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2	nucleus pulposus extrusion in dogs
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- 18 Abstract
- 19

20 Although successful outcomes have been reported after medical and surgical treatment for 21 dogs with cervical hydrated nucleus pulposus extrusion (HNPE), it is unknown which 22 treatment option is preferred. Thirty-four dogs treated medically (n=18) or surgically (n=16) 23 for cervical HNPE were retrospectively identified. Signalment, clinical presentation and 24 imaging findings were compared between medically and surgically treated dogs. Medical 25 management consisted of restricted exercise in combination with physiotherapy. Surgical 26 treatment consisted of a ventral slot procedure. Short-term follow up information was 27 retrieved from re-examination visits. Long-term outcome was obtained via telephone 28 interviews. More dogs in the surgical group demonstrated cervical hyperaesthesia on initial clinical presentation (P = 0.045), otherwise there was no significant difference in signalment, 29 30 clinical presentation, or imaging findings between both groups. Two dogs in the medically 31 managed group underwent surgical decompression due to an unsatisfactory response to 32 medical management. All cases for which long-term information was available (n=30) were 33 neurologically normal at the time of data collection. There were no significant differences for 34 any of the short or long-term outcome variables between both treatment groups. This study 35 demonstrated successful outcomes after medical or surgical treatment and suggests that both 36 treatment modalities can be considered for dogs with cervical HNPE.

38 Introduction

39 Acute intervertebral disc herniation is the most common spinal emergency in dogs and 40 encompasses several pathological processes (Cardy and others 2015). It can be defined as a 41 localised displacement of intervertebral disc material beyond its normal anatomical 42 boundaries (Fardon and Milette 2001). Although acute intervertebral disc herniation or 43 extrusion is most often preceded by advanced degenerative changes, including dehydration 44 and calcification of the nucleus pulposus (Smolders and others 2013), sudden extrusion of 45 well-hydrated and non-degenerate nucleus pulposus material can also occur (De Risio 2015). 46 Although there is some controversy about the most appropriate terminology (Lowrie and 47 others 2014, Falzone 2017), two separate types of herniation of non-degenerate to minimally 48 degenerate nucleus pulposus have been recognised; 'acute non-compressive nucleus pulposus 49 extrusion' and 'hydrated nucleus pulposus extrusion' (De Risio and others 2009, Beltran and 50 others 2012). Acute compressive hydrated nucleus pulposus extrusion (HNPE), formerly 51 referred to as 'intraspinal cyst' (Konar and others 2008), is characterised by sudden extrusion 52 of hydrated, non-degenerate to minimally degenerate nucleus pulposus material which in turn 53 leads to contusion and varying degrees of spinal cord compression (Beltran and others 2012). 54 This condition has a predilection for the cervical vertebral column and is therefore most 55 typically associated with clinical signs of severe cervical spinal cord dysfunction, such as 56 non-ambulatory tetraparesis and even tetraplegia (Konar and others 2008, Beltran and others 57 2012, Dolera and others 2015, Royaux and others 2016). Dogs with cervical HNPE have 58 more severe neurological deficits and less severe signs of cervical hyperaesthesia compared 59 to dogs with other compressive cervical myelopathies (Hamilton and others 2014). Magnetic 60 resonance imaging (MRI) is considered the diagnostic modality of choice (Beltran and others 61 2012, Dolera and others 2015, Falzone 2017). Characteristic MRI findings in dogs with 62 cervical HNPE include extradural compressive material, isointense to hydrated nucleus

