fluid (CSF) of 51 dogs with surgically confirmed intervertebral herniation (IVDH) to predict successful outcome after adjusting for severity of disease via the modified Frankel score (MFS) at admission.

Variable*	**Parameter estimate ($\hat{\beta}$)**	**P-value (Wald)**	**Odds ratio (95% CI)**
MBP ≥ 3.0 ng/ml (versus < 3)	-2.39	0.018	0.09 (0.01, 0.66)
Initial MFS		0.006	
MFS 0-1 (referent)			1.0
MFS 2	2.63	0.043	13.9 (1.08, 179)
MFS 3	2.56	0.017	12.9 (1.57, 105)

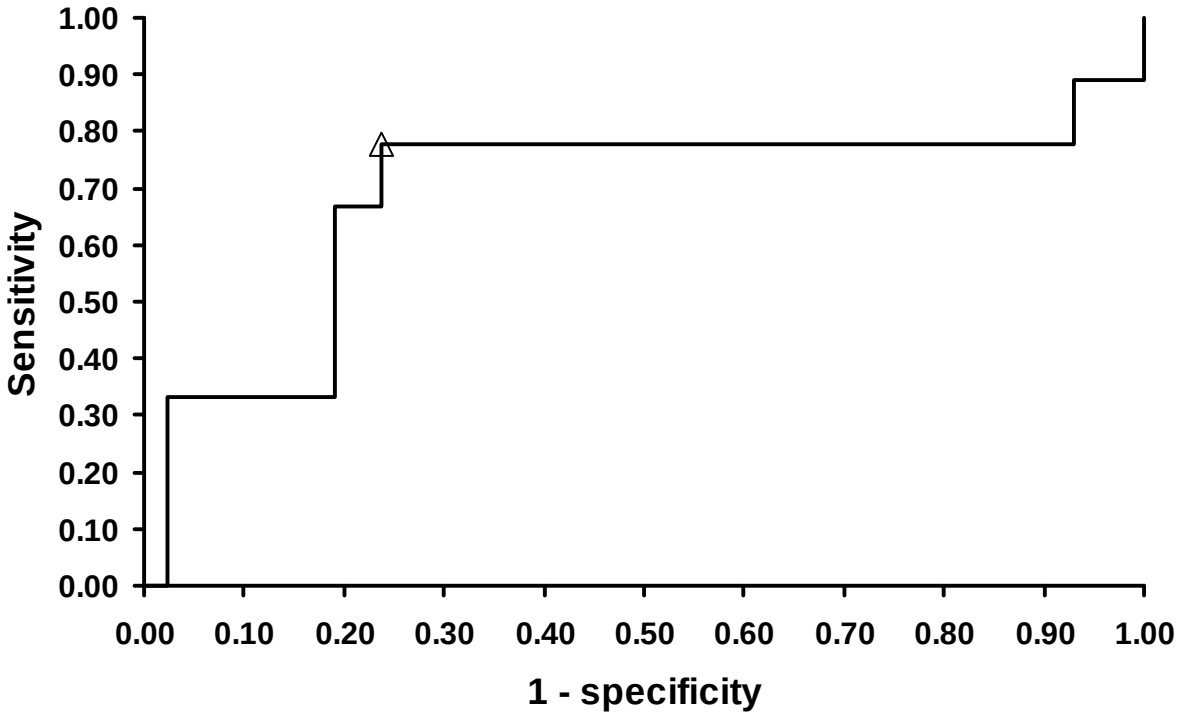

Figure 1. Receiver-operating characteristic curve to predict successful outcome for myelin basic protein (MBP) in the cerebrospinal fluid (CSF) of 51 dogs with surgically confirmed intervertebral disk herniation (IVDH) from a single referral hospital in Texas. Sensitivity and specificity at 3.0 ng/ml were 78% and 76% respectively and designated by a triangle.