Factors associated with recovery from paraplegia in dogs with loss of pain perception in the pelvic limbs following intervertebral disk herniation

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OBJECTIVE
To investigate associations between recovery of locomotion and putative prognostic factors in dogs with loss of deep pain perception in the pelvic limbs caused by intervertebral disk herniation (IVDH).

DESIGN
Prospective cohort study.

ANIMALS
78 client-owned dogs evaluated for IVDH that underwent spinal decompression surgery.

PROCEDURES
Dogs with complete loss of deep pain perception in the pelvic limbs and tail underwent routine examinations, advanced imaging, and spinal decompression surgery in accordance with standards of practice and owner consent. For each dog, information was prospectively collected on duration of clinical signs prior to onset of paraplegia; delay between onset of paraplegia and initial referral evaluation; date of recovery of locomotion, death, or euthanasia (3-month follow-up period); and whether dogs had received corticosteroid drugs before surgery. Severity of spinal cord compression at the lesion epicenter was measured via CT or MRI.

RESULTS
45 of 78 (58%) of dogs recovered the ability to ambulate independently within 3 months after spinal decompression surgery. No evidence of prognostic value was identified for any of the investigated factors; importantly, a greater delay between onset of paraplegia and initial referral evaluation was not associated with a poorer prognosis.

CONCLUSIONS AND CLINICAL RELEVANCE
In this group of dogs with IVDH, immediacy of surgical treatment had no apparent association with outcome. The prognosis for recovery may instead be strongly influenced by the precise nature of the initiating injury. (J Am Vet Med Assoc 2016;248:386–394)

Thoracolumbar spinal cord injury in dogs is often caused by IVDH and is particularly common in chondrodystrophic dogs because of accelerated intervertebral disk degeneration relative to that in other breeds. The resultant injury to the spinal cord almost always involves both an impact injury, conventionally referred to as contusion, and a persistent deformation, referred to as compression. Contusive injury to the spinal cord has been extensively evaluated in laboratory experiments and leads to a chain of events causing tissue destruction, the extent of which depends on the severity of the primary event. Intensive efforts over the past several decades have failed to identify an effective treatment for contusive spinal cord injury beyond maintenance of physiologic stability (eg, blood flow and oxygenation). In contrast, persistent compression of the spinal cord can clearly be alleviated by surgery. Routinely, dogs that become unable to walk independently are considered as potential surgical candidates and, when spinal cord compression can be detected through imaging, will undergo decompressive surgery.

The prognosis for surgically treated dogs with thoracolumbar IVDH varies and appears to be particularly predicted by the presence or absence of deep pain perception in the pelvic limbs. Although the subject is controversial, testing for deep pain perception is a routine component of neurologic examinations involving small animals with spinal cord injury. Deep pain perception is deemed to be intact when a behavioral response consistent with that of a
conscious perception of pain is observed during application of a severely noxious stimulus.

The prognosis for dogs that retain deep pain perception is generally excellent; almost 100% of dogs with thoracolumbar IVDH will recover the ability to walk independently.\textsuperscript{10,12,13} However, the recovery rate for dogs that lack deep pain perception is far worse. Retrospective studies\textsuperscript{10,14–17} have revealed an overall recovery rate of approximately 50%, although rates differ greatly among reports, which may reflect differences in methods of testing.\textsuperscript{1} Investigations into alternative methods to estimate prognosis after severe spinal cord injury in dogs have included evoked potential testing\textsuperscript{18,19} and MRI measurements.\textsuperscript{20–22} However, neither of those methods alone provides prognostic accuracy superior to that of testing for deep pain perception. Measurement of various biomarker concentrations in serum or CSF\textsuperscript{23–26} holds considerable promise for future prognostication but is insufficiently sensitive and specific at present.

Information is lacking to help clinicians predict whether a dog without deep pain perception will recover its ability to walk again, making it challenging to provide owners with a prognosis. Results of experimental research\textsuperscript{27} involving combined contusive and compressive lesions in rodents suggest that greater magnitude of contusive injury, more severe compression, and longer delay between onset and removal of compression reduce the extent of recovery. Similar relationships could be expected in dogs with a spinal cord injury involving contusive-compressive lesions as a result of IVDH.

