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Clinical and Magnetic Resonance Imaging Characteristics of Thoracolumbar Intervertebral Disk Extrusions Intervertebral Disk Protrusions in Large Breed Dogs

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Abstract

Treatment recommendations differ for dogs with intervertebral disk extrusion vs. intervertebral disk protrusion. The aim of this retrospective, cross-sectional study was to determine whether clinical and magnetic resonance imaging (MRI) variables could be used to predict a diagnosis of thoracolumbar intervertebral disk extrusion or protrusion in dogs. Dogs were included if they were large breed dogs, had an MRI study of the thoracolumbar or lumbar vertebral column, had undergone spinal surgery, and had the type of intervertebral disk herniation (intervertebral disk extrusion or protrusion) clearly stated in surgical reports. A veterinary neurologist unaware of surgical findings reviewed MRI studies and recorded number, location, degree of degeneration and morphology of intervertebral disks, presence of nuclear clefts, disk space narrowing, extent, localization and lateralization of herniated disk material, degree of spinal cord compression, intraparenchymal intensity changes, spondylosis deformans, spinal cord swelling, spinal cord atrophy, vertebral endplate changes, and presence of extradural hemorrhage. Ninety-five dogs were included in the sample. Multivariable statistical models indicated that longer duration of clinical signs ($P = 0.01$), midline instead of lateralized disk herniation ($P = 0.007$), and partial instead of complete disk degeneration ($P = 0.01$) were associated with a diagnosis of intervertebral disk protrusion. The presence of a single intervertebral herniation ($P = 0.023$) and dispersed intervertebral disk material not confined to the disk space ($P = 0.06$) made a diagnosis of intervertebral disk extrusion more likely. Findings from this study identified one clinical and four MRI variables that could potentially facilitate differentiating intervertebral disk extrusions from protrusions in dogs.

Introduction

Intervertebral disk herniation is a well-recognized and common spinal cord disorder in dogs.[1-4] Two types of degenerative intervertebral disk herniation have traditionally been recognized: intervertebral disk extrusion or Hansen Type-I, and intervertebral disk protrusion or Hansen Type-II disk herniation.[3] Intervertebral disk extrusion is characterized by sudden herniation of degenerated and calcified nucleus pulposus through a fully ruptured anulus fibrosus, [3,5,6] while intervertebral disk protrusion is characterized by a focal and more gradual extension of the anulus fibrosus and dorsal longitudinal ligament into the vertebral canal. Although recent studies have demonstrated similar pathological abnormalities,[8] intervertebral disk extrusions and protrusions are associated with different clinical characteristics.[6] Intervertebral disk extrusions occur typically in chondrodystrophic dogs, can occur at a young age and is typically associated with an acute onset of neurological signs.[4,6,9] Intervertebral disk protrusions occur typically in non-chondrodystrophic dogs, affected dogs are generally older and can present with a more protracted and insidious clinical history.[4,6,9] Although extrusions typically affect chondrodystrophic and protrusions typically non-chondrodystrophic dogs, [2-4,6,10] large breed dogs can suffer from both types of intervertebral disk herniation. [4,11] Apart from the above mentioned differences in pathophysiology and clinical presentation, intervertebral disk extrusions and protrusions are also associated with different suggested treatment options [4,10,12-14], and possibly also a different prognosis.[4] Intervertebral disk extrusions are typically treated by a hemilaminectomy.[5] Several studies have however suggested this type of surgery would be inadequate for intervertebral disk protrusions and have suggested alternative surgical approaches, including additional vertebral stabilization[10] or a lateral corpectomy.[12,13] While a hemilaminectomy is considered a basic spinal surgical technique, a corpectomy should be considered more technically demanding. Treatment of intervertebral disk protrusions is further complicated by the fact that little is known about the results of medical management and that dogs with protrusions are at increased risk of early postoperative neurological deterioration compared to dogs with extrusions.[4] It seems therefore important to accurately differentiate thoracolumbar intervertebral disk extrusions from protrusions before treatment options and associated outcomes are discussed with owners of affected dogs. Currently, the exact type of intervertebral disk herniation can only be recognized during surgery. If we want to improve our knowledge on the natural evolution and results of medical management, we should improve our knowledge on how to differentiate different types of intervertebral disk herniation without surgical confirmation. Although intervertebral disk herniation can be diagnosed by a variety of imaging modalities, magnetic resonance imaging (MRI) is considered the imaging modality of choice.[15] Several studies have reported MRI findings in dogs with thoracolumbar intervertebral disk herniations,[16-20] establishing further insights into the pathophysiology, diagnosis and treatment of this disorder. Little is however known about specific clinical or MRI abnormalities that can be used to differentiate between thoracolumbar intervertebral disk extrusions and protrusions. The aim of this retrospective, cross sectional study was therefore to evaluate the use of clinical and previously reported MRI characteristics to differentiate between these two specific types of intervertebral disk herniation. It was hypothesized that specific clinical and MRI variables exist that could independently predict the occurrence of intervertebral disk extrusion or protrusion.