63 pulpous on all sequences located immediately dorsal to the affected intervertebral disc space. 64 The affected intervertebral disc space is narrowed and contains a reduced volume of normally 65 hydrated nucleus pulposus (Beltran and others 2012) (Figure 1A and B). Cytologic and 66 histologic evaluation of the extruded material reveals findings consistent with nucleus 67 pulposus with early signs of degeneration (Dolera and others 2015, Manunta and others 2015, 68 Royaux and others 2016, Falzone 2017). Successful outcomes have been reported after both 69 medical and surgical treatment (Beltran and others 2012, Dolera and others 2015, Manunta 70 and others 2015, Royaux and others 2016) and the most appropriate type of treatment is 71 currently unknown (Lowrie and others 2014, Royaux and others 2016). Although it has been 72 suggested that medical management is usually reserved for dogs with a less severe clinical 73 signs and milder degree of spinal cord compression (Beltran and others 2012, Dolera and 74 others 2015, Falzone 2017), the exact role of medical management is currently unclear. The 75 aims of this study were therefore to compare the clinical presentation and outcome after 76 medical and surgical treatment for dogs diagnosed with cervical compressive HNPE. It was 77 hypothesized that no differences would exist in the clinical presentation and imaging findings 78 of dogs treated medically or surgically for cervical compressive HNPE and that although 79 short-term outcomes would be more favourable for surgically treated dogs, no differences 80 would exist for long-term outcomes.

81

82 Materials and Methods

83 This study was approved by the clinical research ethical review board of the Royal
84 Veterinary College, University of London (Ref: 2016/U16).

85

86 The digital medical databases of the Small Animal Referral Hospital, Royal Veterinary
87 College, University of London and the Small Animal Hospital, School of Veterinary

88 Medicine, University of Glasgow were searched for dogs diagnosed with cervical 89 compressive HNPE between January 2012 and January 2017. Search terms included hydrated 90 nucleus pulposus extrusion and HNPE. To be included in this study, animals had to have 91 clinical signs and imaging findings consistent with a diagnosis of cervical HNPE (Beltran and 92 others 2012) and the medical files and imaging studies had to be available for review. The 93 medical records and imaging studies of each potential case were evaluated by a board 94 certified neurologist to determine study eligibility. Dogs were excluded if clinical signs could 95 not solely be attributed to cervical compressive HNPE or if the medical records or imaging 96 studies were not available for review.

97 Information retrieved from the medical records included signalment, bodyweight, duration, 98 onset, type and severity of clinical signs, general physical and neurological examination 99 findings, results of diagnostic investigations and type of treatment. For the specific purpose 100 of this study, onset of clinical signs was determined as acute if clinical signs occurred in a 101 period less than 24 hours, subacute if clinical signs occurred over a period between 24 and 48 102 hours or chronic when clinical signs occurred over a period longer than 48hrs (Beltran and 103 others). The severity of neurological deficits was graded from 0 to 6 and was defined as 104 tetraplegia with reduced/absent nociception with respiratory difficulties/death (grade 0), 105 tetraplegia with intact nociception (grade 1), non-ambulatory tetraparesis (grade 2), 106 ambulatory tetraparesis (grade 3), strongly ambulatory with mild deficits (grade 4), no 107 observational gait abnormalities with cervical hyperaesthesia (grade 5) or neurologically 108 normal (grade 6). This grading system was adapted from a previous study (Fenn and others 2016). 109

Diagnosis of cervical compressive HNPE was made by high-field MRI (1.5T, Intera, Philips
Medical Systems, Eindhoven, The Netherlands or Magnetom, Siemens, Camberley, United
Kingdom) under general anaesthesia in all dogs. All animals underwent MRI within 24 hours