Magnitude of mechanical injury cannot be measured in clinically affected dogs and will vary among individuals, depending on the mass, velocity, and physical character of the herniated material. However, the other factors can be estimated from owners’ reports and from measurements made on preoperative diagnostic images. Indeed, some evidence from retrospective veterinary clinical research suggests that a longer (vs shorter) duration of absence of deep pain perception\textsuperscript{14,15,28} (or more rapid (vs less rapid) onset of paraplegia\textsuperscript{15}) is associated with poorer outcomes. Although it has been suggested that decompressive surgery is unlikely to improve the chance of recovery when the delay between onset of loss of deep pain perception and surgical intervention is > 48 hours,\textsuperscript{29} evidence also exists to contradict this opinion.\textsuperscript{15,16} Overall, considerable discrepancies exist among reported recovery rates, probably because those rates largely originated from retrospective case series. Such data often contain many sources of bias, and many analyses have involved small sample sizes, which yield a higher risk of false discovery than larger sample sizes.\textsuperscript{30}

The purpose of the study reported here was to investigate relationships between recovery of independent (unassisted) locomotion and selected, readily assessed putative prognostic indicators in dogs with loss of deep pain perception in the pelvic limbs after sudden-onset IVDH and to identify factors associated with recovery of locomotion within a 3-month follow-up period. Our hypothesis was that recovery would be more likely for dogs with less severe and less prolonged spinal cord compression.

### Materials and Methods

#### Dogs

Three university veterinary clinical centers (Iowa State University, Texas A&M University, and the University of Bristol) participated in collecting information on dogs for this prospective cohort study. The study was initiated in November 2011 and was planned to continue until a sufficient number of dogs had been enrolled to allow for multivariate analysis, which occurred in February 2014. One author (NG) collected data on dogs evaluated at a private veterinary referral center (On covet, Lille, France) from November 2011 to August 2012 and at the University of Bristol from September 2012 until the end of the collection period.

Dogs evaluated at any of the participating clinics were considered for inclusion in the study when they had paraplegia and absence of deep pain perception, as defined by a lack of behavior consistent with conscious perception of pain (eg, crying, whining, or attempting to bite) when noxious pressure was applied with pliers to the digits, metatarsals, and distal aspect of the tibia of both pelvic limbs and the tail. Dogs were excluded from the study when the cause of paraplegia was a lesion other than extrusive IVDH, the disk extrusion had occurred outside the T10-L3 region of the spinal cord, or the dogs had concurrent neurologic or other medical conditions that might have interfered with collection or interpretation of data (eg, incomplete recovery after a previous spinal lesion).

#### Putative prognostic factors

History taking and physical and neurologic examination were conducted routinely. If absence of deep pain perception was identified, a specific study record was completed for each dog. In clinical practice, it is not possible to determine the precise timing of loss of deep pain sensation (because dog owners do not make this observation); therefore, 2 intervals representing important periods after spinal cord injury were measured: the interval between the point when clinical signs related to spinal cord disease were first identified by the owner and the point when the dog became unable to walk (duration) and the interval between the point when the dog was first observed to be unable to walk and the point when it was initially evaluated at the participating clinic (delay).

Specific items recorded at the initial referral evaluation included dog signalment (age, breed, and sex), interval between first identification of clinical signs and loss of an ability to walk (loss of independent locomotion), interval between onset of loss of independent locomotion and initial referral evaluation, and whether corticosteroid drugs had been administered during the episode of spinal disease for which the dog was being evaluated. Corticosteroid drug administration was included as a putative prognostic factor because
that variable was associated with a poorer prognosis than that achieved with no such administration in a previous study involving conservative management (but not one involving surgical treatment) of affected dogs. Dosage, route, and timing of corticosteroid drug administration by referring veterinarians were highly variable, and no attempt was made to subclassify this intervention. No corticosteroid drugs were administered after the initial referral consultation.

Clinical findings were discussed with owners, including the implication that absence (vs presence) of deep pain perception is associated with a poorer prognosis, and each owner made a decision regarding whether to continue with imaging and possible surgical intervention. After CT or MRI imaging was performed (choice made on the basis of clinician preference or equipment availability), additional entries were made in the study record regarding the cranio-caudal and circumferential location of the herniated disk material. Dogs were subsequently treated in accordance with the recommendations of the attending clinician and wishes of the owners. When the target number of dogs had been enrolled, MRI or CT scans of each dog were examined independently by 2 observers and measurements made to define the maximum severity of spinal cord compression.