Materials and Methods

Criteria for Animal Selection

The digital medical database of the Royal Veterinary College was searched between July 2002 and January 2014 for large breed dogs undergoing MRI and decompressive surgery for thoracolumbar or lumbar intervertebral disk herniation. Search terms were “intervertebral disk extrusion”, “intervertebral disk protrusion”, “intervertebral disk herniation”, “intervertebral disk prolapse”, “intervertebral disk disease” and “MRI”. Dogs were included if (1) they were large breed dogs, defined as a body weight exceeding 20kg [4], (2) underwent an MRI study of the thoracolumbar or lumbar vertebral column, (3) following a diagnosis of intervertebral disk herniation underwent spinal surgery consisting of a hemilaminectomy or hemilaminectomy combined with a partial discectomy and (4) the type of intervertebral disk herniation (intervertebral disk extrusion or protrusion) was clearly noted in the surgical reports. Dogs were excluded if the medical records or imaging studies were incomplete, if they were not available in a digital format, if the type of intervertebral disk herniation (extrusion or protrusion) was not clearly noted in the surgical reports, if more than one type of intervertebral disk herniation (both intervertebral disk extrusion and protrusion), or acute herniations of flaps of anulus were observed during surgery. For inclusion in the study, the surgical treatment had to have consisted of a decompressive hemilaminectomy, a hemilaminectomy combined with an anulectomy, or a hemilaminectomy combined with a partial discectomy. During the latter procedure, a hemilaminectomy had to have been initially performed to allow inspection of the vertebral canal. This had to have been followed by a lateral approach to the affected intervertebral disk, after which the dorsal part of the disk and a portion of the adjacent vertebral endplates were removed by a pneumatic drill or surgical aspirator. For inclusion, all dogs had to have undergone MRI under general anesthesia (1.5T, Intera, Philips Medical Systems, Eindhoven, the Netherlands). If dogs had MRI on multiple occasions for confirmed intervertebral disk herniation, only information from the first visit was used.

Data Recorded

Information retrieved from the medical records included signalment, duration, type, and severity of clinical signs, general physical and neurological examinations findings, and type of surgery. Severity of neurological deficits was graded by the modified Frankel score [21], which was defined as paraplegia with no deep nociception (grade 0), paraplegia with no superficial nociception (grade 1), paraplegia with nociception (grade 2), non-ambulatory paraparesis (grade 3), ambulatory paraparesis and ataxia (grade 4), spinal hyperesthesia only (grade 5), or no dysfunction.

Magnetic resonance imaging studies were anonymized and presented in a randomized order to a board-certified veterinary neurologist (S.D.D.). The observer was only informed on the location of the surgically confirmed intervertebral disk herniation and only T1 –and T2-weighted sequences were presented and assessed. Standard image archiving and communication system software (Osirix Foundation, V.5.5.2 Geneva, Switzerland) was used to view and assess the imaging studies. The selection of MRI variables was based on earlier reported veterinary studies [5,16,22-33] and covered several aspects of intervertebral disk disease (Table 1). Assessed variables included number, degree of degeneration and morphology of affected intervertebral disks, presence of nuclear clefts, narrowing of the intervertebral disk space, extent, localization and lateralization of herniated disk material, degree of spinal cord compression, occurrence and type of intraparenchymal intensity changes, occurrence of spondylosis deformans ventral to the affected intervertebral disk space, spinal cord swelling, spinal cord atrophy, occurrence and type of vertebral endplate changes, and presence of extradural hemorrhage. Since intervertebral disk degeneration is associated with a decrease in nucleus pulposus signal intensity on T2-weighted images [23], assessment of intervertebral disk degeneration was based on nucleus pulposus signal intensity on midsagittal T2-weighted images. A non-degenerate disk (grade 0) had a homogenous hyperintense signal, a partially degenerate disk (grade 1) had heterogeneous loss of hyperintense signal, and a completely degenerate intervertebral disk (grade 2) had complete loss of hyperintense signal.[26] Intervertebral disk morphology was described as bulging, protrusion or extrusion (Figure 1).[16] Bulging was defined as a symmetric, uniform and circumferential extension of the disk margin over the border of the vertebral endplate; protrusion was defined as a focal midline or dorsolateral extension of the disk margin with focal rupture of the anulus fibrosus; extrusion was defined as presence of herniated disk material through all layers of the anulus fibrosus.[16] Intervertebral disk morphology was further determined by the ability or inability to observe the well-defined contour of the anulus fibrosus on transverse T1-weighted images [25] and the ability or inability to identify the distinction between the anulus fibrosus and nucleus pulposus on midsagittal T2-weighted images.[30] Narrowing of the intervertebral disk space was assessed subjectively by visually comparing the affected intervertebral disk space maximum width with the adjacent, cranial and caudal, non-affected intervertebral disk spaces.[31] Nuclear clefts were defined as a focal area of signal loss in the nucleus pulposus on T2-weighted images.[25] Localization of herniated disk material was assessed on T1 -and T2-weighted transverse images, being defined as ventral, lateral, or dorsal relative to the spinal cord. Lateralization of herniated material was further described as being exclusively in the midline or lateralized. Extension of herniated disk material was assessed on T2-weighted sagittal images and characterized as dispersed or confined to the intervertebral disk space. Dispersed disk material was defined as herniated disk material with no clear association with its original intervertebral disk space.[5,16] Disk material confined to the intervertebral disk space was defined as herniated disk material, which did not exceed the limits of the disk space or associated vertebral endplates.[12,29] Presence of spinal cord swelling and spinal cord atrophy were subjectively evaluated on T2-weighted sagittal and transverse images at the spinal segments immediately adjacent to the site of spinal cord compression. Spinal cord swelling was defined as a subjectively decreased area of cerebrospinal fluid and fat relative to a decreased area of spinal cord, while the presence of spinal cord atrophy was defined as an subjectively increased area of cerebrospinal fluid and epidural fat relative to a decreased spinal cord area.[24] Degree of spinal cord compression was determined by calculating the remaining spinal cord area and compression ratio at the site of maximum spinal cord compression. The remaining spinal cord area was defined as the cross sectional area of the spinal cord of the compressed area divided by the cross sectional area at the adjacent, non-compressed segment.[22,33] The compression ratio was determined by dividing the smallest dorsoventral diameter of the spinal cord by the broadest transverse diameter at the same level.[22,33] Intraparenchymal signal intensity changes were assessed on sagittal images and classified as; absent intraparenchymal signal intensity changes on T2 or T1-weighted images (grade 0); light (obscure) hyperintense intraparenchymal signal intensity change on T2-weighted images (grade 1); intense (bright) hyperintense intraparenchymal signal intensity change on T2-weighted images (grade 2); hyperintense intraparenchymal signal intensity change on T2-weighted images, which corresponded to a hypointense intraparenchymal signal intensity change on T1-weighted images (grade 3).[32] Vertebral endplate changes were classified as: no changes (grade 0); hypointense areas on T1-weighted images and hyperintense areas on T2-weighted images (grade 1); hyperintense areas on T1-weighted images and areas of isointense or slightly hyperintense signal intensity on T2-weighted images (grade 2), hypointense signal on both T1 -and T2-weighted images (grade 3).[16] Presence of extradural hemorrhage was defined as a poorly demarcated, extradural area of heterogeneous intensity on T2-weighted images.[28]

