Prevalence and Risk Factors for Presumptive Ascending/Descending Myelomalacia in Dogs after Thoracolumbar Intervertebral Disk Herniation

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Background: Ascending/descending myelomalacia (ADMM) is a severe complication of thoracolumbar intervertebral disk herniation (TL-IVDH) in dogs.

Hypothesis/Objectives: To investigate the prevalence and risk factors for ADMM in nonambulatory dogs with surgically treated TL-IVDH.

Animals: Six-hundred and fifty-two client-owned dogs evaluated for TL-IVDH that underwent decompressive spinal surgery.

Methods: Retrospective medical record review from February 2007 through December 2015.

Results: Thirteen dogs developed ADMM, with an overall prevalence of 2.0%. The prevalence of ADMM was 0% in dogs with neurological signs graded 1 or 2 at admission or before magnetic resonance imaging (MRI) or surgical procedures, 0.6% in dogs with neurological signs graded 3, 2.7% in dogs with neurological signs graded 4, and 14.5% in dogs with neurological signs graded 5. Age (<5.8 years), neurological status (grade 5), site of disk herniation (L5-L6), duration of clinical signs before becoming nonambulatory (<24 hours), detection of intramedullary T2-weighted (T2W) hyperintensity, and a T2 length ratio >4.57 were significant risk factors in the univariate analysis for development of ADMM.

Conclusions and Clinical Importance: The factors identified in this study may be useful for the prediction of ADMM. Multicenter studies with a higher number of dogs with ADMM are required to confirm these data.

Key words: Canine; Contusive injury; Deep pain perception; Spinal cord injury.

Myelomalacia is defined as gross softening of the spinal cord characterized by hemorrhagic necrosis and liquefaction of spinal cord tissue that can occur after acute spinal cord injury.[1–3] Myelomalacia frequently is associated with intervertebral disk herniation (IVDH).[4–6] The pathophysiology of myelomalacia secondary to IVDH involves primary mechanical damage to the spinal cord caused by the concussive and compressive effects of disk herniation, followed by secondary damage caused by decreased vascular perfusion, ischemia, perivascular edema, electrolyte shifts, oxidative stress, release of free radicals and vasoactive molecules, inflammation, and apoptosis.[1,7–9] Myelomalacia may be focal or may ascend and descend along the spinal cord, involving multiple segments or even the entire spinal cord. In the latter case, the condition is defined as ascending and descending myelomalacia

Abbreviations:

ADMM	ascending/descending myelomalacia
CTM	cutaneous trunci muscle
DPP	deep pain perception
IVDH	intervertebral disk herniation
LMN	lower motor neuron
MRI	magnetic resonance imaging
ROC	receiver operating characteristic
T2W	T2 weighted
TL-IVDH	thoracolumbar intervertebral disk herniation
UMN	upper motor neuron

(ADMM).[4,8] The pathophysiology of this phenomenon is not completely understood. Recent studies showed an association among increased intramedullary pressure, the extent of intramedullary and subdural hemorrhage, and oxidative stress with the progression of myelomalacia.[1,8] Ascending/descending myelomalacia after TL-IVDH is reported to develop hours to several days after the onset of paraplegia without deep pain perception (DPP) and affects 9–18% of dogs with such clinical presentation.[5,10–14] Clinical signs of ADMM may include progression from signs of upper motor neuron (UMN) lesion to signs of lower motor neuron (LMN) lesion in the pelvic limbs and tail, total anal areflexia, cranial migration of the caudal border of the cutaneous trunci muscle (CTM) reflex, development of tetraparesis, and death caused by respiratory paralysis.[5,6,11]

Imaging of ADMM has been obtained by myelography and magnetic resonance imaging (MRI).[11,15] Moreover, numerous efforts have been made to identify diagnostic methods, such as MRI and assessment of glial fibrillary acid protein in the blood, to achieve early diagnosis of ADMM.[6,16] Because no treatment for ADMM is available and the prognosis is poor,[2,13] the

identification of risk factors that may predict development of ADMM in dogs suffering from IVDH would be of paramount importance for therapeutic plans and prognostic assessments. To the authors' knowledge however, no such data are available. The aims of this study were as follows: (1) to determine the prevalence of ADMM and (2) to investigate possible risk factors for the development of ADMM in a large number of nonambulatory dogs that underwent spinal decompression surgery for TL-IVDH.

Materials and Methods

Case Selection

The medical record database of the Neurology Unit at the Portoni Rossi Veterinary Hospital was searched for dogs with a diagnosis of TL-IVDH between February 2007 and December 2015.

