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ORIGINAL RESEARCH

Clinical signs, MRI findings and long-term outcomes of foraminal and far lateral thoracolumbar intervertebral disc herniations in dogs

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Abstract

Background: As they have been seldomly described in the veterinary literature, the aims of this retrospective study were to describe the clinical presentation, MRI findings and long-term outcome after medical or surgical treatment of dogs presenting with foraminal and far lateral thoracolumbar intervertebral disc herniations.

Methods: Retrospective multicentre study of dogs diagnosed with foraminal and far lateral thoracolumbar intervertebral disc herniations between 2009 and 2020 in seven referral hospitals.

Results: Thirty-seven dogs were included. Dachshunds and mixed breeds were most affected. Median age at presentation and duration of clinical signs were 6 years and 14 days, respectively. Pain was the most frequent clinical finding (92%), particularly on spinal palpation and/or hip manipulation, followed by pelvic limb lameness (71%). Eighty-seven percent of herniations occurred at L5-L6 or L6-L7. A good to excellent outcome was seen in 95% of surgically and 90% of medically treated dogs.

Conclusion: Although much less frequently recognised than herniation affecting the vertebral canal, foraminal and far lateral thoracolumbar intervertebral disc herniations should be considered in the differential diagnosis list of chondrodystrophic dogs presenting with pain and pelvic limb lameness. Most dogs had a good to excellent outcome following medical or surgical treatment.

INTRODUCTION

Intervertebral disc disease is a common neurological condition in dogs, affecting the thoracolumbar region most frequently.^{1,2} Intervertebral disc herniations most often occur dorsally into the vertebral canal, presumably due to the anatomical conformation of the annulus fibrosus that is thinner in its dorsal portion.³ When this happens, it can cause damage to the spinal cord and clinical signs of myelopathy, characteristic of the spinal cord segments affected. However, in a smaller number of cases, the herniation may occur laterally or dorso-laterally, causing compression of the nerve roots and/or spinal nerve and vessels as

they exit the foramen or distal to it.⁴ These types of herniations have been described, respectively, as intervertebral foraminal or intraforaminal, and lateral, far lateral or extraforaminal extrusions in the veterinary literature,⁴⁻⁷ but the term 'extreme-lateral' has also been used in human medicine.⁸ Clinical signs are secondary to radicular and spinal nerve compression, and include hyperaesthesia and lameness, which could be misinterpreted as a primary orthopaedic disorder.^{4,5,9}

The diagnosis of foraminal or far lateral disc extrusions can be challenging as most cases require advanced imaging techniques, such as MRI or CT.¹⁰ The clinical presentation, MRI features and outcome

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after medical and surgical treatment of intervertebral foraminal extrusions have been previously reported in the cervical region in dogs.¹¹ Although their prevalence in the lumbar region has been reported to range from 0.7% to 11.7% in the human literature,¹² they have seldom been described affecting this region in dogs.⁵ Two case reports have previously described far lateral extrusions in the vertebral column of dogs treated surgically.^{5,9} However, to the authors' knowledge, there are no case series describing foraminal and far lateral thoracolumbar intervertebral disc herniations in dogs and the outcome after medical and surgical treatments.

Therefore, the aims of this retrospective study were to characterise the clinical presentation and to describe the diagnostic imaging findings and long-term outcome after medical or surgical treatment of dogs presenting with foraminal and far lateral thoracolumbar intervertebral disc herniations.

MATERIALS AND METHODS

The study was reviewed and approved by the Research Ethics Committee of the School of Veterinary Medicine of the University of Glasgow (application EA16/19).

The electronic medical records of seven referral hospitals (three in the UK, two in the USA, one in Spain and one in Switzerland) were retrospectively searched for dogs diagnosed with foraminal and far lateral thoracolumbar intervertebral disc herniations between July 2009 and October 2020.