Outcome
The primary outcome assessed was the ability of each dog to walk independently (ie, recovery of independent locomotion) within 3 months after spinal decompression surgery. Independent locomotion was deemed to exist when a dog could walk unaided for 10 consecutive steps on the pelvic limbs, without falling to 1 side sufficiently for the lateral aspect of any part of the limb other than the digits to touch the ground surface. Follow-up information for dogs that had failed to recover by the point of clinic discharge was collected through regular (approx twice-weekly) reexaminations or telephone calls to the owners and referring veterinarians for at least 3 months after spinal decompression surgery or until dogs had been euthanized.

Diagnostic imaging and severity of spinal cord compression
Computed tomographic images were acquired in the transverse plane, and MRI scans were acquired in dorsal, sagittal, and transverse planes. Observers blinded to outcome status used dorsal and sagittal (or reconstructed images for CT) views to identify the site of disk herniation and transverse T2-weighted MRI or bone-window CT images to determine the severity of spinal cord compression. Transverse images were captured at the point where the spinal cord appeared maximally compressed and exactly 1 spinal cord segment cranial to this site where the spinal cord appeared uncompressed, guided by the orientation lines on the sagittal (or reconstructed) images. In situations in which the herniated disk material extended to affect the contour of the adjacent cranial spinal cord segment, the next most cranial segment was used to measure the expected uncompressed cord area. Slices representing sites of maximal compression and no compression were exported to image analysis software to determine the ratio of compressed to uncompressed areas for each dog (therefore smaller values indicated more severe compression). The entire process, from identifying sites of maximal compression and no compression to deriving the compression ratio, was repeated in the same manner by a second observer. Area ratios were then averaged between the 2 observers for subsequent statistical analysis. In situations in which interobserver disagreement was > 20%, a third observer performed the same analysis and the mean of all 3 values was used for statistical analysis.

Treatment
On arrival at the participating referral institution, each dog underwent neurologic examination followed in most situations by imaging and decompressive surgery. Time of arrival was used to calculate the delay between onset of loss of independent locomotion and initial referral evaluation, and, when performed, surgery occurred as rapidly as possible after arrival. Choice of decompressive surgical technique was made on the basis of the location of the compressive material and preference of the attending surgeon, but included hemilaminectomy, pediculectomy, and partial corpectomy. Postoperative care consisted of opioid analgesics, manual bladder expression, and physical therapy tailored to each dog’s requirements.

Statistical analysis
Overall, the study was designed to investigate associations between recovery of locomotion (recorded as a dichotomous outcome [yes vs no]) at 3 months and 5 putative prognostic factors: interval between initial clinical signs and onset of loss of independent locomotion (duration), interval between loss of independent locomotion and initial referral evaluation (delay), severity of spinal cord compression (recorded as a ratio), corticosteroid drug administration (recorded as a dichotomous variable [yes vs no]), and dog age.

The target study sample size was 80; however, determination of appropriate sample sizes for observational studies such as the present study is not straightforward. Our pragmatic approach to sample size was to use the rule of 10 (ie, 10 is often considered a minimum sample size for analysis by logistic regression). We considered it unlikely that all 5 factors would be included in the final statistical model; therefore, the plan was to enroll a sufficient number of dogs to yield 40 dogs with recovery of locomotion. On the basis of findings of previous studies, we estimated that approximately 80 dogs would be necessary to achieve this goal. Dogs were enrolled until this total was attained.

All analyses were performed with statistical software. Initially, each of the putative prognostic factors, which were included as continuous data when...
recorded as such, was examined for an association with recovery of independent locomotion by means of univariate logistic regression. Then, all 5 factors were included in a multivariable model to examine their relationships with recovery of locomotion within the 3-month period, thus allowing for possible interactions among factors. Subsequently, this model was reexamined by both stepwise inclusion and backward elimination of factors in accordance with their probability of a significant association with the outcome; each sequential model was tested for a significant difference from the prior model by means of the likelihood ratio test, with the aim of identifying the most parsimonious model that included all significant associations with outcome.

Subsequent analysis with the prognostic factors restructured into categories was used to check for the possibility of nonlinear relationships, reduce the possible effects of inaccuracy in data recording (through owner misjudgment or inability to determine exact timings), and allow comparison of results with those obtained in previous studies. For compression ratio, the categories were 0 to 0.50, 0.50 to 0.65, 0.65 to 0.80, and 0.80 to 1.00 (to correspond to categories of compression experimentally applied in another study). For duration and delay, the categories were 0 to 12, 12 to 24, 24 to 48, and > 48 hours. For all analyses, ORs and 95% CIs were calculated, and tests of trend for odds were performed to determine whether linear trends existed between series of recorded ORs. Values of \( P < 0.05 \) were considered significant.