To be eligible for inclusion, dogs needed to have had a complete diagnostic evaluation, including physical and neurological examinations performed by a board-certified neurologist (MB) or by neurology residents (FB, SC), MRI of the thoracolumbar spine suggesting a diagnosis of IVDH between the T3 and L6 vertebral segments and confirmation by hemilaminectomy or mini-hemilaminectomy.

Procedures

Information extracted from the medical records included breed, age, sex, body weight, clinical history, neurological status, MRI findings, anatomic localization and type of IVDH (extrusion vs. protrusion), and surgical procedures and outcome, including development of ADMM. The dogs were classified as chondrodystrophic breeds, nonchondrodystrophic breeds, or mixed breeds.[17–19] The dogs were divided into groups based on the severity of neurological dysfunction detected at admission or before diagnostic or surgical procedures should the condition have changed, and graded 1 (spinal hyperesthesia only) to 5 (paraplegia without DPP) according to a grading system described elsewhere.[20,21] For dogs with neurological signs graded 3, 4 and 5, we reported the duration of clinical signs, defined as the interval between the first signs of spinal cord disease and the loss of the ability to walk identified by the owner, and the delay, defined as the interval between the loss of the ability to walk and the neurological evaluation at our hospital, as described previously.[14]

All dogs were anesthetized and had both a survey radiographic study and an MRI (0.22T MrV; Paramed) of the thoracolumbar spine performed. All dogs with neurological signs graded 4 and 5 and the majority of the dogs with neurological signs graded 3 underwent these procedures during the same day of the first clinical evaluation, and within 24 hours for the remaining dogs with neurological signs graded 3. If intramedullary T2-weighted (T2W) hyperintensity was present in the sagittal MRI, we calculated the T2 length ratio, by OsiriX Medical Imaging Software (open source software, www.osirix-viewer.com), as described previously.[22,23] All dogs underwent spinal decompressive surgery (hemilaminectomy or mini-hemilaminectomy) at a different time, depending on the severity of neurological deficits: immediately after diagnostic imaging for all dogs with neurological signs graded 4 or 5 and almost all dogs with neurological signs graded 3; within 24 hours for the remaining dogs with neurological signs graded 3; and within 15 days for dogs with neurological signs graded 1 and 2. All dogs were hospitalized for 2–7 days after surgery. Postoperative neurological status was evaluated daily for any evidence of neurological deterioration compared to the preoperative neurological status.

The dogs were re-examined at our hospital 14 and 30 days after surgery.

Diagnosis of ADMM

A presumptive diagnosis of ADMM was made on the basis of the progression of clinical signs from initial UMN or LMN paraparesis or paraplegia to flaccid paraplegia; total areflexia of the pelvic limbs, tail and anus; loss of DPP caudal to the site of spinal cord injury; cranial migration of the CTM reflex; tetraparesis; loss of thoracic limb reflexes; and respiratory difficulty.[6,11,15]

Statistical Analysis

Statistical analyses were performed by a statistical software packages.[a,b] The prevalence of ADMM across all of the dogs and within each clinical group was calculated. The data from groups with a prevalence of ADMM = 0% were excluded from further statistical analysis. Contingency tables were generated for the categorical variables (sex, body weight, breed, type of IVDH, neurological status, and T2W hyperintensity). For the duration of clinical signs before becoming nonambulatory and the delay between loss of ability to walk and the neurological evaluation, the categories were <24 hours and >24 hours. Receiver operating characteristic (ROC) curve analysis was performed to determine appropriate cutoff values to reclassify the continuous variables of age, body weight, and T2W hyperintensity as categorical. The distribution of factors was compared between dogs with and without ADMM by the chi-square test. Odds ratios and 95% confidence intervals (CIs) were calculated for variables. Factors identified as having a liberal association with ADMM (i.e. $P < .10$) were used to perform multivariate logistic regression. Factors were considered significant when the value of P was <.05 and when the 95% CI of the odds ratio (OR) excluded 1.0. Mann-Whitney U-tests were used to compare T2W length ratio medians within groups.

Results

Prevalence of ADMM and Study Population

Six-hundred and fifty-two dogs met the inclusion criteria and were used for the study.

Based on the neurological status, 34 dogs had neurological signs graded 1, 242 dogs had neurological signs graded 2, 173 dogs had neurological signs graded 3, 148 dogs had neurological signs graded 4, and 55 dogs had neurological signs graded 5. Thirteen dogs developed ADMM, with an overall prevalence of ADMM in the total population of 2.0%. The prevalence of ADMM in dogs with neurological signs graded 1 and 2 was 0%, that in dogs with neurological signs graded 3 was 0.6% (1/173), that in dogs with neurological signs graded 4 was 2.7% (4/148), and that in dogs with neurological signs graded 5 was 14.5% (8/55). For the evaluation of possible risk factors, we considered only the dogs with neurological signs graded 3, 4, and 5. Therefore, 376 dogs were included in further statistical analysis.