Inclusion criteria were complete medical records, clinical signs and neurological examination findings compatible with a diagnosis of foraminal or far lateral thoracolumbar intervertebral disc herniation confirmed by MRI. Foraminal or far lateral thoracolumbar intervertebral disc extrusions were defined as presence of intervertebral disc material within (foraminal) and/or outside the limits of the foramen (far lateral) in the thoracolumbar region of the vertebral column (between the third thoracic and the sixth lumbar vertebra). It was decided to exclude the L7-S1 intervertebral disc space, since foraminal stenosis secondary to lumbosacral disease is frequent and might represent a different pathological process. Another exclusion criterion was the presence of herniated disc material within the vertebral canal causing spinal cord or filum terminale compression.

Data collected for each case included: breed, sex, neuter status, age and weight at diagnosis, clinical signs exhibited at and before presentation, duration of clinical signs, physical, neurological and orthopaedic examination findings, concurrent medical conditions, diagnostic imaging findings (including MRI, but also CT and radiography when available), treatment and outcome.

Onset of signs was classified as acute (onset over 48 hours), subacute (onset over 2–7 days) or chronic (onset over more than 7 days) based on the client-provided history.^{13,14} Duration of signs was quantified as the number of days from the client-reported onset

to presentation. Presence of pain on palpation of the spine, lameness, nerve root signature¹⁴ and neurological deficits were evaluated. Neurological deficits were defined as one or more of the following: paresis, plegia, proprioceptive deficits, reduced pelvic limb spinal reflexes, reduced nociception in the pelvic limbs.

Diagnostic imaging

MRI images were acquired using the following systems: Phillips Intera 1.5 T system (Philips Medical Systems, Nederland, Best, The Netherlands), 1.5 T Magnetom (Siemens, UK), Siemens Magnetom Essenza 1.5 T (Siemens, Munich, Germany), Philips Panorama HFO 1.0 T (Philips Medical Systems), GE Genesis Signa 1.5 T (GE Medical Systems, Fairfield, CT, USA), Siemens Symphony 1.5 T (Siemens Medical Solutions, Malvern, PA, USA), Vet-MR Esaote 0.2 T (Genoa, Italy), Siemens Symphony 1.5 T (Siemens Medical Solutions). T2-weighted (T2W) sagittal and transverse planes were acquired in all dogs. T1-weighted (T1W), fat suppression, volumetric interpolated breath-hold examination (VIBE), T2-star-weighted (T2*W), short tau inversion recovery (STIR), constructive interference in steady state (CISS), half-Fourier acquisition single-shot turbo spin echo (HASTE) and T2-weighted two-dimensional fast low-angle shot for hemosiderin detection in axial projection (T2W-FL2D HEMO), as well as T1W post-gadolinium administration sequences, were additionally acquired at the discretion of the attending clinician. All the MR sequences were reviewed by two of the authors (Sara Silva and Rodrigo Gutierrez-Quintana), one being a board-certified neurologist (Rodrigo Gutierrez-Quintana). The following information was recorded: site and lateralisation of the lesion, degree of intervertebral disc degeneration determined by the Pfirrmann grading system,^{15,16} presence of nerve root/spinal nerve enlargement, nerve root/spinal nerve or perilesional contrast enhancement and changes to the epaxial musculature. The herniation was classified as intervertebral foraminal when the extruded material was confined to the neuroforamen (between the medial and lateral borders of the pedicle), far lateral when the disc material was outside of the neuroforamen (outside the lateral border of the pedicle),^{5,17} and as both foraminal and far lateral when the extruded disc material extended over both regions (Figure 1).

When CT or radiographs were available, the presence of calcified disc material in or outside of the intervertebral foramen was recorded. CT images were obtained using the following systems: 16-slice Mx800 IDT (Philips Medical Systems), two-slice Siemens Somatom Spirit (Siemens, Erlangen, Germany).