Statistical Analyses

Statistical analysis was performed by one of the authors (RMAP) and data were analyzed using statistical software (IBM SPSS Statistics version 19, New York). The binomial outcome variable was diagnosis of intervertebral disk extrusion or protrusion. Associations between the 32 predictor variables (clinical and MRI characteristics) and the outcome variables were screened at the univariable level using Chi-squared analysis for categorical predictors, and the Student's *t*-test or Mann-Whitney *U* test for continuous variables, dependent upon the normality of the distribution of the data, which was determined via visual inspection of histograms. *P* values <0.05 were considered significant in all analyses. Variables significantly associated with diagnosis at the univariable level ($P < 0.05$) were taken forward to be tested in a multivariable model; a binomial logistic regression with diagnosis as the binomial outcome variable, using intervertebral disc extrusion as the reference category. Odds ratios of significant variables were inspected to determine which type of disc disease was more likely based on the predictor variables. Multicollinearity was checked for in all models, identified from inflated standard errors in the models and thus avoided. Model fit was assessed using the Akaike's information criterion (AIC) and percentage correct classification, with lower AIC models favored to reduce residual error in the model while avoiding overfitting. In addition to these analyses, a post hoc receiver operating characteristic (ROC) analysis was used to examine the performance of the significant continuous variable, duration of clinical signs, as an indicator of diagnosis by determining the diagnostic power of the test by measuring the area under the curve (AUC). The reference standard was surgically confirmed diagnosis of intervertebral disk extrusion or protrusion. A perfect test has an AUC value of 1.0, with an AUC of 0.5 means the test performs no better than chance. Youden's index (Youden's J statistic; J = Sensitivity + specificity - 1) was calculated to identify the optimal cut-off value of duration of clinical signs that yielded maximum sums from the ROC curves.

Results

Included animals

A total of 105 large breed dogs underwent MRI and spinal surgery for thoracolumbar intervertebral disk herniation. Ten cases were excluded, as the nature of herniated disk material was not clearly noted in the surgical reports. Ninety-five dogs with intervertebral disk extrusion (n=52) or protrusion (n=43) were therefore included in this study. Magnetic resonance imaging was performed with dogs in dorsal recumbency and by using a dedicated spinal coil. Imaging studies included a minimum of T2-weighted (repetition time (ms) (TR)/ echo time (ms) (TE); 3000/120) and T1-weighted (TR/TE, 400/8) sagittal and transverse images. Slice thickness for sagittal and transverse images were respectively 1.75 and 2.5mm with an interslice gap of 0.3mm in both planes. The transverse images were aligned parallel to the respective intervertebral disks. The surgical appearance of intervertebral disk extrusions was typically characterized as sequestered calcified intervertebral disk material without physical connection with the ruptured anulus fibrosus. The surgical appearance of intervertebral disk protrusion was typically characterized by a focal or broad based dorsal displacement of the intervertebral disk without any defect in the outer layers of the anulus fibrosus.

Breed distribution of 52 dogs with intervertebral disk extrusion was German Shepherd Dog (n=12), Cross breed (seven), Labrador Retriever (six), Basset Hound, English Staffordshire Bull Terrier (both five), Clumber Spaniel, Rottweiler (both four), Rough Collie, Doberman Pinscher, English Pointer, Golden Retriever, Lurcher, English Bull Terrier, Portuguese Waterdog, English Springer Spaniel and Weimaraner (one for each). This group included 27 males and 25 females aged between 1 and 12 years (mean, 6.7 years). Median duration of clinical signs, before referral, was 2 days (25^{th}-75^{th} percentile, 1 - 9.25 days). Dogs presented with neurological grades 0 (n=four dogs), 1 (one), 2 (13), 3 (15), and 4 (19). Affected intervertebral disk spaces in order of occurrence were T13-L1, L1-L2 (both n=11), T12-T13 (nine), L3-L4 (seven), L2-L3 (six), T11-T12, L4-L5 (both three), T3-T4 and T10-L1 (both one). All dogs underwent a decompressive hemilaminectomy.

Breed distribution of 43 dogs with intervertebral disk protrusion was German Shepherd Dog (n = 21), English Staffordshire Bull Terrier (eight), Cross Breed (four), Basset Hound (three), Labrador Retriever (two), Bullmastiff, Dalmatian, English Pointer, Golden Retriever and Rottweiler (one for each). This group included 34 males and nine females aged between 4 and 12.2 years (mean, 8.7 years). The median duration of clinical signs, before referral, was 42 days (25^{th}-75^{th} percentile, 4 - 150 days). Dogs presented with neurological grades 2 (n=one dog), 3 (seven), and 4 (35).

Affected intervertebral disk spaces in order of occurrence were T13-L1 (n=17), T12-T13 (10), L1-L2 (nine), L2-L3 (five), T9-T10 and T11-T12 (both one). All dogs underwent a hemilaminectomy with anulectomy (n=22) or a hemilaminectomy with partial discectomy (21).

