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ORIGINAL ARTICLE

Does surgical timing affect the rapidity of recovery in deep pain-entire non-ambulatory dogs with thoracolumbar intervertebral disk extrusion?

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Objective: To investigate whether the delay between onset of neurological signs and spinal cord decompression affects the time to recovery in non-ambulatory paraparetic/paraplegic dogs with deep pain perception affected by thoracolumbar intervertebral disc extrusion.

Materials and Methods: Data on non-ambulatory dogs with preserved deep pain perception in both hindlimbs and surgically treated for thoracolumbar intervertebral disc extrusion were prospectively collected from three referral hospitals. Cox proportional hazards regression was used to explore the relationship of time until restoration of independent ambulation with age, weight, preoperative use of anti-inflammatory drugs, delay between onset of inability to walk and arrival at the clinic, time between presentation and spinal surgery and surgery time.

Results: One hundred and fifty-one dogs were included. Median time from admission to surgery, including imaging, was 180 (interquartile range, 65.4 to 240) minutes. All dogs were operated within 72 hours. Follow-up was available for all 151 dogs and ranged from 1 to 21 months. All but three dogs, which were all grade IV at presentation, recovered the ability to ambulate. In both univariable and multivariable models, only duration of surgery and neurological (Frankel) grade at presentation were significantly associated with the rapidity of recovery of ambulation.

Clinical Significance: Delay between onset of clinical signs and presentation and time between presentation and spinal surgery was not associated with the rapidity of recovery of ambulation in dogs surgically treated for thoracolumbar intervertebral disc extrusion. These results should be evaluated in the context of a limited range of delay since only 14.5% dogs had a delay ≥6.5 hours. Duration of surgery and neurological grade at presentation were significantly associated with rapidity of recovery of ambulation.

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INTRODUCTION

In veterinary medicine, there is lack of consensus regarding the timing of surgical decompression in non-ambulatory paraparetic/paraplegic dogs with entire deep pain perception. A recent retrospective study (Martin *et al.* 2020) suggested that an overnight delay before spinal decompression marginally increases the risk of non-recovery in non-ambulatory dogs affected by thoracolumbar intervertebral disc extrusion (IVDE). Conversely, a previous retrospective study (Upchurch *et al.* 2019) suggested that delay from onset of neurological signs of IVDE to spinal surgery is unlikely to affect the ultimate outcome or the length of time for a dog to regain pain sensation, urinary continence, or ambulation. In line with these findings, Immekeppel *et al.* (2021) concur that there is no difference in outcome whether dogs are operated on the same day or if the procedure is delayed by 1 or 2 days. Other studies evaluating outcomes have focused on the assessment of the length of recovery, as done by Davis & Brown (2002) and Fenn *et al.* (2020), where the neurological grade and the anaesthetic time were associated with time till recovery.

In human medicine, there is also a lack of agreement on the optimal timing for surgical decompression after acute traumatic spinal injury (Furlan *et al.* 2011, Piazz & Schuster 2017, Wilson *et al.* 2020, Badhiwala *et al.* 2021), although some authors consider that the first 8 to 36 hours after injury may represent a crucial time window for achieving optimal neurological recovery with decompressive surgery following acute spinal cord injury (Badhiwala *et al.* 2021, Hsieh *et al.* 2021). However, a meta-analysis and review of literature did not detect statistical difference in early *versus* late surgical decompression on the rapidity of recovery (Ter Wengel *et al.* 2019). Ethically, these are difficult topics for a randomised controlled trial and therefore decisions rely on observational data, from which it is impossible to remove all bias, notably that delay to surgery in human spinal patients is often dependent on the severity of other injuries, which may in themselves have prognostic importance.

The aim of this study was to investigate whether the delay of spinal cord decompression from the onset of neurological signs was associated with time to recovery in non-ambulatory paraparetic/paraplegic dogs with entire deep pain perception caused by thoracolumbar IVDE.