Results

Dogs

Data from 93 dogs were collected and examined for eligibility (Figure 1). Seven dogs were excluded from the study because they did not have imaging performed; of these, 4 were immediately euthanized at the owners' request and 3 were treated conservatively. All 3 conservatively treated dogs were later euthanized because of signs of myelomalacia (ie, cutoff for cutaneous trunci reflex became progressively more cranial and trunk muscle flaccidity was evident) between 3 and 5 days after imaging. An additional 5 dogs with no evidence of myelomalacia were euthanized at the owners' request at various stages between 0 and 28 days after imaging, and data pertaining to those dogs were excluded from logistic regression analyses (because they did not fairly represent the potential of the study population to recover). One dog died within 24 hours after surgery from suspected pulmonary thromboembolism (acute respiratory distress and rapid death), and data pertaining to it were also excluded from statistical analysis because although this complication might have been a risk of surgery, it was unlikely to have been related to the underlying spinal cord injury. Data pertaining to an additional 2 dogs were excluded from analysis because those dogs were lost to follow-up after clinic discharge (at 5 days after surgery).

Data pertaining to all remaining dogs \( (n = 78) \) were included in the analysis. Forty-four dogs were Dachshunds, and the remaining 34 primarily included various small- to medium-sized purebred dogs or dogs...
of mixed breeding. Estimates of the severity of spinal cord compression (compression ratio) for 25 (29%) of the included dogs differed between the initial 2 observers by > 20%, and discrepancies were resolved by a third blinded observer.

Outcome

Forty-five (58%) dogs had recovery of independent locomotion within the 3-month follow-up period (Table 1). Median interval to recovery for all dogs was 49 days; dogs that recovered within 3 months did so within a median of 27 days. Of the 35 dogs that did not recover, 10 (13% of all dogs) developed signs consistent with progressive (ie, ascending or descending) myelomalacia at a postoperative interval of between 2 and 8 days and were euthanized.

Association of putative prognostic factors with outcome

Univariate logistic regression revealed that none of the factors hypothesized to be associated with recovery of locomotion were significantly associated with prognosis (Table 2). This lack of effect was confirmed through inclusion of all factors in a multivariate analysis, which again revealed that none had a significant association. In additional exploratory analysis, the interaction between spinal cord compression ratio and delay between onset of loss of independent locomotion and initial referral evaluation was also examined and, again, no significant effect was discerned (OR, 1.007; 95% CI, 0.971 to 1.045). When stepwise elimination of the various prognostic factors was used, no significant change was identified in model fit. The last remaining factor (ie, the factor with the lowest $P$ value) was spinal cord compression ratio, and the association of this factor with outcome was subsequently examined in more detail.

Additional univariate analysis involving categorization of the continuous variables duration, compression ratio, and delay resulted in odds of recovery that differed among categories for each variable (Table 3). However, the associated 95% CIs were wide, meaning that there was insufficient evidence to conclude that any of these factors was prognostically important. Specifically, no evidence was identified to support the notion that prognosis for recovery of locomotion was poorer when the delay was greater between onset of loss of independent locomotion and initial evaluation at the participating referral center. However, the power of

Table 1—Characteristics of dogs with loss of deep pain perception in the pelvic limbs following IVDH that recovered (n = 45) or did not recover (33) independent locomotion within 3 months after spinal cord decompression surgery.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Recovered</th>
<th>Did not recover</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>23 (51)</td>
<td>18 (55)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>5.5 ± 2.2</td>
<td>5.2 ± 1.9</td>
</tr>
<tr>
<td>Received corticosteroid drugs</td>
<td>15 (33)</td>
<td>8 (24)</td>
</tr>
<tr>
<td>Duration of clinical signs (h)</td>
<td>47.5 ± 69.2</td>
<td>32.4 ± 49.8</td>
</tr>
<tr>
<td>Delay between onset of loss of</td>
<td>25.1 ± 23.0</td>
<td>23.6 ± 22.9</td>
</tr>
<tr>
<td>independent locomotion and initial</td>
<td></td>
<td></td>
</tr>
<tr>
<td>referral evaluation (h)</td>
<td>0.443 ± 0.188</td>
<td>0.529 ± 0.220</td>
</tr>
</tbody>
</table>

Values are number (%) for sex and receipt of corticosteroid drugs and mean ± SD for all other factors.