Treatment and outcome

Owners were informed about the clinical diagnosis and treatment options for foraminal and far lateral

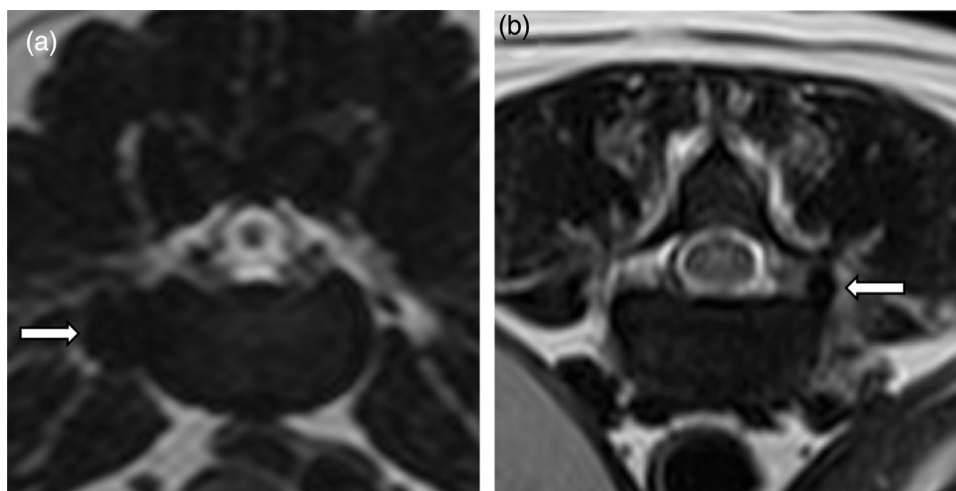


FIGURE 1 T2-weighted transverse images of two cases with thoracolumbar foraminal and far lateral disc herniations. (a) Dog 16—presence of left-sided intervertebral disc material outside of the limits of the foramen at the level of L6-L7 (arrow) consistent with far lateral disc herniation. (b) Dog 8—presence of intervertebral disc material within the right foramen at the level of T12-T13 (arrow) consistent with foraminal herniation

disc herniations by a board-certified neurologist or orthopaedic surgeon, or a veterinary surgeon enrolled in a neurology residency programme. The choice of treatment (medical or surgical) was made by the owner but guided by the attending clinician. Surgical technique was selected by the attending clinician and consisted of hemilaminectomy, foraminotomy, discectomy, corpectomy, a combination of foraminotomy and pediclectomy, or removal of the laterally herniated disc with no drilling of the bone for far lateral disc herniations. Lateral disc fenestration was performed in some cases depending on surgeon preference. Perioperative anaesthetic and analgesic treatments were at the discretion of the anaesthetist and clinician responsible for the case. Postoperative care consisted of restricted exercise for 4 weeks in combination with physiotherapy and appropriate anti-inflammatory and analgesic medication. Medical management was identical to postoperative care for surgical cases. Restricted exercise consisted of allowing the dog to make two or three leashed walks a day for toileting purposes and avoiding jumping, running, excessive playing or any other high-impact movements.

Short-term follow-up information was obtained from the medical records and defined as a period of at least 14 days. Long-term follow-up was defined as a period of more than 3 months and was obtained by a combination of re-examination at the referral centre, evaluation of postdiagnosis clinical records, and when possible, a standardised questionnaire answered by the owners. Complying with ethics and welfare committee guidelines, only owners of dogs that were still alive at time of data collection were contacted to complete the questionnaire. Outcome was defined as: excellent if there was complete resolution of clinical signs; good when all pretreatment clinical signs were resolved, but the dog still had occasional mild signs of pain or pelvic limb weakness/lameness; and poor if the patient failed to improve, deteriorated or experienced a recurrence within the short-term follow-up period.¹⁸

Statistical analysis

Numerical variables were presented as median and range. Categorical variables were described as count and percentage.