Clinical variables associated with intervertebral extrusion or protrusion

Univariable statistical analysis (Table 1) revealed that older age, longer duration of clinical signs, male gender, and a higher neurological grade (less severely affected) were significantly associated with a diagnosis of intervertebral disk protrusion ($P < 0.05$). After performing binomial logistic regression (Table 2), longer duration of clinical signs was the only clinical variable significantly associated with a diagnosis of intervertebral disk protrusion (median duration of clinical signs was two days and 42 days for dogs with intervertebral disk extrusion and protrusion, respectively). With each increasing day that clinical signs were present, there was a significantly increased likelihood of the diagnosis being intervertebral disk protrusion rather than extrusion ($P = 0.011$). ROC-analysis (Figure 1) revealed that duration of clinical signs of 21 days was associated with the highest combined sensitivity (70%) and specificity (87%) to differentiate between both types of intervertebral disk herniation. The area under the curve was 0.79 (95% CI: 0.69-0.88).

MRI-variables associated with intervertebral disk extrusion or protrusion

Univariable statistical analysis (Table 1) revealed that extrusion-morphology, narrowing of the intervertebral disk space, complete intervertebral disk degeneration, presence of nuclear clefts, lateralized disk material, dorsal location of herniated disk material, subjective spinal cord swelling, and presence of epidural hemorrhage, were associated with a diagnosis of intervertebral disk extrusion (*P* < 0.05). Protrusion-morphology, partial disk degeneration, herniated disk material confined to the intervertebral disk space, ventral location of herniated disk material, spinal cord atrophy, lower compression ratio values (indicating more pronounced dorsoventral spinal cord flattening), presence and type of intraparenchymal signal intensity changes, presence and type of endplate changes, presence of multiple intervertebral disk herniations, and presence of spondylosis deformans were significantly associated with a diagnosis of intervertebral disk protrusion. After performing binomial logistic regression, four MRI variables were retained as independent predictors of intervertebral disk protrusion or extrusion (Table 2). Midline instead of lateralized intervertebral disk herniation (Figure 2), and partial instead of complete intervertebral disk degeneration (Figure 3) were significantly associated with a diagnosis of intervertebral disk protrusion. The presence of a single instead of multiple intervertebral disk herniations (Figure 4) and dispersed intervertebral disk material not confined to the disk space (Figure 5) made a diagnosis of intervertebral disk extrusion more likely. Although the latter variable did not reach statistical significance (*P* = 0.06), inclusion of this variable improved model fit (determined by AIC values and percentage correct classification) and it was thus retained in the final model.

Discussion

This study evaluated the application of clinical and previously described MRI characteristics [5,16,22-33] in an attempt to identify specific variables that could be used to differentiate thoracolumbar intervertebral disk extrusions from protrusions. One clinical and four MRI variables were identified as independent predictors for the exact type of intervertebral disk herniation (Table 2). Duration of clinical signs, lateralization of herniated disk material, degree of intervertebral disk degeneration, number of intervertebral disk herniations, and localization of herniated disk material relative to the affected intervertebral disk space were considered the most predictive independent variables to diagnose thoracolumbar intervertebral disk extrusion or protrusion. Differentiating between both types of thoracolumbar intervertebral disk herniation is of clinical importance. Both types of disk herniation can be considered distinct clinical entities and are associated with a different pathophysiology, available treatment options [4,10,12-14], postoperative recovery, and prognosis after medical and surgical treatment.[4] Making informed clinical decisions is however only possible when an accurate diagnosis can be reached.

Longer duration of clinical signs was considered the only clinical variable able to assist in differentiating extrusions from protrusions. This is in agreement with previously reported studies [4,10] and most likely reflects the pathophysiological differences between both types of intervertebral disk herniation. Where intervertebral disk extrusion is characterized by a sudden extrusion of calcified and fragmented nucleus pulposus into the vertebral canal, intervertebral disk protrusion is characterized by a more gradual hypertrophy and hyperplasia of the anulus fibrosus.[3,6,9] Although dogs with both intervertebral disk extrusion and protrusion presented with a large variation in duration of their clinical signs, our results indicate that duration of clinical signs of 21 days could be considered a potential guideline to differentiate between dogs with both types of intervertebral disk herniation.

Midline intervertebral disk herniation was associated with a diagnosis of disk protrusion, while lateralized intervertebral disk herniation was associated with a diagnosis of intervertebral disk extrusion (Figure 2). Intervertebral disk protrusion is characterized by protrusion of the dorsal anulus and the intact dorsal longitudinal ligament into the vertebral canal.[6] Lateral displacement of herniated material is therefore likely limited by the anatomical boundaries of the dorsal longitudinal ligament, which then possibly facilitates midline protrusion. Intervertebral disk extrusion is however often characterized by extrusion of nuclear material through all layers of the anulus fibrosus and through or lateral to the dorsal longitudinal ligament.[6] The dorsal longitudinal ligament therefore does not directly limit lateral displacement of herniated material, which can move more freely into the vertebral canal.