Two-hundred and twenty-six (60.1%) dogs belonged to chondrodystrophic breeds, with Dachshund (128), French Bulldog (28), and Beagle and Cocker Spaniel (10 each) being the most prevalent. The second most represented group was the mixed-breed dogs (n = 115 [30.6%]). The nonchondrodystrophic breeds (n = 35

[9.30%]) included mostly German Shepherds (11) and Labrador Retrievers (4).

The median age was 5.7 years (range, 1.5–15.4 years). There were 210 males and 166 females. The median body weight was 9 kg (range, 1.6–62 kg).

The site of disk herniation ranged from T9–T10 to L5-L6 (Table 1), and several dogs had disk herniation in >1 site. Three-hundred and fifty-six dogs (94.7%) had disk extrusion and 20 dogs (5.3%) had disk protrusion. The duration of clinical signs before becoming nonambulatory was <24 hours for 186 (49.4%) dogs and >24 hours for 190 (50.6%) dogs. The delay between loss of ability to walk and neurological evaluation was <24 hours for 266 (70.8%) dogs and >24 hours for 110 (29.2%) dogs.

One-hundred and fifty-one (40.2%) dogs had intramedullary T2W hyperintensity on sagittal MRI, with a median T2W length ratio of 3.09 (range, 0.37–9.91). The intramedullary T2W hyperintensity and median T2W length ratio for grades 3, 4, and 5 are listed in Table 2.

Risk Factors for the Development of ADMM

Of the 13 dogs that had developed myelomalacia, 4 had signs consistent with descending myelomalacia (progression of clinical signs from initial UMN or LMN paraparesis or paraplegia to flaccid paraplegia; total areflexia of the pelvic limbs, tail and anus; and loss of DPP caudal to the site of spinal cord injury) and 9 had signs consistent with ascending–descending myelomalacia. A clinical diagnosis of ADMM was supported in 2 cases by postsurgical MRI. No dogs underwent a second surgery. For the dogs that showed clinical signs of ADMM, we waited until mechanical ventilation was needed because of respiratory failure, and then, all dogs were euthanized at their owners' request. Dogs with descending myelomalacia all were alive except for 1, which was euthanized on the owner's request 4 days after surgery, with no signs of recovery of DPP, or spinal reflexes and without urinary and fecal continence.

Nine (69.2%) dogs with ADMM belonged to chondrodystrophic breeds: Dachshund (4), French Bulldog

Table 1. Distribution of TL-IVDH sites in all dogs with neurological signs graded 3, 4, and 5 and in dogs with ADMM

Intervertebral Disk Site	Total Number of IVDH	No. (%) of ADMM Cases
T9-T10	2	0 (0)
T10-T11	9	0 (0)
T11-T12	52	2 (3.85)
T12-T13	94	3 (3.19)
T13-L1	78	3 (3.85)
L1-L2	58	1 (1.72)
L2-L3	52	0 (0)
L3-L4	27	0 (0)
L4-L5	23	0 (0)
L5-L6	5	4 (80)

Table 2. Number of dogs with and without ADMM, with neurological signs graded 3, 4, and 5, with intramedullary T2W hyperintensity and median T2 length ratio

Neurological Grade	N° (%) of Dogs with Intramedullary T2W Hyperintensity	Median T2 Length Ratio		
		Dogs without ADMM	Dogs with ADMM	P-value
Grade 3	45 (26%)	2.16	—	—
Grade 4	56 (37.8%)	3.14	4.67	.166
Grade 5	50 (90.9%)	3.57	7.45	<.001

— = Not applicable. Values of $P < .05$ were considered significant and based on Mann-Whitney U-test.

(2), Shih-Tzu, and Miniature Poodle and Cocker Spaniel (1 each). Three (23.1%) dogs with ADMM were mixed breed, and 1 (7.7%) belonged to a nonchondrodystrophic breed (Lagotto). There were 8 females and 5 males. No association was found between breed and sex for the development of ADMM (Table 3). The median age of dogs with ADMM was 4.6 years (range, 2.3–7.1 years), and the median body weight was 10 kg (range, 4.7–20.5 kg). The ROC curve analyses performed for age and body weight yielded optimal cutoff values of 5.8 years and 20.5 kg, respectively, for the creation of categorical variables, corresponding with an area under the curve of 0.66 (sensitivity, 84.6%; specificity, 47.9%) and 0.54 (sensitivity 100%; specificity 15.5%), respectively. When these cutoffs were used, dogs <5.8 years of age were at significantly ($P = .021$) higher odds of developing ADMM than were other dogs. Weight was not significantly associated with development of ADMM (Table 3).