113 after presentation for clinical assessment. Dogs were placed in dorsal recumbency, and 114 protocols included a minimum of T2-weighted (repetition time, 3,000 milliseconds; echo 115 time, 120 milliseconds) and T1-weighted (repetition time, 400 milliseconds; echo time, 8 116 milliseconds) sagittal and transverse images. Slice thickness for sagittal and transverse 117 images were 1.75 mm and 2.5 mm, respectively, with an interslice gap of 0.3 mm in both 118 planes. For each animal the affected intervertebral disc space, the degree of spinal cord 119 compression, and the presence of intraparenchymal spinal intensity (ISI) changes were noted. 120 The degree of spinal cord compression was determined by calculating the remaining spinal 121 cord area, which was defined as the cross sectional area of the compressed spinal cord 122 segment divided by the cross sectional area at the adjacent, non-compressed segment, 123 typically overlying the cranial or caudal vertebral body adjacent to the affected disc space 124 (De Decker and others 2012). Measurements were made on T2-weighted images in the 125 transverse plane. A remaining spinal cord area of 1 represents no spinal cord compression, 126 while a value of 0 would represent complete spinal cord compression. Intraparenchymal 127 spinal intensity (ISI) changes were defined as focal intraparenchymal areas that had a 128 different intensity (hyper or hypointense) compared to the surrounding normal spinal cord 129 parenchyma (da Costa and others 2006). All imaging studies were evaluated and all 130 measurements performed by a board-certified neurologist blinded for the clinical 131 presentation, type of treatment and outcome of the individual dog. Standard image archiving 132 and communication system software (Osirix Foundation, V.5.5.2 Geneva, Switzerland) was 133 used to view and assess the imaging studies. 134 Owners were informed about the clinical diagnosis and treatment options for cervical 135 compressive HNPE by a board-certified neurologist or a veterinary surgeon enrolled in a 136 neurology residency program. The choice of treatment (medical or surgical) was made by the

137 owners. Surgical management consisted of a decompressive ventral slot procedure.

138 Perioperative anesthetic and analgesic treatments were at the discretion of the anaesthetist 139 and clinician responsible for the case. Postoperative care consisted of restricted exercise for 4 140 weeks in combination with physiotherapy and appropriate anti-inflammatory and analgesic 141 medication. Medical management was identical to post-operative care for surgical cases. 142 Restricted exercise was advised in dogs treated medically for cervical HNPE to avoid the 143 potential extrusion of additional nucleus pulposus material. Restricted exercise typically 144 consisted of allowing the dog to make two or three leashed walks a day for toileting purposes 145 and avoiding jumping, running, excessive playing or any other high-impact movements. 146 Owners of both surgically and medically treated dogs were advised to use a body harness 147 instead of a neck collar. For the purpose of this study, dogs that underwent surgical 148 management because of an unsatisfactory response to medical management were included in 149 both groups of dogs. During hospitalisation, all dogs underwent a daily neurological 150 assessment by a board certified neurologist or neurology resident and details of the 151 neurological examination findings were noted in the medical records. 152 For all dogs, the following information was retrieved from the medical records; 153 complications related to treatment or hospitalisation, duration of hospitalisation, time until 154 neurological improvement was seen, and for those dogs that were non-ambulatory, time until 155 dogs were able to ambulate without support after treatment was initiated. For the purpose of 156 this study, neurological improvement was defined as improvement from a lower to at least 157 one higher neurological grade. Occurrence of improvement and neurological grade were 158 determined at the time of discharge from hospitalisation and at re-examination visits 4 to 8 159 weeks after diagnosis. 160 Long-term follow-up was defined as a follow-up period of at least 3 months (Olby and others

161 2004) and was initially obtained via telephone interview with the referring veterinary

162 surgeons. Conforming to local ethics and welfare committee guidelines, only owners of dogs

163 that were believed to be alive at the time of data collection were subsequently contacted. 164 Owners were mailed a letter with study details and a questionnaire that had been reviewed 165 and approved by the Royal Veterinary College Ethics and Welfare committee. This 166 questionnaire covered specific aspects of the disease, such as signs of pain; amount of 167 activity; gait abnormalities, and incontinence; type of medical and surgical treatment 168 received; and response to treatment. Telephone interviews were conducted by one of the 169 authors (TB) for patients from the Royal Veterinary College and by another author for 170 patients from Glasgow University (RGQ). A successful outcome was defined as resolution or 171 improvement of clinical signs with the dog being able to ambulate independently, able to 172 voluntarily control urination and defecation, and considered by the owner to have no signs of 173 pain.