Partial intervertebral disk degeneration, represented by the preservation of some hyperintensity in the nucleus pulposus on T2-weighted images, was associated with a diagnosis of intervertebral disk protrusion, while complete disk degeneration, represented by complete loss of hyperintense signal was associated with a diagnosis of intervertebral disk extrusion. This is consistent with published studies indicating that uniformly hyperintense signal on T2-weighted images of a non-degenerated intervertebral disk is caused by the high water content of the healthy nucleus pulposus.[25,30,31] The hallmark of Hansen Type I disk degeneration, which precedes intervertebral disk extrusion, is the transition from a gelatinous, semi-fluid nucleus pulposus into a drier and more rigid structure.[3,6,9] This is caused by a decrease of water-binding proteoglycans, including chondroitin sulfate, and an increase in collagen content. [6,34,35] While the primary target of degeneration is the nucleus pulposus in dogs with intervertebral disk extrusion, this is not necessarily true in dogs with intervertebral disk protrusion. Mineralization of the nucleus pulposus is not always seen in dogs with disk protrusions and degenerative changes of the anulus can occur earlier, before pathological changes are seen in the nucleus pulposus.[3,6,9,35,36] This could explain why dogs with intervertebral disk protrusion can still demonstrate hydration of the nucleus pulposus with preservation of hyperintensity on T2-weighted images. In agreement with previous studies, presence of a single intervertebral disk herniation was associated with disk extrusions, while the presence of multiple compressive lesions was associated with a diagnosis of intervertebral disk protrusion.[4] Although this finding is difficult to explain, it is possibly related to the different pathological mechanisms underlying these two types of intervertebral disk disease. Sudden extrusion of disk material in intervertebral disk extrusion results most often in both contusion and compression of the spinal cord.[37] It is therefore less likely that disk extrusions will occur without noticeable clinical signs. In contrast, intervertebral disk protrusion is typically associated with gradual spinal cord compression without contusion.[38] Disk-associated spinal cord compression has been demonstrated in clinically normal dogs [26,39] and a remarkable degree of progressive spinal cord compression can occur before clinical signs eventually develop.[33] It is therefore possible that multiple spinal cord compressions of variable severity can co-exist before clinical signs appear. It is also possible that intervertebral disk protrusion is an intrinsically more multifocal disease process, facilitating concurrent intervertebral disk herniations. Additionally, dogs with intervertebral disk protrusions were significantly older than dogs with intervertebral disk extrusions. Intervertebral disk degeneration and herniation has been suggested to represent a physiological age related process.[39] This could also have contributed to the higher number of disk herniations in dogs with intervertebral disk protrusions. Occurrence of multiple lumbar disk protrusions poses difficulties in selecting the most appropriate treatment modality. While specific surgical techniques, including stabilization, have been suggested [10,13], the presence of multiple disk protrusions has also been associated with a reluctance to perform surgery.[4]

In agreement with previous findings [4] dispersion of herniated disk material beyond the borders of the affected disk space was associated with a diagnosis of intervertebral disk extrusion, while confinement to the borders of the intervertebral disk space was associated with a diagnosis of intervertebral disk protrusion (Figure 5). This finding can most likely be explained by the fact that the dorsally displaced nucleus pulposus remains contained within the outer layers of the anulus fibrosus in dogs with disk protrusions [3,6,9], while calcified nucleus pulpous ruptures through all layers of the anulus in dogs with intervertebral disk extrusion and can therefore be more easily displaced beyond the boundaries of the affected intervertebral disk space.[5]

This study is limited by its retrospective nature, which complicated standardized patient assessment and correlation of MRI and surgical findings. Although the selection of MRI variables was based on previously published veterinary and human neuroradiology studies, it is possible that some of the variables were not necessarily associated with a perfect diagnostic accuracy for the intended purpose. For example, assessment of epidural haemorrhage was based on the presence of a poorly demarcated, extradural area of heterogeneous intensity on sagittal T2-weighted images [28], which could be considered an unspecific imaging finding. Although it is possible that inclusion of gradient echo sequences would have improved diagnostic accuracy, results of a recent study suggest that identification of a susceptibility artifact on gradient echo spinal MRI studies is also not specific for epidural hemorrhage in dogs with intervertebral disk extrusions.[40] It should further be emphasized that this study did not evaluate the diagnostic accuracy or reliability of the blinded observer and that interpretation of most evaluated MRI variables were likely associated with inherent subjectivity. Previous studies have questioned the reliability of some of the evaluated MRI variables, including subjective evaluation of intervertebral disk width.[41,42] Subjective evaluation of intervertebral disk width using MRI has been associated with considerable disagreement between and within observers [41,42], while objective measurements have been associated with good inter –and intraobserver agreement.[43] Absolute measurements were however not included in this study due to concerns about heterogeneity of included breeds and dog sizes. Although this study has identified one clinical and several MRI-variables that are independently associated with a diagnosis of intervertebral disk extrusion or protrusion, it is currently unclear if application of these variables into a clinical setting will result in an improved differentiating of both clinical entities. Furthermore, it is currently unclear how well or poor intervertebral disk extrusion and protrusion can be differentiated without assistance of these variables. Further studies are therefore needed to determine the necessity, accuracy and reliability of the identified variables as diagnostic guidelines to differentiate both types of intervertebral disk herniation.

In summary, this study identified potential clinical and MRI-variables to improve differentiation of thoracolumbar intervertebral disk extrusions from protrusions. More specifically, duration of clinical signs, lateralization of herniated disk material, degree of intervertebral disk degeneration, presence of multiple intervertebral disk herniations, and confinement of herniated disk material to the affected intervertebral disk space were identified as independent variables to predict a diagnosis of intervertebral disk extrusion or intervertebral disk protrusion. Further studies are necessary to evaluate the use of these variables to improve reaching a correct diagnosis of thoracolumbar intervertebral disk extrusion or protrusion.

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Figure Legends

Table 1. IVDH, intervertebral disk herniation: IVDS, intervertebral disk space; ISI, intraparenchymal intensity; SE, standard error; %, percentile; non-significant values indicated by *P*-value >0.05

Table 2. IVD, intervertebral disk; IVDH, intervertebral disk herniation; IVDP, intervertebral disk protrusion; IVDE, intervertebral disk extrusion, OR, odds ratio; CI, confidence interval; significant variables ($P < 0.05$) marked by asterisk (*). Although 'IVDH not confined to IVDS' did not reach statistical significance, inclusion of this variable improved model fit.

Figure 1. Receiver operating characteristic curve for duration of clinical signs in 52 dogs with thoracolumbar intervertebral disk extrusion and 43 dogs with intervertebral disk protrusion. A duration of clinical signs of 21 days (asterisk) corresponded with the highest combined sensitivity and specificity to differentiate between both types of intervertebral disk herniation.