Of the 13 dogs with ADMM, 1 had neurological signs graded 3, 4 had neurological signs graded 4, and 8 had neurological signs graded 5. The dog with clinical signs graded 3 and 1 of the dogs with clinical signs graded 4 had a second MRI performed 6 days after surgery. An intramedullary hyperintensity in the entire spinal cord, without signs of a new IVDH, was detected. Both dogs developed respiratory failure. Dogs with neurological signs graded 5 had significantly ($P < .001$) higher odds of developing ADMM than other dogs (Table 3). The sites of disk herniation in dogs with ADMM were L5-L6 in 4 dogs, T12-T13 in 3 dogs, T13-L1 in 3 dogs, T11-T12 in 2 dogs, and L1-L2 in 1 dog. Dogs with disk herniation at the level of intervertebral disk space L5-L6 had significantly ($P < .001$) higher odds of developing ADMM than other dogs with IVDH located at different sites. None of the dogs with ADMM had multiple sites of disk herniation. None of the dogs with ADMM had disk protrusion, preventing the ability to evaluate any association between disk protrusion and ADMM.

The duration of clinical signs before becoming nonambulatory was <24 hours for 10 (76.9%) dogs and >24 hours for 3 (23.1%) dogs. The delay between loss of ability to walk and the neurological evaluation was

Table 3. Results of univariate analysis to identify factors unconditionally associated with development of ADMM in 376 dogs after spinal decompression surgery for thoracolumbar IVDH.

Factor	No. (%) with ADMM	No. (%) without ADMM	OR	95% CI	*P*-value
Breed					
Chondrodystrophic	9 (69.2%)	217 (59.8%)	1.41	0.17–11.48	.746
Mixed	3 (23.1%)	112 (30.8%)	0.91	0.09–9.06	.938
Nonchondrodystrophic	1 (7.7%)	34 (9.4%)	Referent	—	—
Age					
≤5.8 year	11(84.6%)	189 (52.1%)	5.06	1.11–23.17	.021
>5.8 year	2 (15.4%)	174 (47.9)	Referent	—	—
Sex					
Female	8 (61.5%)	158 (43.5%)	2.07	0.66–6.46	.198
Male	5 (38.5%)	205 (56.5%)	Referent	—	—
Body weight					
≤20.5 kg	12 (92.3%)	282 (77.7%)	2.21	0.28–17.38	.438
>20.5 kg	1 (7.7%)	52 (22.3%)	Referent	—	—
Neurological grade					
Grade 5	8 (61.5%)	47 (12.9%)	10.75	3.37–34.26	<.001
Grade 3 and 4	5 (38.5%)	316 (87.1%)	Referent	—	—
Site of IVDH					
L5-L6	4 (30.8%)	1 (0.3%)	171.55	17.39–1692.14	<.001
Other	9 (69.2%)	386 (99.7%)	Referent	—	—
Duration of clinical signs to become nonambulatory					
≤24 hours	10 (76.9%)	176 (48.5%)	3.54	0.96–13.08	.043
>24 hours	3 (23.1%)	187 (51.5%)	Referent	—	—
Delay between loss of ability to walk and the neurological evaluation					
≤24 h	11 (84.6%)	255 (70.2%)	2.33	0.51-10.69	.263
>24 h	2 (15.4%)	108 (29.8%)	Referent	—	—
Intramedullary T2W Hyperintensity					
Presence	11 (84.6%)	140 (38.6%)	8.76	1.91–40.11	<.001
Absence	2 (15.4%)	223 (61.4%)	Referent	—	—
T2 length ratio					
>4.57	9 (81.8%)	29 (20.7%)	17.22	3.52–84.10	<.001
≤4.57	2 (18.2%)	111 (79.3%)	Referent	—	—

— = Not applicable. Values of *P* < .05 were considered significant.

For percentage calculations, the denominator is the total number of dogs with ADMM (13) or without ADMM (363) for breed, age, sex, body weight, neurological grade, duration of clinical signs, delay, and intramedullary T2W hyperintensity.

For percentage calculations, the denominator is the total number of intervertebral disk sites affected in dogs with (13) or without ADMM (387) for site of IVDH.

For percentage calculations, the denominator is the number of dog with intramedullary T2W hyperintensity with (11) and without (140) ADMM for T2 length ratio.

<24 hours for 11 (84.6%) dogs and >24 hours for 2 (15.4%) dogs.

The duration of clinical signs to become nonambulatory was significantly associated with the development of ADMM (*P* = .043). Dogs with a duration of clinical signs <24 hours were 3.54 times more likely to develop ADMM than were the dogs with a duration of clinical signs >24 hours. The delay between loss of ability to walk and the neurological evaluation was not significantly associated with the development of ADMM (Table 3).

