UNIVERSIDADE FEDERAL DO PARANÁ

FERNANDO SWIECH BACH

CLINICAL AND SURGICAL STUDIES OF SELECTED CANINE CENTRAL NERVOUS SYSTEM DISEASES – CERVICAL DISC HERNIATION AND MENINGOENCEPHALOMYELITIS

CURITIBA
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CLINICAL AND SURGICAL STUDIES OF SELECTED CANINE CENTRAL NERVOUS SYSTEM DISEASES – CERVICAL DISC HERNIATION AND MENINGOENCEPHALOMYELITIS

Tese apresentada ao curso de Pósgraduação em Ciências Veterinárias, Setor de Ciências Agrárias, Universidade Federal do Paraná, como requisito parcialà obtenção do título de Doutor.

Orientador: Prof. Dr. Fabiano MontianiFerreira.

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TERMO DE APROVAÇÃO

Os membros da Banca Examinadora designada pelo Colegiado do Programa de Pós-Graduação CIÊNCIAS VETERINÁRIAS da Universidade Federal do Paraná foram convocados para realizar a arguição da tese de Doutorado de FERNANDO SWIECH BACH intitulada: CLINICAL AND SURGICAL STUDIES OF SELECTED CANINE CENTRAL NERVOUS SYSTEM DISEASES - CERVICAL DISC HERNIATION AND MENINGOENCEPHALOMYELITIS. Sob orientação do Prof. Dr FABIANO MONTIANI FERREIRA, que após terem inquirido o aluno e realizada a avaliação do trabalho, são de parecer pela sua APROVAÇÃO no rito de defesa.

A outorga do título de doutor está sujeita à homologação pelo colegiado, ao atendimento de todas as indicações e correções solicitadas pela banca e ao pleno atendimento das demandas regimentais do Programa de Pós-Graduação.

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RESUMO

A presente tese compreende dois capítulos, cada qual composto por um artigo cientifico distinto. Tais capítulos englobam temas relevantes da neurológica veterinária. Os dois estudos foram realizados pelo autor e orientador, por meio de pacientes oriundos do serviço de neurologia do hospital veterinário CLINIVET. O primeiro artigo cientifico denominado “Clinical Outcome After Ventral Slot Decompression for Cervical Disc Extrusion In 57 Dogs. An Analysis of Association Between Spinal Cord Compression Ratio in Magnetic resonance imaging, Initial Neurological StatusGrade and Recovery After Surgery” este capítulo apresenta 5 objetivos principais para tentar responder questões ainda não bem esclarecidas e tem resultados inéditos que podem auxiliar os médicos veterinários que atuam na área da neurologia. O segundo capítulo possui o artigo cientifico denominado “An Etiological Study Of Presuntive Meningoencephalomyelitis In Dogs With Cerebral Spinal Fluid (Csf) Analysis And Neurological Panel (Pcr) Of 194 Cases” que tem como objetivo principal determinar a porcentagem de cães com meningoencefalites infecciosas e auto-imunes em Curitiba, Paraná, Brazil, também auxiliando do ponto de vista epidemiológico médicos veterinários que trabalham na área de neurologia.

Palavras-chaves: Neurologia, hérnia de disco, slot ventral, ressonância magnética, meningoencefalite, liquor.

ABSTRACT

The present thesis encompasses two different chapters. Each one of these chapters comprises a distinct scientific manuscript, bringing relevant information about the veterinary neurology field. The two studies were carried out by the author and advisor through patients from the neurology service of the CLINIVET veterinary hospital. The first scientific paper called “Clinical Outcome After Ventral Slot Decompression for Cervical Disc Extrusion In 57 Dogs. An Analysis of Association Between Spinal Cord Compression Ratio in Magnetic resonance imaging, Initial Neurological Status Grade and Recovery After Surgery” this chapter has 5 main objectives to try to answer questions that are not yet well clarified and has unprecedented results that can help veterinarians working in the area of neurology. The second chapter has the scientific article called “An Etiological Study of Presumptive Meningoencephalitis in Dogs with Cerebrospinal Fluid (CSF) Analysis and Neurological PCR Panel of 194 Cases” whose main objective is to determine the percentage of dogs with infectious and autonomic meningoencephalitis. -immune in Curitiba, Paraná, Brazil, also helping from the epidemiological point of view veterinarians working in the neurology field.

Keywords: Neurology, herniated disc, ventral slot, magnetic resonance imaging, meningoencephalitis, cerebrospinal fluid.

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SUMMARY

1 CHAPTER1: CLINICAL OUTCOME AFTER VENTRAL SLOT DECOMPRESSION FOR CERVICAL DISC EXTRUSION IN 57 DOGS. AN ANALYSIS OF ASSOCIATION BETWEEN SPINAL CORD COMPRESSION RATIO IN MAGNETIC RESONANCE IMAGING, INITIAL NEUROLOGICAL STATUS GRADE AND RECOVERY AFTER SURGERY

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Keywords: Cervical Herniation, Intervertebral Disc Disease, Extrusion, Ventral Slot, Surgery (Min.5-Max. 8)

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1.1 Abstract

The primary aims of this study were to evaluate transverse images obtained from magnetic resonance imaging (MRI) of dogs with cervical intervertebral disc extrusion before being submitted to ventral slot surgical decompression (VSD). Dogs were re-evaluated systematically at 10 and 30 days after surgery. We investigated the association between: 1) Spinal cord compression ratio (SCCR) and pre-surgical Neurological Status (NS) grade; 2) NS grade and postoperative recovery; 3) SCCR and postoperative recovery. Our original hypotheses were: 1) Dogs with greater SCCR will have higher pre-surgical NS grades; 2) Higher pre-surgical NS grade will have longer postoperative recovery time; 3) Higher SCCR will have longer postoperative recovery time. The secondary aims were: 4) Compare NS grades and recovery times between dogs with cranial and caudal cervical disc herniations and 5) Compare the length of cerebral spinal fluid (CSF) attenuation on HASTE images with NS grade and recovery time. Our original hypotheses were: 4) Dogs with caudal cervical disc herniations will have higher NS grade and longer recovery time; 5) Dogs with longer HASTE CSF attenuation will have higher NS grade and longer time to recovery.

Of the 57 dogs subjected to VSD, 44/57 dogs (77.19%) showed complete clinical recovery within 10 days, 9/57dogs (15.79%) showed complete recovery within 30 days, 3/57 (5.26%) improved the NS but grade did not make a full recovery and 1/57 (1.76%) had no improvement in NS grade.

The lack of strong association between SCCR and NS grade suggests that this relationship in the cervical region is similar to what is observed in the thoracolumbar region, rejecting our first hypothesis. Dogs with NS grades 1-2-3 recovered overall faster than those with NS grade 4, accepting our second hypothesis. There was no correlation between SCCR derived from MRI transverse images and recovery time, rejecting our third hypothesis. Caudal cervical herniation did not show higher NS grade or longer recovery time than cranial herniation, rejecting our fourth hypothesis. CSF attenuation length ratio on HASTE images was not significantly correlated with NS grade but may weakly correlate with post-surgical recovery time, only partially accepting our fifth hypothesis.

1.2 Introduction

Intervertebral disc herniation (IDH) is the main cause of spinal cord compression in dogs, with the cervical region being affected in approximately 15% of cases (1). According to the literature, the most commonly affected spaces in the cervical region are C2-C3 and C3-C4 (1). Small dogs, mainly chondrodystrophic, are predisposed to degenerative intervertebral disc disease (IVDD) followed by herniation and spinal cord compression (2). The amount of herniated disc material, the force of the extrusion and duration of compression are factors that may contribute to the severity of neurological deficits (1). Any breed can be affected; however, the disease is more prevalent in Dachshunds, followed by Lhasa Apsos, Shi tzus, Beagles and French Bulldogs (2). Most commonly, the affected dogs are older than two years of age (2). Currently, IVDD is subdivided as: 1) Extrusion of the intervertebral disc (Hansen type 1, acute); 2) Acute intervertebral disc extrusion with extensive epidural hemorrhage; 3) Protrusion of the intervertebral disc (Hansen type 2, chronic); 4) Acute non-compressive nucleus pulposus extrusion; 5) Hydrated nucleus pulposus extrusion; 6) Intradural/intramedullary intervertebral disc extrusion; 7) Traumatic intervertebral disc extrusion. The term disc herniation also can be used and interpreted as disc material exerting some degree of spinal compression(3). Hyperesthesia is the most common clinical sign in cervical disc herniation; tetraplegia is less frequent compared to paraplegia in thoracolumbar disc herniation, possibly to the larger diameter of the vertebral canal in the cervical region (4). NS grade for cervical spinal cord injury ranges from cervical pain to tetraplegia, with neurogenic respiratory failure (Table 1) (5-6).

The diagnostic imaging modality considered the “gold standard” for disc herniation is magnetic

resonance imaging (MRI), as it can distinguish anatomical structures such as nerve roots, spinal cord parenchyma, epidural fat, cerebrospinal fluid and intervertebral disc layers (7). Ventral slot decompression (VSD) is the most widely used surgical treatment for ventral cervical disc herniation in dogs and has a good long-term prognosis (8). Risks related to this technique include hemorrhage, cardiac arrhythmias, cardiopulmonary arrest, aspiration pneumonia, spinal instability, and damage to adjacent structures such as the esophagus, trachea, vagosympathetic trunk and laryngeal recurrent nerve (8). The mortality rate for VSD in cervical herniation is around 8%, with a poor prognostic factor being preoperative non-ambulatory tetraparesis (8-9).

There are no well-defined guidelines for classifying the severity of spinal cord compression on cross-sectional images; however, several studies have used some form of classification using spinal cord compression ratios (SCCR), especially in caudal cervical spondylomyelopathy (10–11). Other authors have described cutoff points for the severity of compression such as mild compression, when less than 25% of the vertebral canal's cross-sectional area is occupied by compressive material; moderate compression, from 25% to 50%; and severe compression, when greater than 50% (12). To the authors' knowledge, there are no previous study using a similar scale for cervical disc extrusion and evaluating potential association with pre-surgical NS grade and post-surgical recovery. There still are uncertainties regarding the associations between NS grade and SCCR, NS grade and postoperative recovery, SCCR and postoperative recovery. In a study including 33 dogs with cervical disc extrusion, Ryan et al (2008) found correlation between pre-surgical NS grade and size of spinal compression (16). However, they found no correlation between spinal cord compression size and recovery. Da Costa et al studied cervical caudal myelopathy and did not find correlation between size of compression and NS grade (11).

In contrast to previous reports (13), we have the clinical impression that there is no association between degree of compression in cervical disc extrusion and neurologic status grade at presentation.

Such association was not found for thoracolumbar disc herniation, and the authors underscored the importance of other factors not reflected by the degree of physical compression, such as spinal cord contusion (14).

Several veterinary texts, citing work by Waters et al. (15), state that cranial cervical disc herniation show better outcome than caudal cervical herniations, but this has not been our clinical impression and there are still uncertainties as to whether this is true.

Finally, there are few studies showing the prognostic factors of CSF attenuation length measured on HASTE pulse sequence in dogs with thoracolumbar disc herniation (16). To the authors' knowledge, there is no veterinary study looking at this in dogs with cervical disc herniation.

The primary objectives of this article are to investigate the associations among the following parameters in a large group of dogs with cervical disc herniation treated by VSD: 1) The maximal SCCR (as seen on transverse MRI images) and pre-surgical NS grade; we hypothesized that dogs with greater SCCR will have higher NS grades at presentation; 2) NS grade and postoperative recovery; we hypothesized that higher cervical NS grade will influence postoperative recovery time; 3) SCCR and postoperative recovery; we hypothesized that dogs with higher SCCR will have longer recovery time. The secondary objectives are: 4) Compare outcomes between cranial and caudal cervical disc herniations; we hypothesized that caudal cervical herniation will have longer time to recovery; 5) Compare ventral longitudinal extension of CSF signal loss on HASTE pulse sequence with NS grade and time to recovery; we hypothesized that longer HASTE CSF attenuation will have higher NS grade and longer time to recovery.

1.3 Materials and Methods

1.3.1 Inclusion criteria

The database of the neurology service at Clinivet Veterinary Hospital, Curitiba-PR, Brazil was searched over a period of four years (2017 to 2021) for dogs that presented with clinical signs of cervical spine dysfunction. Dogs were included if: (1) cervical disc herniation was confirmed with MRI, (2) spinal cord decompression by ventral slot surgery was performed within a maximum of two weeks after onset of clinical signs, and (3) clinical follow-up was available at 10 and 30 days after surgery. In dogs older than seven years of age, the preoperative work-up included thoracic radiographs and abdominal ultrasonography to rule out potential concomitant diseases that could contribute to poor patient recovery after spinal surgery. All included animals were deemed healthy enough to undergo VSD, with complete blood count and blood chemistry (including glucose, urea, creatinine, albumin, and alanine aminotransferase levels).

1.3.2 Clinical evaluation and data collection

The cervical NS grade of each included patient was quantified using a grading system (0-5) previously described (5,6) and is available in Table 1. A single observer (FB) determined the pre- and post- surgical NS grade. Additional data collected from the medical records included breed, sex, age. Prospective review of the MRI images (see below) was conducted to record affected cervical intervertebral discs, size of herniation, and length of CSF signal loss on HASTE pulse sequence.

Neurologic Status Grade	Clinical signs
1	Neck pain, hyperesthesia, walking with head down, vocalization.
2	Ambulatory tetraparesis. Mild motor deficit or ataxia in the 4 limbs.
3	Ambulatory tetraparesis. Moderate motor deficit or ataxia in the 4 limbs.
4	Non-ambulatory tetraparesis or tetraplegia. Not walking.
5	Tetraplegia. Not walking and neurogenic hypoventilation.

Table 1 - Classification of neurological status grade based on clinical signs

1.3.3 Imaging techniques and morphometric measurements.

The diagnosis of cervical disc herniation was confirmed by MRI (1.5 Tesla Avanto, Siemens, Erlangen, Germany), performed with patients anesthetized using intravenous propofol (B.Braun, Melsungen, Germany) at 6 mg/kg and placed in dorsal recumbency. The anesthesiologist stayed in the exam room to administer propofol as needed, based on respiratory frequency, heart rate, and palpebral reflex, until the end of MRI exam. Each exam took around 25 minutes to be completed. Pulse sequences included were sagittal plane T1-weighted, T2-weighted, HASTE, STIR, transverse plane T2-weighted, dorsal plane STIR and sagittal/transverse plane post-contrast T1-weighted with fat suppression after administration of intravenous paramagnetic contrast medium (gadoteridol - 0.5 mmol/ml, ProHance Bracco imaging, Germany) at a dose of 0.1 mmol/kg. All MRI exams were performed in a human hospital.

Measurements of SCCR was performed using transverse T2-weighted images at the level of the spinal cord compression and were performed using the region of interest and surface area tool of a DICOM viewer (Horos for OS X, version 3 - LGPL-3.0). To determine the SCCR, the surface area of the non-compressed spinal cord at

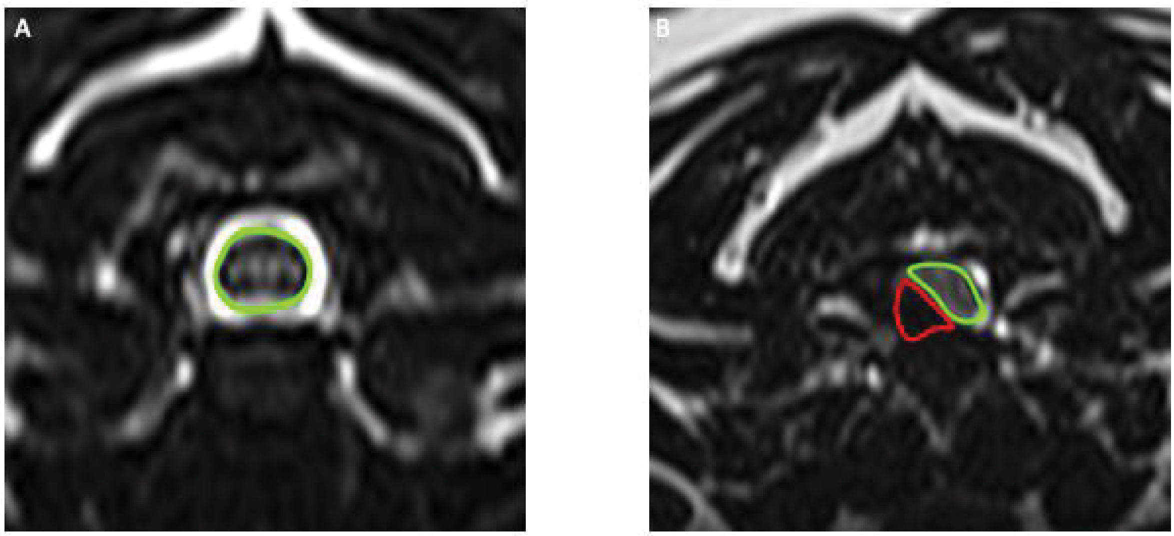

Figure 1 - A) T2-weighted transverse MRI of the cervical spine of a dog, with the uncompressed spinal cord highlighted in green. B) T2-weighted transverse MRI of the compressed spinal cord (green) and extradural disc material (red) in a dog with intervertebral disc extrusion.

the disc space cranial to the compression site was measured as well as the surface area of the cord at the site of maximal compression, determined by visual assessment scrolling through the image series (Figure 1). The exact SCCR was then computed using the formula: SCCR = [(Surface area of non-compressecord – Surface area of compressed cord) / Surface area of non-compressed cord] * 100. The exact SCCR was used to calculate correlations. Each case was also assigned to a categorical score of SCCR: mild compression for SCCR<25%, moderate compression for SCCR >25% and <50% and severe compression for SCCR >50% (12) (Figure 2).

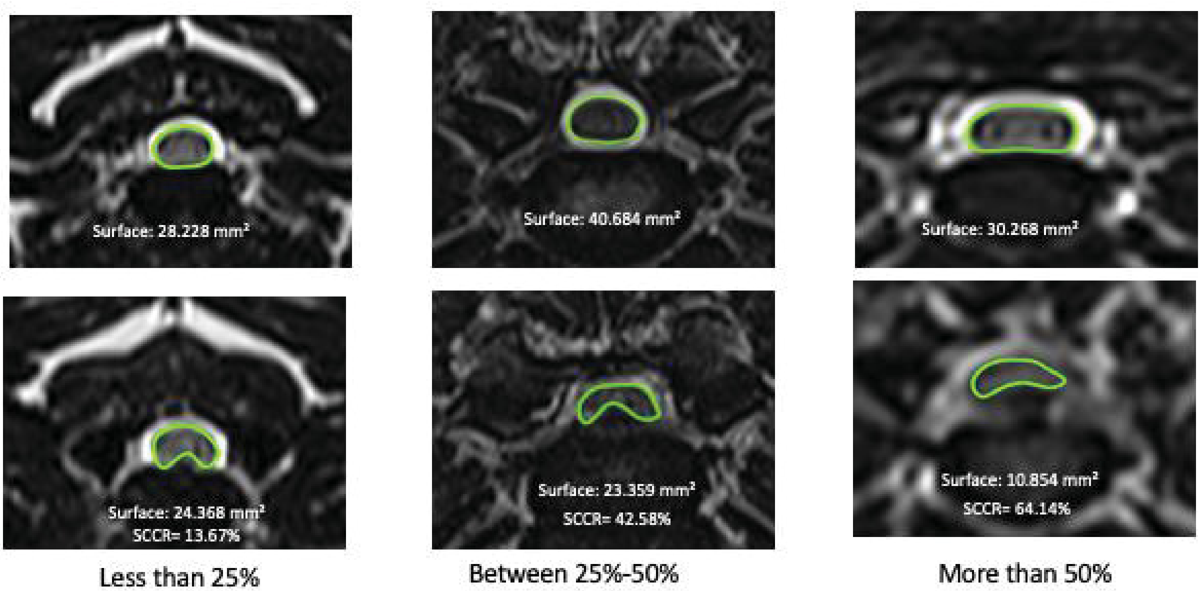

Figure 2 - Examples of Spinal Cord Compression Ratio scores; mild, moderate and severe spinal compression based on measurement of surface area of the spinal cord at site of maximal compression vs normal spinal cord at the disc space cranial to the compression. The top images represent the cranial normal disc space in the same dog with the spinal cord outlined; the images at the bottom are the sites of maximal spinal cord compression with the spinal cord outlined in green.