RESULTS

Thirty-seven dogs were included. Additionally, one dog presented on two different occasions with disc herniations at different sites. The most affected breeds were Dachshund and mixed breed, both representing 22% of the study population (8/37), followed by Cocker Spaniel (16%, 6/37), Beagle (11%, 4/37), Shih Tzu (5%, 2/37), and one each of the following: French Bulldog, Lhasa Apso, Poodle, Greyhound, German Shepherd, German Pointer, Cavalier King Charles Spaniel, Field Spaniel and Jack Russel Terrier. Median age at presentation was 6 years (range 2.5–12 years) and weight was 11.25 kg (range 4.6–37 kg). Sixteen animals were female, 14 of those neutered, and 21 were male, 13 neutered. Median duration of clinical signs was 14 days (range 1–660 days). Information on progression of clinical signs was available in 23 cases. It was progressive in 10, non-progressive in 10 and intermittent in three. Lameness was observed in 71% of cases (27/38) (Video S1). Pain was noted in 92% of cases (35/38). Out of these, 49% on lumbar palpation (17/35), 57% on hip extension (20/35), 20% on lumbosacral palpation (7/35), 6% on thoracolumbar palpation (2/35) and 6% on tail manipulation (2/35). In two cases, although pain was not detected on examination, intermittent yelping episodes were reported by the owner. Postural reactions were normal in 53% of cases (20/38), reduced in 32% (12/38) and absent in 16% (6/38). Postural reactions were unilaterally abnormal in 29% of cases (11/38) and bilaterally abnormal in 18% (7/38). Pedal withdrawal reflexes were abnormal in 34% of cases (13/38), unilaterally in 12 and bilaterally in one case. Patellar reflex was abnormal in 26% of cases (10/38), unilaterally in nine

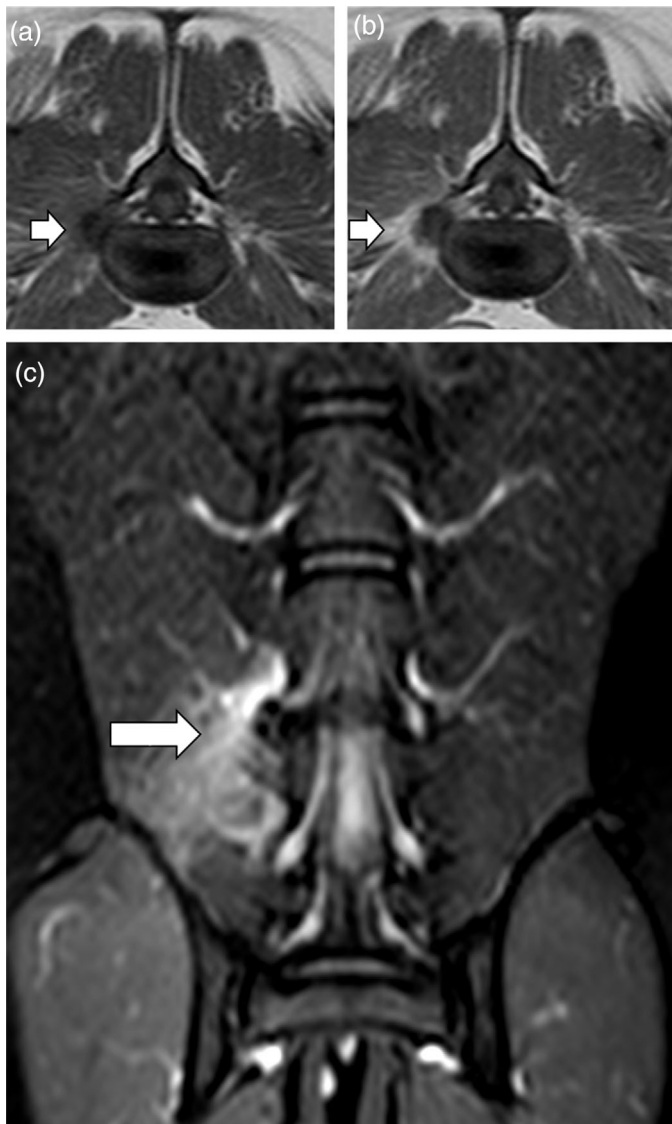


FIGURE 2 (a) Dog 13—T1-weighted transverse image of a dog with a left-sided L6-L7 far lateral disc herniation. (b) Postcontrast T1-weighted transverse image of the same dog showing nerve root and perilesional contrast enhancement (arrow). (c) Dog 12—short tau inversion recovery (STIR) dorsal image of another dog revealing right-sided hyperintensity of the epaxial musculature adjacent to the herniated disc material at L5-L6 (arrow)