Eleven (84.6%) dogs with ADMM (4 with neurological signs graded 4 and 7 with neurological signs graded 5) had intramedullary T2W hyperintensity, with a median T2W length ratio of 7.19 (range, 2.12-9.84). Two dogs with ADMM (1 with neurological signs graded 3 and 1 with neurological signs graded 5) had no signs of intramedullary T2W hyperintensity at the time of the IVDH diagnosis. The presence of intramedullary T2W hyperintensity was strongly associated with development of ADMM (*P* < .001). The ROC curve analysis performed for T2W length ratio yielded an optimal cutoff value of 4.57 for the creation of categorical variables, corresponding to an area under the curve of 0.85 (sensitivity, 81.8%; specificity, 79.2%). When this cutoff value was used, dogs with a T2W length ratio >4.57 were 17.2 times more likely to develop ADMM as were other dogs. Comparing median T2W length ratio in dogs with and without ADMM within each clinical grade, only in dogs with neurological signs graded 5 was the median T2W length ratio of dogs with ADMM (7.45) significantly different (*P* < .001) from the median T2W length ratio of dogs without ADMM (3.57) (Table 2). The number of dogs with IVDH at the level of intervertebral disk space L5-L6, compared to other intervertebral disk spaces, was too low to be considered for the multivariate analysis. Thus, factors included in the multivariate regression model were as follows: age, clinical grade, and duration of clinical signs before becoming nonambulatory and T2 length ratio. Multivariate analysis

indicated that only a T2 length ratio >4.57 maintained a significant association ($P < .001$) with the development of ADMM, whereas age, clinical grade, and duration of clinical signs failed to reach significance in this model (Table 4).

Discussion

Our study shows that the overall prevalence of ADMM in dogs with TL-IVDH was 2.0%, ranging from 0 to 14.5% depending on clinical grading, showing a close correlation with neurological status.

The prevalence of ADMM in paraplegic dogs without DPP found in our population agrees with that of other studies, where the prevalence of ADMM ranged from 9 to 18%.[5,10,12–14,24] Ascending/descending myelomalacia as a consequence of TL-IVDH has been described almost exclusively in dogs with neurological signs graded 5.[4–6,10,12–14,16,24,25] In 1 study, 2 of the 7 dogs that finally developed ADMM presented upon admission to the hospital paraplegic with DPP. The DPP was lost within the next 2 hours.[11] Moreover, in a large population study evaluating long-term outcome in dogs with surgically treated TL-IVDH, a dog with neurological signs graded 3 developed ADMM after surgery and died. In that dog, ADMM was believed to be caused by iatrogenic damage to the spinal cord that occurred in the attempt to remove the herniated disk.[24]

In our population of myelomalacic dogs, neurological signs in 1 dog were graded 3 and those in 4 dogs were graded 4 before the anesthesia for diagnostic and surgical procedures. In all of these cases, the spinal cord was compressed by blood and soft nuclear disk material that were easy to remove with minimal manipulation of the nervous tissue. The surgical procedure was determined to be uneventful in these cases. Moreover, in 4 of 5 cases, the spinal cord had a reddish to bluish discoloration below the dura mater, and a durotomy was performed in 1 dog. All of these dogs were paraplegic without DPP 12–24 hours after surgery at the first re-evaluation. Although intraoperative iatrogenic damage of the spinal cord cannot be ruled out, we believe that ADMM was a consequence of the IVDH.

Ascending/descending myelomalacia is the final result of a cascade of detrimental secondary events, occurring from 24 hours to several days after severe spinal cord injury caused by IVDH.[5,6,11,13,14] Myelomalacic dogs with neurological signs initially graded 3 and 4 likely had been evaluated in the initial phase of the secondary injury events, when spinal function still was partially preserved. To the authors' knowledge, ours is the first study to show that ADMM can develop in dogs with neurological signs graded 3 and 4 at presentation. The potential to develop ADMM therefore must be considered even in dogs that usually have a highly positive postsurgical outcome, ranging from 86 to 98.7%.[24,26]

The second aim of this study was to investigate possible risk factors for the development of ADMM in dogs with TL-IVDH. We found that age (<5.8 years), neurological status (grade 5), site of disk herniation (L5-L6), duration of clinical signs before becoming nonambulatory (<24 hours), detection of intramedullary T2W hyperintensity, and a T2 length ratio >4.57 represented potential risk factors for the development of ADMM. In contrast, no association was found among sex, body weight, breed, or delay between loss of ability to walk and neurological evaluation and development of ADMM.