Data analysis was performed with the assistance of a standard statistical software package
(SPSS, V.21.01, SPSS, Chicago, Illinois, USA). Data were assessed for normal distribution
using the Shapiro-Wilk test for normality. Median values were reported for variables that
were not normally distributed. Continuous variables were compared using a Mann-Whitney
U test. Categorical variables were compared using either a Fisher's Exact or Chi Square test.
Values of P<0.05 were considered statistically significant.

180 **Results**

Thirty-three dogs were initially diagnosed with cervical compressive HNPE during the study period. Eighteen dogs were initially treated medically, 14 surgically and one dog was euthanised without treatment attempted. This dog presented with non-ambulatory tetraparesis and had a remaining spinal cord area of 0.71. The owners requested euthanasia due to concerns about long-term recovery and quality of life. Two dogs that underwent initial medical management, underwent eventual surgical decompression due to an unsatisfactory response to medical management. This resulted in a total of 16 surgically treated dogs, 18

188 medically treated dogs and a total of 34 dogs in which some for of treatment was attempted

189 (Table 1).

190

191	Table 1. Signalment, clinical presentation, imaging findings and outcome of 34 dogs treated
192	medically (n=18) or surgically (n=16) for cervical compressive hydrated nucleus pulposus
193	extrusion

VARIABLE	MEDICALLY TREATED DOGS (N=18)	SURGICALLY TREATED DOGS (N=16)	P-VALUE
Median age in months	96	101.5	0.48
Median weight in kg	10.8	18.8	0.16
Male dogs (%)	14 (78)	12 (75)	1.0
Median duration clinical signs in hours	12	12	0.22
Median neurological grade at presentation	2	2	0.06
Ambulatory at presentation (%)	5 (28)	3 (19)	0.69
Cervical hyperaesthesia at presentation (%)	7 (39)	12 (75)	0.045
ISI change present (%)	7 (39)	7 (44)	1.0
Median remaining spinal cord area	0.79	0,79	0.90
Median days to neurological improvement	2	2	0.32
Median days of hospitalisation	4	5	0.061
Ambulatory on discharge from hospitalisation (%)	15 (83)	12 (75)	0.33
Median days to regain ambulation	2	5	0.052
Neurologically improved on reexamination visit (%)*	9 (100)	7 (100)	0.47
Neurologically normal on reexamination visit (%)*	5 (56)	3 (43)	0.64

	Neurologically improved on long-term follow-up (%)**	16 (100)	14 (100)	1.0	
	Neurologically normal on long-term follow-up (%)**	16 (100)	14 (100)	1.0	
195	Successful outcome (%) ***	16 (89)	14 (100)	1.0	
196	ISI = Intraparenchymal spinal intensity. * information available for 9 medically and 7				
197	surgically treated dogs. ** information available for 16 medically treated and 14 surgically				
198	treated dogs. *** information available for 18 medically and 14 surgically treated dogs.				

199 Cervical hyperaesthesia on presentation was the only significantly different variable between

200 dogs treated medically or surgically for cervical compressive hydrated nucleus pulposus

extrusion.

202

203

204 Medically treated dogs

205

206 Eighteen dogs were treated medically for cervical compressive HNPE. This group consisted 207 of 14 males (5 neutered) and four females (2 neutered) aged between two and 12.5 years old 208 (median 8 years) and weighing between five and 37 kg (median 10.75kg). Affected breeds 209 included Yorkshire terrier (n=4), Border collie, Labrador retriever and Shih Tzu (n=2 for 210 each) and eight breeds were represented by one dog. Duration of clinical signs ranged from 211 12 hours to seven days (median 12 hours) and onset of clinical signs was considered acute in 212 17 dogs and chronic in one dog. Thirteen dogs presented with non-ambulatory tetraparesis 213 (grade 2) and five dogs with ambulatory tetraparesis (grade 3). During neurological 214 examination seven dogs displayed cervical hyperaesthesia. All 18 dogs could urinate 215 voluntarily. The most frequently affected intervertebral disc space was C4-C5 (n=8 dogs), 216 followed by C5-C6, C3-C4 (n=4 for both), C2-C3 and C6-C7 (n=1 for both). In seven dogs