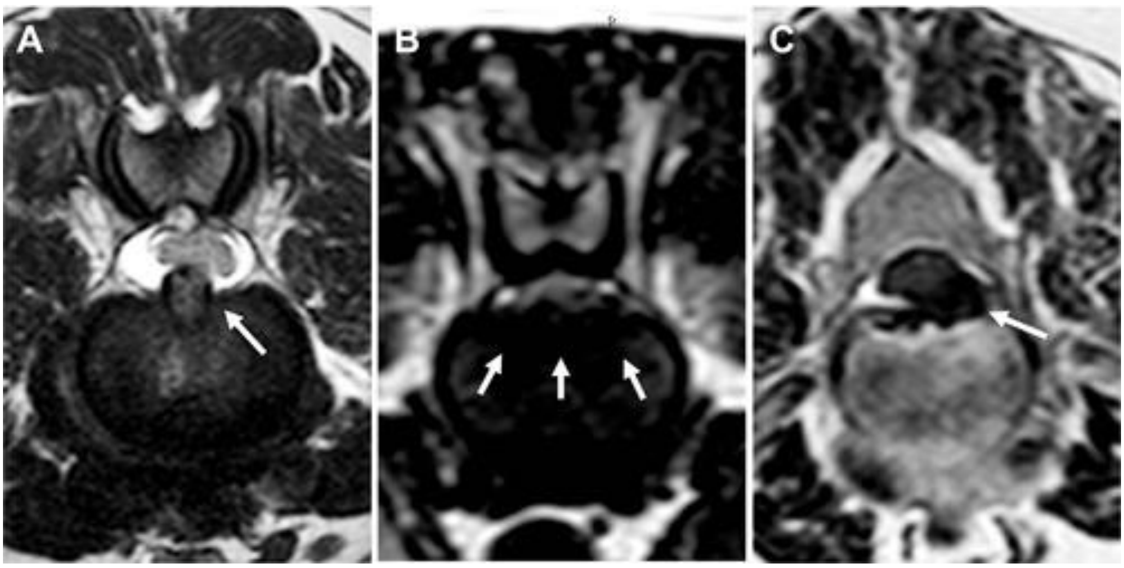

Figure 2. T2W transverse images of dogs with a surgically confirmed thoracolumbar intervertebral disk protrusion (A and B) and a dog with surgically confirmed intervertebral disk extrusion (C). (A and B) Midline intervertebral disk herniation (arrows) was predictive for a diagnosis of disk protrusion, while lateralized intervertebral disk herniation (arrow) was predictive for intervertebral disk extrusion (B). Presented intervertebral disk herniations represent protrusion (A), bulging (B), and extrusion (C) morphology

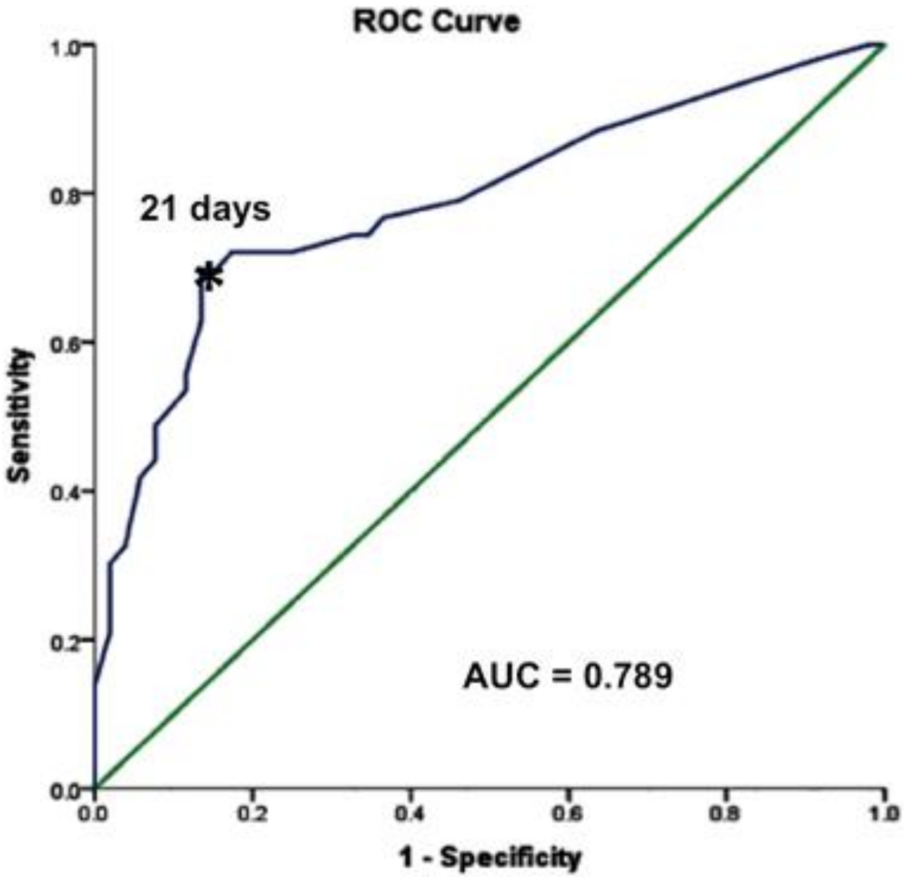

Figure 3. T2W sagittal images of a clinically normal dog (A), a dog with surgically confirmed thoracolumbar intervertebral disk protrusion (B), and a dog with a surgically confirmed intervertebral disk extrusion (C). Partial loss of nucleus pulposus signal intensity (B) was associated with disk protrusion, while complete loss of hyperintense signal (C) was associated with disk extrusion. Non-degenerated disk with homogenous hyperintense nucleus pulposus for comparison (A).