In the analysis, dogs <5.8 years of age were 5 times more likely to develop ADMM than were other dogs, but this factor was no longer significant ($P = .121$) after other variables were controlled. This result is consistent with the data reported in a previous study, where the mean age of dogs that developed ADMM was 4.5 ± 1.9 years.[6] This correlation likely is simply a consequence of the peak incidence of intervertebral disk disease for chondrodystrophic dogs (4–6 years of age).[27]

Dogs with neurological signs graded 5 at the initial evaluation were 10 times more likely to develop ADMM compared to the other dogs in the univariate analysis. This factor was no longer significant ($P = .053$) in the multivariate analysis. A significant association between the severity of neurological dysfunction and the severity of spinal cord damage was identified in 1 study, in which paraplegic dogs without DPP had the most severe spinal cord damage.[21] Presumably, concussive damage, intramedullary and subdural hemorrhage, and secondary damage leading to ADMM are more likely to develop in the severely injured spinal cord, allowing close correlation between the severity of clinical presentation, and severity of spinal cord damage and development of ADMM.

We found that dogs that had IVDH located at L5-L6 were at higher risk for developing ADMM ($P < .001$) than were dogs with IVDH in a different site. Although this result should be considered with caution because of the low number of dogs with IVDH at this level compared to other intervertebral disk spaces, a possible explanation may be related to the blood supply of the spinal cord. Normal blood supply to the thoracolumbar spinal cord comes from the spinal branches of the intercostal and lumbar arteries that give rise to small spinal segmental arteries.[28,29]

In addition, in a large percentage of dogs, there is a larger feeder artery, named the great radicular artery (*arteria radicularis magna*), that usually enters the vertebral canal at L5,[28,30,31] supplies the major part of the ventral two-thirds of the caudal half of the spinal cord and gives rise, cranially, to an important branch of the ventral spinal artery.[30] It has been hypothesized that damage of this artery during IVDH could produce a

Table 4. Results of multivariate logistic regression to identify factors significantly associated with ADMM.

Factor	OR (95% CI)	*P*-value
Age ≤5.8 year (vs >5.8 year)	3.71 (0.71–19.48)	.121
Neurological grading 5 (vs 3 and 4)	3.97 (0.98–16.09)	.053
Duration of clinical signs ≤24 hours (vs >24 hours)	3.75 (0.89–15.88)	.072
T2 length ratio >4.57 (vs ≤4.57)	15.15 (2.90–79.13)	<.001

Values of $P < .05$ were considered significant.

large area of the spinal cord ischemia and necrosis, which initiates the cascade of events leading to ADMM.[28]

In this study, dogs that became nonambulatory in <24 hours had 3.54-fold higher odds of developing ADMM than dogs that presented with a duration of clinical signs >24 hours, although this factor was no longer significant ($P = .072$) after other variables were controlled. This result is in agreement with those of previous studies describing ADMM after IVDH.[6,13,15] The rapidity of onset of paraplegia without DPP usually is connected with the severity of the injury caused by IVDH, in particular with contusive parenchymal injury.[2,7,32] These results suggest that the rapidity of becoming nonambulatory must to be considered a risk factor for the development of ADMM, even in dogs that retain some motor function and presence of DPP at the time of clinical evaluation.

The detection of intramedullary hyperintensity in T2W sagittal MRI sequences represents an important risk factor ($P < .001$) in the univariate analysis for the development of ADMM. However, intramedullary T2 hyperintensity after IVDH is a rather nonspecific MRI finding because this abnormality can reflect spinal cord edema, inflammation, hemorrhage, gliosis, and necrosis, along with myelomalacia.[22,33] More important is the result of this study showing that dogs with T2 length ratio > 4.57 were 17.2 times more likely to develop ADMM as were other dogs, and this factors also maintained its significance in the multivariate analysis ($P < .001$). Moreover, in dogs with neurological signs graded 5, the median T2 length ratio of dogs with ADMM was significantly different ($P = .001$) from the median T2 length ratio of dogs without ADMM. These results reinforce the finding in previous studies that the longitudinal extent of intramedullary T2W hyperintensity is correlated with outcome in patients with IVDH.[22,23]

Two dogs (1 with neurological signs graded 3 and 1 with neurological signs graded 5 at admission) with ADMM in this study had no signs of intramedullary T2W hyperintensity at the time of the IVDH diagnosis.[33–35] The dog with neurological signs graded 3 had a second MRI 6 days after surgery, and intramedullary T2 hyperintensity was detected in the entire spinal cord. Therefore, the absence of intramedullary T2 hyperintensity at the time of the IVDH diagnosis does not rule out the development of ADMM.

In this study, none of the dogs with intervertebral disk protrusion had signs of ADMM, because of the different pathophysiology of spinal cord damage, which is typically slowly compressive.[7] Finally, we did not find any predisposition for ADMM in chondrodystrophic breeds in comparison with nonchondrodystrophic and mixed breeds.