MATERIAL AND METHODS

Three referral hospitals participated in this observational study. Dogs diagnosed with IVDE between the third thoracic and third lumbar spinal segments, presenting as grade III (non-ambulatory paraparesis) and grade IV (paraplegia with deep pain preservation), modified Frankel scoring system (Frankel *et al.* 1969, Van Wie *et al.* 2013), and undergoing decompressive surgery were consecutively collected between September 2019 and June 2021. There were no exclusion criteria in this study.

All dogs underwent routine neurological examination and neurological grade at presentation and before surgery was attributed using the modified Frankel Score (Frankel *et al.* 1969, Van Wie *et al.* 2013). After collection of the clinical history from each owner, dogs were divided into four categories according to time elapsed between losing the ability to ambulate and presentation to the referral hospital: Category 1 included dogs that lost ambulation in up to 8 hours; category 2 dogs lost ambulation in a period of more than 8 but up to 12 hours; category 3 included dogs that lost ambulation in a period of more than 12 hours but up to 24 hours; category 4 was formed by the dogs that lost ambulation over a period of more than 24 hours. In cases for which the owner was unable to precisely determine when ambulation was lost, the latter information was calculated from the time that the dog was last seen walking.

All dogs underwent general anaesthesia and MRI exam of the thoracolumbar area (0.4 T, Hitachi APERTO Grande, Steinhausen, Switzerland; 0.3 T, Hitachi AIRIS II, Tokyo, Japan; 0.25 T, Hitachi Iris light, Tokyo, Japan) before decompressive spinal surgery. Removal of the herniated intervertebral disc material and subsequent spinal cord and peripheral nerve(s) decompression were achieved via a mini-hemilaminectomy or hemilaminectomy (Hoerlein 1953, Jeffrey 1988, Scott 1997) using a surgical microscope in all hospitals (Zeiss NC31, Switzerland; Zeiss NC2, Switzerland). Pre-, intra- and postoperative analgesia and anaesthesia protocols were prescribed by the anaesthetist in charge of each case, and included opioids, non-steroidal anti-inflammatory drugs (NSAIDs), gabapentin and paracetamol (acetaminophen) administered at standard dosages.

Other recorded variables included: time for imaging (hours), defined as the delay from admission to the moment that the MRI was completed; delay till surgery (hours), defined as the delay between admission and commencement of surgery (including imaging time); and, duration of the surgical procedure (minutes).

Additional data, including age, breed, weight, affected disc site, severity of spinal cord compression, administration of NSAIDs or corticosteroids before the consultation and during or after spinal surgery along with the analgesic protocols were recorded. The spinal cord compression ratio was defined as the ratio of cross-sectional area (transverse images) between maximal compression of the spinal cord and the corresponding site cranial to this where the spinal cord was uncompressed. These sites were selected according to orientation lines on the sagittal or reconstructed images (Jeffery *et al.* 2016) using imaging analysis software (Osirix, Pixmeo, Bernex, Switzerland; Horos, Version 3, Horos Project).

Neurological grade at the time of discharge, hospitalisation time and the time required for recovery of ambulation were also recorded. Recovery of ambulation (yes or no) was defined as the ability to walk at least 10 consecutive steps with both pelvic legs combined (i.e. at least five steps with each pelvic limb) without collapsing and with minimal or no support (minimal support was defined as the use of an abdominal sling to maintain balance but not to take weight off the pelvic limbs). This subjective evaluation was performed by the clinician in charge of the case (ECVN diplomate or ECVN resident).

Statistical analysis

The original aim was to examine the effect of various pre- and intra-operative variables on *whether* dogs recovered the ability to walk again. However, only three dogs in this series did not recover and so the statistical analysis was re-focused instead on the rapidity of recovery of ambulation. Cox proportional hazards regression was used to explore the relationship between age, weight, preoperative use of NSAIDs, use of corticosteroids, delay between time until independent ambulation (10 steps unaided or assisted ambulation) was recovered (outcome) and onset of inability to walk and arrival at the clinic, delay to surgery while in hospital, surgery time (exposure variables). Owing to the large differences between clinics in some of these factors, *clinic* was included as a "frailty" factor in the analysis (allowing for random effects associated with the variable *clinic*). Following univariable analysis of the association of time to recover ambulation, a multivariable model was constructed using forward and backward stepwise models and minimisation of the Bayesian information criterion (BIC) to determine the most appropriate final multivariable model. Analysis was carried out in Stata 17 (StataCorp, College Station, TX) and $P<0.05$ were taken to suggest rejection of null hypotheses.