The HASTE images were evaluated for presence or absence of CSF signal attenuation. When CSF signal attenuation was present, the maximal craniocaudal length of ventral CSF attenuation was measured using the same measurement tool as described above. The length of the C3 vertebral body was measured on sagittal T2-weighted images. A CSF length attenuation ratio was then calculated by dividing the length of CSF attenuation on HASTE by the length of C3 vertebral body (Figure 3).

To avoid interobserver discrepancies, all MRI images were prospectively evaluated by the same examiner (FB).

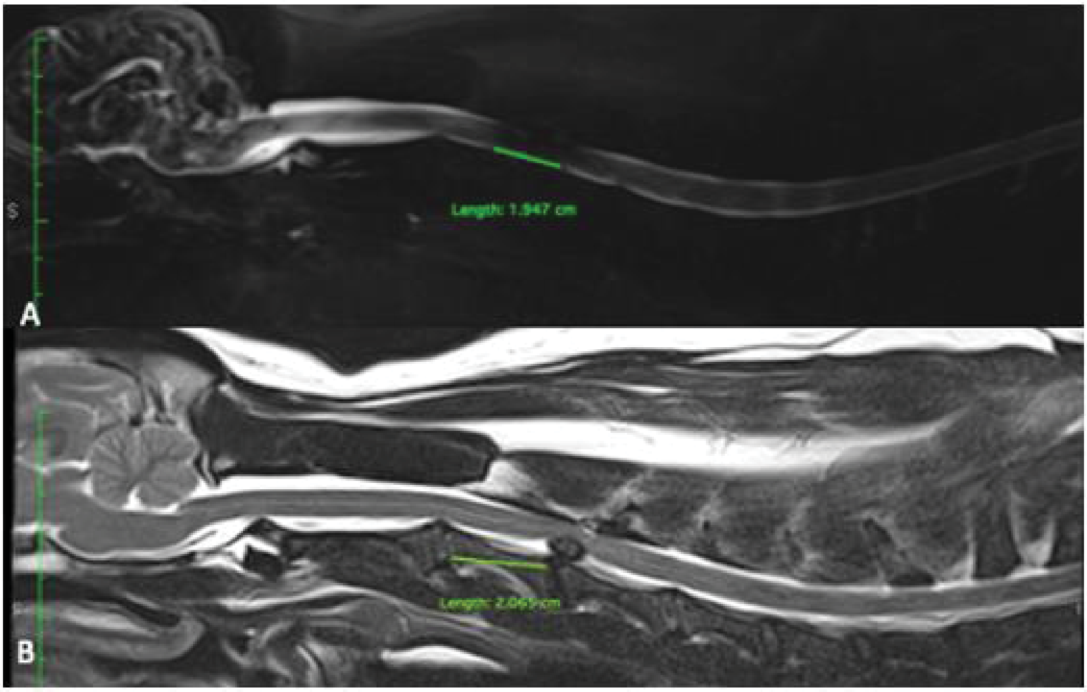

Figure 3 - Measure of spinal cord lesion on HASTE (A) comparing sizes with length of C3 on T2 weight images (B).

1.3.4 Anesthesia and surgical technique

Pre-anesthetic medication varied for each specific patient, but as a basic protocol, intravenous midazolam (0.25 mg/kg) and ketamine hydrochloride (1 mg/kg) were used followed by an intravenous bolus of propofol (5 mg / kg). Anesthesia was maintained using isoflurane as well as a continuous infusion of fentanyl (10 µg/kg/hour). The same surgeon (FB), with substantial neurosurgical experience, performed all surgeries, using the technique described in the literature (17). The patient was positioned in dorsal recumbency, and the neck gently extended under a folded towel, which allows widening of the intervertebral disc spaces. The ventral cervical area was prepared for surgery by clipping the hair and local application of povidone-iodine. A sterile patch (Opsite Incise; Smith and Nephew, London, United Kingdom) was placed over the surgical field. Surgical material used for surgery was standard, including Surgairtome drill, Kerrison forceps, special curettes, burs and absorbable gelatin sponge (Surgifoam, Ethicon, USA). In a few dogs, additional disc fenestrations were performed at disc spaces where severe disc mineralization/dehydration or very minimal disc protrusion were noted on MRI, as a preventative measure to future clinical disc herniation.

1.3.5 Postoperative care and hospital discharge

The dogs were monitored for 48 hours in the hospital's semi-intensive care unit. During this period, analgesia was performed by continuous infusion of fentanyl at a dose of 2 μg/kg/hour. After 24 hours, the infusion was discontinued and analgesia was performed with tramadol hydrochloride and sodium dipyrone subcutaneously at a dose of 3 and 30 mg/kg respectively, every 8 hours, for 5 days. Prophylactic antibiotic therapy was performed by intravenous cephalothin administration at a dose of 30 mg/kg a few minutes before skin incision and every 6 hours on the first postoperative day. Anti-inflammatory drugs were used if dogs showed signs of pain including vocalization, cervical stiffness or head ventroflexion after the surgery. In dogs that were receiving steroidal anti-inflammatory drugs prior to surgery, dexamethasone was administered at a dose 0.1 mg/kg subcutaneously once a day. In dogs that were receiving non-steroidal anti-inflammatory drugs prior to surgery, carprofen was administered at a dose at 2.2 mg/kg subcutaneously once a day. Steroidal and non-steroidal anti-inflammatory drugs were never used in combination.

All dogs remained in individual cages, with controlled room temperature, food and water. Each animal remained two days in the semi-intensive care unit and one day in the regular surgical wards until hospital release. At the time of discharge, owners were instructed to maintain activity restriction, monitor defecation and urination, in addition to light physical therapy exercises in tetraparetic dogs. The dogs were re-evaluated at 10 and 30 days by the same observer (FB) after hospital discharge.

1.4 Statistical analyses

Descriptive and inferential statistical analyses were performed. Spearman's rank-order correlation was used to analyze possible associations between variables (SCCR vs pre-surgical NS grade, SCCR vs recovery time, CSF attenuation length ratio vs NS grade and recovery time). Wilcoxon signed-ranks tests were used to compare overall and pairwise differences, respectively, between non-normally distributed paired data (pre-surgical NS grade, NS grade at 10 and 30 days after surgery, and NS grade difference at 10 and 30 days). In order to increase the statistical power, dogs with ambulatory status (NS grades 1, 2, 3) were grouped and compared with dogs with a non-ambulatory status (NS grade 4) comparing recovery times using Fisher's exact test. Mann-Whitney test was used to compare Ns grade and recovery times between dogs with cranial vs caudal cervical discs. P values < 0.05 were deemed significant.

1.5 Results

A total of 57 dogs fitted the inclusion criteria. The overall median age was 8.39 years (range 3 to 16 years). 31/57 dogs (54.39%) were males and 26/57 (45.61%) were females. There were 18 different breeds; the two most affected breeds were mixed breed 12/57 (21.05%), followed by French bulldog 10/57 (17.54%) (Table 2).

Breed	Number
Mixed-breed dog	12
French Bulldog	10
Dachshund	4
Yorkshire Terrier	4
Beagle	3
Lhasa Apso	3
Shit-tzu	3
Miniature Pincher	3
Rottweiler	3
Pekingese	2
Standart Poodle	2
Miniature Schnauzer	2
Spitz	1
Dobermann Pincher	1
Jack Russel	1
Labrador Retriever	1
Maltese	1
Pug	1
Total	**57**

Table 2 - Distribution of breeds with Cervical Intervertebral Disk Extrusion

The most affected disc space was C3-C4 in 17/57 (29.82%) and C4-C5 in 17/57 (29.82%) followed by C2-C3 in 12/57 (21.05%), C5-C6 in 6/57 (10.52%) and C6-C7 in 5/57 dogs (8.77%) (Figure 4). Slight lateralized disc herniation was observed in 8/57 dogs (14.03%).

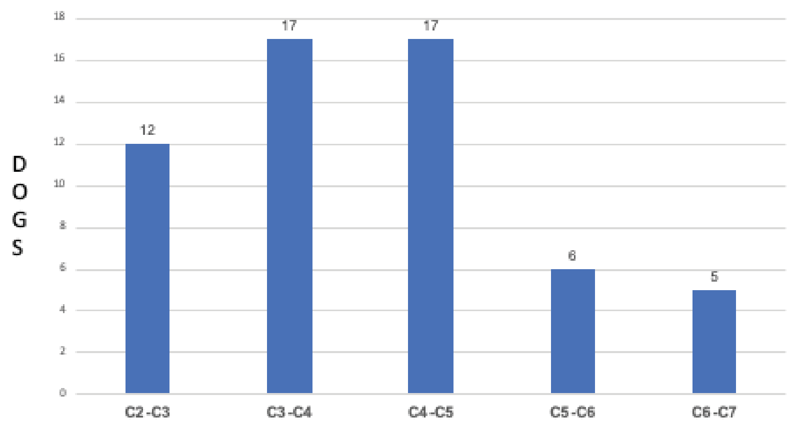

Figure 4 - Distribution of Dogs and Spinal Cord Compression sites.

Of the 57 dogs submitted to VSD, 44/57 dogs (77.19%) showed complete clinical recovery within 10 days, 9/57 dogs (15.79%) showed complete recovery within 30 days, 3/57 (5.26%) had an improved NS grade at 30 days but did not reach full recovery and 1/57 (1.76%) had no improvement in NS grade at the 30 days recheck. Overall, 56/57 dogs (98.24%) had an improved NS grade within 30 days.

Surgery duration was consistently between 60 and 90 minutes. No significant complication (such as hemorrhage requiring transfusion, laryngeal paralysis, severe edema or hematoma in the muscles, subcutaneous tissues or skin around the neck) was observed. Surgical findings correlated with the imaging diagnosis in all cases. Additional disc fenestration was performed in 8/57 dogs (14.03%) at the following disc spaces: C3-C4 (four dogs), C4-C5 (two dogs) and C5-C6 (two dogs). All dogs in this study received a single VSD. No dogs had deterioration of their NS grade after surgery.

There was a weak (r_s 0.24) but non-significant ($p=0.07$) positive correlation between pre-surgical NS grade and SCCR (Figures 5 and 6). At presentation, 32/57 dogs (56.14%) were NS grade 1, 6/57 (10.53%) were grade 2, 5/57 (8.77%) were grade 3, 14/57 (24.56%) were grade 4. Quantitative measurements of spinal cord compression severity by means of the SCCR calculation showed that 3/57 (5.26%) dogs had mild compression (2/3 dogs (66.66%) were NS grade 1 and 1/3 (33.34%) was NS grade 2), 34/57 dogs (59.65%) had moderate compression (22/34 (64.70%) were NS grade 1, 1/34 (2.94%) were NS grade 2, 1/34 (2.94%) were NS grade 3 and 10/34 (29.41%) were NS grade 4). 20/57 dogs (35.09%) had severe compression (8/20 (40%) were NS grade 1, 4/20 (20%) were NS grade 2, 4/20 (20%) were NS grade 3 and 4/20 (20%) were NS grade 4).

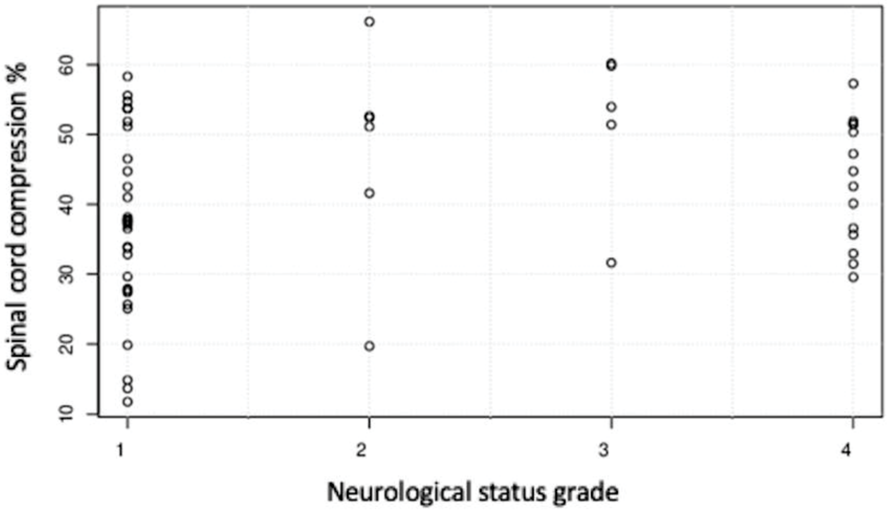

Figure 5 – Relationship between spinal cord compression ratio and the neurological status grade of 57 dogs with cervical intervertebral disc disease before undergoing surgery.

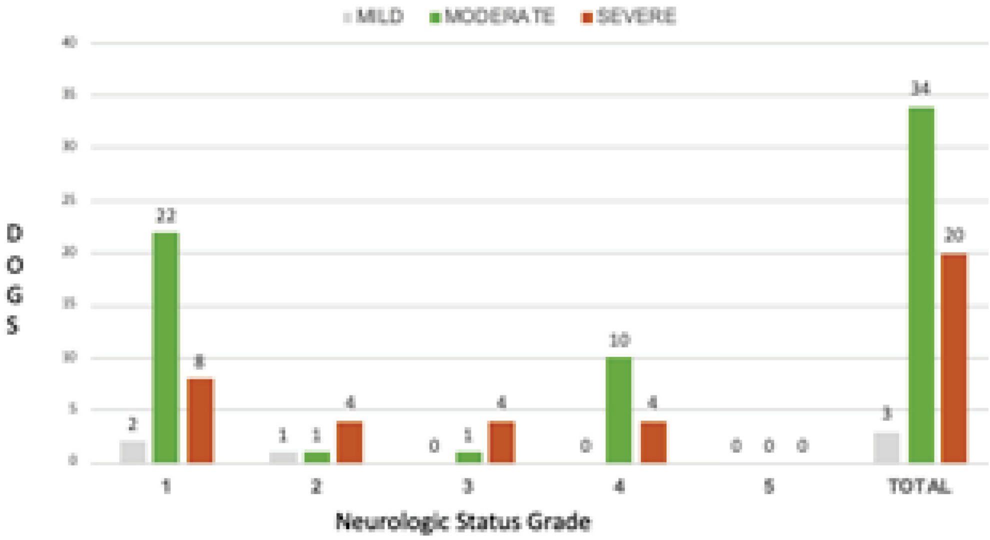

Figure 6 – Distribution of Spinal Cord Compression ratio in each of the NS grades.

There was an overall significant difference (P<0.001) comparing pre-surgical NS grade with NS grade at 10 days and 30 days after surgery) (Figure 7). NS grade at 10 days after surgery and NS grade at 30 days after surgery (P=0.0031). When considering all ambulatory dogs (pre-surgical NS grade 1, 2 and 3), a total of 40/43 dogs (93.02%) recovered in 10 days and 2/43 (4.65%) recovered in 30 days; 1/43 (2.32%) did not completely recover. Regarding non-ambulatory dogs (NS grade 4), 4/14 dogs (28.57%) had full recovery in 10 days and 7/14 dogs (50%) had full recovery in 30 days; 3/14 (21.43%) dogs did not make a complete recovery (two with partial improvement and one with no improvement). There was a statistically significant difference (P< 0.001) in the proportion of dogs that had complete recovery at 10 days vs 30 days in the group of ambulatory dogs (NS grades 1-2-3). There was no statistically significant difference in the proportion of non-ambulatory dogs (NS grade 4) that had complete recovery at 10 days vs 30 days in dogs (P=0.5). This may suggest that dogs with NS grade 4 (non-ambulatory) will need more time to recovery compared with dogs with NS grade 1, 2 and 3 (ambulatory).

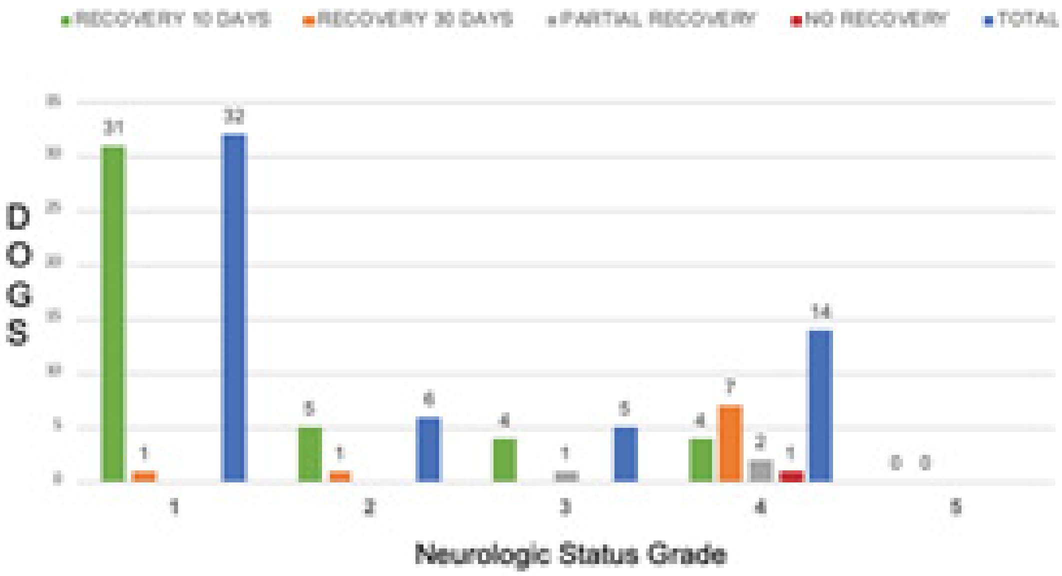

Figure 7 - Distribution of recovery times in each of the NS grades.

There was a negligible (r_s -0.0053) and non-statistically significant (P=0.97) negative correlation between categorical SCCR and post-surgical recovery time at 10 days. There was a negligible (r_s -0.0041) and non-statistically significant (P=0.76) negative correlation between categorical SCCR and post-surgical recovery time at 30 days (Figure 8). SCCR was mild in three dogs, and all (100%) recovered completely in 10 days. Of the 34 dogs that had moderate SCCR, 24/34 (70.59%) had full recovery at 10 days, 7/34 (20.58%) had full recovery at 30 days and 2/32 (5.88%) had an improved NS grade at 30 days but did not achieve full recovery; 1/34 dog (2.95%) had no improvement in NS grade at 30 days. Finally, 20 dogs had severe SCCR; of those, 17/20 (85%) had complete recovery at 10 days after surgery, 2/20 (10%) had complete recovery at 30 days after surgery and only 1/20 (5%) had improved NS grade at 30 days, but still had clinical signs (Figure 8). In all three groups of SCCR, the vast majority of dogs (44/57 or 77.2%) made a complete recovery at 10 days after surgery.