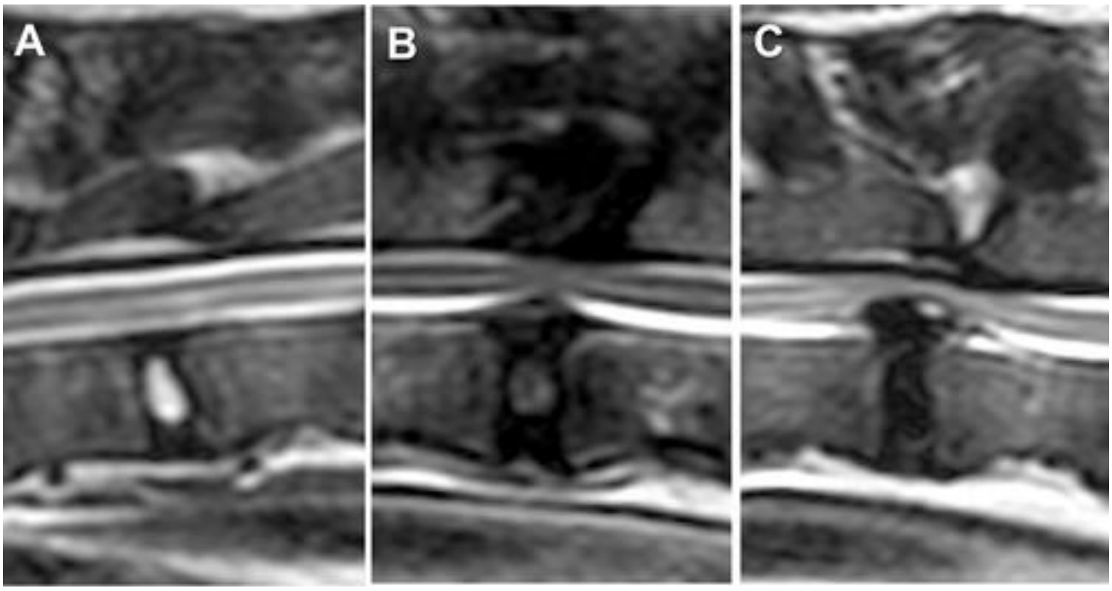

Figure 4. T2W sagittal images of a dog with surgically confirmed thoracolumbar intervertebral disk protrusions (A), and a dog with intervertebral disk extrusion (B). (A) Presence of multiple intervertebral disk herniations was predictive for a diagnosis of disk protrusion (arrows), while presence of a single intervertebral disk herniation (arrow) was predictive for disk extrusion (B).

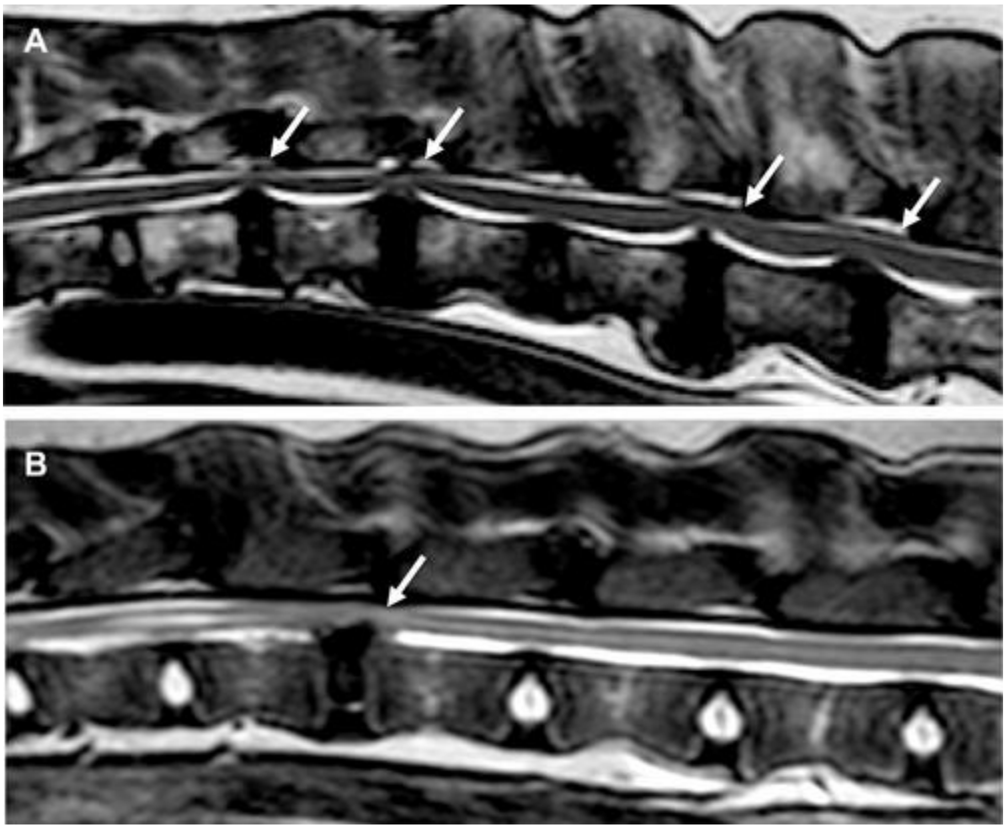

Figure 5. T2W sagittal images of a dog with two surgically confirmed thoracolumbar intervertebral disk protrusions (A), and a dog with a surgically confirmed intervertebral disk extrusion (B). Presence of herniated disk material confined to the intervertebral disk space (arrows) was predictive for protrusion (A), while herniated disk material exceeding the limits of the intervertebral disk space (arrows) was predictive for extrusion (B). Both intervertebral disk protrusions (A) demonstrate partial intervertebral disk degeneration, while the intervertebral disk extrusion (B) demonstrates complete intervertebral disk degeneration.

