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Preliminary study of presumptive intradural-intramedullary intervertebral disc extrusion in 20 dogs

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Conflict of Interest

The authors declare no conflicts of interest.

ABSTRACT

Background: Intradural-intramedullary intervertebral disc extrusion (IIVDE) is a rare condition of intervertebral disc disease. However, the diagnosis of IIVDE is challenging because the prognosis and imaging characteristics are poorly characterized.

Objectives: We aimed to describe the clinical and imaging characteristics of tentatively diagnosed IIVDE in dogs to assess the prognostic utility of neurological grade and magnetic resonance imaging (MRI) findings.

Methods: Twenty dogs were included in this retrospective cohort study.

Results: Nonchondrodystrophic breeds (n = 16) were more predisposed than chondrodystrophic breeds. Most dogs showed acute onset of clinical signs. Neurological examination at admission showed predominant non-ambulatory paraparesis (n = 9); paresis (n = 16) was confirmed more frequently than paralysis (n = 4). Follow-up neurological examination results were only available for 11 dogs, ten of whom showed neurological improvement and 8 showed successful outcomes at 1 month. The characteristic MRI findings include thoracic vertebra (T)2 hyperintense, T1 hypointense, intramedullary linear tracts with reduced disc volume, and cleft of the annulus fibrosus. None of the MRI measurements were significantly correlated with neurological grade at admission. Neurological grade did not differ according to the presence of parenchymal hemorrhage, parenchymal contrast enhancement, and meningeal contrast enhancement. Neurological grades at admission showed a statistical correlation with those observed at the 1-month follow-up ($r = 0.814$, $p = 0.02$).

Conclusions: IIVDE is a rare form of disc extrusion commonly experienced after physical activity or trauma and most frequently affects the cranial-cervical and thoracolumbar regions of nonchondrodystrophic dog breeds. Neurological score at admission emerged as a more useful prognostic indicator than MRI findings in dogs with suspected IIVDE.

Keywords: 3D dimensional T2-weighted fast spin echo sequence; dog; intradural-intramedullary intervertebral disc extrusion; intervertebral disc disease; magnetic resonance imaging

INTRODUCTION

Intervertebral disc disease (IVDD) is one of the most common vertebral and spinal disorders in dogs [1] and is traditionally categorized as either a Hansen type I extrusion or a Hansen type II

Author Contributions

Conceptualization: Kim J, Eom K; Data curation: Kim J; Formal analysis: Kim J; Funding acquisition: Kim J, Eom K; Investigation: Kim J, Kim H, Hwang J; Methodology: Kim J, Kim H, Hwang J; Project administration: Kim J, Eom K; Resources: Kim J; Software: Kim J; Supervision: Kim J, Eom K; Validation: Kim J, Eom K; Visualization: Kim J, Eom K; Writing - original draft: Kim J, Kim H, Hwang J; Writing - review & editing: Kim J, Eom K.

protrusion [2]. Type I extrusion is associated with chondroid degeneration in chondrodystrophic breeds and type II protrusion with fibroid degeneration in nonchondrodystrophic breeds [1]. Recently, various subcategories of IVDD such as far lateral lumbar disc extrusion, hydrated nucleus pulposus extrusion, acute non-compressive nucleus pulposus extrusion (ANNPE), and intradural-intramedullary intervertebral disc extrusion (IIVDE) have been reported in dogs [3,4].

In IIVDE, the nucleus pulposus damages the spinal cord parenchyma through a dural tear [5]. Because the non-degenerative nucleus pulposus ruptures at high velocity during physical activity or a traumatic event, it can completely penetrate the spinal cord or part of the disc material can become embedded in the spinal parenchyma. Although a few cases of IIVDE have been reported in dogs and cats [3,6-9], the prognosis and imaging characteristics of this condition are poorly characterized. In our experience, IIVDE is uncommon but sometimes encountered in daily veterinary practice, presenting with characteristic magnetic resonance imaging (MRI) findings.

We aimed to describe the clinical and imaging characteristics of tentatively diagnosed IIVDE in dogs to assess the prognostic utility of neurological grade and MRI findings.