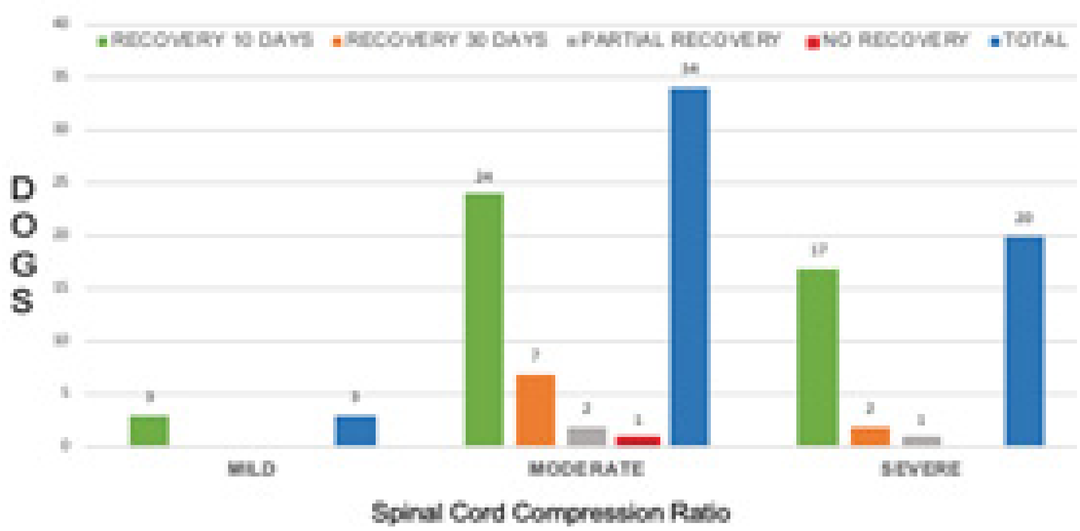

Figure 8 - Distribution of recovery times in each of the Spinal Cord Compression ratios.

Forty-six dogs had VSD in cranial segments (C2-C3, C3-C4 and C4-C5). Of these, 33/46 (71.73%) dogs were NS grade 1, 2 and 3 and 13/46 (28.27%) dogs were NS grade 4. 35/46 dogs (76.08%) had full recovery in 10 days, 8/46 (17.40%) had full recovery in 30 days and 3 dogs did not recover completely. There were 11 dogs with VSD in the caudal cervical spine (C5-C6 and C6-C7). Of these, 10/11 dogs (90.90%) were NS grade 1, 2 and 3 and 1/11 (9.09%) was NS grade 4. Nine of these 11 dogs (81.8%) had full recovery at 10 days and 1 (9.09%) at 30 days; one dog did not have complete recovery at 30 days. There was no significant association between NS grade groups and site of herniation (cranial vs caudal) (P=0.71) (Figure 9). In addition, there was no significant association between recovery time and site of herniation (cranial vs caudal) (P=0.69) (Figure 10).

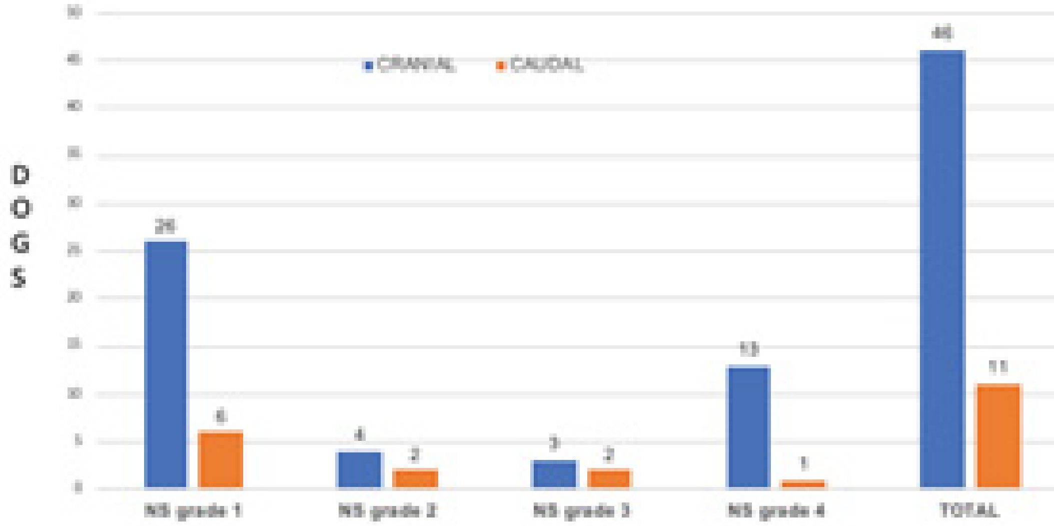

Figure 9 – Distribution of Neurologic Status grade at cranial disc and caudal disc herniations.

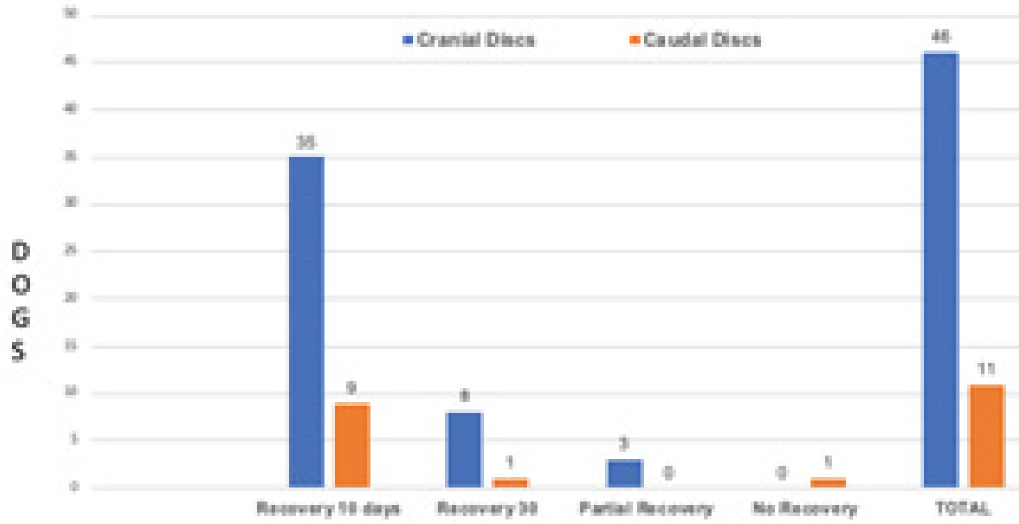

Figure 10 - Distribution of recovery times at cranial disc and caudal disc herniations.

The median CSF length attenuation ratio measured on HASTE images was 0.39 times the length of C3 (range 0.1-0.9). There was a very weak (r_s 0.046) but non statistically significant (P=0.73) correlation with pre NS grade. There was a weak (r_s 0.26) positive correlation with recovery time, with a trend towards statistical significance (P=0.05).

There were three dogs (5.3%) that had only partial improvement in NS grade over the 30-day post-surgical period but did not make a full recovery. One dog had a C2-C3 disc herniation with a moderate SCCR and a CSF attenuation ratio of 0.2 times length of C3. The pre-surgical NS grade was 3 and improved to NS grade 1 at 30 days post-surgery (minimal residual pain). The other two dogs had disc herniation at C3-C4: one had severe, and one had moderate SCCR; both had a CSF attenuation ratio of 0.3 times the length of C3. Both dogs were NS grade 4 before surgery, and at 30 days after surgery, they had NS grades of 3 (dog with severe SCCR) and 2 (dog with moderate SCCR). Hence, both of these dogs regained ambulatory status. Finally, one dog (1.75%) had no post-surgical clinical improvement; this was a 12-year-old Labrador retriever with co-morbidities (diabetes mellitus); this dog had disc herniation at C6-C7 with a NS grade of 4 and lower motor neuron (LMN) signs in the thoracic limbs.

1.6 Discussion

The present study showed that dogs with severe SCCR due to cervical discs herniation presented a great variation regarding clinical signs ranging from neck pain to non-ambulatory tetraparesis. This corroborates findings in the only similar study in the literature (13). Interestingly, our study showed a weak but non-significant correlation between SCCR and pre-surgical NS grade, which was different from the previously cited study (13). Nevertheless, our study showed that none of the patients with NS grade 3 and 4 had spinal compression classified as mild. There was a similar proportion of dogs presenting with NS grade 1 and NS grade 4 that had severe cord compression (25% and 28.57% respectively). Overall, the lack of correlation between compression severity and NS grade likely reflects the fact that other factors contribute to the severity of spinal cord injury, such as degree of spinal cord contusion. A similar amount of compression could be associated with a range of contusive spinal cord injuries, probably dependent upon the mechanical concussive forces exerted during the extrusion event. A comparison between the degree of cervical spinal compression and the relationship with clinical signs was investigated in Dobermans with caudal cervical spondylomyelopathy (CSM) (11). In that study, it was found that clinically normal patients may have severe cervical spinal compressions. In sixteen clinically normal Dobermans, all had some degree of disc protrusion, which was considered mild in 11 dogs, moderate in 2 dogs, and severe in 3 dogs. Remarkably, in that study the degree of spinal compression at MRI was more severe in normal dogs than in those with cervical hyperesthesia or mild ataxia (11). Doberman pinschers affected with CSM usually have chronic spinal cord injury secondary to disc protrusion and hypertrophy of the ligamentum flavum. However, the pathophysiology of CSM is different from spinal injury associated with acute disc extrusion, therefore these findings may not be applicable to dogs with acute disc extrusion. Penning et al. (14) similarly observed no association between the NS grade and SCCR documented with MRI in dogs with thoracolumbar disc extrusion. Once again, this is not surprising, because spinal cord injury following intervertebral disc extrusion is due to a combination of concussive and compressive forces and further complicated by secondary mechanisms of injury (14). Jones and Inzana (18) found severe intervertebral disc changes using CT in the lumbosacral region in five out of six asymptomatic dogs. Overall, these studies and our findings suggest that there is no clear association between degree of compression and observed clinical signs in the cervical, and thoracolumbar regions. Ryan et al. (13) found in 33 dogs that severity of cervical spinal cord compression was significantly correlated with the presurgical NS grade (rs. 0.37 and P=0.04) but not with the postsurgical NS grade. In addition, they found that on cross-sectional images, the median area of spinal cord compression was 26% (varied from 11 to 71%) (13). Our study revealed a weaker correlation between severity of compression and presurgical NS grade (r_s 0.24) and this did not reach statistical significance (P=0.07). Possible explanations for this difference include a larger sample size in our study, and a bigger median area of compression in our study group (41%, range 13-66%).

Our study found that the majority of dogs with NS grade 4 recovered at 30 days while the majority of dogs with NS grade 1, 2 and 3 had a complete recovery at the 10 days recheck. These differences however must be interpreted with caution, since the group of dogs with NS grade 4 was small (14 dogs) compared to dogs with NS grades 1-2-3 (43 dogs). We used the recheck time points of 10- and 30-days post-surgery as these are the time intervals used as standard of care in our hospital (stiches removal at 10 days and last recheck at 30 days before ending cage restriction), and hence these time points were consistently available for data collection in all dogs of our study group. Indeed, some dogs across all NS grades improved completely as early as 1-3 days after surgery. That corroborates others studies that claim that the prognosis after cervical disc surgery is favorable (13,19). Although a previous study suggested that pre-surgical neurologic status were prognostic indicators of outcome, larger and more recent studies do not support these findings (20). Seim and Prata (21) reported post-surgical recovery times in 54 dogs with cervical disc herniations and found complete recovery in 47 of 54 cases after one month. In dogs with only cervical pain (NS Grade 1), 73% recovered in 7 days and 91% recovered in 28 days. In dogs with ambulatory tetraparesis (NS Grade 2 and 3), 71% and 86% recovered at 7 and 28 days respectively. Finally in non-ambulatory dogs (NS Grade 4 and 5), recovery occurred by 7 days in 56% of dogs and by 28 days after surgery in 78%. Waters (15) reported outcomes in 12 non-ambulatory dogs with cervical disc herniation: seven dogs (58%) had complete recovery, two (17%) had partial recovery and three (25%) died or were euthanized. Our outcomes are overall better than reported by these studies, but this may reflect more accurate diagnostic methods (MRI vs radiography) and improved surgical equipment.

In our study, there was no significant association between SCCR and recovery rates at 10 days and 30 days post-surgery. Those findings are similar to the study by Ryan et al (13) in 33 dogs with cervical disc herniation, which found no association between the degree of spinal cord compression and the clinical outcome (13). Similarly, another study in the thoracolumbar spine by Penning et al (14) did not find association between degree of spinal cord compression and surgical outcome. Again, this underscores the fact that other factors than the severity of the compression contribute to the outcome, such as the degree of spinal cord contusion, which is difficult to objectively quantify at MRI.

The most affected space was C3-C4 in 17/57 (29.82%) and C4-C5 in 17/57 (29.82%) followed by C2-C3 in 12/57 (21.08%). This is in agreement with other studies (1, 2, 4) that showed that intervertebral disc disease is more common in the cranial cervical region. Waters' study found that cranial cervical lesions (C2-C3, C3-C4) were associated with greater likelihood of complete recovery than caudal cervical herniations (15). Our study did not find significant differences in post-surgical recovery time between cranial and caudal disc herniation. This corroborates results from a study by Hillman et al (22), which found that site of disc herniation was not a significant predictor of complete recovery and that dogs with cranial cervical disc herniations did not actually have a higher likelihood of complete recovery compared to dogs that had caudal cervical disc herniations. In addition, our study did not find differences in NS grades between dogs with caudal vs cranial cervical disc herniation. This corroborates Cherrone´s study (1) that found no association between intervertebral disc space involved and ambulatory status. Overall, our findings seem to refute the notion that the site of disc herniation are useful predictors of outcome and severity of neurological signs.

One application of HASTE MRI pulse sequence is to obtain a “myelogram effect” on sagittal images, using heavy T2-weighting that highlights the signal from the CSF. This sequence is excellent for a rapid evaluation of the subarachnoid space, and in dogs with acute disc herniation, allows a quick localization of areas of extradural spinal cord compression and/or cord swelling from contusion and edema (12). HASTE pulse sequence was reported to be a potential prognostic tool in dogs with thoracolumbar disc extrusion and found that dogs with longitudinal extension of loss of CSF signal of <7.4 times the length of L2 were less likely to develop progressive myelomalacia (23,25). In our study in dogs with cervical disc herniation, we did not observe a significant correlation of extent of loss of CSF signal on HASTE images with NS grade at presentation and only a weak positive correlation with recovery time. Overall, the length of loss of CSF signal on HASTE observed in our study was much shorter than the one reported by Gilmour et al (24), however only dogs with paraplegia and loss of deep pain perception secondary to thoracolumbar discs herniation were included in that study. Therefore, a direct comparison to the clinical features observed in the group of dogs analyzed here is not possible. The possibly larger diameter of the vertebral canal in the cervical area is the most likely explanation for potential differences in length of CSF attenuation when comparing cervical and thoracolumbar disc herniation using HASTE images.

In this study, chondrodystrophic breeds such as the French bulldog, Dachshund, Lhasa Apso, Shi tzu, Pekingese and Beagle had a high prevalence, together making up 42% of the study group. This is not unexpected as chondrodystrophic breeds are predisposed to disc herniation (2). The average age in our group was 8.4 years, in agreement with previous studies where the mean age of the affected animals was 8.6 years (13).

All 57 dogs had VSD. We performed disc fenestration in 8/57 dogs (14.03%) at the same time as VSD surgery. Although the value of fenestration has been questioned, it should prevent further extrusion of disc material into the vertebral canal thereby reducing the recurrence of compressive myelopathy; it also appears effective in dogs with discogenic pain (17). Fenestration was performed in dehydrated discs (as seen on MRI by complete loss of T2-weigthed signal) or in areas of minimally compressive disc protrusion. These procedures were performed to avoid potential clinically significant herniation and compression in the future. However, it was beyond the scope of this study to evaluate recurrence rate. The choice of disc space to perform the ventral slot was based on the site of the most severe spinal compression observed at neuroimaging. No dogs had more than one VSD in this study. No dog was re-imaged or needed re-intervention in the 30-day post-operative period. The only dog that was not improved was a 12-year-old Labrador with diabetes mellitus that had a SCCR of 41.13%. Ideally, re-imaging this dog would have been indicated but for financial reasons the owner decided to not repeat MRI. This particular dog had a C6-C7 disc herniation and presented with lower motor neuron signs in the thoracic limbs and a NS grade of 4. Lower motor neuron lesions usually carry a worse prognosis than upper motor neuron lesions. However, only 10 other dogs had caudal disc herniation (C5-C6 or C6-C7) and because they had NS grade 1 (n=6), 2 (n=2) or 3 (n=2) with only discrete or moderate motor deficits, an accurate determination of lower vs upper motor neuron lesions was not possible. Therefore, it was not feasible in our study to assess the influence of upper vs lower motor neuron signs on recovery.

Ryan et al. (13) observed 3/33 (9.09%) dogs had deterioration of the NS grade after cervical decompression surgery. In another study of 173 dogs with thoracolumbar disc herniation, Forterre et al. (24) observed clinical deterioration within 1–10 days after hemilaminectomy in 5.8% of cases. We did not observe clinical deterioration in our study. Of the three dogs that had an NS grade improvement but did not show full recovery, two had moderate and one had severe SCCR. Post-surgically, one dog had minimal residual neck pain and two dogs were walking with mild ataxia and were pain-free. Due to financial reasons, no re-imaging procedures were performed to evaluate any remaining disc material. In these dogs, the median CSF length attenuation ratio measured on HASTE images was 0.2-0.3, i.e. lower than the median across all 57 dogs (0.39 times the length of C3).

In the literature, mortality associated with cervical decompressive surgery in dogs ranges from 1% to 25%, with a non-ambulatory preoperative neurologic status being reported as a risk factor for mortality (8, 9, 20). Despite having 14/57 dogs (24.56%) with a non-ambulatory preoperative status (NS Grade 4), we observed no mortality in our study group.

In our study, four cases were initially managed conservatively before surgery. They all presented with a NS grade 1. At MRI, three dogs had mild compression and one had moderate compression. These dogs were closely monitored and eventually received surgery within the 2-week period after onset of clinical signs, due to worsening clinical NS grade or increasing pain. The conservative treatment consisted of restricting physical activity and cage confinement to reduce the risk of continuous extrusion while the ruptured annulus fibrosus heals. Physical therapy, administration of analgesics, muscle relaxants and anti-inflammatory drugs are also used (17, 20, 25).

This study has some limitations. The same surgeon reevaluated the dogs at 10 and 30 days, which could lead to some judgment bias. The SCCR was measured at the point of maximal compression and did not account for any dispersal of disc material or the longitudinal extent of spinal cord compression. Our observation time points for post-surgical recovery were set at 10 and 30 days but recovery may have occurred earlier than these delays in many dogs. These time points were chosen because they are consistent recheck points for all dogs undergoing VSD surgery at our hospital (removal of stitches at 10 days after surgery and last clinical recheck before lifting exercise restriction at 30 days after surgery). Finally, no neuroimaging after surgery was performed, to see how much disc material remained; although re-imaging is not a very common procedure in veterinary ventral slot surgery, it certainly should be considered in dogs that do not improve after surgery.