and bilaterally in one case. Patellar reflex was reduced in 24% (9/38) and absent in one case. Half of the cases with abnormal patellar reflex (5/10) also had abnormal withdrawal reflex. In all unilaterally affected cases the side of the deficit was the same as the herniation. Unilateral pelvic limb paresis was observed in 21% of cases (8/38), pelvic limb ataxia in 13% (5/38) and paraparesis in 11% (4/38). Concurrent relevant or previously diagnosed diseases were documented in eight dogs as follows: hip osteoarthritis (two), previous thoracolumbar disc extrusions at another site treated surgically or medically (two), resolved undiagnosed back pain (three), chronic neck pain secondary to cervical intervertebral disc protrusion (one).

Diagnostic imaging

A total of 38 foraminal and/or far lateral intervertebral disc herniations were documented. They were at the level of intervertebral disc spaces L5-L6 in 50% (19/38), L6-L7 in 37% (14/38), T12-T13 in 5% (2/38), L1-L2 in 5% (2/38) and L4-L5 in 3% (1/38). They were right sided in 50% (19/38) and left sided in 50% (19/38). In 42% of cases, herniations were defined as both far

lateral and foraminal (16/38). In the remaining cases, 34% were far lateral (13/38) and 24% were foraminal (Figure 1). Degree of intervertebral disc degeneration of the affected sites assessed with use of the Pfirrmann grading system was four in 84% (32/38) and three in the remaining 16% of cases (6/38). Nerve root enlargement was observed in 89% (34/38) of cases. T1W post-gadolinium administration sequences were acquired in 19 cases. In all but one (95%), contrast enhancement was observed. Both nerve root and perilesional contrast enhancement were seen in 63% (12/19) (Figure 2a,b), perilesional enhancement alone in 16% (3/19) and nerve root enhancement exclusively in 16% (3/19). Dorsal STIR sequences were obtained in 23 cases. In 57% (13/23), hyperintensity of the epaxial musculature was observed (Figure 2c).

Radiography was performed in 12 cases. In 11 cases, there was evidence of calcification in the region of the herniated intervertebral disc, six had mineral opacification at the level of the intervertebral foramen, in five there was presence of mineralised material lateral to and/or at the level of the foramen (Figure 3a,b), and two had narrowing of the affected intervertebral disc space. CT was available in two cases. There was evi-