*Compression ratio (ratio of compressed to uncompressed area) was calculated from transverse MRI or CT images captured at the point where the spinal cord appeared maximally compressed and exactly 1 spinal cord segment cranial to this site where the spinal cord appeared uncompressed. The compression ratio was unobtainable (ie, images were not retrievable) for 2 dogs, both of which recovered.

Table 2—Results of univariate and multivariate analyses to examine relationships between putative prognostic factors and recovery of locomotion in 78 dogs with loss of deep pain perception in the pelvic limbs following IVDH.

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
<th>SE</th>
<th>$P$ value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Univariate analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>1.130</td>
<td>0.137</td>
<td>0.313</td>
<td>0.891–1.433</td>
</tr>
<tr>
<td>Compression ratio*</td>
<td>0.149</td>
<td>0.180</td>
<td>0.114</td>
<td>0.014–1.584</td>
</tr>
<tr>
<td>Duration of clinical signs (h)</td>
<td>1.005</td>
<td>0.004</td>
<td>0.259</td>
<td>0.996–1.013</td>
</tr>
<tr>
<td>Delay between onset of loss of</td>
<td>1.007</td>
<td>0.011</td>
<td>0.527</td>
<td>0.986–1.029</td>
</tr>
<tr>
<td>independent locomotion and initial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>referral evaluation (h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroid drugs received</td>
<td>1.334</td>
<td>0.670</td>
<td>0.567</td>
<td>0.498–3.572</td>
</tr>
<tr>
<td>Multivariate analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>1.051</td>
<td>0.141</td>
<td>0.711</td>
<td>0.808–1.367</td>
</tr>
<tr>
<td>Compression ratio*</td>
<td>0.188</td>
<td>0.235</td>
<td>0.187</td>
<td>0.015–2.284</td>
</tr>
<tr>
<td>Duration of clinical signs (h)</td>
<td>1.004</td>
<td>0.005</td>
<td>0.396</td>
<td>0.995–1.013</td>
</tr>
<tr>
<td>Delay between onset of loss of</td>
<td>1.003</td>
<td>0.012</td>
<td>0.833</td>
<td>0.979–1.028</td>
</tr>
<tr>
<td>independent locomotion and initial</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>referral evaluation (h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corticosteroid drugs received</td>
<td>1.104</td>
<td>0.625</td>
<td>0.865</td>
<td>0.362–3.347</td>
</tr>
</tbody>
</table>

See Table 1 for key.
this analysis was low because few dogs were included in the categories representing the greatest delay.

**Discussion**

The exploratory study reported here was designed to investigate whether recovery of locomotion by dogs with absence of deep pain perception in the pelvic limbs following IVDH would be associated with prognostic factors that could readily be determined in the clinic. Most importantly, we found no evidence to support the notion that the 2 factors over which veterinarians presumably have the most control (delays between onset of paraplegia and spinal decompression surgery or corticosteroid drug administration) had an effect on prognosis within the 3-month follow-up period. Most surprisingly, no evidence was obtained to suggest a poorer prognosis for dogs that had absence of deep pain perception for > 48 hours after onset of paraplegia than the prognosis for dogs in which it had been absent for < 48 hours.

The lack of associations identified in the present study conflicted with other reported findings from retrospective studies. In studies in which little or no evidence of an association is detected, the possibility typically exists that inadequate power was available to detect a true association. However, results of the present study could be considered more reliable than those of the other studies because data were collected prospectively on sequentially evaluated dogs, more dogs were included than in the other studies, and almost complete follow-up information was available for each. Indeed, the present study involved the largest sample of dogs with loss of deep pain sensation following IVDH to be analyzed for prognostic factors. Furthermore, the point estimates of effect obtained with both univariate and multivariate analyses in the present study were centered on the null value (ie, OR = 1) and many had reasonably narrow 95% CIs, suggesting that increasing the number of dogs would have been unlikely to have yielded considerably different results.

Results of corollary analyses yielded little reason to believe that interactions between severity of spinal cord compression and either of the temporal factors (duration of clinical signs before onset of paraplegia and delay between onset of clinical signs and initial referral evaluation) would affect prognosis, although those analyses involved a smaller number of dogs and therefore had less power to detect associations. Provision of sufficiently precise 95% CIs to completely rule out significant interactions between factors would have required data from many hundreds of dogs, necessitating collaboration between many neurosurgical centers over many years.