1.7 Conclusions

Ventral Slot Decompression is a safe technique for the treatment of cervical disc extrusions and, when properly performed, has an excellent prognosis. The lack of strong association between SCCR and NS grade suggests that this relationship in the cervical region is similar to that observed in the thoracolumbar region, rejecting our first hypothesis. Regarding pre-surgical NS grade and recovery time after VSD, statistically significant association was found; dogs with NS grade 4 tended to have longer post-surgery recovery times if compare to dogs with NS grade 1, 2 and 3, accepting our second hypothesis . The degree of spinal cord compression as measured by MRI-derived SCCR was not associated with the recovery time after surgery, rejecting our third hypothesis. Caudal cervical herniation did not show higher NS grades or a longer recovery time than cranial herniation, rejecting our fourth hypothesis. CSF attenuation length ratio on HASTE images was not significantly correlated with NS grade, but weakly correlated with post-surgical recovery time, only partially accepting our fifth hypothesis.

1.8 Conflict of Interest:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

1.9 Author Contributions

FB: Performed the neurologic examinations, MRI and images analyses, surgeries and reevaluated all patients

WM: Improved English syntax and grammar, and provided input as far as the methods, analysis of results and discussion.

LW: Helped with manuscript writing and reference organization.

JV: Helped with manuscript writing

LB: Helped with clinical data acquisition

FF: Principal investigator, helped with manuscript writing and statistical analyses

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1.13 Supplementary Material

grades.

Figure 7 – Distribution of recovery times in each of the NS grades.

Figure 8 – Distribution of recovery times in each of the Spinal Cord Compression ratios.

Figure 9 – Distribution of Neurologic Status grade at cranial disc and caudal disc herniations.

Figure 10 - Distribution of recovery times at cranial disc and caudal disc herniations

2 CHAPTER 2 - AN ETIOLOGICAL STUDY OF MENINGOENCEPHALOMYELITIS IN DOGS – CEREBRAL SPINAL FLUID ANALYSIS AND PCR NEUROLOGICAL PANEL OF 194 CASES

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AN ETIOLOGICAL STUDY OF PRESUNTIVE MENINGOENCEPHALOMYELITIS IN DOGS WITH CEREBRAL SPINAL FLUID (CSF) ANALYSIS AND PCR NEUROLOGICAL PANEL OF 194 CASES

Objectives: The study aims to perform a retrospective investigation of meningoencephalomyelitis (ME) cases reporting how many of these cases had the condition caused by an infectious agent, identified by using a polymerase chain reaction (PCR) commercial neurologic test panel.

Materials and Methods: ME diagnosis was presumptive by clinical, cerebral spinal fluid (CSF) analysis and/or computed tomography (CT) and/or magnetic resonance imaging (MRI). Breed, sex, age, neurological examination, neuroimaging, CSF analysis and PCR results of 194 dogs are analyzed. In addition, the relationships between test results are interpreted and discussed with 168 dogs that had advance neuroimaging.

Results: Out of the 194 dogs with CSF analysis, neurological panel (PCR) and neurological clinical signs of central nervous system (CNS) disease, 138/194 (71.13%) had abnormal CSF results. Fifty six of 194 (28.87%) had normal CSF results. Out of the abnormal CSF results, 126/138 (91.30%) had negative results for the PCR neurologic panel and 12/138 (8.70%) had positive results. Fifty one of 56 dogs (91.07%) of normal CSF analysis had negative results for PCR. Five normal CSF of 56 (8.93%) had positive neurologic panel (four positive for canine distemper virus (CDV) and one for *Borrelia Burgadorferi*). The most common infection in CSF samples was CDV 10/17 (58.82%). In ME of unknown origin (MEUO) 64/177 (36.15%), the most common neurological sign was seizure, which also was the most common clinical sign in the group of infectious ME (IME) 5/17 (29.41%). Out of 194 cases with CSF analysis, 168 (86.59%) also had advanced neuroimaging, being 130 magnetic resonance imaging (MRI) and 38 computed tomography (CT). 25% of normal brain MRI had abnormal CSF analysis.

Conclusion/ Clinical significance: The most common clinical sign observed of ME is seizures. The majority of cases (90%) had ME auto-imunne and 10% of the ME have positive infections result for the PCR panel. Normal CSF not exclude infection ME in 8.93%. A PCR panel should always be performed to exclude IME cases.

2.1 Introduction

The term meningoencephalomyelitis (ME) implies inflammation of the meninges, brain and spinal cord. Meningoencephalitis can be defined as inflammation of meninges (pia mater and arachnoid) and brain, the term meningitis is used to define the inflammation of the meninges only, even though it can be clinically challenging to determine the exact extension of the inflammatory process (1). ME is not a single disease, but rather is a group of syndromes (2). These central nervous system (CNS) syndromes are somewhat common in small animal neurology practice (2). ME can be classified into two general categories: 1) Infectious ME – caused by bacterial, viral, protozoal, fungal or parasitic agents; 2) Non-infectious/auto immune ME - which in dogs also may be broadly referred to as Meningoencephalitis of Unknown Origin (MUO) (2,3). MUO may be defined as and idiopathic noninfectious neuro-inflammatory of central nervous system (CNS) of dogs, which an immune-mediated pathogenesis is suspected (3,4). The classification of MUO also has subtypes, including necrotizing meningoencephalitis (NME), necrotizing leukoencephalitis (NLE), and granulomatous meningoencephalomyelitis (GME). However, even with similar characteristics, each subtype of the disease may possess a unique histopathological feature (2,3,4). Exact details of the etiopathogenesis of MUO is still unknown. What is known so far is that all studies looking for an infectious etiology have failed to reveal a consistent infectious agent. (2,5,6,7,8).

The clinical presentation of ME depends on the severity and localization of the lesions within the CNS. The most common clinical signs observed in a study of 94 patients diagnosed with MUO were abnormal mentation or behavior, proprioceptive deficits, cranial nerve deficits, ataxia and seizure activity (6) The most common clinical signs in infectious ME depend of the infectious agent. However, CNS inflammatory disorders may frequently be very similar to those of infectious diseases and even to those of neoplastic disease (4). Diagnosis usually is based on advanced diagnostic imaging (CT or MRI), cerebrospinal fluid (CSF) analysis, PCR and serologic tests that are designed to rule out infectious disease. In most cases, neoplastic lesions, which are generally focal may be differentiated from inflammatory disease, which are usually multifocal. Therefore, a major challenge is to first differentiate between infectious and noninfectious ME. In more developed countries, noninfectious inflammatory diseases of the CNS are much more common than infection. Definitive diagnosis of MUO requires histopathological examination. For a presumptive diagnosis, conversely, a multimodal approach is needed (4). Although magnetic resonance imaging (MRI) can identify abnormalities consistent with inflammatory disease in the brain or spinal cord, is not always possible to define the diagnosis just by using MRI. Therefore, the safest route for an ante mortem diagnosis of MUO or infection ME is a cerebrospinal fluid (CSF) analysis and PCR panels investigating the most common infectious agents (4). The CSF analysis on MUO cases usually demonstrate mononuclear pleocytosis and high protein concentration, which can vary considerably in severity (9,10,11,12). Results of the CSF analysis on infectious ME might depend of the infectious agent. Usually, in bacterial infection will show neutrophilic/degenerative pleocytosis, high protein and low glucose. Viral infections usually show pleocytosis lymphocytes and high protein. Protozoal infections may show eosinophil pleocytosis and high protein (13).

It is estimated that 56% of dogs diagnosed with MUO die shortly after the presumptive diagnosis, with a survival interval of 0 to 52 days after the start of treatment. Therefore, aggressive therapies with immunosuppressant agents even before a conclusive diagnosis for non-infectious disease are justified by the high mortality rate within a short time of evolution (14). The survival time for infectious ME will depend of the agent. After ruling out the possibility of being an infectious disease with serology and PCR tests, treatment with immunosuppressive drugs such as steroids may start, which have been somewhat effective in alleviating the signs and prolonging the patient's survival in MUO cases. This response to treatment required itself to be an immune-mediated disease (3). Other drugs beyond of corticosteroids were also explored in some studies, as cytosine arabinoside (CA) (15), leflunomide (16), procarbazine (17), lomustine (18), mycophenolate mofetil (19), azathioprine (20). In addition, supportive treatment for the patient's neurological conditions, like preventing seizures must be considered (3). Because of the imunosupressive treatment should start soon as possible in MUO it is important rule out infectious diseases by performing serology and PCR tests. In some instances, test results can return in 10-15 days. This delay can make the treatment decision challenging. Usually, the prognosis of untreated MUO is unfavorable (3) The factors that indicate the prognosis have not been well defined, however, the prognosis is evaluated by the progression of the disease and the seriousness of the clinical signs (21). It varies considerably according to the specific geolocation and respective common Infectious agents. In Brazil, for example, there are some studies on CDV meningoencephalitis, which demonstrate to be the most common infectious agent (22,23). In the present study, medical records of 194 dogs with clinical signs of inflammatory/infectious CNS diseases were retrospectively evaluated. The aim of this study were to present the incidence of inflammatory diseases in the central nervous system of dog secondary to infectious diseases, in Curitiba, Paraná, Brazil, discuss the main clinical signs presented, compare neuroimaging findings and results of the CSF analysis.

2.2 Materials and Methods

2.2.1 Ethics Committee

The present animal study was reviewed and approved by the Ethics Committee of Pontifical Catholic University of Paraná (PUCPF), Brazil. A written informed consent was obtained from each owner authorizing the participation of their respective animals in this study.

2.2.2 Type of study

Retrospective, transversal, uncontrolled and non-randomized.

2.2.3 Inclusion Criteria

The data were provided from a private veterinary hospital in Curitiba, Paraná, Brazil. A total of 194 canine cases of ME with CSF samples and neurological panel (PCR) from 2015 to 2021 were investigated. Data collection included age, breed, sex, and medical history of previous diseases.

All canine patients needed to possess the following inclusion criteria: neurological examination, neurological clinical signs, blood work, including blood count, alt, creatinine, urea, albumin, glucose, ammonia, cerebrospinal fluid (CSF) analysis and a PCR panel that included *Bartonella* spp*, Borrelia burgdorfi, Blastomyces dermatitidis,* CDV*, Coccidioides* spp*, Cryptococcus* spp*, Histoplasma capsulatum*, *Neospora* spp, *Borrelia burgdorferi*, *Toxoplasma gondii* and West Nile Virus. Of the 194 dogs analyzed, 168 dogs also had results from neuroimaging analysis by either CT or MRI. Thirty-eight dogs with computed tomography (CT) and 130 dogs with magnetic resonance imaging (MRI) results.

2.2.4 Anesthesia, technique to collect CSF and analysis.

Anesthesia was induced by an intravenous administration of 5 mg/kg propofol (B.Braun, Melsungen, Germany) and intubated. The same person (FB) performed all CSF sample collections, at the level of cisterna magna, using the technique described in the literature (24). Briefly, the patient was positioned in lateral recumbency and the neck flexed until form 90 angle between nasal bone and cervical spine, which allows widening of cisternal space. The puncture area was prepared for surgery by clipping the hair and local application of 1% povidone-iodine. A sterile spinal needle was used to perform the punction, the CSF collected were immediately send to the laboratory to analysis. No CSF bacterial culture were performed. When dogs had neuroimaging the collect of CSF was performed immediately after this procedure.

CSF samples with blood contamination of >5000 RBC/μL were excluded from the study. Results of CSF analysis were considered abnormal if the protein concentration was >30 mg/dL or if the nucleated cell count was >5 cells/μL.

2.2.5 Criteria used to diagnose MUO

Criteria that were used for a diagnosis of MUO were presence of neurological clinical signs, breed, negative neurologic PCR panel, CSF results with an increase in nucleated cells (>5) and or proteins (>30) and, finally, results of neuroimaging tests (CT and/or MRI) showing irregular and multifocal hypersignal lesions on T2 or Flair with or without contrast enlargement.

2.2.6 Criteria used for ME of Infectious origin

The criteria used for a diagnosis of meningoencephalitis of infectious origin were the presence of neurologic clinical signs, patient's history of previous infectious diseases, presence of microorganisms at CSF sample and a positive result in neurological panel (PCR).

2.2.7 Neuro Imaging techniques

MRI (1.5 Tesla Avanto, Siemens, Erlangen, Germany) was performed with patients anesthetized using intravenous propofol (5 mg/kg), intubated and placed in dorsal recumbency. Pulse sequences for the brain exams included, T2 sagittal plane, T1-weighted, T2-weighted and Flair in transversal planes, diffusion, ADC and SWI in transverse planes, plus T1-weighted with fat suppression in three planes (sagittal, transversal and dorsal) after administration of intravenous paramagnetic contrast medium, gadoteridol 0.5 mmol/ml (ProHance Bracco Imaging, Germany) at a dose of 0.1 mmol/kg. For the spinal images pulse sequences included were sagittal plane T1-weighted, T2-weighted, HASTE and STIR, transverse plane T2-weighted, dorsal plane STIR and sagittal/transverse plane post-contrast T1-weighted with fat suppression after administration of intravenous paramagnetic contrast medium at same dose that in brain exams. All MRI exams were performed in a human hospital.

A CT scan system (Somatom Spirit multislice, Siemens, Munich, Germany) was used to perform exams with the patients under sedation, using intravenous dexmedetomidine (Zoetis, São Paulo-SP, Brazil) 10 mcg/kg and placed in dorsal recumbency. CT scans were performed without contrast and after intravenous contrast iohexol (Omnipaque 300, GE Healthcare, Barueri, SP, Brazil) at a dose of 1.5 ml/kg, injected intravenous. All CT exams were performed at Clinivet Veterinary Hospital.

All CSF samples were collected immediately after neuroimaging when performed. To avoid interobserver discrepancies, all MRI and CT images were prospectively evaluated by the same examiner (FB), with more than 15 years of clinical experience in neurology, neuro-imaging studies and neurosurgery.

Dogs with solitary masses that suggested brain neoplasia were excluded. Dogs with neuroimaging that suggested vascular disease (ischemic or hemorrhagic) like restriction on diffusion images and hyposignal o ADC images also were excluded.

2.2.8 Groups analyzed.

Positive neurological panel (PCR) vs abnormal cerebrospinal fluid (CSF).
Positive neurological panel (PCR) vs normal cerebrospinal fluid (CSF).
Negative neurological panel (PCR) vs abnormal cerebrospinal fluid (CSF).
Negative neurological panel (PCR) vs normal cerebrospinal fluid (CSF).

2.2.9 Correlation neuroimaging analyzed vs CSF analysis.

MRI:
Total MRI brain cases, cervical and thoracolumbar.

Total MRI in CSF normal.
Total MRI in CSF abnormal.
Normal MRI in CSF normal.
Abnormal MRI in CSF normal.
Normal MRI in CSF abnormal.
Abnormal MRI in CSF abnormal.

CT:
Total CT brain cases and thoracolumbar.
Total CT in CSF normal.
Total CT in CSF anormal.
Normal CT in CSF normal.
Abnormal CT in CSF normal.
Normal CT in CSF abnormal.
Abnormal CT in CSF abnormal.

2.2.10 Statistical Analyses

The results of the statistical analysis of the data contingency table tests were submitted to Chi-squat test and Fisher's exact tests. P< 0.05 were deemed significant.

2.3 Results

A total of 194 cases were analyzed, of which 117/194 (60.31%) were females and 77/194 (39.69%) were male. The overall median age was 5 years (range 2 months to 15 years). In the MUO group the median age was 5.5 years (range 4 months to 11 years) in ME infection group the median age was 4.5 years (range 2 months to 15 years) . Among the 194 dogs in the present study, the two most affected breeds were mixed breed dogs (54/194 dogs, 27.84%), followed by Maltese (24/194 dogs, 12,37%), and others 29 breeds. (Table 1).

Breed	Frequency	Percentage %
Mixeed breed	54	28%
Maltese	24	12%
Yorkshire Terrier	13	7%
Lhasa Apso	11	6%
French Bulldog	10	5%
German Sptiz	10	5%
Shi-tzu	9	5%
Pincsher	8	4%
Pug	8	4%
Poodle	7	4%
Schnau	5	3%
Chihuahua	4	2%
Golden Retriever	4	2%
Labrador Retriever	4	2%
Beagle	3	2%
Border Collie	3	2%
Brazillian Terrier	2	1%
Pomerian Lulua	2	1%
Akita	1	1%
American Staffordshire	1	1%
Boxer	1	1%
English Cocker Spaniel	1	1%
Cotton de Tulear	1	1%
Dachshund	1	1%
Siberian Husky	1	1%
Pekings	1	1%
Pitbull	1	1%
Pointer	1	1%
Rotweiller	1	1%
Sharpei	1	1%
Newfoundland dog	1	1%
Total	**194**	**100%**

Table 1 - Representation of breeds in the present in the study.

Of the 194 dogs submitted to this study 108 dogs had a high count of white cells > 5 mm3 and 111 dogs had protein high >30 mg/dl in the CSF analysis. Overall 138/194 (71.13%) had the condition of abnormal CSF (high than 5 cells per mm^3, high than 30 mg/dl of protein or both abnormalities). The median of abnormal CSF number of nucleated cells was 111.26 and (range from 6 to 2224 white cells), the median of abnormal CSF protein was 65.07 and (range from 31 to 720 mg/dl). In this data collection, no samples with microorganisms were detected directly in CSF microscopy. Of the 138 dogs with abnormal CSF analysis results, in 126/138 (91.30%) the neurological panel had negative results and in 12/138 (8.7%) the neurological panel had positive results. We had a total of 56/194 (28.87%) normal CSF analysis, of those CSF analysis 5/56 (8.92%) had positive neurological PCR panel, 4/56 (7.14%) with CDV) and 1/56 (1.7%) *(Borrelia burgdorferi)*. Four agents diagnosed by neurological panel (PCR), in the normal and abnormal CSF analysis and they were: CDV 10/17 (58.82%), *Toxoplasmosis gondii* 3/17 (17.65%), *Borrelia burgdorferi* 3/17 (17.65%) and *Neospora* sp. 1/17 (5.88%). Just one dog had more than one positive infectious agent together and was toxoplasmosis and neosporosis. Interesting that in 16 dogs tested for conjunctival swab test for CDV disease (Allere PCR rapid test) all 16 were negative and in two of these dogs had a neurological PCR panel positive 2/10 (20%) to CDV. That means the false negative results were found in 20% of these dogs.

2.3.1 CSF vs neurologic PCR panel results:

Group: Positive neurological panel (PCR) vs Abnormal cerebrospinal fluid (CSF) 12/138 (8.7%).
Group: Positive neurological panel (PCR) vs Normal cerebrospinal fluid (CSF) 5/56 (8.9%)
Group: Negative neurological panel (PCR) vs Abnormal cerebrospinal fluid (CSF) 126/138 (91.3%).
Group: Negative neurological panel (PCR) vs Normal cerebrospinal fluid (CSF) 51/56 (91.1%).

In CDV cases 6/10 (60%) showed abnormal CSF analysis. 6/10 (60%) showed pleocytosis, 5/10 (showed high than 30 of protein) and 5/10 (50%) showed pleocytosis and increase of protein in CSF analysis. 4/10 (40%) CSF analysis were considered normal. 3/5 (60%) had seizures.

2.3.2 Correlation Neuroimaging results and CSF.

In addition to the CSF analysis and the neurological panel, the majority of CSF samples had neuroimaging as a diagnostic aid 168/194 (86.59%).

Thirty-eight CT and 130 MRIs. The correlations regarding CSF and neuroimaging were made; (Table 2).