RESULTS

A total of 151 cases were included in this observational study. There were 94 grade IV dogs and 57 grade III dogs; two dogs had different neurological scores for each pelvic limb and were graded by the most functional neurological score (e.g. considered grade III, if there was voluntary movement in one limb only). The breeds were as follows: dachshund (49), cross-breed (32), French bulldog (22), Jack Russell terrier (10), cocker spaniel (six), Maltese (six), pinscher (five), beagle (four), other breeds were represented from three or less dogs. The median weight was 8 kg [interquartile range (IQR): 6 to 12.6] and the median age was 72 months (IQR: 48 to 103).

With regards to the time elapsed between losing the ability to ambulate and presentation to the referral hospital, dogs were allocated to four categories as follows: 53 of 151 dogs [35%; 95% confidence interval (CI): 28% to 43%] lost ambulation in up to 8 hours; 23 of 151 dogs (15%; 95% CI: 10% to 22%) lost ambulation in a period of more than 8 hours but up to 12 hours; 41 of 151 (27%; 95% CI: 21% to 35%) lost ambulation in a period of more than 12 hours but up to 24 hours; and 35 of 151 (23%; 95% CI: 17% to 31%) lost the ambulation over a period of more than 24 hours. Time from admission to the completion of imaging procedures was performed in a median of 120 (IQR: 60 to 120) minutes. Median time from admission to surgery, including imaging, was 180 (IQR: 65.4 to 240) minutes. All dogs were operated within 72 hours. The median duration time for the surgical procedure was 120 (IQR: 120 to 150) minutes. The median spinal cord compression ratio was 0.57 (IQR: 0.47 to 0.68). The median hospitalisation time was 3 (IQR:2 to 4) days.

Follow-up was available for all 151 dogs and ranged from 1 to 21 months. All but three dogs, which were all grade IV at presentation, recovered the ability to ambulate. Of the three non-recovering dogs, one developed myelomalacia 3 days after surgery and died, the other two remained grade III at 18 and 4 months, respectively. The remaining 148 dogs recovered the ability to ambulate. For the dogs that lost ambulation in less than 8 hours before presentation 50 of 53 (94%) recovered the ability to walk, all dogs in all other categories recovered the ability to walk. At the time of data collection, 81 dogs were grade II, four dogs were grade I and 63 were considered neurologically normal. The median time to recover ambulation was 5 (IQR: 1 to 9.5) days. The median time to recover of grade III dogs was 2 days (IQR: 1 to 4) and for grade IV dogs was 5 days (IQR: 2 to 10). All dogs that recovered ambulation did so within 30 days.

There were numerous differences between hospitals in time to surgery (delay from admission to surgery), duration of surgery and time to recover ambulation and therefore the Cox regression analysis used a fragility term to allow a random effects model for the variable *clinic*. In univariable models, only duration of surgery and severity of injury (Frankel grade) were significantly associated with the rapidity of recovery of ambulation. Weight, age, NSAID use, corticosteroid use, delay till presentation, severity of compression and time from admission to surgery were not significantly associated with the rapidity of recovery of ambulation (Table 1). Stepwise subtraction and forward model building, together with use of the BIC suggested that the optimal model included only severity of neurologic deficits and surgery time associated with rapidity of recovery of ambulation (Tables 2 and 3). Our data implied that surgery time had a mild to moderate association with rapidity of recovery of ambulation (i.e. the association that is made here in our data is that a dog operated for 30 minutes longer than another, with all other factors held equal, will have a 19% reduction in chance of recovery at any specific instant.)