Our study has several limitations, mainly related to the retrospective study design. The first limitation concerns the accuracy of data collection in a study that encompasses a period of almost 9 years. A second important limitation is the evaluation of the duration of the clinical signs before becoming nonambulatory based on owner assessment and recall, which obviously may be inaccurate. However, because of its intrinsic nature, this bias cannot be completely eliminated. A third limitation is the lack of accuracy of medical records of dogs with neurological signs graded 3 and 4 that developed ADMM, regarding the exact time point of loss of DPP after surgery, because the first postsurgical re-evaluation was performed the morning after the day of surgery. Earlier and regular neurological evaluations may have helped in detecting the exact time point for loss of DPP. Finally, histopathologic confirmation of ADMM was lacking, because the owners declined pathological assessment.

In conclusion, dogs with neurological signs graded 3, 4, and 5 can develop ADMM after IVDH. The absence of intramedullary T2 hyperintensity does not rule out the possibility of the development of ADMM. Finally, dogs that presented with paraplegia without DPP with a duration of clinical signs before becoming nonambulatory <24 hours and with a T2 length ratio >4.57 were at higher risk of developing ADMM after IVDH. These results may represent important tools for clinicians. However, because of the low prevalence of ADMM, these results should be confirmed by multicenter studies involving a larger population of dogs with IVDH.

Footnotes

Acknowledgments

References

1. Marquis A, Packer RA, Borgens RB, et al. Increase in oxidative stress biomarkers in dogs with ascending–descending myelomalacia following spinal cord injury. J Neurol Sci 2015;353:63–69.

2. Fingeroth JM, de Lahunta A. Ascending/descending myelomalacia secondary to intervertebral disc herniation. In: Fingeroth JM, Thomas WB, eds. Advances in Intervertebral Disc Disease in Dogs and Cats. Ames, IA: Wiley-Blackwell; 2014:115–120.

3. Zachary JF. Pathological Basis of Veterinary Disease. St. Louis: Elsevier; 2017.

4. Griffiths IR. The extensive myelopathy of intervertebral disc protrusions in dogs ('the ascending syndrome'). J Small Anim Pract 1972;13:425–437.

5. Olby N, Levine J, Harris T, et al. Long-term functional outcome of dogs with severe injuries of the thoracolumbar spinal cord: 87 cases (1996–2001). J Am Vet Med Assoc 2003;222:762–769.

6. Okada M, Kitagawa M, Ito D, et al. Magnetic resonance imaging features and clinical signs associated with presumptive and confirmed progressive myelomalacia in dogs: 12 cases (1997–2008). J Am Vet Med Assoc 2010;237:1160–1165.

7. Jeffery ND, Levine JM, Olby NJ, et al. Intervertebral disk degeneration in dogs: Consequences, diagnosis, treatment, and future directions. J Vet Intern Med 2013;27:1318–1333.

8. Henke D, Gorgas D, Doherr MG, et al. Longitudinal extension of myelomalacia by intramedullary and subdural hemorrhage in a canine model of spinal cord injury. Spine J 2016;16:82–90.

9. Mayer D, Oevermann A, Seuberlich T, et al. Endothelin-1 Immunoreactivity and its association with intramedullary hemorrhage and myelomalacia in naturally occurring disk extrusion in dogs. J Vet Intern Med 2016;30:1099–1111.

10. Scott HW, McKee WM. Laminectomy for 34 dogs with thoracolumbar intervertebral disc disease and loss of deep pain perception. J Small Animal Practice 1999;40:417–422.

11. Lu D, Lamb CR, Targett MP. Results of myelography in seven dogs with myelomalacia. Vet Radiol Ultrasound 2002;43:326–330.

12. Muguet-Chanoit AC, Olby NJ, Lim J-H, et al. The cutaneous trunci muscle reflex: A predictor of recovery in dogs with acute thoracolumbar myelopathies caused by intervertebral disc extrusions. Vet Surg 2012;41:200–206.

13. Olby NJ, Muguet-Chanoit AC, Lim JH, et al. A placebo-controlled, prospective, randomized clinical trial of polyethylene glycol and methylprednisolone sodium succinate in dogs with intervertebral disk herniation. J Vet Intern Med 2016;30:206–214.

14. Jeffery ND, Barker AK, Hu HZ, et al. Factors associated with recovery from paraplegia in dogs with loss of pain perception in the pelvic limbs following intervertebral disk herniation. J Am Vet Med Assoc 2016;248:386–394.