MRI:

Total MRI 130: Brain cases (106) Cervical (14) and thoracolumbar (10).
Total MRI in CSF abnormal 95/138 (68.84%) of abnormal CSF performed MRI.
Group: Normal MRI and CSF abnormal 24/95 (25.26%)
Group: Abnormal MRI and CSF abnormal 71/95 (74.73%)

Total MRI in CSF normal: 35/56 (62.5%) of normal CSF performed MRI.
Group: Abnormal MRI and CSF normal 16/35 (45.71%)
Group: Normal MRI and CSF normal 19/35 (54.29%)

Group: Myelopathies: a total of spine MRI 20 dogs. Eight of 20 (33.33%) had hypersignal at sequence T2 intra medullary, syringohydromyelia, meningeal or lesion with contrast enlargement, 16/20 (80%) had abnormal CSF analysis, 1/20 had positive neurologic panel (Toxoplasmosis and Neosporosis) with contrast enlargement intra medullary in the cervical (C1-C5).

CT:

Total CT 38 cases: Brain cases (30), cervical (4) and thoracolumbar (4).
Total CT in CSF abnormal 26/38 (68.42%) of abnormal CSF performed CT.
Group: Normal CT and CSF abnormal 14/26 (53.84%)
Group: Abnormal CT in CSF abnormal 12/26 (46.16%)

Total CT in CSF normal 5/56 (8.92%) of normal CSF performed CT.
Group: Abnormal CT in CSF normal 2/5 (40%)
Group: Normal CT in CSF normal 3/5 (60%)
Group: Myelopathies:

NEUROIMAGING COMPARISON	MRI/CT	CSF	%
MRI Normal x CSF Normal	19	35	54.29
MRI Normal x CSF Abnormal	24	95	25.26
MRI Abnormal x CSF Normal	16	35	45.71
MRI Abnormal x CSF Abnormal	71	95	74.74
CT Normal x CSF Normal	3	5	60
CT Normal x CSF Abnormal	14	26	46.16
CT Abnormal x CSF Normal	2	5	40
CT Abnormal x CSF Abnormal	12	26	54.84

Table 2 - Correlation between neuroimaging and CSF analysis

Total of spine CT 8 dogs: 4/8 (50%) (abnormal CT), 7/8 (87.5%) abnormal CSF analysis. 2/4 (50% meningeal or lesion with contrast enlargement.

Of all brain MRIs, the most common abnormal neuroimaging finds are multiple lesions with hypersignal on T2 and Flair, following or not with contrast enlargement in the meninges and/or multiple lesions.

The total of 168 neuroimaging spinal cord was involved in 32/168 cases (19.04%).

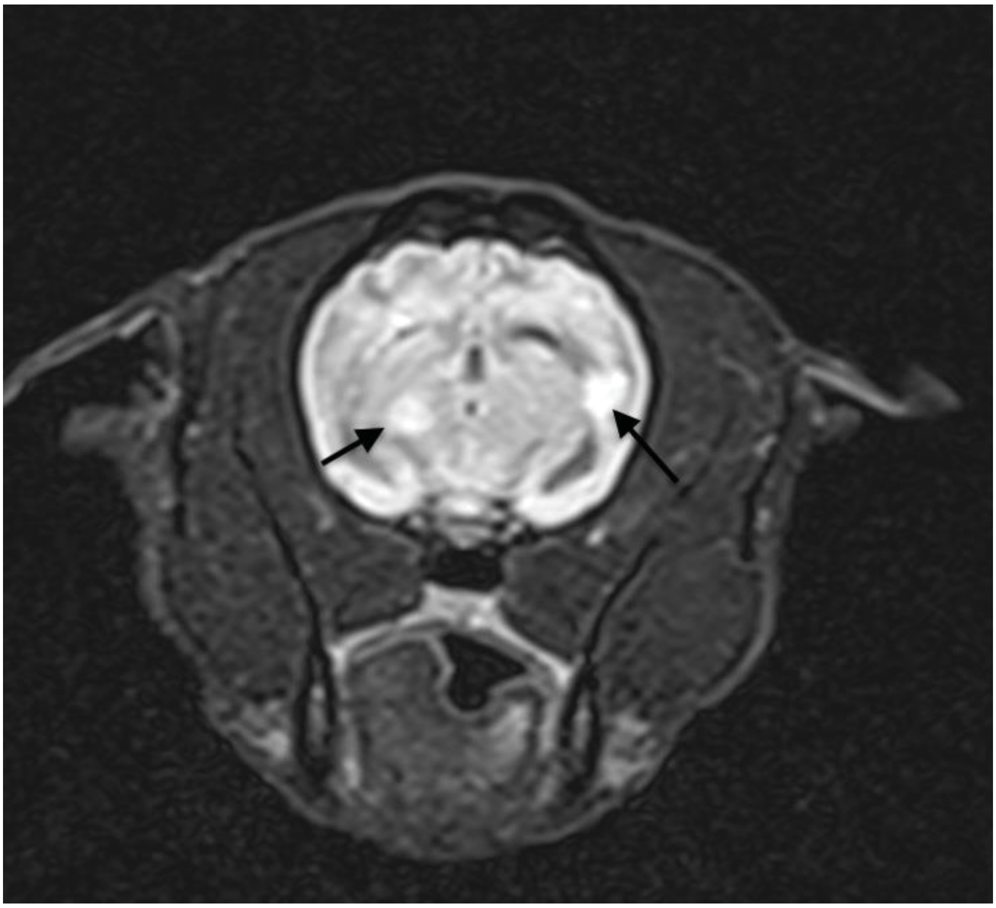

Figure 11 - Transversal, FLAIR T2 weighted MRI showing hypersignal in multifocal lesions suggesting MUO

2.3.3 Neurological clinical signs

In patients with abnormal CSF findings and neurological clinical signs, it was possible to perceive that the main neurological clinical signs presented by the patients during the anamnesis was seizure in the MUO group 64/177 (36.15%) and in ME infection 5/17 (29.41%). Following ataxia 37/177 (20.90%) in MUO group and 3/17 (17.65%) in ME infection, complete neurological signs showed in Error! Reference source not found. and

Table 3 – Neurological signs of dogs with presumptive Meningoencephalitis uncommon origin

.

Neurology clinical signs	Frequency	Percentage
Seizure	65	36.84
Ataxia	50	28.24
Neck pain	12	6.77
Visula Deficit	10	5.65
Trigemial nerve paralysis	9	5.08
Difuse spinal pain	9	5.08
Proprioceptive deficit	7	3.95
Myoclonus	4	2.25
Paraparesis/paraplegia	4	2.25
Mental Status Change	3	1.70
Tetraparesis	2	1.12
Hemiparesis	1	0.55
Nystagmus	1	0.55
Total	177	100%

Table 3 – Neurological signs of dogs with presumptive Meningoencephalitis uncommon origin

Neurology clinical signs	Frequency	Percentage (%)
Seizure	5	29.41
Ataxia	3	17.65
Myoclonus	3	17.65
Neck pain	3	17.65
Visual deficit	3	17.65
Total	**17**	**100%**

Table 4 - Neurological signs of positive for infection diseases in CSF

Myoclonus was detected in seven dogs, of those, six had CSF abnormal and one normal, two were positive to CDV and one toxoplasmosis and neosporosis. The total of 32/194 (16.49%) of dogs with neurological signs that could involve myelopathies as (diffuse spine pain, neck pain, tetraparesis and paraparesis).

2.4 Discussion

In the present study, 194 cases with neurological signs, CSF analysis, PCR panel neurologic and/or advanced neuro imaging suggesting ME were analyzed. Of those, 138 dogs had CSF abnormalities which is closer in Coelho et all study who found 76% of abnormalities in CSF analysis (25). Meningoencephalitis of inflammatory/autoimmune/ meningoencephalitis of unknown origin (MUO) represented approximately 90% of abnormal CSF analysis and 10% of these tests were positive for infectious disease in our study. This proportion corroborates with a previous study that found immune-mediated disease in 83.6%, being more common than infectious conditions 16.4% (26). The most common immune-mediated conditions diagnosed were (MUO) (25). Tests for infectious diseases like PCR panels are very important and should be performed in all cases suspect of ME (3). Our study showed a slight high proportion of normal CSF analysis in MUO cases (28.86%). In another published study, normal CSF analysis was found in 22% of MUO cases (21). Regarding neurological panel in our study showed the total of four agents diagnosed by neurological panel (PCR): CDV, *Toxoplasmosis gondii*, *Borrelia burgdorferi* and *Neospora* sp. The proportion of our infection agents were different than an England study that found a higher number of bacterial infections than CDV (26). Five dogs that had a positive result in the neurological panel had a CSF analysis within normal limits; four were positive to CDV and one for *Toxoplasma gondii* and *Neospora* sp. That is important information that one CSF analysis normal not exclude the possibility of a positive neurologic panel. CDV usually showed abnormal CSF analysis in 77.3% (high protein) and pleocytosis (50.72%) of dogs (27). That corroborates with our study that showed 60% of abnormal CSF analysis in CDV cases. The total of 58% of all infection cases were positive to CDV which means that agent still being the most common infection agent in Brazil. The conjunctival swab test for CDV disease (Allere, PCR rapid test) were not very sensible because it missed the diagnostic in 2/10 cases (20%) and this study recommend perform the PCR tests.

Bacterial culture from CSF samples was not performed in this investigation. When an infectious organism is suspected to be the cause of a CNS disease, both aerobic and anaerobic bacterial cultures of CSF may be performed. However, positive bacterial culture results in confirmed cases of bacterial meningitis are extremely uncommon (28). A negative culture may be the result of inappropriate sample handling or culture media, in addition to a low number of organisms in the CSF (28).

Neuro imaging and CSF This investigation showed abnormal MRI results in 75 % of cases in CSF abnormal. Conversely we found 25% of normal MRI with abnormal CSF analysis, with corroborates with Lamb study that found abnormal MRI in 76% in dogs with inflammatory CSF and 24% of dogs with inflammatory CSF had images interpreted as normal, which emphasizes that a normal MRI scan does not rule out the possibility of intracranial inflammatory disease (28,29). Forty five percent of cases that had normal CSF analysis had some abnormal MRI findings whereas 40% of normal CSF analysis had some abnormal CT findings. In our study MRI findings suggested ME when it showed meningeal or multifocal lesions with hypersignal on T2 weighted or Flair images with or without contrast enlargement. This is in accordance to previous study that states that dogs with multifocal contrast-enhancing brain lesions consistent with GME and normal CSF results have also been reported (29). Generally, there was much variability in CSF cell count in MUO dogs and around of 22% of the cases the cell count can be normal and a normal CSF not exclude the MUO (21).

In our study, abnormal CSF in 53% was found in patients without abnormalities observed using CT imaging and that is twice than MRI. That information suggests that MRI is more sensible to CT regarding abnormality detection in brain images that had abnormal CSF analysis. This corroborates the previously published statement that MRI is more sensitive than computed tomography (CT) for lesions associated with intracranial inflammation in dogs (29). An important limitation of CT scan is that it produces a beam hardening artefact (due to preferential absorption of low energy x-ray beams), most notably adjacent to the petrous parts of the temporal bones. This artefact may obscure the clinician’s ability to interpret brainstem and cerebellar lesions, although MUO lesions can affected these places (2). The availability of CT scans systems in Brazil for veterinary use is more common than MRI examinations. CT scans provide limited soft tissue detail but when performed with CSF analysis, it may help to provide evidence of ME. CT scans however will miss some lesions that MRI hypothetically would not (4). However, again if collect the CSF together with CT it will increase your accuracy to get the final diagnosis. CSF analysis is more sensitive than CT and MR imaging in identifying abnormalities consistent with inflammatory disease, normal CSF analysis has been described in 20% of cases with histopathologically confirmed inflammatory CNS disease (31).

Although there are overlapping clinical and histopathological features among the possible ME cases, the topographical distribution of the lesions (for example, NME versus NLE) and presence or absence of necrosis (for example, GME versus NLE) constitute imaging features that may help direct a presumptive antemortem diagnosis (4). The presence or absence of contrast enhancement with inflammatory brain disease depends upon the degree of blood brain barrier (BBB) breakdown (4). Enhancement of meninges and in the lesions was identified in 28% and 36% respectively of dogs with inflammatory CSF, our study showed enhancement meningeal plus lesions in 44%. Intracranial neoplasms in dogs are usually solitary, although metastasis may result in multifocal lesions. Inflammatory conditions are more likely to result in multifocal or diffuse lesions, although granulomatous meningoencephalitis can cause solitary mass lesions that appear similar to neoplasms (4). Meningeal enhancement may also prove to be a relatively nonspecific sign as it has been described in dogs with inflammatory conditions including bacterial and cryptococcal meningitis and granulomatous meningoencephalitis and in dogs with intracranial neoplasia, usually lymphoma (4).

Neurological clinical signs

Joan R. Coates and Nick Jeffery study (4) stated that although the syndrome can affect any dog aged between approximately 3 and 7 years are most commonly affected by all subtypes of MUO (4). Wong et all study (40 cases) states that regarding age at initial examination ranged from 7.5 months to 9 years, median 4 years for MUO cases (20). Our findings regarding age (median 5 years) showed some younger dogs comparing with previous studies. Regarding breeds our study found Maltese as second breeds most coomon with MUO with corroborates with Wong et all study (20) which founds Maltese as one breed with prevalence with MUO.

Wong et al. study (20) found several neurological signs such as seizures, compulsive circling, altered behavior or degree of consciousness, blindness, vestibular dysfunction, and cerebellar dysfunction in dogs with MUO (20). CDV also can cause neurological signs as central vestibular disease (head tilt, nystagmus, and tendency to fall, cranial nerve and conscious proprioceptive deficits), cerebellar disease and generalized or partial seizures (26). In our investigation, seizure was the more common neurological signs in the MUO group 36% and in ME infection 29%. Following ataxia 20% in MUO group and 17% in ME.

According to GRANGER et al. (21) eight percent of dogs diagnosed with GME resented neurological deficits suggestive of a myelopathy (21). The myelopathy could be localized anywhere in the spinal cord, and there were clinical sings ranging from general proprioceptive ataxia to paresis or even plegia; spinal hyperesthesia also was a common finding (21). However, the present study showed spinal signs in 16% of the cases.

Since MUO includes several subtypes, including steroid responsive meningitis-arteritis (SRMA), eosinophilic meningoencephalitis (EME), granulomatous meningoencephalomyelitis (GME) and necrotizing encephalitis (NE; including necrotizing meningoencephalomyelitis (NME) and necrotizing leucoencephalitis (NLE), the absence of histopathology diagnosis in the MUO group is a limitation of the study. It is beyond the scope of this paper to explain survival times or to evaluate any specific treatment on MUO or infectious ME. However, the cases with MUO received a standard protocol suggesting by Lowie (22) using immunosuppressive doses of prednisolone and cytosine araboniside.

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3 ANEXOS

3.1 Aprovação do comitê de ética.

Pontifícia Universidade Católica do Paraná
Pró-Reitoria de Pesquisa, Pós-Graduação e Inovação
Comissão de Ética em Pesquisa no Uso de Animais

PARECER CONSUBSTANCIADO DA CEUA

TÍTULO DA PESQUISA	Clinical Outcome After Ventral Slot Decompression for Cervical Disc Extrusion In 57 Dogs. An Analysis of Association Between Spinal Cord Compression Ratio, Initial Neurological Status Grade and Recovery After Surgery		
Nº DO PARECER / VERSÃO	02239		
PESQUISADOR RESPONSÁVEL	JOSE ADEMAR VILLANOVA JUNIOR		
ESPECIE DO ANIMAL	*Canis familiaris*	**Nº DE ANIMAIS**	57
NOME COMUM DO ANIMAL	cão-doméstico	**Nº SISBIO** (animais de vida livre)	*Não se aplica*
SEXO / IDADE / PESO	Não especificado	**ATIVIDADES** (animais de vida livre)	*Não se aplica*
ORIGEM DO ANIMAL	Clinica Veterinária da PUCPR e Hospital Veterinário Clinivet (Curitiba, Paraná)	**GP TAXONÔMICOS** (animais de vida livre)	*Não se aplica*
DATA DE INICIO DA PESQUISA	2020	**LOCAL (IS)** (animais de vida livre)	*Não se aplica*
DATA DE TÉRMINO DA PESQUISA	2022	**Nº SISGEN**	*Não se aplica*
APRESENTAÇÃO DO PROJETO	A hérnia de disco intervertebral (HDI) é a principal causa de compressão medular em cães, sendo a região cervical acometida em aproximadamente 15% dos casos (1,2,3). De acordo com a literatura, os espaços mais comumente acometidos na região cervical são C2-C3 e C3-C4 (3). Cães de pequeno porte, principalmente condrodistróficos, estão predispostos à doença degenerativa do disco intervertebral (DDIV) seguida de hérnia e compressão da medula espinhal. A quantidade de material do disco herniado, a força de extrusão e a duração da compressão são fatores que podem contribuir para a gravidade dos déficits neurológicos (3). Qualquer raça pode ser afetada, no entanto, a doença é mais prevalente em Dachshunds, seguido por Lhasa Apsos, Shi tzus, Beagles e Bulldogs Franceses (3-6). Mais comumente, os cães afetados têm mais de dois anos de idade (7). Atualmente, o DDIV é subdividido em: 1) Extrusão do disco intervertebral (Hansen tipo 1, agudo); 2) Extrusão aguda do disco intervertebral com extensa hemorragia epidural; 3) Protrusão do disco intervertebral (Hansen tipo 2, crônica); 4) Extrusão aguda não compressiva do núcleo pulposo; 5) Extrusão do núcleo pulposo hidratado; 6) Extrusão de disco intervertebral intradural/intramedular; 7) Extrusão traumática do disco intervertebral. De um modo geral, o termo hérnia de disco também pode ser usado e interpretado como material discal exercendo algum grau de compressão espinhal (8). A hiperestesia é o sinal clínico mais comum na hérnia de disco cervical; a tetraplegia é menos frequente em relação à paraplegia na hérnia de disco toracolombar, devido ao maior diâmetro do canal vertebral na região cervical (3–7,9). O grau de status neurológico (ST) para lesão medular cervical varia de dor cervical a tetraplegia, com insuficiência respiratória neurogênica (10,11). A modalidade de diagnóstico por imagem considerada "padrão ouro" para hérnia de disco é a ressonância magnética (RM), pois pode distinguir estruturas anatômicas como raízes nervosas, parênquima medular, gordura epidural, líquor e camadas do disco intervertebral (12). A tomografia computadorizada (TC) sem contraste e a TC-mielografia têm sensibilidade de 88,6% e 97%, respectivamente (13,14). A descompressão cirúrgica pela formação de fenda vertebral (DCFFV) é o tratamento cirúrgico mais utilizado para hérnia de disco cervical em cães e tem bom prognóstico a longo prazo (15). Os riscos relacionados a essa técnica incluem hemorragia, arritmias cardíacas, parada cardiorrespiratória,		