- T2-weighted hyperintense ISI changes were present at the site of compression and the remaining spinal cord area ranged from 0.55 to 0.92 (median 0.79).
- 219

220 Two medically treated dogs, which both presented with non-ambulatory tetraparesis (grade 221 2), did not demonstrate any improvement and therefore underwent surgical treatment two and 222 five days respectively after medical treatment was started. Surgery was uneventful in both 223 cases, with both dogs demonstrating gradual neurological improvement. They were 224 discharged six and five days respectively after surgery both being strongly ambulatory with 225 mild neurological deficits (grade 4). Duration of hospitalisation for the remaining 16 dogs 226 ranged from one to six days (median 4 days). Fifteen dogs were ambulatory at the time of 227 discharge. For the one dog that was non-ambulatory at the time of discharge, time to regain 228 ambulation was 28 days (median time to regain ambulation was 2 days). Time to neurological 229 improvement ranged from one to 28 days (median 2 days). 230 Eight of these 16 dogs were re-examined four to eight weeks after a diagnosis of cervical 231 compressive HNPE was made. At this time, all eight dogs had an improved neurological 232 status and were ambulatory, and four were considered to be neurologically normal. Long-233 term follow-up information was available for all 16 dogs and was obtained from the referring 234 veterinary surgeon (n=4) or both the referring veterinary surgeon and the owner (n=12). Duration of follow-up ranged from three to 32 months (median 8 months). All dogs had 235 236 demonstrated a neurological improvement with all dogs ambulatory and considered to be 237 neurologically normal.

In summary, medical treatment resulted in a successful outcome in 16 of 18 dogs (88.9%).
The remaining two dogs did not demonstrate improvement after medical management and
experienced a complete neurological recovery after undergoing subsequent surgical

241 management.

242

243 Surgically treated dogs

244 Sixteen dogs underwent surgery for cervical compressive HNPE. Fourteen dogs underwent 245 surgery immediately after diagnosis, while two dogs underwent surgery after an unsuccessful 246 response to medical management. This group consisted of 12 males (6 neutered) and four 247 females (2 neutered) aged between three and 14 years old (median 8.5 years) and weighing 248 between 9.5 and 40 kg (median 18.73kg). Affected breeds included English Cocker Spaniel 249 (n=3), Whippet (n=2), nine breeds were represented by one dog each and two dogs were 250 crossbreeds. Duration of clinical signs ranged from 12 hours to two days (median 12 hours) 251 and onset of clinical signs was considered acute in 13 dogs and subacute in three dogs. Six 252 dogs presented with tetraplegia with intact nociception (grade 1), seven with non-ambulatory 253 tetraparesis (grade 2), two with ambulatory tetraparesis (grade 3) and one with cervical 254 hyperaesthesia without a gait abnormality (grade 5). Cervical hyperaesthesia could be elicited 255 in 12 dogs during neurological examination and four dogs were considered unable to urinate 256 voluntarily. The most often affected intervertebral disc space was C3-C4 (n=9), followed by 257 C4-C5, C5-C6 (n=3 for each), and C2-C3 (n=1). In seven dogs T2-weighted hyperintense ISI 258 changes were present at the site of compression and the remaining spinal cord area ranged 259 from 0.55 to 0.999 (median 0.79). Surgery was uneventful in all cases and surgery revealed 260 white or transparent water-like or gelatinous extradural compressive material in all cases. 261

Duration of hospitalisation ranged from two to 16 days (median 5 days). Twelve dogs were ambulatory at discharge and for dogs that were non-ambulatory at the time of diagnosis, time to regain ambulation ranged from seven to 28 days (median time to regain ambulation was 5 days). Time to neurological improvement ranged from one to 28 days (median 2 days). For

dogs that were unable to urinate voluntarily at the time of diagnosis (n=4), time to regain
voluntary control of urination ranged from two to five days (mean 3.5 days).