MATERIALS AND METHODS

The care, maintenance, and study design followed the protocols approved by the Institutional Animal Care and Use Committee of Konkuk University. From January 2017 to May 2019, dogs diagnosed with IIVDE by MRI at our institution were included. To diagnose IIVDE, we used 3-dimensional (3D) thoracic vertebra (T)2-weighted fast spin echo sequence (CUBE; GE Healthcare, USA). Inclusion criteria were: 1) availability of an MRI image series including 3D T2-weighted, T1-weighted, T2-weighted, or gradient recalled echo (GRE); and T1-weighted post-contrast image MRI findings characterized as follows: 2) the nucleus pulposus decreased in size and signal intensity on a T2-weighted sagittal image; and 3) presence of the intramedullary disc material or a linear tract that originated from the intervertebral disc space. We retrieved clinical data including breed, age, sex, body weight, neurological score, and onset of clinical signs from the hospital database.

Neurological examination

Based on a previous report [10], the results of neurological examinations at admission and follow-up a month later were collected. The criteria for neurological scoring were: grade 0, normal; grade 1, cervical or thoracolumbar pain, hyperesthesia; grade 2, paresis, muscle weakness with decreased proprioception, ambulatory; grade 3, severe paresis with absent proprioception, non-ambulatory; grade 4, paralysis, decreased or no bladder control, preserved nociception; and grade 5, paralysis, urinary and fecal incontinence, absence of nociception.

MRI

MRI was performed under general anesthesia using a 1.5-Tesla system (Signa HDxt; GE Healthcare). Anesthesia was induced with propofol (6 mg/kg, IV; Provive 1%; Myungmoon Pharmaceutical Co., Korea) and was maintained with 1.5% isoflurane (Foran solution; Choongwae Pharma Corporation, Korea) in 100% oxygen via endotracheal intubation. The dog was positioned in dorsal recumbency on the 8-channel phased-array spine coil. 3D T2-weighted images were obtained with the following parameters: repetition time, 2,600 ms; echo time, 121 ms; spacing 0.5 mm; flip angle, 90°; field of view, 12 × 12 cm; acquisition time, 4 min 30 sec. Based on the 3D T2-weighted transverse images, multiplanar images were

obtained with a 0.5 mm slice thickness. Post-contrast T1-weighted images were acquired following 0.15 mmol/kg intravenous administration of contrast agent manually (Magnevist; Bayer, USA). Detailed parameters are summarized in **Appendix 1**.

MRI analysis

MRI analysis was performed using commercially available software (Osirix DICOM viewer; Pixmeo, Switzerland). The location, direction of disc penetration, number of lesions, and measurements of the T2 hyperintensity were analyzed on MRI (**Fig. 1**). The length of the T2 hyperintense lesion on the sagittal image was measured and expressed relative to either the 6th cervical or 2nd lumbar vertebral length (length of the spinal lesion [LL]: length of the vertebra [VL]), depending on whether the lesion was identified in the cervical or the thoracolumbar spinal cord, respectively. The ratios between the diameter of the linear tract to spinal diameter (diameter of the spinal lesion [LD]: diameter of the spinal cord [SD]), and the maximal cross-sectional area of the lesion as a percentage of the cross-sectional area of the spinal cord at the same level (PCSAL) were obtained on the transverse images. The presence/absence of spinal parenchymal and epidural hemorrhages on GRE sequence was