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	pneumonia aspirativa, instabilidade espinhal e danos a estruturas adjacentes, como esôfago, traqueia, tronco vagossimpático e nervo laríngeo (15-19). A taxa de mortalidade por DCFFV na hérnia cervical é em torno de 8%, sendo fator de mau prognóstico a tetraparesia pré-operatória não ambulatorial (20). Não há diretrizes bem definidas para classificar a gravidade da compressão da medula espinhal em imagens transversais, no entanto, vários estudos usaram alguma forma de classificação usando a média de compressão medular (MCM), especialmente na espondilomielopatia cervical caudal (21–23).
OBJETIVO DA PESQUISA	Os objetivos deste artigo são investigar as associações entre os seguintes parâmetros em cães com hérnia de disco cervical tratados por DCFFV: 1) grau ST e MCM (como visto na ressonância magnética); 2) grau ST e recuperação pós-operatória; 3) MCM e recuperação pós-operatória. Além disso, procuramos determinar se havia diferença no tempo de recuperação pós-cirurgia entre cães de raças pequenas/médias e grandes, e se havia diferença no grau ST e tempo de recuperação pós-cirúrgico com base na localização cranial ou caudal dos discos afetados.
RISCOS E ATITUDES MITIGATÓRIAS	Não se aplica por se tratar de dados já coletados
CONSIDERAÇÕES SOBRE A PESQUISA	Utilizaram os dados ja coletados da Clinica Veterinária da PUCPR e Hospital Veterinário Clinivet (Curitiba, Paraná) oriundos de prontuários médicos e imagens de ressonância magnética. O referido projeto 02239 apresentou pendências, as quais são descritas abaixo: 1. Falta os termos de autorização da utilização dos dados e prontuarios ja coletados que se encontram sobre responsabilidade da Clinica Veterinária da PUCPR e Hospital Veterinário Clinivet (Curitiba, Paraná) 2. No item 8 metodologia descrever com detalhes qual será a metodologia utilizada para a utilização dos dados, quais os dados a seram analisados e ou comparados.E retirar a metodologia descrita no formulario , pois descreve a manipulação dos animais e no presente estudo somente será de utilização de dados já coletados. 3. No item justificativa descrever qual a justificativa da utilização desde dados especificos. 4. Ficou uma duvida se os dados que serão utilizados fazem parte de algumo projeto que tem um parecer aprovado ? 5. No item 17 descrever somente Não se aplica por se tratar de dados já coletados
CONSIDERAÇÕES SOBRE OS TERMOS DE APRESENTAÇÃO OBRIGATÓRIA	Favor apresentar os termos de autorização da utilização dos dados, prontuarios e exames de imagens da Clínica Veterinária da PUCPR e Hospital Veterinário Clinivet (Curitiba, Paraná).
RECOMENDAÇÕES	Sugere-se que todas as considerações realizadas pelo relator sejam realizadas.
CONCLUSÕES OU PENDÊNCIAS E LISTA DE INADEQUAÇÕES	O referido projeto 02239 apresentou pendências, as quais são descritas abaixo: 1. Faltam os termos de autorização da utilização dos dados e prontuários já coletados que se encontram sob responsabilidade da Clínica Veterinária da PUCPR e Hospital Veterinário Clinivet (Curitiba, Paraná); 2. No item 8 (metodologia) descrever com detalhes qual será a metodologia empregada para a utilização dos dados e quais dados

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	serão analisados. É recomendado retirar a metodologia descrita no formulário, pois descreve a manipulação dos animais, o que não é necessário constar, uma vez que o presente estudo somente utilizará os dados já coletados. 3. No item "Justificativa" descrever qual a razão pela utilização destes dados específicos. 4. Não ficou claro se os dados que serão utilizados fazem parte de algum projeto que já tem um parecer aprovado, pois parece se tratar de um projeto de pesquisa que havia sido planejado anteriormente. 5. No item 17 descrever somente "Não se aplica" por se tratar de dados já coletados.
CONSIDERAÇÕES FINAIS	O pesquisador tem 60 dias, após a ciência do parecer com pendência para responder aos quesitos formulados pela CEUA-PUCPR em seu parecer, os quais devem ser respondido no formulário de pendência. Após este prazo o projeto será considerado "Retirado". Conforme RESOLUÇÃO N. º 036/2016 - CONSUN. Informamos que as pendências devem ser respondidas pelo link https://pucpr.co1.qualtrics.com/jfe/form/SV_3eEQgHGiDk0KO45, obrigatóriamente, não sendo possível avaliação caso seja enviado por outros meios.

SITUAÇÃO DO PARECER	**Com pendências porém caso sejam apresentados os itens solicitados "pendências" não há necessidade de ressubmeter e/ou reavaliar o projeto em nova reunião.**

CURITIBA, 18 de abril de 2022.

PROF. DR. SÉRGIO LUIZ ROCHA
Coordenador CEUA-PUCPR

A validade deste documento pode ser confirmada pelo e-mail ceua@pucpr.br informando o número do parecer.

3.2 Trabalho submetido.

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Clinical Outcome After Ventral Slot Decompression for Cervical Disc Extrusion In 57 Dogs. An Analysis of Association Between Spinal Cord Compression Ratio in Magnetic resonance imaging, Initial Neurological Status Grade and Recovery After Surgery

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Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest

Author contribution statement

FB: Performed the neuro examinations, MRI and images analyses, surgeries and reevaluated all patients
WM: Improved the use of English language, suggested mores statistical analyses and provided input as far as the methods and analysis of results.
LW: Helped with manuscript writing and reference organization.
JV: Helped with the helped with manuscript writing
LB: Helped with clinical data acquisition
FF: Principal investigator, helped with manuscript writing and statistical analyses

Keywords

Cervical herniation, Intervertebral disc disease, Extrusion, Ventral slot, Surgery (Min.5-Max. 8

Abstract

Word count: 347

The primary aims of this study were to evaluate transverse images obtained from magnetic resonance imaging (MRI) of dogs with cervical intervertebral disc extrusion before being submitted to ventral slot surgical decompression (VSD). Dogs were re-evaluated systematically at 10 and 30 days after surgery. We investigated the association between: 1) Spinal cord compression ratio (SCCR) and pre-surgical Neurological Status (NS) grade; 2) NS grade and postoperative recovery; 3) SCCR and postoperative recovery. Our original hypotheses were: 1) Dogs with greater SCCR will have higher pre-surgical NS grades; 2) Higher pre-surgical NS grade will have longer postoperative recovery time; 3) Higher SCCR will have longer postoperative recovery time. The secondary aims were: 4) Compare NS grades and recovery times between dogs with cranial and caudal cervical disc herniations and 5) Compare the length of cerebral spinal fluid (CSF) attenuation on HASTE images with NS grade and recovery time. Our original hypotheses were: 4) Dogs with caudal cervical disc herniations will have higher NS grade and longer recovery time; 5) Dogs with longer HASTE CSF attenuation will have higher NS grade and longer time to recovery.

Of the 57 dogs subjected to VSD, 44/57 dogs (77.19%) showed complete clinical recovery within 10 days, 9/57dogs (15.79%) showed complete recovery within 30 days, 3/57 (5.26%) improved the NS grade but did not make a full recovery and 1/57 (1.76%) had no improvement in NS grade.

The lack of strong association between SCCR and NS grade suggests that this relationship in the cervical region is similar to what is observed in the thoracolumbar region, rejecting our first hypothesis. Dogs with NS grades 1-2-3 recovered overall faster than those with NS grade 4, accepting our second hypothesis. There was no correlation between SCCR derived from MRI transverse images and recovery time, rejecting our third hypothesis. Caudal cervical herniation did not show higher NS grade or longer recovery time than cranial herniation, rejecting our fourth hypothesis. CSF attenuation length ratio on HASTE images was not significantly correlated with NS grade but may weakly correlate with post-surgical recovery time, only partially accepting our fifth hypothesis.

Contribution to the field

Transverse images obtained from MRI of dogs with cervical intervertebral disc extrusion were evaluated before being submitted to VSD. Dogs were re-evaluated systematically at 10 and 30 days after surgery. We investigated the association between: 1) SCCR and pre-surgical NS grade; 2) NS grade and postoperative recovery; 3) SCCR and postoperative recovery. Our original hypotheses were; 1) Dogs with greater SCCR will have higher pre-surgical NS grades 2) Higher pre-surgical NS grade will have longer postoperative recovery time; 3) Higher SCCR will have longer postoperative recovery time. 4) Compare NS grades and recovery times between dogs with cranial and caudal cervical disc herniations and 5) Compare the length of cerebral spinal fluid (CSF) attenuation on HASTE images with NS grade and recovery time. Our original hypotheses were: 4) Dogs with caudal cervical disc herniations will have higher NS grade and longer recovery time; 5) Dogs with longer HASTE CSF attenuation will have higher NS grade and longer time to recovery. (1) We have the clinical impression that there is NO association between degree of compression and neurologic score at presentation in cervical disk extrusion. There is just one paper regarding this topic and they state there IS an association. (2) Just to further illustrate the matter, such association was NOT found for thoracolumbar disc herniation, in past publications. (3) The only previous study looking at similar features (Ryan et al 2008) had a low number of dogs (33, versus the 57 dogs in the current study). The referred study (Ryan et al 2008) had inconsistent surgical methods (some dogs had dorsal laminectomy) with different surgeons. These factors could strongly influence the outcome. (4) The prognostic factors for

surgically treated dogs with thoracolumbar disk herniation are well established, not much is known about which factors predict complete recovery in dogs with non ambulatory tetraparesis secondary to cervical disk herniation. The prognostic factors, like site of disk herniation (cranial x caudal) still in textbooks. (Hillman 2009). Although a previous study suggested that lesion localization (cranial cervical better than caudal cervical) and neurologic status were prognostic indicators of outcome, larger and more recent studies do not support these findings. (Brisson 2010). (5) Finally, there are few studies showing the prognostic factors of CSF attenuation length measured on HASTE pulse sequence in dogs with thoracolumbar disc herniation. To the authors' knowledge, there is no veterinary study looking at this in dogs with cervical disc herniation.

Ethics statements

Studies involving animal subjects

Generated Statement: The animal study was reviewed and approved by Comissão de Ética no Uso de Animais (CEUA) da PUCPR. Written informed consent was obtained from the owners for the participation of their animals in this study.

Studies involving human subjects

Generated Statement: No human studies are presented in this manuscript.

Inclusion of identifiable human data

Generated Statement: No potentially identifiable human images or data is presented in this study.

Data availability statement

Generated Statement: The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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Clinical Outcome After Ventral Slot Decompression for Cervical Disc Extrusion In 57 Dogs. An Analysis of Association Between Spinal Cord Compression Ratio in Magnetic resonance imaging, Initial Neurological Status Grade and Recovery After Surgery

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Keywords: Cervical Herniation, Intervertebral Disc Disease, Extrusion, Ventral Slot, Surgery (Min.5-Max. 8)

Abstract

The primary aims of this study were to evaluate transverse images obtained from magnetic resonance imaging (MRI) of dogs with cervical intervertebral disc extrusion before being submitted to ventral slot surgical decompression (VSD). Dogs were re-evaluated systematically at 10 and 30 days after surgery. We investigated the association between: 1) Spinal cord compression ratio (SCCR) and pre-surgical Neurological Status (NS) grade; 2) NS grade and postoperative recovery; 3) SCCR and postoperative recovery. Our original hypotheses were: 1) Dogs with greater SCCR will have higher pre-surgical NS grades; 2) Higher pre-surgical NS grade will have longer postoperative recovery time; 3) Higher SCCR will have longer postoperative recovery time. The secondary aims were: 4) Compare NS grades and recovery times between dogs with cranial and caudal cervical disc herniations and 5) Compare the length of cerebral spinal fluid (CSF) attenuation on HASTE images with NS grade and recovery time. Our original hypotheses were: 4) Dogs with caudal cervical disc herniations will have higher NS grade and longer recovery time; 5) Dogs with longer HASTE CSF attenuation will have higher NS grade and longer time to recovery.

Of the 57 dogs subjected to VSD, 44/57 dogs (77.19%) showed complete clinical recovery within 10 days, 9/57dogs (15.79%) showed complete recovery within 30 days, 3/57 (5.26%) improved the NS grade but did not make a full recovery and 1/57 (1.76%) had no improvement in NS grade.

The lack of strong association between SCCR and NS grade suggests that this relationship in the cervical region is similar to what is observed in the thoracolumbar region, rejecting our first hypothesis. Dogs with NS grades 1-2-3 recovered overall faster than those with NS grade 4, accepting

our second hypothesis. There was no correlation between SCCR derived from MRI transverse images and recovery time, rejecting our third hypothesis. Caudal cervical herniation did not show higher NS grade or longer recovery time than cranial herniation, rejecting our fourth hypothesis. CSF attenuation length ratio on HASTE images was not significantly correlated with NS grade but may weakly correlate with post-surgical recovery time, only partially accepting our fifth hypothesis.

1 Introduction

Intervertebral disc herniation (IDH) is the main cause of spinal cord compression in dogs, with the cervical region being affected in approximately 15% of cases (1). According to the literature, the most commonly affected spaces in the cervical region are C2-C3 and C3-C4 (1). Small dogs, mainly chondrodystrophic, are predisposed to degenerative intervertebral disc disease (IVDD) followed by herniation and spinal cord compression (2). The amount of herniated disc material, the force of the extrusion and duration of compression are factors that may contribute to the severity of neurological deficits (1). Any breed can be affected; however, the disease is more prevalent in Dachshunds, followed by Lhasa Apsos, Shi tzus, Beagles and French Bulldogs (2). Most commonly, the affected dogs are older than two years of age (2). Currently, IVDD is subdivided as: 1) Extrusion of the intervertebral disc (Hansen type 1, acute); 2) Acute intervertebral disc extrusion with extensive epidural hemorrhage; 3) Protrusion of the intervertebral disc (Hansen type 2, chronic); 4) Acute non-compressive nucleus pulposus extrusion; 5) Hydrated nucleus pulposus extrusion; 6) Intradural/intramedullary intervertebral disc extrusion; 7) Traumatic intervertebral disc extrusion. The term disc herniation also can be used and interpreted as disc material exerting some degree of spinal compression (3). Hyperesthesia is the most common clinical sign in cervical disc herniation; tetraplegia is less frequent compared to paraplegia in thoracolumbar disc herniation, possibly to the larger diameter of the vertebral canal in the cervical region (4). NS grade for cervical spinal cord injury ranges from cervical pain to tetraplegia, with neurogenic respiratory failure (Table 1) (5-6).

The diagnostic imaging modality considered the "gold standard" for disc herniation is magnetic resonance imaging (MRI), as it can distinguish anatomical structures such as nerve roots, spinal cord parenchyma, epidural fat, cerebrospinal fluid and intervertebral disc layers (7). Ventral slot decompression (VSD) is the most widely used surgical treatment for ventral cervical disc herniation in dogs and has a good long-term prognosis (8). Risks related to this technique include hemorrhage, cardiac arrhythmias, cardiopulmonary arrest, aspiration pneumonia, spinal instability, and damage to adjacent structures such as the esophagus, trachea, vagosympathetic trunk and laryngeal recurrent nerve (8). The mortality rate for VSD in cervical herniation is around 8%, with a poor prognostic factor being preoperative non-ambulatory tetraparesis (8-9).

There are no well-defined guidelines for classifying the severity of spinal cord compression on cross-sectional images; however, several studies have used some form of classification using spinal cord compression ratios (SCCR), especially in caudal cervical spondylomyelopathy (10–11). Other authors have described cutoff points for the severity of compression such as mild compression, when less than 25% of the vertebral canal's cross-sectional area is occupied by compressive material; moderate compression, from 25% to 50%; and severe compression, when greater than 50% (12). To the authors' knowledge, there are no previous study using a similar scale for cervical disc extrusion and evaluating potential association with pre-surgical NS grade and post-surgical recovery. There still are uncertainties regarding the associations between NS grade and SCCR, NS grade and postoperative recovery, SCCR and postoperative recovery. In a study including 33 dogs with cervical disc extrusion, Ryan et all (2008) found correlation between pre-surgical NS grade and size of spinal compression (16). However, they found no correlation between spinal cord compression size and recovery. Da Costa et all studied cervical caudal myelopathy and did not find correlation between size of compression and NS grade (11).

In contrast to previous reports (13), we have the clinical impression that there is no association between degree of compression in cervical disc extrusion and neurologic status grade at presentation. Such association was not found for thoracolumbar disc herniation, and the authors underscored the importance of other factors not reflected by the degree of physical compression, such as spinal cord contusion (pening 14).

Several veterinary texts, citing work by Waters et al. (waters 15), state that cranial cervical disc herniation show better outcome than caudal cervical herniations, but this has not been our clinical impression and there are still uncertainties as to whether this is true.

Finally, there are few studies showing the prognostic factors of CSF attenuation length measured on HASTE pulse sequence in dogs with thoracolumbar disc herniation (16). To the authors' knowledge, there is no veterinary study looking at this in dogs with cervical disc herniation.

The primary objectives of this article are to investigate the associations among the following parameters in a large group of dogs with cervical disc herniation treated by VSD: 1) The maximal SCCR (as seen on transverse MRI images) and pre-surgical NS grade; we hypothesized that dogs with greater SCCR will have higher NS grades at presentation; 2) NS grade and postoperative recovery; we hypothesized that higher cervical NS grade will influence postoperative recovery time; 3) SCCR and postoperative recovery; we hypothesized that dogs with higher SCCR will have longer recovery time. The secondary objectives are: 4) Compare outcomes between cranial and caudal cervical disc herniations; we hypothesized that caudal cervical herniation will have longer time to recovery; 5) Compare ventral longitudinal extension of CSF signal loss on HASTE pulse sequence with NS grade and time to recovery; we hypothesized that longer HASTE CSF attenuation will have higher NS grade and longer time to recovery.

2 Materials and Methods

2.1 Inclusion criteria

The database of the neurology service at Clinivet Veterinary Hospital, Curitiba-PR, Brazil was searched over a period of four years (2017 to 2021) for dogs that presented with clinical signs of cervical spine dysfunction. Dogs were included if: (1) cervical disc herniation was confirmed with MRI, (2) spinal cord decompression by ventral slot surgery was performed within a maximum of two weeks after onset of clinical signs, and (3) clinical follow-up was available at 10 and 30 days after surgery.

In dogs older than seven years of age, the preoperative work-up included thoracic radiographs and abdominal ultrasonography to rule out potential concomitant diseases that could contribute to poor patient recovery after spinal surgery. All included animals were deemed healthy enough to undergo VSD, with complete blood count and blood chemistry (including glucose, urea, creatinine, albumin, and alanine aminotransferase levels).

2.2 Clinical evaluation and data collection

The cervical NS grade of each included patient was quantified using a grading system (0-5) previously described (5,6) and is available in Table 1. A single observer (FB) determined the pre- and post- surgical NS grade. Additional data collected from the medical records included breed, sex, age. Prospective review of the MRI images (see below) was conducted to record affected cervical intervertebral discs, size of herniation, and length of CSF signal loss on HASTE pulse sequence.

2.3 Imaging techniques and morphometric measurements.

The diagnosis of cervical disc herniation was confirmed by MRI (1.5 Tesla Avanto, Siemens, Erlangen, Germany), performed with patients anesthetized using intravenous propofol (B.Braun, Melsungen, Germany) at 6 mg/kg and placed in dorsal recumbency. The anesthesiologist stayed in the exam room to administer propofol as needed, based on respiratory frequency, heart rate, and palpebral reflex, until the end of MRI exam. Each exam took around 25 minutes to be completed. Pulse sequences included were sagittal plane T1-weighted, T2-weighted, HASTE, STIR, transverse plane T2-weighted, dorsal plane STIR and sagittal/transverse plane post-contrast T1-weighted with fat suppression after administration of intravenous paramagnetic contrast medium (gadoteridol - 0.5 mmol/ml, ProHance Bracco imaging, Germany) at a dose of 0.1 mmol/kg. All MRI exams were performed in a human hospital.

Measurements of SCCR was performed using transverse T2-weighted images at the level of the spinal cord compression and were performed using the region of interest and surface area tool of a DICOM viewer (Horos for OS X, version 3 - LGPL-3.0). To determine the SCCR, the surface area of the non-compressed spinal cord at the disc space cranial to the compression site was measured as well as the surface area of the cord at the site of maximal compression, determined by visual assessment scrolling through the image series (Figure 1). The exact SCCR was then computed using the formula: SCCR = [(Surface area of non-compressed cord – Surface area of compressed cord) / Surface area of non-compressed cord] * 100. The exact SCCR was used to calculate correlations. Each case was also assigned to a categorical score of SCCR: mild compression for SCCR<25%, moderate compression for SCCR >25% and <50% and severe compression for SCCR >50% (12) (Figure 2).