268

269 Seven of 16 dogs returned for re-examination visits four to eight weeks after diagnosis. At 270 that time six dogs had an improved neurological status, all seven were ambulatory and two 271 were neurologically normal. One of these seven dogs presented seven weeks after surgery for 272 sudden onset of cervical hyperaesthesia. Repeat MRI was suggestive for a collapsed ventral 273 slot (Figure 1) with compression of the left nerve root. Medical treatment was initiated with 274 Gabapentin (10mg/kg, PO, every 8 hours for 2weeks) and a recommendation of four weeks 275 restricted exercise. This dog demonstrated gradual neurological improvement and was 276 considered neurologically normal three months after surgery. Long-term follow-up 277 information was available for 14 dogs and was obtained from the referring veterinary surgeon 278 (n=5) or both the referring veterinary surgeon and the owner (n=9). Duration of follow-up 279 ranged from three to 33 months (median 18.5 months). One dog had died of an unrelated 280 cause 26 months after surgery and was, at this time, considered to be neurologically normal. 281 Of the remaining 13 dogs, all had demonstrated a neurological improvement, with all dogs 282 ambulatory and neurologically normal at the time of data collection. 283 In summary, surgical management resulted in a successful long-term outcome in all dogs 284 with available long-term information. One of 16 dogs (6.25%) experienced a surgical 285 complication, which was responsive to medical management. 286 287 Comparison between medically and surgically treated dogs 288 Cervical hyperaesthesia on initial clinical presentation was significantly more often reported

289 in dogs that underwent surgical management compared to medical management (P=0.045).

290 There were no significant differences between both treatment groups for age, bodyweight,

gender, neutering status, duration of clinical signs, ambulatory status at presentation,
neurological grade, affected intervertebral disc space, ISI changes, and remaining spinal cord
area (P>0.05). There were also no significant differences between both treatment groups for
time until neurological improvement, duration of hospitalisation, ambulatory status on
discharge, degree of neurological improvement on discharge, time to regain ambulatory
status, neurological improvement, neurological grade and likelihood of regaining a
'neurologically normal' status at short-term or long-term follow-up (P>0.05) (Table 1).

299 Discussion

300 This study evaluated and compared the clinical presentation, imaging findings and outcome 301 of dogs treated medically or surgically for cervical compressive HNPE. The signalment and 302 clinical presentation of dogs included in this study were similar to those reported previously 303 (Beltran and others 2012, Hamilton and others 2014, Dolera and others 2015). A variation of 304 small and large, predominantly non-chondrodystrophic dog breeds with an acute onset of 305 severe neurological deficits were included. Non-ambulatory tetraparesis was the most 306 common clinical presentation and that the majority of dogs presented within 24 hours of onset of clinical signs. Despite the severity of clinical signs, all dogs with available long-term 307 308 follow-up information experienced a successful outcome and were considered to be 309 neurologically normal at the time of data collection. This finding is in agreement with 310 previous studies suggesting a good to excellent prognosis for full neurological recovery in 311 dogs with cervical compressive HNPE (Kamishina and others 2009, Beltran and others 2012, 312 Dolera and others 2015, Royaux and others 2016, Falzone 2017). Although successful 313 outcomes have been reported after both medical and surgical management of cervical 314 compressive HNPE, it is currently unclear which type of treatment is associated with more 315 favourable outcomes (Lowrie and others 2014, Manunta and others 2015, Royaux and others