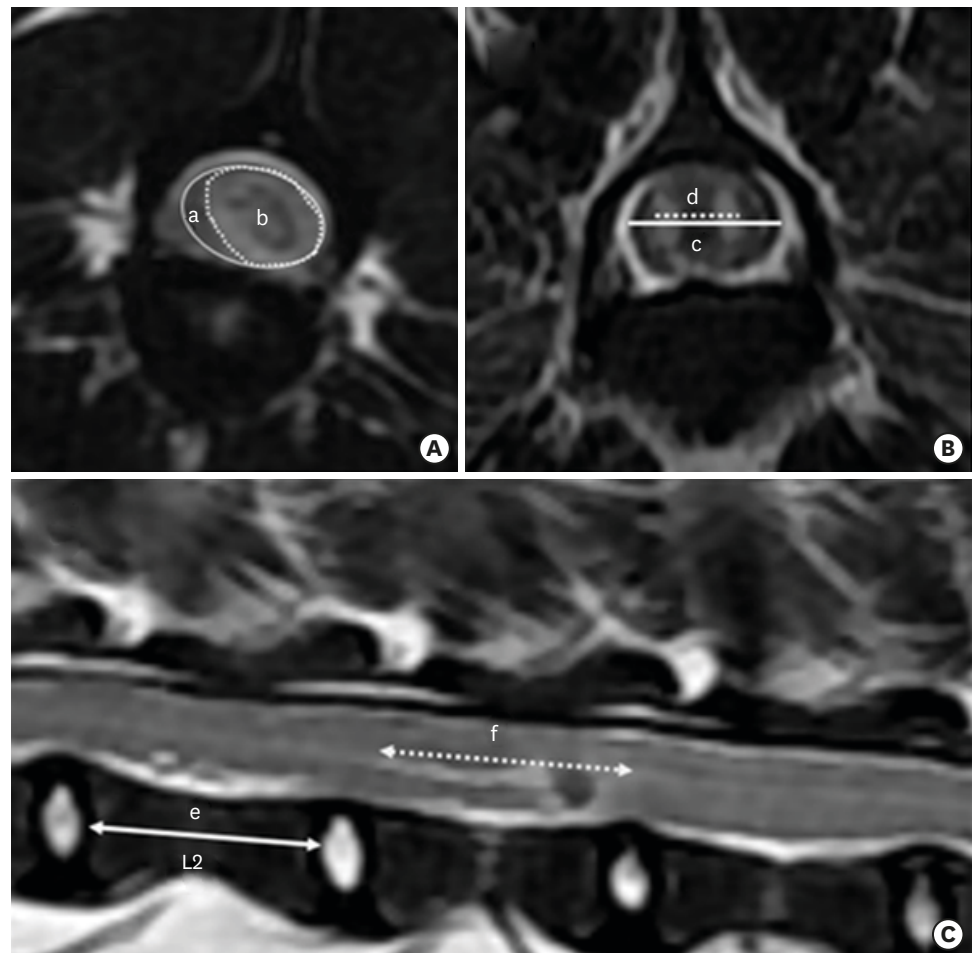


Fig. 1. Measurements on magnetic resonance images in dogs with intradural-intramedullary intervertebral disc extrusion. Three parameters (PCSAL, b/a ; $LD:SD$, d/c ; $LL:VL$, f/e) were calculated as follows: (A), On the T2-weighted transverse plane, the ratio of CSA of hyperintensity (b) to CSA of spinal cord (a). (B), On the T2-weighted transverse plane, the diameter of the linear tract (d) to the spinal diameter (c). (C) On the T2-weighted sagittal plane, the length of the hyperintense lesion to the length of the 6th cervical or 2nd lumbar vertebra.

PCSAL, the maximal cross-sectional area of the lesion as a percentage of the cross-sectional area of the spinal cord at the same level; LD, diameter of the spinal lesion; SD, diameter of the spinal cord; LL, length of the spinal lesion; VL, length of the vertebra, CSA, cross-sectional area.

determined. On the post-contrast image, the presence/absence of spinal parenchymal and meningeal contrast enhancement was determined. The cleft of annulus fibrosus was defined as the hyperintense gap located dorsal to the nucleus pulposus. The presence of the cleft was assessed on both T2- and 3D T2-weighted transverse images. All measurements were made 3 times by a single experienced veterinary radiologist, and the mean of these replicates was used in all analyses.

Statistical analysis

Statistical analyses were conducted using commercially available software (SPSS 21.0; IBM Corp., USA). Kolmogorov-Smirnov and Shapiro-Wilk tests were used to identify normal distributions. Pearson's correlations were used to identify correlations between MRI measurements and neurological scores on admission. Differences between neurological scores of patients grouped according to presence/absence of MRI findings such as parenchymal hemorrhage, parenchymal contrast enhancement, and meningeal contrast enhancement, were assessed using the student's *t*-test. For all comparisons, the level of significance was set at $p < 0.05$.

RESULTS

Inclusion criteria were met by 20 dogs of 10 breeds: Spitz ($n = 5$), Chihuahua ($n = 4$), Pomeranian ($n = 3$), Maltese ($n = 1$), Dachshund ($n = 1$), Italian Greyhound ($n = 1$), Poodle ($n = 1$), French Bulldog ($n = 1$), English Bulldog ($n = 1$), and mixed breed ($n = 1$). Nonchondrodystrophic breeds ($n = 16$) were more predisposed to IIVDE than chondrodystrophic breeds ($n = 4$). The sex distribution included entire males ($n = 3$), castrated males ($n = 9$), females ($n = 6$), and spayed females spayed ($n = 2$). Age at diagnosis ranged from 1 to 7 years (mean \pm SD, 4.5 ± 2.7). Body weight ranged from 2 to 23 kg (7.2 ± 4.8 kg). All dogs showed acute onset of clinical signs less than 24 h after the physical activity ($n = 5$) or trauma ($n = 12$), except for 3 dogs who had undergone no identifiable causative events, and their clinical histories were unclear.