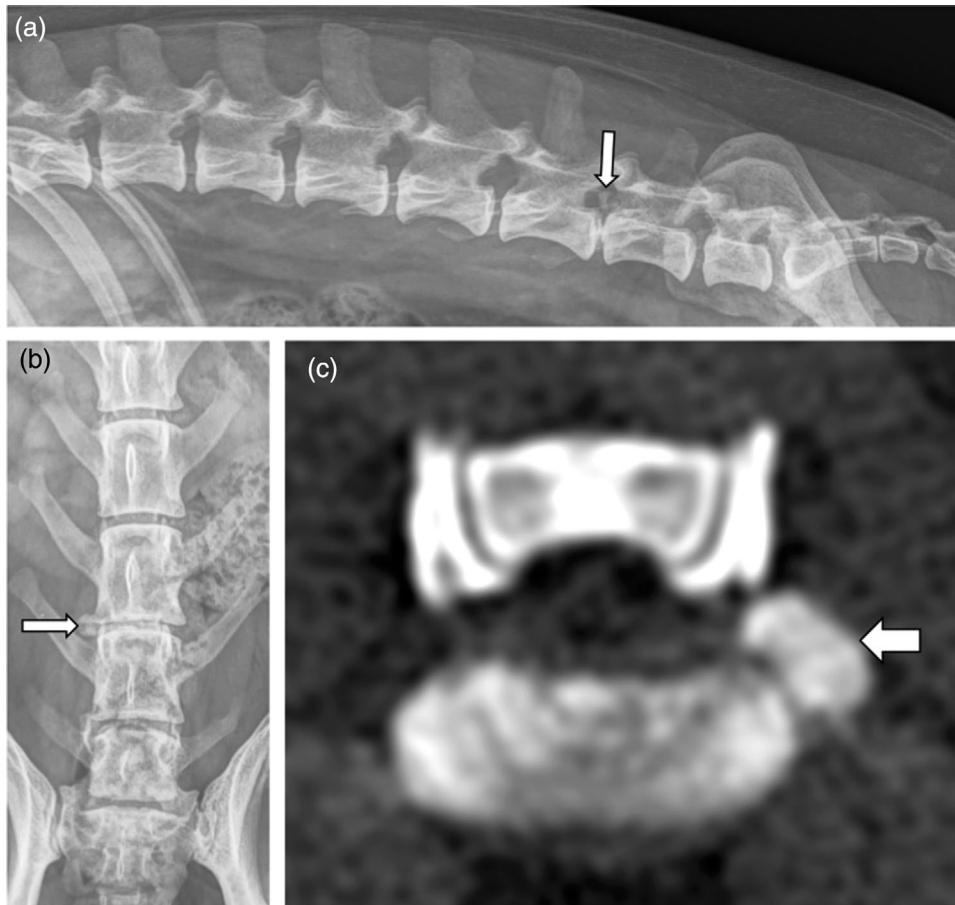


FIGURE 3 Radiographs and CT of the lumbar spine. (a) Dog 12—latero-lateral view showing mineral opacity and narrowing of the L5-L6 intervertebral disc space with mineral opacification of the right foramen (arrow). (b) Ventro-dorsal view of the same dog demonstrating mineral opacity lateral to the foramen (arrow). (c) Dog 7—CT transverse image at the level of L6-L7 showing calcified disc material in and outside of the right foramen (arrow)

dence of intra and/or extraforaminal calcified material in both (Figure 3c).

Treatment and outcome

Thirty-eight percent of cases were treated conservatively (15/38), all with gabapentin. Of these, 53% were additionally treated with NSAIDs (8/15) and 33% with prednisolone (5/15). Sixty-one percent of cases were treated surgically (23/38). All of these either failed to respond to conservative treatment or had recurrence of clinical signs following medical treatment. Hemilaminectomy was performed in 52% (12/23). In half of these it was performed alone (6/12), in four in combination with fenestration, one combined with corpectomy and one with foraminotomy. Nerve root decompression without bone drilling was performed in 26% of cases (6/23), in half of these alone. Foraminotomy was performed in 22% of cases (5/23). Information on medication regimen for surgically treated animals was available in 22 cases. Ninety-one percent were treated with gabapentin (20/22) and 77% were treated with NSAIDs (17/22). In 23% of cases a fentanyl patch was applied (5/22) and 14% were treated with prednisolone (3/22).

Short-term outcome information was available in 18 cases. Median time of follow-up assessment was 30 days (range 14–90 days). Of the medically treated cases (four), outcome was good in three and excellent in one. Of the surgically treated cases (14), outcome was good in eight and excellent in six. Recurrence of clinical signs was reported 3 months following initial diagnosis and once the dog was off medication in one of the cases treated medically. MRI revealed a foraminal intervertebral disc extrusion at a different site than the previously documented one, so the case was re-enrolled in the study.

Long-term outcome information was available in 31 dogs. In 25, this was obtained via standardised questionnaire answered by the owners. In the remaining ones, outcome was assessed via re-examination at the referral centre, the referring veterinarian, or examination of the animals' medical records. Eight dogs had died at the time of outcome assessment. Median time of follow-up assessment was 36 months (range 3–108 months). Overall outcome was considered excellent in 77% of dogs (24/31) and good in 16% (5/31). Of the surgically treated cases (21), 86% (18/21) had an excellent outcome and 10% (2/21) had a good outcome. The remaining case had intermittent episodes of back pain and pelvic limb lameness

responding to pain relief and crate resting. This animal had also been previously diagnosed with bilateral luxating patellae. Of the medically treated cases (10), 70% (7/10) and 20% (2/10) had an excellent and good outcome, respectively. In the other dog treated medically, daily elbow and hip pain and lameness were documented. This dog suffered from bilateral elbow and hip osteoarthritis for which it received gabapentin and amantadine.