The HASTE images were evaluated for presence or absence of CSF signal attenuation. When CSF signal attenuation was present, the maximal craniocaudal length of ventral CSF attenuation was measured using the same measurement tool as described above. The length of the C3 vertebral body was measured on sagittal T2-weighted images. A CSF length attenuation ratio was then calculated by dividing the length of CSF attenuation on HASTE by the length of C3 vertebral body (Figure 3).

To avoid interobserver discrepancies, all MRI images were prospectively evaluated by the same examiner (FB).

2.4 Anesthesia and surgical technique

Pre-anesthetic medication varied for each specific patient, but as a basic protocol, intravenous midazolam (0.25 mg/kg) and ketamine hydrochloride (1 mg/kg) were used followed by an intravenous bolus of propofol (5 mg / kg). Anesthesia was maintained using isoflurane as well as a continuous infusion of fentanyl (10 µg/kg/hour). The same surgeon (FB), with substantial neurosurgical experience, performed all surgeries, using the technique described in the literature (17). The patient was positioned in dorsal recumbency, and the neck gently extended under a folded towel, which allows widening of the intervertebral disc spaces. The ventral cervical area was prepared for surgery by clipping the hair and local application of povidone-iodine. A sterile patch (Opsite Incise; Smith and Nephew, London, United Kingdom) was placed over the surgical field. Surgical material used for surgery was standard, including Surgairtome drill, Kerrison forceps, special curettes, burs and absorbable gelatin sponge (Surgifoam, Ethicon, USA). In a few dogs, additional disc fenestrations were performed at disc spaces where severe disc mineralization/dehydration or very minimal disc protrusion were noted on MRI, as a preventative measure to future clinical disc herniation.

2.5 Postoperative care and discharge

The dogs were monitored for 48 hours in the hospital's semi-intensive care unit. During this period, analgesia was performed by continuous infusion of fentanyl at a dose of 2 μg/kg/hour. After 24 hours, the infusion was discontinued and analgesia was performed with tramadol hydrochloride and sodium dipyrone subcutaneously at a dose of 3 and 30 mg/kg respectively, every 8 hours, for 5 days. Prophylactic antibiotic therapy was performed by intravenous cephalothin administration at a dose of 30 mg/kg a few minutes before skin incision and every 6 hours on the first postoperative day. Anti-inflammatory drugs were used if dogs showed signs of pain including vocalization, cervical stiffness or head ventroflexion after the surgery. In dogs that were receiving steroidal anti-inflammatory drugs prior to surgery, dexamethasone was administered at a dose 0.1 mg/kg subcutaneously once a day. In dogs that were receiving non-steroidal anti-inflammatory drugs prior to surgery, carprofen was administered at a dose at 2.2 mg/kg subcutaneously once a day. Steroidal and non-steroidal anti-inflammatory drugs were never used in combination.

All dogs remained in individual cages, with controlled room temperature, food and water. Each animal remained two days in the semi-intensive care unit and one day in the regular surgical wards until hospital release. At the time of discharge, owners were instructed to maintain activity restriction, monitor defecation and urination, in addition to light physical therapy exercises in tetraparetic dogs. The dogs were re-evaluated at 10 and 30 days by the same observer (FB) after hospital discharge.

Materials and Methods

2.6 Statistical analyses

Descriptive and inferential statistical analyses were performed. Spearman's rank-order correlation was used to analyze occurrence of associations between variables (SCCR vs pre-surgical NS grade, SCCR vs recovery time, CSF attenuation length ratio vs NS grade and recovery time). Wilcoxon signed-rank test was used to compare overall and pairwise differences, respectively, between non-normally distributed paired data (pre-surgical NS grade, NS grade at 10 and 30 days after surgery). Recovery time analysis for both ambulatory (NS grades 1, 2, 3) and non-ambulatory groups (NS grade 4) was performed by Fisher's exact test. As a consequence of that a posteriori grouping, the "n" and statistical power were increased. Mann-Whitney test was used to compare NS grade and recovery times between dogs with cranial vs caudal cervical disc herniation. P values < 0.05 were deemed significant.

3 Results

A total of 57 dogs fitted the inclusion criteria. The overall median age was 8.39 years (range 3 to 16 years). 31/57 dogs (54.39%) were males and 26/57 (45.61%) were females. There were 18 different breeds; the two most affected breeds were mixed breed 12/57 (21.05%), followed by French bulldog 10/57 (17.54%) (Table 2). The most affected disc space was C3-C4 in 17/57 (29.82%) and C4-C5 in 17/57 (29.82%) followed by C2-C3 in 12/57 (21.05%), C5-C6 in 6/57 (10.52%) and C6-C7 in 5/57 dogs (8.77%) (Figure 4). Slight lateralized disc herniation was observed in 8/57 dogs (14.03%).

Of the 57 dogs submitted to VSD, 44/57 dogs (77.19%) showed complete clinical recovery within 10 days, 9/57 dogs (15.79%) showed complete recovery within 30 days, 3/57 (5.26%) had an improved NS grade at 30 days but did not reach full recovery and 1/57 (1.76%) had no improvement in NS grade at the 30 days recheck. Overall, 56/57 dogs (98.24%) had an improved NS grade within 30 days.

Surgery duration was consistently between 60 and 90 minutes. No significant complication (such as hemorrhage requiring transfusion, laryngeal paralysis, severe edema or hematoma in the muscles, subcutaneous tissues or skin around the neck) was observed. Surgical findings correlated with the imaging diagnosis in all cases. Additional disc fenestration was performed in 8/57 dogs (14.03%) at the following disc spaces: C3-C4 (four dogs), C4-C5 (two dogs) and C5-C6 (two dogs). All dogs in this study received a single VSD. No dogs had deterioration of their NS grade after surgery.

There was a weak (r_s 0.24) but non-significant (p=0.07) positive correlation between pre-surgical NS grade and SCCR (Figures 5 and 6). At presentation, 32/57 dogs (56.14%) were NS grade 1, 6/57 (10.53%) were grade 2, 5/57 (8.77%) were grade 3, 14/57 (24.56%) were grade 4. Quantitative measurements of spinal cord compression severity by means of the SCCR calculation showed that 3/57 (5.26%) dogs had mild compression (2/3 dogs (66.66%) were NS grade 1 and 1/3 (33.34%) was NS grade 2), 34/57 dogs (59.65%) had moderate compression (22/34 (64.70%) were NS grade 1, 1/34 (2.94%) were NS grade 2, 1/34 (2.94%) were NS grade 3 and 10/34 (29.41%) were NS grade 4). 20/57 dogs (35.09%) had severe compression (8/20 (40%) were NS grade 1, 4/20 (20%) were NS grade 2, 4/20 (20%) were NS grade 3 and 4/20 (20%) were NS grade 4).

There was an overall significant difference (P<0.001) comparing pre-surgical NS grade with NS grade at 10 days and 30 days after surgery (Figure 7). In addition, there was an significant difference (P=0.0031) between NS grade at 10 days after surgery vs at 30 days after surgery. When considering all ambulatory dogs (pre-surgical NS grade 1, 2 and 3), a total of 40/43 dogs (93.02%) recovered in 10 days and 2/43 (4.65%) recovered in 30 days; 1/43 (2.32%) did not completely recover. In this subgroup (ambulatory dogs), the proportion of dogs that had complete recovery at 10 days was significantly higher than in 30 days (P< 0.001). Regarding non-ambulatory dogs (NS grade 4), 4/14 dogs (28.57%) had full recovery in 10 days and 7/14 dogs (50%) had full recovery in 30 days; 3/14 (21.43%) dogs did not make a complete recovery (two with partial improvement and one with no improvement). There was no significant difference in the proportion of non-ambulatory dogs (NS grade 4) that had complete recovery at 10 days vs 30 days in dogs (P=0.5).. This may suggest that dogs with NS grade 4 (non-ambulatory) will need more time to recovery compared with dogs with NS grade 1, 2 and 3 (ambulatory).

There was a negligible (r_s -0.0053) and non-statistically significant (P=0.97) negative correlation between categorical SCCR and post-surgical recovery time at 10 days. There was a negligible (r_s -0.0041) and non-statistically significant (P=0.76) negative correlation between categorical SCCR and post-surgical recovery time at 30 days (Figure 8). SCCR was mild in three dogs, and all (100%) recovered completely in 10 days. Of the 34 dogs that had moderate SCCR, 24/34 (70.59%) had full recovery at 10 days, 7/34 (20.58%) had full recovery at 30 days and 2/32 (5.88%) had an improved NS grade at 30 days but did not achieve full recovery; 1/34 dog (2.95%) had no improvement in NS grade at 30 days. Finally, 20 dogs had severe SCCR; of those, 17/20 (85%) had complete recovery at 10 days after surgery, 2/20 (10%) had complete recovery at 30 days after surgery and only 1/20 (5%) had improved NS grade at 30 days, but still had clinical signs (Figure 8). In all three groups of SCCR, the vast majority of dogs (44/57 or 77.2%) made a complete recovery at 10 days after surgery.

Forty-six dogs had VSD in cranial segments (C2-C3, C3-C4 and C4-C5). Of these, 33/46 (71.73%) dogs were NS grade 1, 2 and 3 and 13/46 (28.27%) dogs were NS grade 4. 35/46 dogs (76.08%) had full recovery in 10 days, 8/46 (17.40%) had full recovery in 30 days and 3 dogs did not recover completely. There were 11 dogs with VSD in the caudal cervical spine (C5-C6 and C6-C7). Of these, 10/11 dogs (90.90%) were NS grade 1, 2 and 3 and 1/11 (9.09%) was NS grade 4. Nine of these 11 dogs (81.8%) had full recovery at 10 days and 1 (9.09%) at 30 days; one dog did not have complete recovery at 30 days. There was no significant association between NS grade groups and site of herniation (cranial vs caudal) ($P=0.71$) (Figure 9). In addition, there was no significant association between recovery time and site of herniation (cranial vs caudal) ($P=0.69$) (Figure 10).

The median CSF length attenuation ratio measured on HASTE images was 0.39 times the length of C3 (range 0.1-0.9). There was a very weak (r_s 0.046) and non-statistically significant ($P=0.73$) correlation with pre-surgical NS grade. There was a weak (r_s 0.26) positive correlation with recovery time, with a trend towards statistical significance ($P=0.05$). There were three dogs (5.3%) that had only partial improvement in NS grade over the 30-day post-surgical period but did not make a full recovery. One dog had a C2-C3 disc herniation with a moderate SCCR and a CSF attenuation ratio of 0.2 times length of C3. The pre-surgical NS grade was 3 and improved to NS grade 1 at 30 days post-surgery (minimal residual pain). The other two dogs had disc herniation at C3-C4: one had severe, and one had moderate SCCR; both had a CSF attenuation ratio of 0.3 times the length of C3. Both dogs were NS grade 4 before surgery, and at 30 days after surgery, they had NS grades of 3 (dog with severe SCCR) and 2 (dog with moderate SCCR). Hence, both of these dogs regained ambulatory status. Finally, one dog (1.75%) had no post-surgical clinical improvement; this was a 12-year-old Labrador retriever with co-morbidities (diabetes mellitus); this dog had disc herniation at C6-C7 with a NS grade of 4 and lower motor neuron (LMN) signs in the thoracic limbs.

4 Discussion

The present study showed that dogs with severe SCCR due to cervical discs herniation presented a great variation regarding clinical signs ranging from neck pain to non-ambulatory tetraparesis. This corroborates findings in the only similar study in the literature (13). Interestingly, our study showed a weak but non-significant correlation between SCCR and pre-surgical NS grade, which was different from the previously cited study (13). Nevertheless, our study showed that none of the patients with NS grade 3 and 4 had spinal compression classified as mild. There was a similar proportion of dogs presenting with NS grade 1 and NS grade 4 that had severe cord compression (25% and 28.57% respectively). Overall, the lack of correlation between compression severity and NS grade likely reflects the fact that other factors contribute to the severity of spinal cord injury, such as degree of spinal cord contusion. A similar amount of compression could be associated with a range of contusive spinal cord injuries, probably dependent upon the mechanical concussive forces exerted during the extrusion event. A comparison between the degree of cervical spinal compression and the relationship with clinical signs was investigated in Dobermans with caudal cervical spondylomyelopathy (CSM) (11). In that study, it was found that clinically normal patients may have severe cervical spinal compressions. In sixteen clinically normal Dobermans, all had some degree of disc protrusion, which was considered mild in 11 dogs, moderate in 2 dogs, and severe in 3 dogs. Remarkably, in that study the degree of spinal compression at MRI was more severe in normal dogs than in those with cervical hyperesthesia or mild ataxia (11). Doberman pinschers affected with CSM usually have chronic spinal cord injury secondary to disc protrusion and hypertrophy of the ligamentum flavum. However, the pathophysiology of CSM is different from spinal injury associated with acute disc extrusion, therefore these findings may not be applicable to dogs with acute disc extrusion. Penning et al. (14) similarly observed no association between the NS grade and SCCR documented with MRI in dogs with thoracolumbar disc extrusion. Once again, this is not surprising, because spinal cord injury following intervertebral disc extrusion is due to a combination of concussive and compressive forces and further complicated by secondary mechanisms of injury (14). Jones and Inzana (18) found severe intervertebral disc changes using CT in the lumbosacral region in five out of six asymptomatic dogs. Overall, these studies and our findings suggest that there is no clear association between degree of compression and observed clinical signs in the cervical, and thoracolumbar regions. Ryan et al. (13) found in 33 dogs that severity of cervical spinal cord compression was significantly correlated with the presurgical NS grade (rs. 0.37 and P=0.04) but not with the postsurgical NS grade. In addition, they found that on cross-sectional images, the median area of spinal cord compression was 26% (varied from 11 to 71%) (13). Our study revealed a weaker correlation between severity of compression and presurgical NS grade (r_s 0.24) and this did not reach statistical significance (P=0.07). Possible explanations for this difference include a larger sample size in our study, and a bigger median area of compression in our study group (41%, range 13-66%).

Our study found that the majority of dogs with NS grade 4 recovered at 30 days while the majority of dogs with NS grade 1, 2 and 3 had a complete recovery at the 10 days recheck. These differences however must be interpreted with caution, since the group of dogs with NS grade 4 was small (14 dogs) compared to dogs with NS grades 1-2-3 (43 dogs). We used the recheck time points of 10- and 30-days post-surgery as these are the time intervals used as standard of care in our hospital (stiches removal at 10 days and last recheck at 30 days before ending cage restriction), and hence these time points were consistently available for data collection in all dogs of our study group. Indeed, some dogs across all NS grades improved completely as early as 1-3 days after surgery. That corroborates others studies that claim that the prognosis after cervical disc surgery is favorable (13,19). Although a previous study suggested that pre-surgical neurologic status were prognostic indicators of outcome, larger and more recent studies do not support these findings (20). Seim and Prata (21) reported post-surgical recovery times in 54 dogs with cervical disc herniations and found complete recovery in 47 of 54 cases after one month. In dogs with only cervical pain (NS Grade 1), 73% recovered in 7 days and 91% recovered in 28 days. In dogs with ambulatory tetraparesis (NS Grade 2 and 3), 71% and 86% recovered at 7 and 28 days respectively. Finally in non-ambulatory dogs (NS Grade 4 and 5), recovery occurred by 7 days in 56% of dogs and by 28 days after surgery in 78%. Waters (15) reported outcomes in 12 non-ambulatory dogs with cervical disc herniation: seven dogs (58%) had complete recovery, two (17%) had partial recovery and three (25%) died or were euthanized. Our outcomes are overall better than reported by these studies, but this may reflect more accurate diagnostic methods (MRI vs radiography) and improved surgical equipment.

In our study, there was no significant association between SCCR and recovery rates at 10 days and 30 days post-surgery. Those findings are similar to the study by Ryan et al (13) in 33 dogs with cervical disc herniation, which found no association between the degree of spinal cord compression and the clinical outcome (13). Similarly, another study in the thoracolumbar spine by Penning et al (14) did not find association between degree of spinal cord compression and surgical outcome. Again, this underscores the fact that other factors than the severity of the compression contribute to the outcome, such as the degree of spinal cord contusion, which is difficult to objectively quantify at MRI.

The most affected space was C3-C4 in 17/57 (29.82%) and C4-C5 in 17/57 (29.82%) followed by C2-C3 in 12/57 (21.08%). This is in agreement with other studies (1, 2, 4) that showed that intervertebral disc disease is more common in the cranial cervical region. Waters' study found that cranial cervical lesions (C2-C3, C3-C4) were associated with greater likelihood of complete recovery than caudal cervical herniations (15). Our study did not find significant differences in post-surgical recovery time between cranial and caudal disc herniation. This corroborates results from a study by Hillman et al (22), which found that site of disc herniation was not a significant predictor of complete recovery and that dogs with cranial cervical disc herniations did not actually have a higher likelihood of complete recovery compared to dogs that had caudal cervical disc herniations. In addition, our study did not find differences in NS grades between dogs with caudal vs cranial cervical disc herniation. This corroborates Cherrone´s study (1) that found no association between intervertebral disc space involved and ambulatory status. Overall, our findings seem to refute the notion that the site of disc herniation are useful predictors of outcome and severity of neurological signs.

One application of HASTE MRI pulse sequence is to obtain a "myelogram effect" on sagittal images, using heavy T2-weighting that highlights the signal from the CSF. This sequence is excellent for a rapid evaluation of the subarachnoid space, and in dogs with acute disc herniation, allows a quick localization of areas of extradural spinal cord compression and/or cord swelling from contusion and edema (12). HASTE pulse sequence was reported to be a potential prognostic tool in dogs with thoracolumbar disc extrusion and found that dogs with longitudinal extension of loss of CSF signal of <7.4 times the length of L2 were less likely to develop progressive myelomalacia (21, 23). In our study in dogs with cervical disc herniation, we did not observe a significant correlation of extent of loss of CSF signal on HASTE images with NS grade at presentation and only a weak positive correlation with recovery time. Overall, the length of loss of CSF signal on HASTE observed in our study was much shorter than the one reported by Gilmour et al (24), however only dogs with paraplegia and loss of deep pain perception secondary to thoracolumbar discs herniation were included in that study. Therefore, a direct comparison to the clinical features observed in the group of dogs analyzed here is not possible. The possibly larger diameter of the vertebral canal in the cervical area is the most likely explanation for potential differences in length of CSF attenuation when comparing cervical and thoracolumbar disc herniation using HASTE images.

In this study, chondrodystrophic breeds such as the French bulldog, Dachshund, Lhasa Apso, Shi tzu, Pekingese and Beagle had a high prevalence, together making up 42% of the study group. This is not unexpected as chondrodystrophic breeds are predisposed to disc herniation (2). The average age in our group was 8.4 years, in agreement with previous studies where the mean age of the affected animals was 8.6 years (13).