In the neurological examination conducted at admission (**Table 1**), paresis (grades 2 and 3, $n = 16$) was more frequently confirmed than paralysis (grades 4 and 5, $n = 4$). Non-ambulatory paraparesis ($n = 9$) was the most common neurological abnormality. All dogs with an IIVDE in the thoracolumbar region either had paraparesis ($n = 12$) or paraplegia ($n = 3$). Moreover, hemiparesis ($n = 3$), tetraplegia ($n = 1$), and tetraparesis ($n = 1$) were identified among the dogs with a cervical lesion. Two dogs who developed loss of nociception had urinary incontinence.

Only 11 of the 20 dogs had the results of a follow-up neurological examination performed 1 month post-admission. Ten of these 11 dogs showed neurological improvement (improvement in their neurological grade on follow-up compared to at first admission), and 8 of the 11 dogs showed successful ambulatory outcomes (able to walk without any assistance). In the 2 dogs with a grade 5 score at admission, one showed no neurological improvement,

Table 1. Summarized results of neurological examinations of dogs with intradural-intramedullary intervertebral disc extrusion

Assessments	Results
Neurological grade	Grade 1 (0), grade 2 (7), grade 3 (9), grade 4 (2), grade 5 (2)
Neurological grade at follow-up	Grade 1 (2), grade 2 (6), grade 3 (1), grade 4 (1), grade 5 (1)
Nociception	Normal (18), abnormal (2)
Urinary function	Normal (18), abnormal (2)

Values are presented as number.

Table 2. Summarized magnetic resonance imaging findings in dogs with intradural-intramedullary intervertebral disc extrusion

MRI assessments	MRI results
T2-weighted images	Hyperintense (20*), isointense (0), hypointense (0)
T1-weighted images	Hyperintense (0), isointense (5), hypointense (15)
LL:VL ratio (range)	1.18 (0.37–3.63)
LD:SD ratio (range)	0.33 (0.18–0.61)
PCSAL (%) (range)	0.48 (0.18–0.71)
Parenchymal hemorrhage	Present (7/20), absent (13/20)
Epidural hemorrhage	Present (2/20), absent (18/20)
Parenchymal contrast enhancement	Present (5/20), absent (15/20)
Meningeal contrast enhancement	Present (10/20), absent (10/20)
Cleft of the annulus fibrosis†	Present (13/20), absent (7/20)

T, thoracic vertebra; LL, length of the spinal lesion; VL, length of the vertebra; LD, diameter of the spinal lesion; SD, diameter of the spinal cord; PCSAL, the maximal cross-sectional area of the lesion as a percentage of the cross-sectional area of the spinal cord at the same level.

*Five dogs showed a hypointense center consistent with a parenchymal hemorrhage with hyperintense linear tracts; †The clefts were identified using 3D T2-weighted images.

whilst the other showed neurological improvement (grade 4 at follow-up); however, no further improvement was observed.

The MRI findings are summarized in **Table 2**. On sagittal T2-weighted images, all dogs showed a single linear hyperintense intramedullary lesion along the craniodorsal (n = 14) or dorsal (n = 6) direction (**Fig. 2**). Most dogs showed a linear tract with a T2 hyperintense and