A summary of the signalment, clinical signs, lesion localisation, treatment and long-term outcome of each dog is presented in Supplementary Table 1.

DISCUSSION

In the present study, sex and age appear to have similar distribution to that of previous reports of thoracolumbar intervertebral disc herniations in dogs.¹⁹ Breed mostly follows the same trend, except for the fact that mixed breed dogs were among the most affected groups. Although specific lineage information was not available for the population of mixed breed dogs included in this study, the authors hypothesise that this may be due to the increasing popularity of hybrid breeds deriving from the crossing of chondrodystrophic and other breeds predisposed to developing intervertebral disc herniations. The small sample size may equally account for this finding.

All cases presented with pelvic limb lameness or pain (signs consistent with nerve root signature), 63% of them showing both concomitantly, which is in agreement with findings of previous case reports.^{5,9} Interestingly, in 24% of cases pain or lameness were the only clinical examination findings, with the remaining showing more specific neurological deficits such as segmental spinal reflex abnormalities, postural reaction deficits, ataxia or paresis. This highlights the importance of a thorough neurological and orthopaedic examination in patients presenting with pelvic limb lameness, back or hip pain. Bilateral postural reaction abnormalities were seen in 18% of cases. None of these was more severe on the affected side than on the contralateral one. Although the reason behind this is still unclear, in human literature it has been hypothesised that traction forces to the contralateral nerve root secondary to extrusion in lateralised herniations may be the cause of contralateral signs.²⁰ The possibility of these bilateral deficits being secondary to previous intervertebral disc herniations not visible on imaging studies performed cannot equally be excluded.

The majority of intervertebral disc herniations in our population occurred at the level of L5-L6 or L6-L7. This finding is similar to what is described in foraminal and far lateral intervertebral disc herniations in humans, which also appear to more commonly occur at the lower lumbar level.²¹ The authors hypothesise that, in this region, foraminal and far lateral herniations will often cause more noticeable signs of lameness than those in a more cranial loca-

tion, which will be more likely to be noticed by the owners. Additionally, morphometric studies of the intervertebral disc in Dachshunds have demonstrated that the dorsal portion of the annulus fibrosus between T10 and L1 is thinner than in the caudal lumbar intervertebral discs, while the thickness of the lateral portion remains constant throughout the thoracolumbar spine.⁵ This may equally account for the higher number of foraminal and far lateral caudal lumbar intervertebral disc herniations observed in our population. In most cases in which STIR sequences were obtained, some degree of perilesional or nerve root hyperintensity was seen. Additionally, nerve root or perilesional contrast enhancement was observed in all but one case in which gadolinium was administered. Contrast enhancement is believed to be due to the herniated disc material mimicking a soft tissue mass and secondary to the compression and inflammation of the nerve root.²² The use of STIR sequences and administration of gadolinium was considered helpful by the observers, particularly in more discrete herniations. The authors therefore suggest the use of a dorsal STIR, T1W post-gadolinium administration at the level of the intervertebral disc and foramen, or a three-dimensional reconstruction technique, in cases where clinical signs compatible with a foraminal or far lateral disc herniation. Although MRI is a more sensitive and specific method to identify nerve root compression, in its absence radiography and CT may be valuable tools in identifying or suspecting foraminal and far lateral herniations in dogs, especially if the herniated disc material is mineralised.

Regarding the influence of severity of neurological deficits on the choice of surgical versus medical treatment, 61% of dogs with pain and/or lameness as only clinical signs were treated surgically, and the remaining 39% medically. Out of dogs with more severe neurological deficits such as paresis or ataxia, 60% underwent surgery and the remaining 40% was treated conservatively. It therefore appears that the presence of these neurological signs did not influence choice of treatment in this population of dogs.