Overall, there was little variation in the delay to surgery in our population, only 22 of 151 (14.5%) had a delay of more than 6.5 hours between presentation and surgery. During the period from admission to commencement of surgery, nine of 151 (6%) deteriorated from non-ambulatory paraparesis to paraplegia and two of 151(1.3%) improved from paraplegia to non-ambulatory paraparesis. Of the dogs that deteriorated, three were in the category of more than 12 hours up to 24 hours, one was in the category of (>8 ≤12 hours) and five were in the category of up to 8 hours. No dogs deteriorated from deep pain positive to deep pain negative (Figs 1 and 2).

DISCUSSION

The primary aim of this study was to investigate whether the time between the onset of neurological signs and spinal cord decompression affected whether grade III to IV dogs, with thoracolumbar IVDE, recovered independent ambulation. However, almost the entire study population (98%) recovered the ability to ambulate and so we focused instead on the effect of pre- and intraoperatively variables on the *rapidity* of recovering ambulation. As previously reported (Davis & Brown 2002, Ruddle *et al.* 2006, Jeffery *et al.* 2016, Olby *et al.* 2016) time between onset

Table 1. Cox regression analysis – univariable model

Variable	Hazard ratio	95% CI	P
Weight	0.988	0.961 to 1.015	0.393
Age	0.991	0.932 to 1.053	0.766
NSAID	1.082	0.753 to 1.556	0.670
Corticosteroids	0.718	0.462 to 1.116	0.141
Delay	0.986	0.849 to 1.144	0.851
Grade	0.605	0.428 to 0.853	0.004
Compression	0.862	0.276 to 2.696	0.799
Time to surgery	1.001	0.976 to 1.026	0.950
Surgical time	0.992	0.987 to 0.997	0.002

CI Confidence interval, NSAID, non-steroidal anti-inflammatory drug

Table 2. Cox regression analysis – multivariable model

Variable	Hazard ratio	95% CI	P
Weight	0.996	0.965 to 1.027	0.803
Age	0.994	0.931 to 1.056	0.856
NSAID	0.827	0.539 to 1.267	0.383
Corticosteroids	0.573	0.350 to 0.936	0.026
Delay	1.076	0.907 to 1.278	0.401
Grade	0.675	0.467 to 0.974	0.036
Compression	0.937	0.269 to 3.260	0.918
Time to surgery	1.019	0.988 to 1.050	0.225
Surgical time	0.991	0.986 to 0.997	0.001

CI Confidence interval, NSAID, non-steroidal anti-inflammatory drug

Table 3. Best model analysis after stepwise subtraction and forward model building, together with use of the Bayesian information criterion (BIC)

Variable	Hazard ratio	95% CI	P
Grade	0.655	0.463 to 0.925	0.016
Surgical time	0.993	0.987 to 0.997	0.005

CI Confidence interval

of neurological signs and spinal cord decompression, age, weight or the use of NSAIDs or corticosteroids were not associated with rapidity of recovery, but there were associations with the duration of the surgical procedure and neurological grade before surgery.

In our study, the median time to recover ambulation was 5 days, and all dogs that recovered ambulation did so within 30 days. The time to recover ambulation has been evaluated in several studies, and our results are broadly in line with previous reports. Davis & Brown (2002) reported a median recovery time for grade III dogs of 7.9 and 16.4 days for grade IV. Aikawa *et al.* (2012) reported 75% grade IV and 82% of grade III being ambulatory within 14 days, while Rousse *et al.* (2016) reported that 80% grade III and 64% grade IV dog had good stepping ability within 2 weeks, that all grade III were able to ambulate within 4 weeks, and that grade IV were within 6 weeks. Skytte & Schmökel (2018) also reported a median time of 6.9 days for non-ambulatory paraparetic dogs and 28 days for paraplegic dogs. Langerhuus & Miles 2017 reported a median time to recovery ambulation for grade III dogs of 10 days, and 15 days for grade IV dogs. In our analysis, a more severe neurological grade was associated with slower recovery of ambulation, in agreement with some previous reports (Davis & Brown 2002, Skytte & Schmökel 2018). On the other hand, Ferreira *et al.* (2002) did not find an association between the duration of clinical signs and recovery of ambulation in non-ambulatory dogs with IVDE, but they did report correlation between how suddenly the damage occurred and the clinical outcome, which would support the theory of IVDE often being predominantly an acute contusive lesion. This aspect of spinal cord injury, associated with disc extrusion, was not examined in our study.