316 2016). Previous studies have suggested that medical management in dogs with spinal disease 317 is usually reserved for dogs with less severe clinical signs and less severe spinal cord 318 compression (Hillman and others 2009, Beltran and others 2012, De Decker and others 2014, 319 Crawford and others 2017). More severe spinal cord compression observed on MRI has 320 indeed been considered the most important indicator to elect surgery over medical treatment 321 in dogs with cervical compressive HNPE (Beltran and others 2012). In contrast, the study 322 presented here failed to demonstrate any important differences in signalment, clinical 323 presentation and imaging findings, including degree of spinal cord compression, between 324 dogs treated medically or surgically for cervical HNPE. The only significant difference 325 between the two treatment groups was that cervical hyperaesthesia was significantly more 326 often noted in dogs treated surgically compared to dogs treated medically. Furthermore, no 327 significant differences were observed for any of the short and long-term outcome measures 328 between both treatment groups. Although these results should be interpreted with caution, our 329 findings suggest that medical treatment can result in rapid and complete neurological 330 recovery in dogs with even severe clinical signs. This finding is of major clinical importance 331 because not every animal is a suitable surgical candidate and not every owner will be able or 332 prepared to pursue surgical intervention for their dog. The clinical importance of this finding 333 is illustrated by the fact that one of the dogs in this study was euthanised after a diagnosis of 334 cervical HNPE was made without any form of treatment attempted due to uncertainties about 335 the long-term prognosis and quality of life after non-surgical treatment. Two dogs underwent 336 surgery because of a perceived unsatisfactory response to medical management. The decision 337 to perform surgery was taken after respectively two and five days and both dogs eventually 338 experienced a complete neurological recovery. Although it cannot be excluded that both dogs 339 would have experienced eventual good recoveries if given more time, these results also

340 suggest that results of surgical treatment are not necessarily negatively influenced by giving341 considerations to initial medical management.

342 The fact that dogs with cervical compressive HNPE seem to respond favourably to medical 343 management is possibly explained by several factors. Development of clinical signs in 344 animals with acute extrusion of degenerate and calcified nucleus pulposus ('Hansen type I' 345 intervertebral disc disease) is multifactorial with spinal cord contusion and ongoing spinal 346 cord compression considered two important factors (Jeffery and others 2013). Ongoing spinal 347 cord compression results in decreased spinal cord perfusion and damage to myelin and axons 348 (Olby and others 2004). Although the optimal timing of decompressive surgery is somewhat 349 controversial, early surgical decompression has been suggested to improve outcome in people 350 with acute spinal cord injury and ongoing spinal cord compression (Yousefifard and others 351 2017). The acute onset of severe neurological deficits suggests also an important role for 352 spinal cord contusion in the pathophysiology of cervical HNPE (Beltran and others 2012, 353 Jeffery and others 2013). Median duration for neurological improvement and time to regain 354 ambulation after initiation of medical management were however only two days. This rapid 355 neurological improvement without surgical decompression could question the role of 356 sustained spinal cord compression in the pathophysiology of cervical HNPE. In contrast to 357 extruded nucleus pulposus in dogs with "Hansen type I" intervertebral disc disease, the 358 extruded material in dogs with HNPE has been described as a gelatinous liquid, water-like or 359 lumpy liquid (Dolera and others 2015, Falzone 2017). It is possible that the soft texture of 360 extruded material in HNPE is therefore not necessarily associated with sustained spinal cord 361 compression. It has also been suggested that the biochemical characteristics of the almost 362 healthy extruded nucleus pulposus in cervical HNPE could allow spontaneous and rapid 363 resorption (Manunta and others 2015). Previous reports have indeed demonstrated complete 364 disappearance of extruded material when follow-up MRI was performed 1.5 to six months

after medical treatment for cervical compressive HNPE was started (Kamishina and others
2010, Manunta and others 2015).

367

368 Surgery by a decompressive ventral slot procedure is an accepted treatment modality for 369 cervical compressive HNPE in dogs and can be justified by the combination of severe clinical 370 signs and the presence of extradural, moderately compressive material (Beltran and others 371 2012, Dolera and others 2015, Falzone 2017). In agreement with previous studies, surgical 372 treatment resulted in rapid improvement and excellent outcomes. This study failed however 373 to demonstrate a clear benefit from surgical intervention over medical management. Spinal 374 surgery is furthermore associated with increased expenses and potential complications. 375 Although a ventral slot procedure can be considered a standard surgical technique, potential 376 complications include intraoperative haemorrhage of the internal vertebral venous plexus, 377 vertebral subluxation, a collapsed ventral slot, respiratory compromise, and infection (Sharp 378 and Wheeler 2005). One dog included in this study experienced a postoperative complication, 379 consisting of a collapsed ventral slot. Although severe complications after ventral slot surgery 380 are rare and this dog improved with subsequent medical management, these findings illustrate 381 that the decision to perform decompressive spinal surgery should be carefully considered and 382 should ideally be reserved for dogs unlikely to recover after medical management. Further 383 studies are therefore needed to identify prognostic factors for medical management and 384 identify reliable surgical indicators for dogs with cervical compressive HNPE.