The present findings were surprising, considering that evidence from experimentally induced disease in small groups of rodents (42 rodents separated into 5 groups) suggests that severity and duration (equivalent to delay in the present study) of spinal cord compression are associated with extent of recovery in that species. Some evidence also exists to suggest that

Table 3—Results of univariate analysis to examine relationships between putative prognostic factors and recovery of independent locomotion in dogs with loss of deep pain perception in the pelvic limbs following IVDH (n = 78), after reclassification of selected continuous factors as categorical variables.

<table>
<thead>
<tr>
<th>Factor</th>
<th>No. (%) that recovered</th>
<th>No. (%) that did not recover</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compression ratio*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–0.50</td>
<td>20 (47)</td>
<td>14 (42)</td>
<td>1.429</td>
<td>0.722–2.828</td>
<td>0.188</td>
</tr>
<tr>
<td>0.50–0.65</td>
<td>18 (42)</td>
<td>10 (30)</td>
<td>1.800</td>
<td>0.831–3.899</td>
<td>—</td>
</tr>
<tr>
<td>0.65–0.80</td>
<td>4 (9)</td>
<td>6 (18)</td>
<td>0.667</td>
<td>0.188–2.362</td>
<td>—</td>
</tr>
<tr>
<td>0.80–1.00</td>
<td>1 (2)</td>
<td>3 (9)</td>
<td>0.333</td>
<td>0.035–3.205</td>
<td>—</td>
</tr>
<tr>
<td>Duration of clinical signs (h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–12</td>
<td>20 (44)</td>
<td>15 (45)</td>
<td>1.333</td>
<td>0.683–2.604</td>
<td>0.214</td>
</tr>
<tr>
<td>12–24</td>
<td>8 (18)</td>
<td>12 (36)</td>
<td>0.667</td>
<td>0.273–1.631</td>
<td>—</td>
</tr>
<tr>
<td>24–48</td>
<td>6 (13)</td>
<td>2 (6)</td>
<td>3.000</td>
<td>0.606–14.864</td>
<td>—</td>
</tr>
<tr>
<td>&gt; 48</td>
<td>11 (24)</td>
<td>4 (12)</td>
<td>2.750</td>
<td>0.876–8.636</td>
<td>—</td>
</tr>
<tr>
<td>Delay between onset of loss of independent locomotion and initial referral evaluation (h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–12</td>
<td>18 (40)</td>
<td>16 (48)</td>
<td>1.125</td>
<td>0.574–2.206</td>
<td>0.395</td>
</tr>
<tr>
<td>12–24</td>
<td>14 (31)</td>
<td>11 (33)</td>
<td>1.272</td>
<td>0.578–2.803</td>
<td>—</td>
</tr>
<tr>
<td>24–48</td>
<td>9 (20)</td>
<td>3 (9)</td>
<td>3.000</td>
<td>0.812–11.081</td>
<td>—</td>
</tr>
<tr>
<td>&gt; 48</td>
<td>4 (9)</td>
<td>3 (9)</td>
<td>1.333</td>
<td>0.298–5.957</td>
<td>—</td>
</tr>
</tbody>
</table>

For percentage calculations, the denominator is the total number of dogs that did (43 dogs for compression ratio and 45 dogs for the other 2 factors) or did not (33 dogs) recover for which data were available. — = Not applicable. See Table 1 for remainder of key.
immediacy of surgery in humans with spinal cord injury is associated with a superior recovery rate, although this finding is highly controversial. Indeed, results of a study involving humans with a severity of spinal injury similar to that of dogs without deep pain sensation (ie, American Spinal Injury Association grade A patients) suggest that an increase in delay to surgery does not affect outcome. Prior experimental laboratory studies and the present study differed in 2 important ways. First, in the most relevant experiment involving rats, spinal cord compression persisted for a matter of hours, whereas in the present study, compression may have been left untreated for several days (the duration of clinical signs). Second, injury causing loss of deep pain perception in dogs is more severe than that generally evaluated in rats.