Our data would also suggest that delaying decompressive surgery up to 72 hours in grade III and IV dogs, might not affect the rapidity of recovery – both the time between the onset of clinical signs and admission, and the time from admission to spinal surgery were not associated with the overall outcome. A reasonable explanation for this finding might be that such delay is too

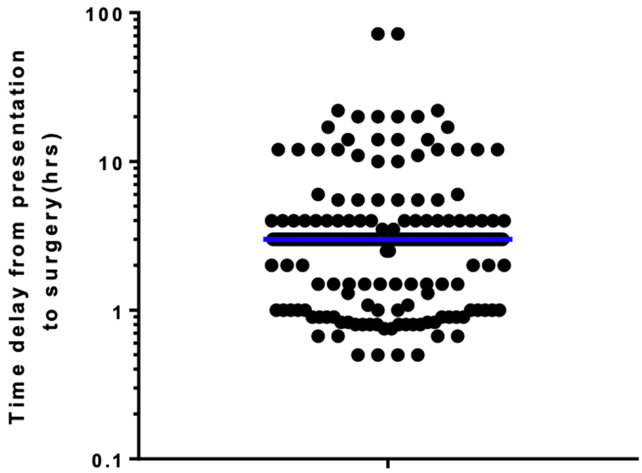

FIG 1. Dot plot illustrating range of delay from presentation to surgery. The blue line shows median value (at 3 hours). Twenty-two dogs had a delay of 6.5 or more hours between presentation and surgery (=14.5%). Note the log scale on the y-axis

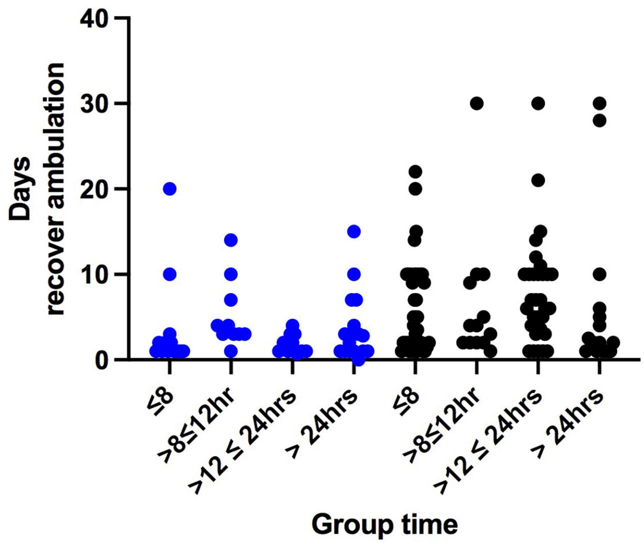

FIG 2. Dot plot illustrating the recovery time in days (y value). On the columns on the left the grade III (blue dots) dogs are represented and divided within the timing groups for losing ambulation (x-values) and on the columns on the right the same is represented with the grade IV dogs (black dots)

short to ultimately affect outcome, especially since there is little variability in our dataset. If all our cases were operated within the – unknown – time period that is required to prevent further spinal cord injury, then it would account for why there is no apparent effect of delay in our data. An alternative explanation is the contrary position, where the time delay in all cases was sufficiently long that the effects of the disc extrusion had already reached their maximum and that surgery played no overall role in recovery in this sample population.

Several studies have attempted to identify prognostic factors for recovery in dogs with spinal cord injury secondary to IVDE, but consensus is still lacking. Over the past decades there has been a trend towards recommending early decompression for cases presenting as paraplegic, probably due to the belief that leaving material in the vertebral canal might promote further damage to the spinal cord. Our results indicate that there is no correlation between severity of compression and rapidity of recovery; therefore, the role of the extradural compression in canine spinal cord injury, and the need to actively decompress the spinal cord, remain unknown (Moore *et al.* 2020). Our data echoes the idea that the contusive injury is the primary cause of clinical signs, and that remaining extradural spinal cord compression is not a source of further injury – as previously suggested (Jeffery *et al.* 2016). This would also be in agreement with recent literature reviews, comparing prognostic factors and outcomes for different types of intervertebral disc diseases (Olby *et al.* 2020). These suggest very good outcomes despite persistent spinal cord compression and spinal cord injury: 98.5% of recovery in hydrated nucleus pulposus extrusion and 100% in acute non-compressive nucleus pulposus extrusion with conservative management only.