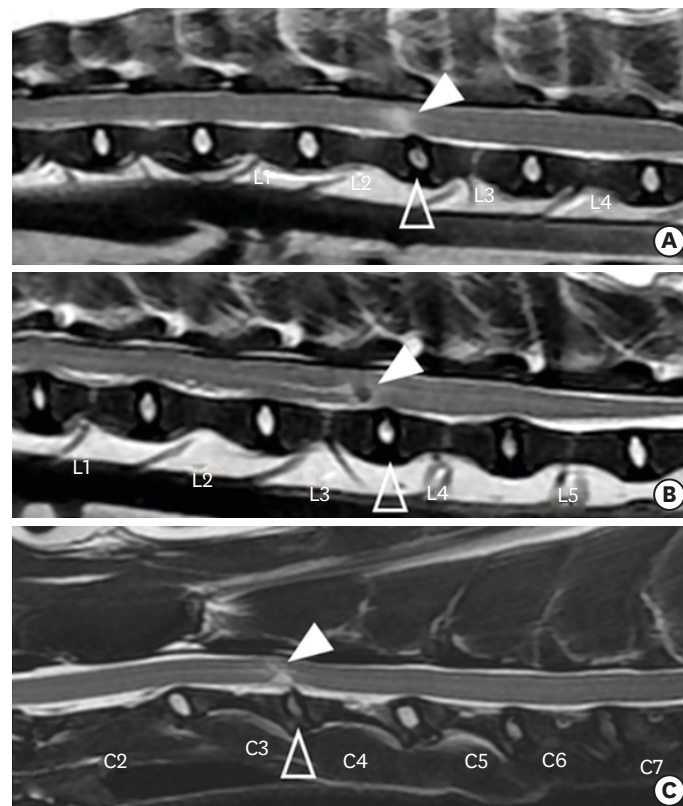


Fig. 2. T2-weighted mid-sagittal images of dogs with intradural-intramedullary intervertebral disc extrusion. Although lesions can be seen at various locations and lengths, note that there are commonly identified linear tracts (arrowheads) and decreased disc volumes (open arrowheads). L, lumbar vertebra; C, cervical vertebra; T, thoracic vertebra.