385

This study is obviously limited by its retrospective study design. Allocation of included dogs to medical or surgical treatment was not randomised and direct comparisons between both treatment modalities should therefore be done with caution. Efforts were however made to compare the signalment, clinical presentation and imaging findings between both treatment

390 groups. Although the final decision to perform surgery or pursue medical management was 391 made by the owners of the individual dogs, it cannot be excluded that owners were 392 influenced by preferences and previous experience of the responsible clinician. Furthermore, 393 only a small number of dogs could be included in this study. A small sample size can be 394 associated with a type II error or the failure to detect an effect that is actually present. It can 395 therefore not be excluded that differences in clinical presentation and outcome would have 396 become apparent with a larger population size. A sample size calculation based on the results 397 of this study indicated that we should have included 174 dogs if we we would have wanted to 398 demonstrate a significant difference in successful outcome between medical and surgical 399 treatment for cervical compressive HNPE.

400

401 Despite these limitations, the results of this study provide important new information. 402 Excellent outcomes, characterised by rapid and complete neurological recovery were 403 observed after both medical and surgical treatment for cervical compressive HNPE. In 404 agreement with previous suggestions (Munanta and others 2015), medical management 405 should, despite the severity of clinical signs, be considered a viable treatment option in dogs 406 with cervical compressive HNPE. Further studies are necessary to identify surgical 407 indications and objectively compare outcome after medical and surgical treatment for 408 cervical compressive HNPE.

409

410 **Conflicts of interest**

411 The authors declare that there were no conflicts of interest.

412

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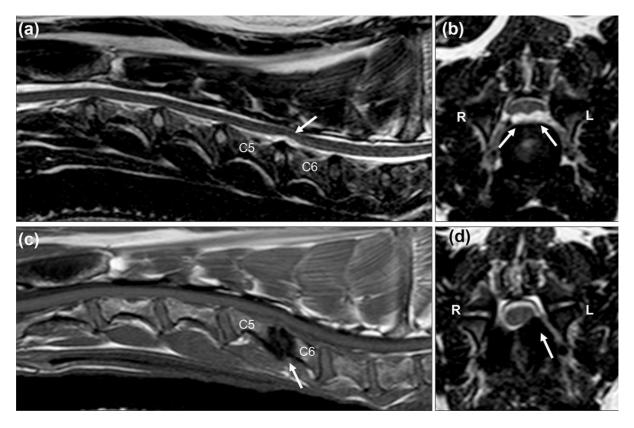
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497 Figure Legends



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499 Figure 1. T2-weighted sagittal (A) and transverse (B) magnetic resonance (MR) images of an 500 8-year-old, male, Doberman Pinscher with cervical hyperaesthesia and no other neurological 501 deficits. (A) A ventral extradural compression overlying the C5-C6 intervertebral disc is 502 visible (arrow). The compressive material has the same intensity as normally hydrated 503 nucleus pulposus. The intervertebral disc space is mildly narrowed and contains a reduced 504 volume of normally hydrated nucleus pulposus. (B) The material has the typical bilobed or 505 'seagull' appearance (arrows) and causes moderate spinal cord compression. T1-weigted 506 sagittal (C) and T2-weighted transverse (D) MR images of the same dog 7 weeks after a 507 ventral slot procedure was performed. (C) The C5-C6 intervertebral disc space is collapsed 508 (arrow). (D) A left sided extradural compression of the spinal cord and C6 nerve root (arrow) 509 510 511