Interestingly, in our study the duration of the surgical procedure was also negatively associated with the speed of recovery, which is in line with previously published data, where dogs that recovered ambulation, the recovery was faster if they had shorter surgical anaesthetic time (Fenn *et al.* 2020, Immekeppel *et al.* 2021). It is important to consider that the obvious conclusion of causality (i.e. longer anaesthetic/surgical time *causes* worse outcome) may not be correct. There are other equally valid explanations, such as that more complicated cases, or those with less obvious, or more inaccessible lesions, are likely to require additional anaesthetic (for imaging) or surgical (to locate and remove lesions) time than more straightforward lesions. Considering the minimal associative effects, and while our data analysis *does* indicate an association, it is important to note that this does not necessarily prove a causal effect. Correlation does not imply causality! (Smith 2020).

Data analysis also highlighted that 25% of dogs were imaged within 120 minutes and that the surgical procedure itself also lasted 120 minutes. The authors believe that this may be the result of a standardised/protocolary approach. In addition, anaesthetic sheets are not continuously monitored but more likely at intervals of 5 minutes; therefore, all the timings for the procedures would be a result of roughly 5-minute intervals. Overall, it is reasonable to think that a standard spinal surgery may took 120 minutes.

Our evaluation is an observational study, assessing how grade III and grade IV dogs with thoracolumbar IVDE recovered after standard procedures. This evaluation was based on several factors, such as clinician availability and hospital capacity; therefore, all the cases were evaluated consecutively with no exclusion. It may well be that, in view of a recent publication (Martin *et al.* 2020), clinicians have chosen to take to surgery more severely affected dogs faster than those less severely affected. While this decision making would be considered standard practice in clinical practice (Moore *et al.* 2020), it might have influenced data collection and results, reducing the chances of detecting the effects of delay on slowing recovery of ambulation. Ideally, blinded prospective randomised studies would be required to better clarify on this association, but these are likely to encounter ethical difficulties.

In conclusion, our study suggests that delay in performing decompressing spinal surgery in grade III and IV dogs may not affect the rapidity of recovery; however, it is particularly important to highlight that only a limited proportion of dogs experienced long delays, with only 14.5% (22 dogs) having a delay of more than 6.5 hours. Although all 22 dogs recovered the ability to ambulate, such cut-off should be interpreted carefully as further studies are necessary to strength these data. Also, the time between onset of clinical signs and admission, and the time from admission to spinal surgery do not influence the overall outcome. It is also possible, as suggested previously (Martin *et al.* 2020), that the time window in which the spinal cord requires surgical decompression so as to maximise recovery and its rapidity is so short that it is not practically attainable in many, or even all, canine clinical cases.

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Author contributions

L. Vicens Zanoguera: Conceptualization (supporting); data curation (lead); formal analysis (supporting); investigation (equal); methodology (supporting); project administration (lead); validation (lead); visualization (lead); writing – original draft (lead); writing – review and editing (lead). **C. Pauciulo:** Data curation (equal); validation (equal); writing – review and editing (supporting). **D. Corlazzoli:** Data curation (equal); validation (equal); writing – review and editing (supporting). **A. Cauduro:** Data curation (equal); validation (equal); writing – review and editing (supporting). **L. Motta:** Conceptualization (lead); investigation (equal); methodology (equal); project administration (lead); supervision (lead); writing – original draft (equal); writing – review and editing (equal).

Conflict of interest

None of the authors of this article has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

Ethics statement

Ethical approval was not granted for this study as this was observational, and enrolment had no influence on how the dogs were treated. All clients had signed a consent form, allowing the use of relevant data for scientific divulgation.

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