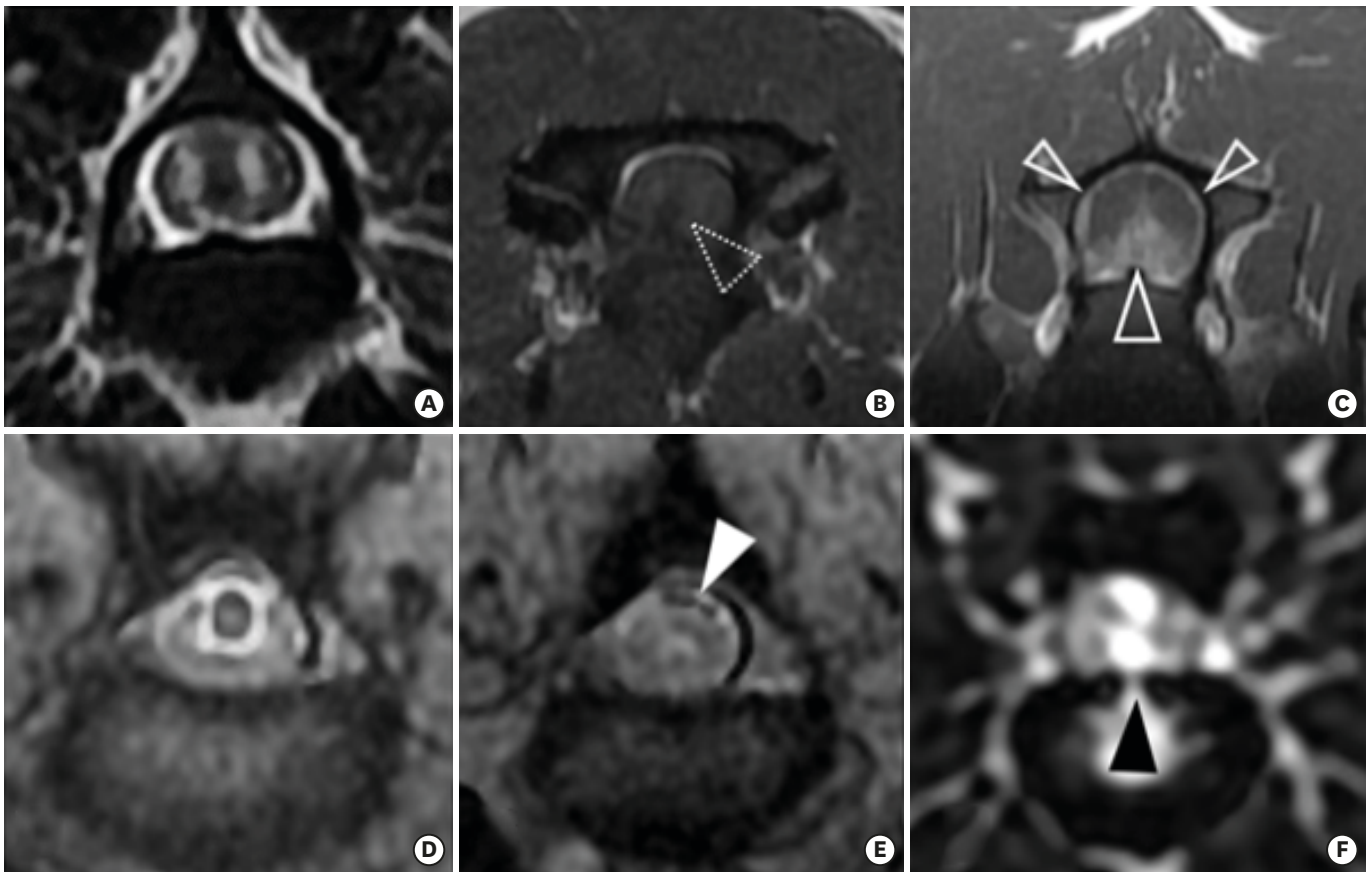


Fig. 3. Magnetic resonance imaging findings of dogs with intradural-intramedullary intervertebral disc extrusion. (A) On the T2-weighted image, a linear, hyperintense lesion with a hypointense center consistent with parenchymal hemorrhage is identified. (B), On the T1-weighted image, a linear hypointense lesion arising from the disc is seen (dashed arrowhead). (C), On the T1-weighted, post-contrast image, parenchymal and meningeal contrast enhancements are distinctly seen (open arrowheads). Strong contrast enhancement is observed along the linear tract on the spinal parenchyma. (D, E), on the gradient recalled sequence, intraparenchymal and epidural hemorrhage (white arrowhead) are seen. (F), On the 3-dimensional T2-weighted image, the cleft of the annulus fibrosus in the dorsal direction (black arrowhead) is clearly identified.

T1 hypointense intramedullary lesion on the transverse plane (**Fig. 3**). Five dogs exhibited spinal parenchymal hemorrhage causing hyperintense lesion with a hypointense area on the T2-weighted images. On the 3D T2-weighted transverse images, 13 of the 20 dogs showed the cleft of annulus fibrosus dorsal to the nucleus pulposus. However, among them, only 3 dogs showed the cleft on conventional T2-weighted transverse images. IIVDE was predisposed at the cranial-cervical ($n = 5$) and thoracolumbar ($n = 15$) regions (**Fig. 4**), with the most frequent location between the 12th and 13th thoracic vertebrae ($n = 6$).

None of the MRI measurements were significantly correlated with neurological grade at admission ($p = 0.461$ in LL:VL; $p = 0.618$ in LD:SD; $p = 0.313$ in PCSAL). Neurological grade did not differ according to the MRI measurements ($p = 0.391$, parenchymal hemorrhage; $p = 0.361$, parenchymal contrast enhancement; and $p = 0.425$, meningeal contrast enhancement). There were no differences in the neurological grade between the 2 groups separated by the presence/absence of parenchymal hemorrhage, parenchymal contrast enhancement, and meningeal contrast enhancement. Neurological grades at admission showed a statistical correlation with those observed at the 1 month follow-up ($r = 0.814$, $p = 0.02$). In particular, 2 of the 11 dogs with persistent paralysis (grade 4 and 5) at follow-up had initially presented with severe neurological dysfunction (grade 5) at admission.

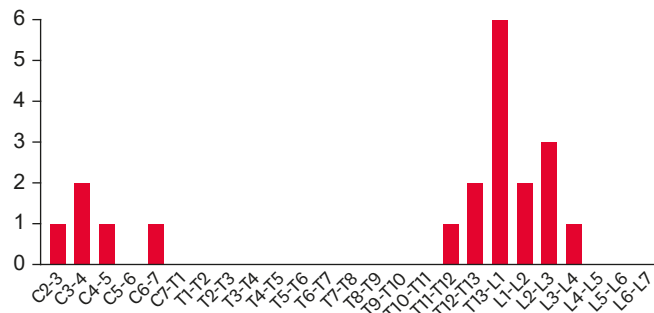


Fig. 4. Frequency distribution of sites of intradural-intramedullary intervertebral disc extrusion. Similar to the typical intervertebral disc disease in dogs, the lesion most frequently observed in the thoracolumbar and cranial-cervical region.
C, cervical vertebra; T, thoracic vertebra; L, lumbar vertebra.