In most cases, a combination of two or more surgical procedures was performed. This was not only due to surgeon preference, but also because of the characteristics of these intervertebral disc herniations. In cases in which foraminal involvement was observed, osteotomy procedures (hemilaminectomy, foraminotomy, corpectomy) were required for decompression, whereas in some cases in which the extruded disc material was in a far lateral location, nerve root decompression was deemed more appropriate and there was no need for bone drilling. Hemilaminectomy was performed in a relatively large proportion of cases with foraminal intervertebral disc herniations. Although if extended to the level of the foramen this may provide adequate exposure for decompression, a foraminotomy might have been a more appropriate technique to address this type of herniation. Interestingly, 68% of intervertebral disc herniations that affected the intervertebral foramen were treated

surgically, versus 46% of the strictly far lateral intervertebral disc herniations. This finding might suggest that a larger proportion of intervertebral foraminal herniations may require surgical treatment, when compared to far lateral herniations.

All cases in which outcome information was available had a good to excellent short-term outcome for both surgically and medically treated herniations at a median of 30 days after discharge. Eighty-six percent and 70% of surgically and medically treated dogs, respectively, had an excellent long-term outcome. The remaining cases had a good outcome, except for two dogs that although overall improved following treatment, had lameness and pain suspected to be secondary to orthopaedic disease. Both dogs were deemed by the owners to have a good quality of life. An even greater variety of surgical procedures to treat foraminal and far lateral herniations than those described in this study has been reported in the human literature. The rate of good to excellent outcome in humans following surgery ranges from 68% to 91%,²¹ which is similar to this study (95%). When it comes to conservative management, human studies have reported a success rate ranging from 10% to 71%,²¹ which appears lower than that reported in this study (90%).

Considering the small sample size, the fact that surgical and medical treatment protocols were not standardised due to the retrospective nature of the study, the clinical presentation of surgically and medically treated dogs differed, and that all surgically treated animals underwent various types of medical management before surgery, it was not deemed appropriate to perform statistical comparisons between surgically and conservatively treated animals in this study. Overall, long-term outcome was considered good or excellent in 93% of dogs, which leads the authors to believe this presentation of thoracolumbar intervertebral disc herniation appears to be associated with a favourable prognosis.

This study was hampered by several limitations, mostly those inherent to its retrospective and observational nature. Long-term outcome was, in most cases, assessed via a standardised questionnaire answered by the owners, which is a subjective tool. The use of objective and validated outcome assessment measures would have been preferable. Additionally, long-term outcome information was only available in 84% of dogs. This was mostly due to ethics and welfare committee guidelines which dictated only owners of animals alive at the time of outcome assessment were contacted. Treatment choice was also clinician dependent, which is a source of selection bias. Finally, all included cases were seen at referral centres, which may have skewed the population towards more severe presentations that did not respond to initial medical management.

In conclusion, most dogs in the present study had a good to excellent outcome following medical or surgical treatment. Considering that most cases presented with at least one neurological examination abnormality besides lameness and back or hip pain, this study

reinforces the need for neurological examination and cross-sectional advance imaging in dogs presenting with pelvic limb lameness or lumbar or hip pain, without an obvious orthopaedic cause. Further studies with higher number of cases and prospective and standardised treatment and outcome assessment methodologies are required to compare the results of conservative and surgical management of foraminal and far lateral intervertebral disc herniations in dogs.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

Conceptualisation: Sara Silva, Julien Guevar and Rodrigo Gutierrez-Quintana. *Methodology:* Sara Silva, Julien Guevar and Rodrigo Gutierrez-Quintana. *Data collection:* Sara Silva, Julien Guevar, Roberto José-López, Steven De Decker, Josep Brocal, Cristian de la Fuente, Alexane Durand, Franck Forterre, Natasha Olby and Rodrigo Gutierrez-Quintana. *Writing original draft:* Sara Silva and Rodrigo Gutierrez-Quintana. *Writing review and editing:* Sara Silva, Julien Guevar, Roberto José-López, Steven De Decker, Josep Brocal, Cristian de la Fuente, Alexane Durand, Franck Forterre, Natasha Olby and Rodrigo Gutierrez-Quintana. All authors have read and agreed to the publish version of the manuscript.

ETHICS STATEMENT

The study was reviewed and approved by the Research Ethics Committee of the School of Veterinary Medicine of the University of Glasgow (application EA16/19).


DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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