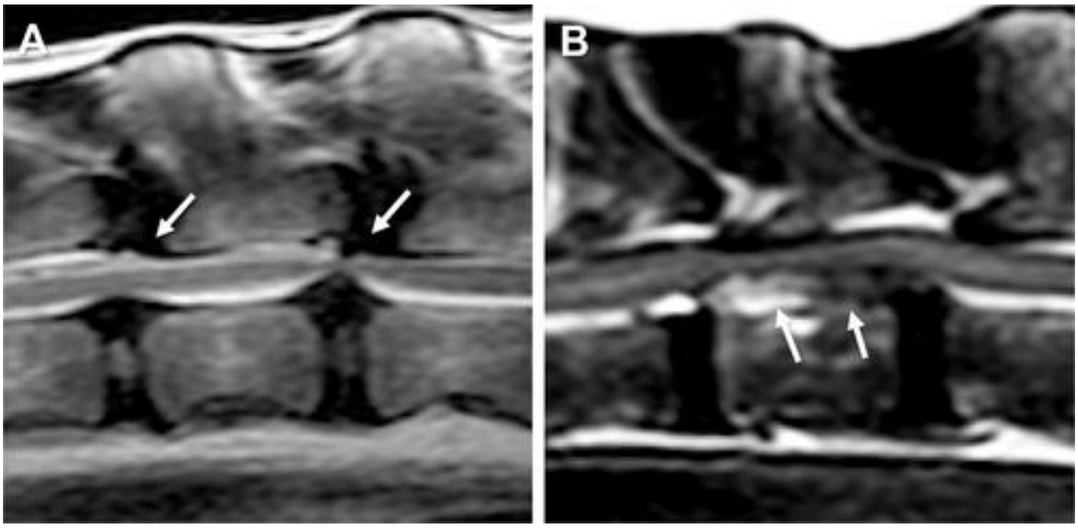

Table 1. Results of univariate statistical analysis for clinical and MRI variables for 52 dogs with intervertebral disk extrusion and 43 dogs with intervertebral disk protrusion

Variable	**Intervertebral disk extrusion (n=52)**	**intervertebral disk protrusion (n=43)**	***P*-Value**
Male	27 (51.9%)	34 (79.1%)	0.006
Neutered	24 (46.2%)	19 (44.2%)	>0.05
Age (mean, SE)	6.7 years (0.34)	8.7 (0.34)	< 0.001
Duration signs (median, 25^{th}-75^{th} percentile)	2 days (1.0 – 9.25)	42 days (4.0-150)	< 0.001
Neurological grade			<0.001
Grade 1	4 (7.7%)	0 (0%)	
Grade 2	13 (25.0%)	1 (2.3%)	
Grade 3	15 (28.8%)	7 (16.3%)	
Grade 4	19 (36.5%)	35 (81.4%)	
IVDH confined to IVDS	17 (32.7%)	42 (97.7%)	<0.001
IVDH lateralized	43 (82.7%)	8 (18.6%)	<0.001
Dorsal disk material	17 (32.7%)	1 (2.3%)	<0.001
Ventral disk material	37 (71.2%)	43 (100%)	<0.001
Lateral disk material	33 (63.5%)	0 (0%)	<0.001
Bulging morphology	3 (5.8%)	13 (30.2%)	0.002
Protrusion morphology	4 (7.7%)	24 (55.8%)	<0.001
Extrusion morphology	43 (82.7%)	6 (14%)	<0.001
Nuclear cleft present	34 (65.4%)	16 (37.2%)	0.006
Distinct contour anulus fibrosus	10 (19.2%)	12 (27.9%)	>0.05
Distinction anulus and nucleus	6 (11.5%)	9 (20.9%)	>0.05
IVD degeneration			0.048
Grade 0	5 (9.6%)	2 (4.7%)	
Grade 1	20 (38.5%)	27 (62.8%)	
Grade 2	27 (51.9%)	14 (32.6%)	
Multiple IVDH present	9 (17.3%)	33 (76.7%)	<0.001
Narrowed IVDS	42 (80.8%)	15 (34.9%)	<0.001
ISI change present	27 (51.9%)	32 (74.4%)	0.045
ISI changes			0.036
Type 0	25 (48.1%)	11 (25.6%)	
Type 1	24 (46.2%)	22 (51.2%)	
Type 2	2 (3.8%)	7 (16.3%)	
Type 3	1 (1.9%)	3 (7.0%)	
Extradural hemorrhage	35 (67.3%)	1 (2.3%)	<0.001
Spondylosis deformans	9 (17.3%)	21 (48.8%)	0.001
Endplate changes present	12 (23.1%)	22 (51.2%)	0.016
Endplate changes			0.025
Type 0	40 (76.9%)	21 (48.8%)	
Type 1	2 (3.8%)	5 (11.6%)	
Type 2	5 (9.6%)	12 (27.9%)	
Type 3	5 (9.6%)	5 (11.6%)	
Spinal cord swelling	37 (71.2%)	2 (4.6%)	<0.001
Spinal cord atrophy	2 (3.8%)	14 (32.7%)	<0.001
Remaining spinal cord area (mean, SE)	0.62 (0.02)	0.66 (0.03)	>0.05
Compression ratio (mean, SE)	0.50 (0.03)	0.39 (0.02)	0.004

Table 2. Results of multivariate statistical analysis for clinical and MRI variables for 52 dogs with intervertebral disk extrusion and 43 dogs with intervertebral disk protrusion

Risk Factor	**Type of IVDH**	**OR**	**95% CI**	***P*-value**
Longer duration of clinical signs	IVDP more likely	1.02	1.01-1.04	0.01*
Partial instead of complete IVD degeneration	IVDP more likely	16.58	1.95-141.3	0.01*
IVDH NOT lateralized	IVDP more likely	14.19	2.1 – 97.6	0.007*
Multiple IVDHs NOT present	IVDE more likely	0.17	0.04 – 0.78	0.023*
IVDH not confined to IVDS	IVDE more likely	0.09	0.01 – 1.08	0.06