DISCUSSION

Our study highlighted both similarities and differences between IIVDE and typical IVDD in dogs. Type I extrusion is commonly associated with degenerative changes in the annulus fibrosis and is usually more prevalent in chondrodystrophic breeds. IIVDE has been partially described as a subtype of disc extrusion in dogs and cats [5,9,11,12]. IIVDE occurs when the disc is severely ruptured by high pressure and momentary external force, causing some of the disc material to penetrate the adjacent spinal cord after the causative trauma or physical activity [3,6]. Interestingly, although IIVDE is a type of disc extrusion, most dogs in the present study were nonchondrodystrophic breeds. IIVDE is a type of non-degenerative disc rupture, which occurs when the disc experiences high pressure for a short time. Therefore, dogs belonging to nonchondrodystrophic breeds that have slow degenerative changes in the annulus fibrosus may frequently develop IIVDE. Notably, the most frequently affected sites of IIVDE in our study were the cranial-cervical and thoracolumbar regions, especially between the 12th and second lumbar vertebrae. These regions are predisposed to developing spontaneous IVDD [13], probably because the biomechanical forces are the greatest at these static-dynamic junctions.

A definitive diagnosis of IIVDE can be made when extrusion of the intramedullary disc material is surgically and histologically confirmed [6]; however, surgical treatment is rare unless compression of the spinal cord is evident. In addition, most dogs in the present and previous studies showed a good prognosis without surgical decompression [7,14,15]. Therefore, MRI is key for the diagnosis of IIVDE. As in previous studies [5,11], our common MRI findings for IIVDE were reduced disc volume and linear tract of the spinal cord. The decrease in signal intensity of the disc is considered proportional to the amount of disc extrusion. If the decrease can be quantified, it may be helpful to evaluate the prognosis of dogs. However, in the present study, because some dogs were older than 5 years, multifocal disc degeneration and dehydration made it difficult to quantify the disc volume reduction attributable to IIVDE. Notably, in addition to the linear tract, clefts in the annulus fibrosus were identified on 3D T2-weighted images for more than half the patients in our study, suggesting that this finding might provide distinct evidence of disc extrusion. In some dogs, intramedullary hyperintensity occasionally accompanied by a hypointense center within the linear tracts was observed on T2-weighted images. This mixed signal intensity was consistent with a parenchymal hemorrhage on GRE sequence. However, although MRI findings of IIVDE have been described in a few case reports [3,4], concurrent hemorrhage and changes

in signal intensity over time are not well-established for such findings. Further studies are needed to establish a comprehensive spectrum of MRI findings in dogs with IIVDE.

The neurological score is a more important prognostic factor than MRI findings for prognosis assessment in dogs with IVDD [1,2]. MRI findings such as spinal cord compression rate, length and area of the parenchymal lesion, and the presence of parenchymal hemorrhage are not known to be correlated with the prognosis of IVDD in dogs. However, we considered it possible that criteria for prognostic evaluation might be different for IIVDE, in which spinal cord injury results from penetrating disc material. However, the neurological grades reported in this study are more important prognostic factors than MRI findings, which were similar to that reported in previous studies on IVDD. Therefore, the value of MRI in dogs with suspected IIVDE may be limited to that of accurate diagnosis and lesion identification. The prognosis of such dogs should be evaluated through the neurological scores, as in typical IVDD.

In the present study, most dogs with lower neurological grades (paresis) on admission progressively improved and showed successful outcomes after 1 month. The small number of dogs that presented with preserved nociception on admission improved to paresis within a month. However, dogs with a loss of nociception had unsuccessful outcomes at follow-up. This suggests that in most cases, the prognosis of IIVDE with conservative treatments, including analgesics, exercise restriction, and occasional steroid administration, is relatively good despite the risk of intramedullary damages. At the 1 month follow-up, more than two thirds of the 11 dogs examined showed an improvement and could ambulate without assistance. Our results, along with those of a previous study that reported successful outcomes in 67% of dogs with ANNPE [16], suggest that contrary to expectation, intramedullary spinal damage may have an unexpectedly small effect on prognosis.