All 57 dogs had VSD. We performed disc fenestration in 8/57 dogs (14.03%) at the same time as VSD surgery. Although the value of fenestration has been questioned, it should prevent further extrusion of disc material into the vertebral canal thereby reducing the recurrence of compressive myelopathy; it also appears effective in dogs with discogenic pain (17). Fenestration was performed in dehydrated discs (as seen on MRI by complete loss of T2-weigthed signal) or in areas of minimally compressive disc protrusion. These procedures were performed to avoid potential clinically significant herniation and compression in the future. However, it was beyond the scope of this study to evaluate recurrence rate. The choice of disc space to perform the ventral slot was based on the site of the most severe spinal compression observed at neuroimaging. No dogs had more than one VSD in this study. No dog was re-imaged or needed re-intervention in the 30-day post-operative period. The only dog that was not improved was a 12-year-old Labrador with diabetes mellitus that had a SCCR of 41.13%. Ideally, re-imaging this dog would have been indicated but for financial reasons the owner decided to not repeat MRI. This particular dog had a C6-C7 disc herniation and presented with lower motor neuron signs in the thoracic limbs and a NS grade of 4. Lower motor neuron lesions usually carry a worse prognosis than upper motor neuron lesions. However, only 10 other dogs had caudal disc herniation (C5-C6 or C6-C7) and because they had NS grade 1 (n=6), 2 (n=2) or 3 (n=2) with only discrete or moderate motor deficits, an accurate determination of lower vs upper motor neuron lesions was not possible. Therefore, it was not feasible in our study to assess the influence of upper vs lower motor neuron signs on recovery.

Ryan et al. (13) observed 3/33 (9.09%) dogs had deterioration of the NS grade after cervical decompression surgery. In another study of 173 dogs with thoracolumbar disc herniation, Forterre et al. (25) observed clinical deterioration within 1–10 days after hemilaminectomy in 5.8% of cases. We did not observe clinical deterioration in our study. Of the three dogs that had an NS grade improvement but did not show full recovery, two had moderate and one had severe SCCR. Post-surgically, one dog had minimal residual neck pain and two dogs were walking with mild ataxia and were pain-free. Due to financial reasons, no re-imaging procedures were performed to evaluate any remaining disc material. In these dogs, the median CSF length attenuation ratio measured on HASTE images was 0.2-0.3, i.e. lower than the median across all 57 dogs (0.39 times the length of C3).

In the literature, mortality associated with cervical decompressive surgery in dogs ranges from 1% to 25%, with a non-ambulatory preoperative neurologic status being reported as a risk factor for mortality (8, 9, 20). Despite having 14/57 dogs (24.56%) with a non-ambulatory preoperative status (NS Grade 4), we observed no mortality in our study group.

In our study, four cases were initially managed conservatively before surgery. They all presented with a NS grade 1. At MRI, three dogs had mild compression and one had moderate compression. These dogs were closely monitored and eventually received surgery within the 2-week period after onset of clinical signs, due to worsening clinical NS grade or increasing pain. The conservative treatment consisted of restricting physical activity and cage confinement to reduce the risk of continuous extrusion while the ruptured annulus fibrosus heals. Physical therapy, administration of analgesics, muscle relaxants and anti-inflammatory drugs are also used (17, 20, 26).

This study has some limitations. The same surgeon reevaluated the dogs at 10 and 30 days, which could lead to some judgment bias. The SCCR was measured at the point of maximal compression and did not account for any dispersal of disc material or the longitudinal extent of spinal cord compression. Our observation time points for post-surgical recovery were set at 10 and 30 days but recovery may have occurred earlier than these delays in many dogs. These time points were chosen because they are consistent recheck points for all dogs undergoing VSD surgery at our hospital (removal of stitches at 10 days after surgery and last clinical recheck before lifting exercise restriction at 30 days after surgery). Finally, no neuroimaging after surgery was performed, to see how much disc material remained; although re-imaging is not a very common procedure in veterinary ventral slot surgery, it certainly should be considered in dogs that do not improve after surgery.

5 Conclusions

Ventral Slot Decompression is a safe technique for the treatment of cervical disc extrusions and, when properly performed, has an excellent prognosis. The lack of strong association between SCCR and NS grade suggests that this relationship in the cervical region is similar to that observed in the thoracolumbar region, rejecting our first hypothesis. Regarding pre-surgical NS grade and recovery time after VSD, statistically significant association was found; dogs with NS grade 4 tended to have longer post-surgery recovery times if compare to dogs with NS grade 1, 2 and 3, accepting our second hypothesis . The degree of spinal cord compression as measured by MRI-derived SCCR was not associated with the recovery time after surgery, rejecting our third hypothesis. Caudal cervical herniation did not show higher NS grades or a longer recovery time than cranial herniation, rejecting our fourth hypothesis. CSF attenuation length ratio on HASTE images was not significantly correlated with NS grade, but weakly correlated with post-surgical recovery time, only partially accepting our fifth hypothesis.

6 Conflict of Interest:

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

7 Author Contributions

FB: Performed the neurologic examinations, MRI and images analyses, surgeries and reevaluated all patients

WM: Improved English syntax and grammar, and provided input as far as the methods, analysis of results and discussion.

LW: Helped with manuscript writing and reference organization.

JV: Helped with manuscript writing

LB: Helped with clinical data acquisition

FF: Principal investigator, helped with manuscript writing and statistical analyses

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11 Supplementary Material

Table 1 – Classification of neurological status grade based on clinical signs.

Table 2 - Distribution of breeds with Cervical Intervertebral Disk Extrusion.

Figure 1 – A) T2-weighted transverse magnetic MRI of the cervical spine of a dog, with the uncompressed spinal cord highlighted in green. B) T2-weighted transverse image of the compressed spinal cord (green) and extradural disc material (red) in a dog with intervertebral disc extrusion.

Figure 2 – Examples of Spinal Cord Compression Ratio scores; mild, moderate and severe spinal compression based on measurement of surface area of the spinal cord at site of maximal compression vs normal spinal cord at the disc space cranial to the compression. The top images represent the cranial normal disc space in the same dog with the spinal cord outlined in blue; the images at the bottom are the sites of maximal spinal cord compression with the spinal cord outlined in green.

Figure 3 – Measure of spinal cord lesion on HASTE (A) comparing sizes with length of C3 on T2 weight images (B).

Figure 4 – Distribution of Dogs and Spinal Cord Compression sites.

Figure 5 – Relationship between spinal cord compression ratio and the neurological status grade of 57 dogs with cervical intervertebral disc disease before undergoing surgery.

Figure 6 – Distribution of Spinal Cord Compression ratio in each of the NS grades.

Figure 7 – Distribution of recovery times in each of the NS grades.

Figure 8 – Distribution of recovery times in each of the Spinal Cord Compression ratios.

Figure 9 – Distribution of Neurologic Status grade at cranial disc and caudal disc herniations.

Figure 10 - Distribution of recovery times at cranial disc and caudal disc herniations.

Figure 1.TIFF

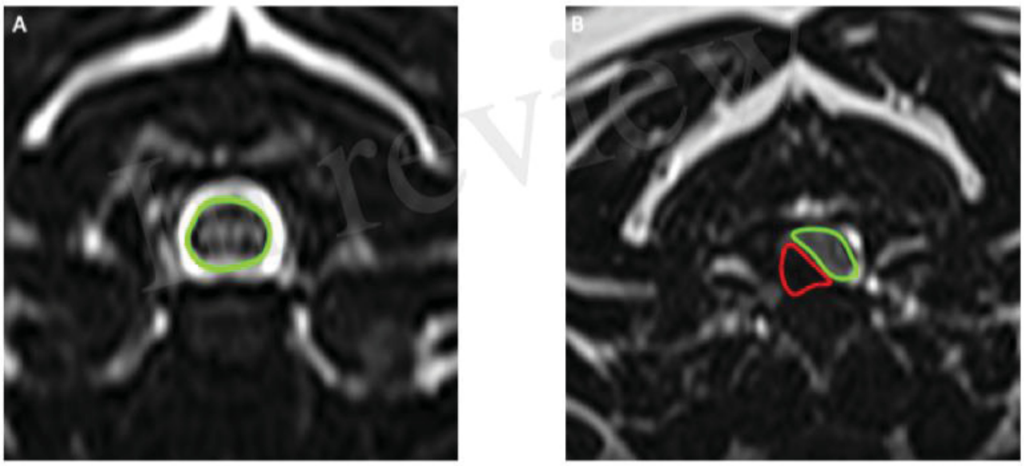

Figure 1 – A) T2-weighted transverse MRI of the cervical spine of a dog, with the uncompressed spinal cord highlighted in green (C3-C4) B) T2-weighted transverse image of the compressed spinal cord (green) and extradural disc material (red) in the same dog with intervertebral disc extrusion (C4-C5).

Figure 2.TIFF

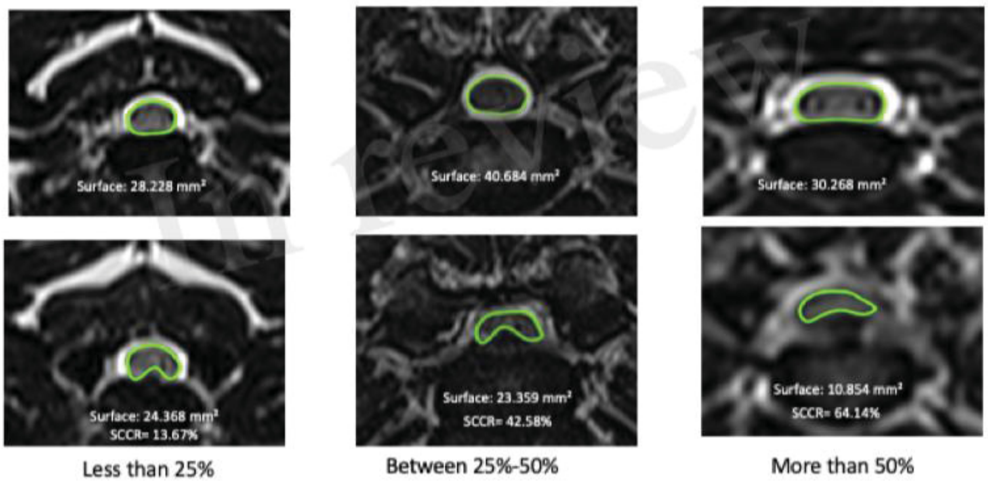

Figure 2 – Examples of Spinal Cord Compression Ratio Score; mild, moderate and severe spinal compression based on % of the vertebral canal occupied by disc material using MRI. The picture above corresponding the cranial normal disc space in the same dog.

Figure 3.TIFF

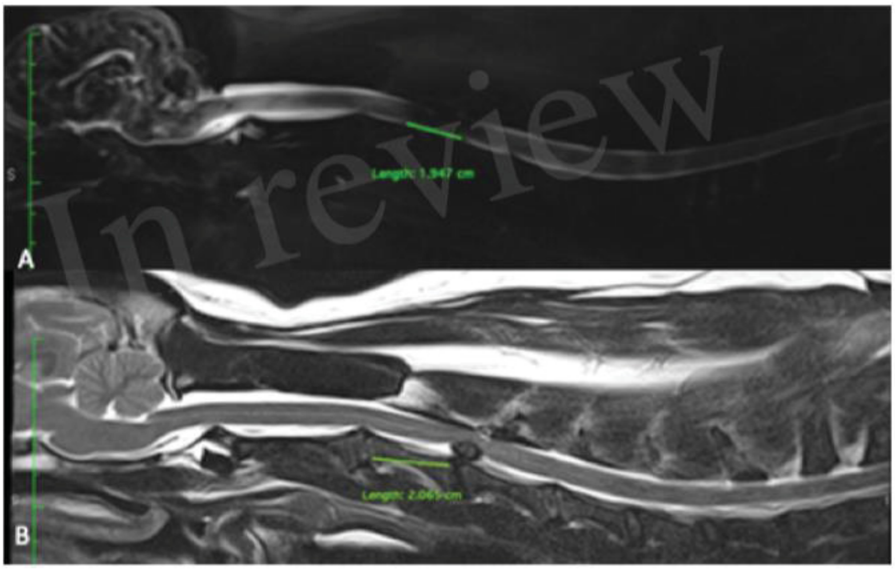

Figure 3 – A) Measure of CSF attenuation on HASTE.
B) Measure of lenght of C3 and C3-C4 disc herniation..

Figure 4.TIFF

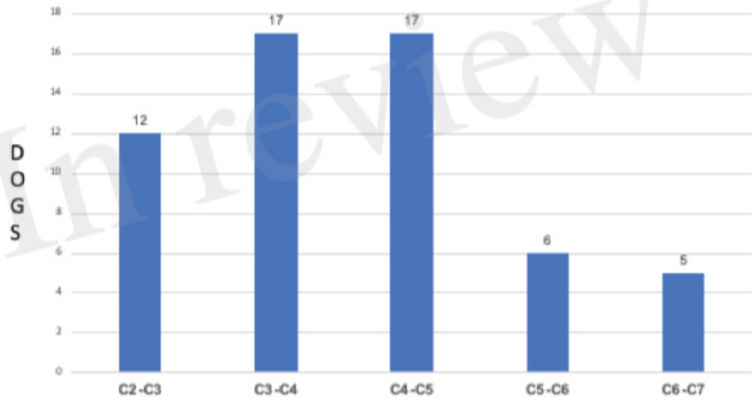

Figure 4 – Distribution of Dogs and Spinal Cord Compression sites.

Figure 5.TIFF

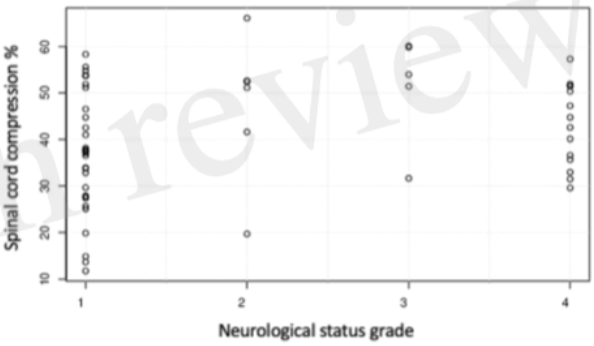

Figure 5 – Relationship between spinal cord compression ratio and the neurological status grade of 57 dogs with cervical intervertebral disc disease before undergoing surgery.

Figure 6.TIFF

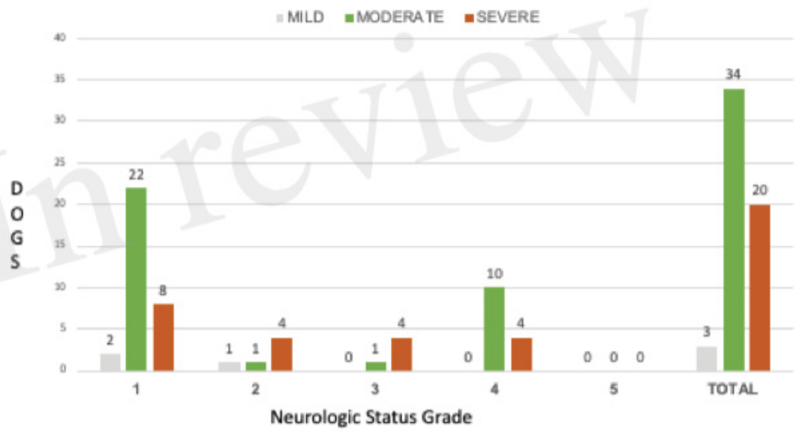

Figure 6 – Distribution of Spinal Cord Compression ratio in each of the NS grades.

Figure 7.TIFF

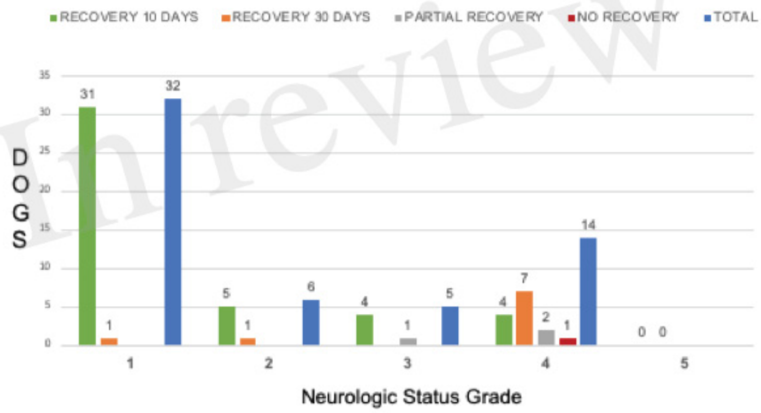

Figure 7 – Distribution of recovery times in each of the NS grades.

Figure 8.TIFF

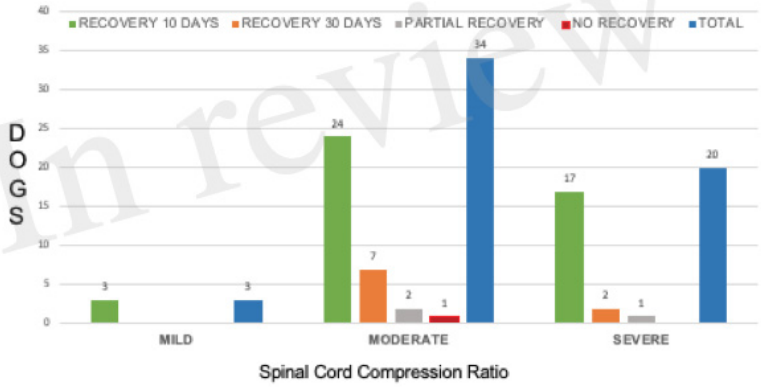

Figure 8 – Distribution of recovery times in each of the Spinal Cord Compression ratios.

Figure 9.TIFF

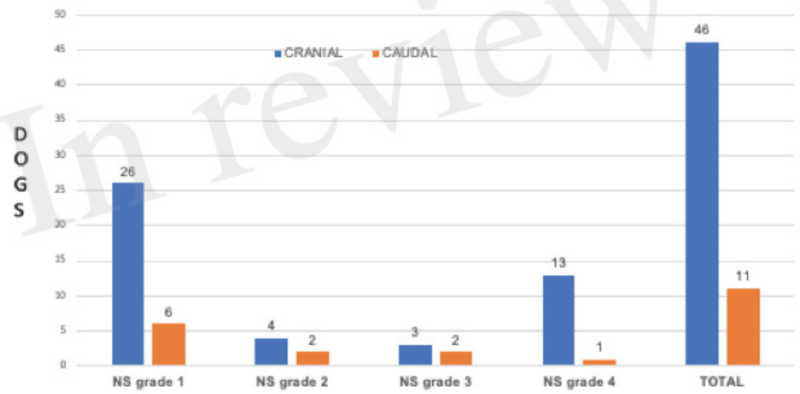

Figure 9 – Distribution of Neurologic Status Grade at Cranial and Caudal discs herniations.

Figure 10.TIFF

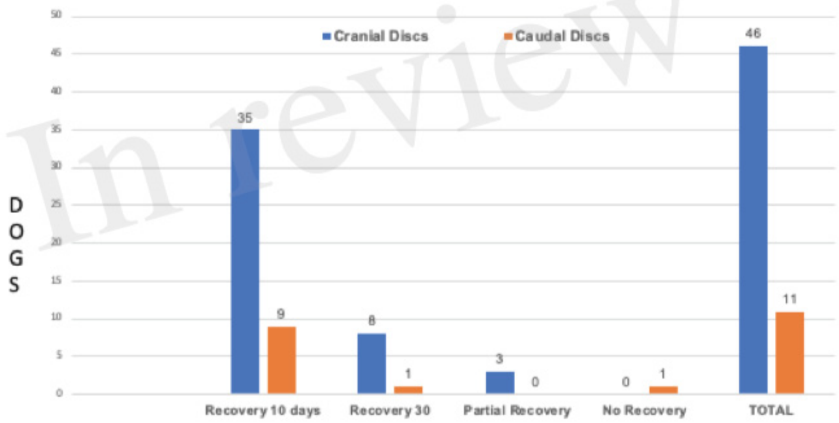

Figure 10 – Distribution of recovery times at cranial discs and caudal discs herniations.

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