15. Platt SR, McConnell JF, Bestbier M. Magnetic resonance imaging characteristics of ascending hemorrhagic myelomalacia in a dog. Vet Radiol Ultrasound 2006;47:78–82.

16. Sato Y, Shimamura S, Mashita T, et al. Serum glial fibrillary acidic protein as a diagnostic biomarker in dogs with progressive myelomalacia. J Vet Intern Med 2013;75:949–953.

17. Bergknut N, Auriemma E, Wijsman S, et al. Evaluation of intervertebral disk degeneration in chondrodystrophic and non-chondrodystrophic dogs by use of Pfirrmann grading of images obtained with low-field magnetic resonance imaging. AJRV 2011;72:893–898.

18. Kranenburg HC, Grinwis GCM, Bergknut N, et al. Intervertebral disc disease in dogs – Part 2: Comparison of clinical, magnetic resonance imaging, and histological findings in 74 surgically treated dogs. Vet J 2013;195:164–171.

19. Smolders LA, Bergknut N, Grinwis GCM, et al. Intervertebral disk degeneration in the dog. Part 2: Chondrodystrophic and non-chondrodystrophic breeds. Vet J 2013;195:292–299.

20. Penning V, Platt SR, Dennis R, et al. Association of spinal cord compression seen on magnetic resonance imaging with clinical outcome in 67 dogs with thoracolumbar intervertebral disc extrusion. J Small Animal Practice 2006;47:644–650.

21. Henke D, Vandevelde M, Doherr MG, et al. Correlations between severity of clinical signs and histopathological changes in 60 dogs with spinal cord injury associated with acute thoracolumbar intervertebral disc disease. Vet J 2013;198:70–75.

22. Ito D, Matsunaga S, Jeffery ND, et al. Prognostic value of magnetic resonance imaging in dogs with paraplegia caused by thoracolumbar intervertebral disk extrusion: 77 cases (2000–2003). J Am Vet Med Assoc 2005;227:1454–1460.

23. Levine JM, Fosgate GT, Chen AV, et al. Magnetic resonance imaging in dogs with neurologic impairment due to acute thoracic and lumbar intervertebral disk herniation. J Vet Intern Med 2009;23:1220–1226.

24. Aikawa T, Fujita H, Kanazono S, et al. Long-term neurologic outcome of hemilaminectomy and disk fenestration for treatment of dogs with thoracolumbar intervertebral disk herniation: 831 cases (2000–2007). J Am Vet Med Assoc 2012;241:1617–1626.

25. Laitinen OM, Puerto DA. Surgical decompression in dogs with thoracolumbar intervertebral disc disease and loss of deep pain perception: A retrospective study of 46 cases. Acta Vet Scand 2005;46:79–85.

26. Ferreira AJ, Correia JH, Jaggy A. Thoracolumbar disc disease in 71 paraplegic dogs: Influence of rate of onset and duration of clinical signs on treatment results. J Small Anim Pract 2002;43:158–163.

27. Priester WA. Canine intervertebral disc disease — Occurrence by age, breed, and sex among 8,117 cases. Theriogenology 1976;6:293–303.

28. de Lahunta A, Glass E, Kent M. Veterinary Neuroanatomy and Clinical Neurology. St. Louis: Elsevier; 2015:146–147.

29. Bezuidenhout A. The heart and arteries. In: Evans HE, de Lahunta A, eds. Miller's Anatomy of the Dog. St. Louis: Sanders; 2013:428–508.

30. Pais D, Casal D, Arantes M, et al. Spinal cord arteries in Canis familiaris and their variations: Implications in experimental procedures. Braz J Morphol Sci 2007;24:224–228.

31. Kato S, Kawahara N, Tomita K, et al. Effects on spinal cord blood flow and neurologic function secondary to interruption of bilateral segmental arteries which supply the artery of adamkiewicz. Spine 2008;33:1533–1541.

32. Amsellem PM, Toombs JP, Laverty PH, et al. Loss of deep pain sensation following thoracolumbar intervertebral disk herniation in dogs: Pathophysiology. Compend Contin Educ Pract Vet 2003;25:256–264.

33. Boekhoff TM, Flieshardt C, Ensinger EM, et al. Quantitative magnetic resonance imaging characteristics: Evaluation of prognostic value in the dog as a translational model for spinal cord injury. J Spinal Disord Tech 2012;25:E81–E87.

34. Shinzato J, Yoshizumi K, Sakamoto Y, et al. MRI evaluation of sequential changes of the injured spinal cord. Neuroradiology 1991;33:158–160.

35. Okada S, Saito T, Kawano O, et al. Sequential changes of ascending myelopathy after spinal cord injury on magnetic resonance imaging: A case report of neurologic deterioration from paraplegia to tetraplegia. Spine J 2014;14:e9–e14.