Traditionally, ANNPE and fibrocartilaginous embolism (FCE) have been considered as differential diagnoses because they commonly show decreased disc volume without distinct spinal cord compression on MRI [17]. Furthermore, they are clinically similar in that they both show an acute post-traumatic onset of clinical signs [14]. FCE has been differentiated from ANNPE on the basis of largely asymmetrical intramedullary lesions, including gray matter, with generally longer lesions than in cases with ANNPE [18]. Although ANNPE and IIVDE both involve extrusion of non-degenerative nucleus pulposus, our study has revealed some distinct MRI findings for IIVDE: longer hyperintense spinal lesion, more frequent parenchymal hemorrhage, and less contrast enhancement than previously reported for ANNPE patients [4,17]. We consider that among dogs presenting with IIVDE, intramedullary penetration or embedding of extruded disc materials causes severe parenchymal changes and more frequent hemorrhages than are observed among ANNPE patients. Additionally, previous studies differentiate ANNPE and intradural extramedullary disc extrusion without a definitive distinction from IIVDE [13,15,17]. Because it is likely that some of the dogs diagnosed as ANNPE in previous reports were actually IIVDE, previously reported prognostic factors may differ from those suggested by our study. Indeed, in our study, some dogs were misdiagnosed as having ANNPE based on the findings of conventional T2-weighted images; the linear tracts in these cases were only visible on 3D T2-weighted images. In addition, the cleft of annulus fibrosus, a potential pathway for extrusion of the nucleus pulposus in response to mechanical forces exerted on the spinal column, was visualized in more than 70% dogs only on 3D T2-weighted images. As a result, IIVDE could be misdiagnosed as ANNPE when only conventional T2-weighted images are used for diagnosis; therefore, we

recommend that future evaluations of ANNPE and IIVDE in dogs should use high-field MRI with a 3D T2-weighted sequence for definitive diagnosis.

T2-weighted imaging has been used for the assessment of IVDD in dogs, but limitations of this technique include the wide interslice gap and operator dependency that manifests especially in small breed dogs [1]. In human medicine, 3D T2-weighted imaging is widely applied because it yields excellent spatial resolution [19], multiplanar reconstruction, and thin slices [20]. Especially in veterinary medicine, 3D T2-weighted imaging is potentially useful because of the small body size of many subjects, and the time-consuming procedure to get multiplanar imaging under general anesthesia. However, it has been applied mainly in research settings because of the need for high Tesla MRI equipment, and lack of previous studies [19]. As mentioned above, because the diagnostic MRI findings of IIVDE such as linear tracts and annulus tears require confirmation on 3D T2-weighted images in some dogs, we recommend 3D T2-weighted imaging for definitive diagnosis in dogs with suspected IIVDE.

The limitations of our study were firstly that intramedullary disc material was not identified surgically and histologically in all dogs in the absence of spinal compression. Because the study was designed based on a tentative diagnosis through MRI findings, we included only dogs that showed definite IIVDE through a 3D T2-weighted sequence in the study cohort. Therefore, we may have excluded IIVDE cases that showed unclear findings on MRI. Second, the prognostic power of our statistical analysis was limited by the small sample size, particularly for the follow-up neurological examination and MRI findings such as epidural hemorrhages. Third, the follow-up period was set at 1 month, which is too short for clear determination of improvement or deterioration in neurological signs. Lastly, due to the retrospective nature of our study, not all individuals received the same conservative treatment including physical rehabilitation, corticosteroid injection, and hyperbaric oxygen therapy.

In conclusion, IIVDE is a rare form of disc extrusion commonly experienced after physical activity or trauma and most frequently affects the cranial-cervical and thoracolumbar regions of nonchondrodystrophic dog breeds. In dogs with IIVDE, the characteristic MRI findings include T2 hyperintense, T1 hypointense, intramedullary linear tracts with reduced disc volume, and cleft of the annulus fibrosus. However, the neurological score at admission emerged as a more useful prognostic indicator than MRI findings.

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Appendix 1. Parameters of the magnetic resonance imaging sequences

MRI parameters	T1W transverse	T1W sagittal	T2W transverse	T2W sagittal	GRE
Sequence	FSE	FSE	FSE	FSE	GRE
FOV (cm)	12	20	12	20	12
Slice thickness (mm)	3	3	3	3	3
Interslice gap (mm)	0.3	0.3	0.3	0.3	0.3
Relaxation time (ms)	400–600	400–600	3,000	3,000	400–600
Echo time (ms)	12	12	80	95	5.8
Flip angle	110	110	160	160	-
Matrix	288 × 224	320 × 224	288 × 224	320 × 224	256 × 192
Nex	4	4	4	4	2

T1W, T1-weighted sequence; T2W, T2-weighted sequence; CE, contrast enhanced; GRE, gradient recalled echo; FSE, fast spin echo; FOV, field of view.