Instead, findings of the study reported here suggested that the prognosis for many dogs lacking deep pain perception following IVDH may be more or less fixed at the point of injury (ie, the damage may be irreparable in some dogs). The unknown factor responsible for induction of irreversible injury could perhaps be the primary mechanical injury, the magnitude of which cannot be measured in clinically affected dogs but which can be controlled in laboratory investigations. Contusion initiates a cascade of destructive secondary events, and laboratory experiments involving rats have revealed that subtle differences in various aspects of the mechanical injury can yield quite profound differences in outcome. A so-called switch effect has been suggested on the basis of findings involving humans with brain injury after stroke, in whom pericyte death causes shutdown of regional blood flow. With the techniques available at the time of the present study, we were unable to identify dogs that would be unable to recover.

Ascending myelomalacia was identified in approximately 10% of the surgically treated dogs in the present study, which was similar to proportions reported previously. This small proportion made it difficult to identify what may be important causal factors. Instead, a cohort study with a sufficient number of dogs to examine this outcome (approx 500 dogs with absence of deep pain perception) or a case-control study would be required to identify specific risk factors.

Although the present study yielded no evidence that the physical and temporal factors examined had prognostic importance, results should be interpreted with caution. Some of the measurements may have been unreliable. For example, owner-reported timing of specific events may have been inaccurate because of difficulty in owner assessment or recall, thereby obscuring the results. However, we considered this potential problem before performing the analyses and therefore used logistic regression (for dichotomous differentiation of recovery of locomotion rather than time-to-event analysis) plus reanalysis of continuous data as categorical data (to reduce the effect of imprecise measurements). We consequently believe that

Other potential sources of inaccuracy in the study reported here included measurements of the severity of spinal cord compression. Moderate disagreement was common between measurements made by 2 observers, and the consequent likely loss of accuracy might have obscured important relationships between compression severity and outcome. Such inaccuracy might be resolved in the future as the quality of clinical imaging increases. No constraints were placed on mode of imaging (CT or MRI) used for measurements of spinal cord compression because the study involved many clinics and many clinicians with different preferences or available equipment. To control for these differences, we chose to assess severity of spinal cord compression by calculating ratios of compressed to uncompressed areas (rather than measuring only the compressed area) by use of the same sequence and imaging modality for each dog. However, failure to use a single modality may have obscured relationships between compression severity and outcome.

Lastly, assessment of absence of deep pain sensation and detection of independent locomotion could have involved some imprecision. Assessment of deep pain sensation was subjective, although no different in nature from other neurologic assessments used for veterinary species or those used in human clinical trials. Of course, other observers may have graded the degree of deep pain perception differently than the clinicians involved in the present study, through differences in technique or interpretation. In addition, recovery of independent locomotion as defined in the present study may have been difficult for owners to accurately identify. The study design also did not account for the possibility that some dogs might have been able to walk without recovery of deep pain perception, although this ability usually takes many months to develop. To rule out that possibility, we collected information on other variables such as recovery of voluntary tail wag and development of urinary continence in situations requiring follow-up telephone conversations, and many dogs were reexamined at the participating clinics at or after the 3-month follow-up period.

Results of the study reported here indicated that the putative temporal and physical prognostic factors evaluated had little value in predicting recovery of independent locomotion (within 3 months) in dogs with paraplegia and loss of pain sensation in the pelvic limbs. Most notably, the data suggested that, as a whole, dogs with paraplegia and loss of deep pain sensation did not necessarily require immediate surgical intervention. Findings also suggested the possibility that the ability to recover locomotion may have already been determined prior to initial referral evalu-
ation. The mechanism for such a determination likely involved control of blood flow to the damaged region; therefore, we recommend that future investigations of prognostic factors for recovery of independent locomotion in dogs with loss of deep pain perception following IVDH focus on detection of biomarkers for this type of injury.

Acknowledgments

Dr. Hu is supported by a grant from the International Spinal Research Trust.

Footnotes

a. Image J, version 1.50a, National Institutes of Health, Bethesda, Md.
b. Osirix, version 5.8.2, Pixmeo, Bernex, Switzerland.
c. Stata, version 11.2, StataCorp, College Station, Tex.

References


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From this month’s *AJVR*

**Radiographic evaluation of the width of the femorotibial joint space in horses**

Pierre Trencart et al

**OBJECTIVE**

To measure the minimal joint space width (mJSW) in caudocranial radiographic views of orthopedically normal femorotibial joint of horses, to compare the accuracy of measurements with those of a software program designed for humans, and to identify the ideal caudocranial radiographic projection angle for mJSW measurement.

**ANIMALS**

12 healthy mares (22 femorotibial joints) and 3 equine cadavers (6 stifle joints).

**PROCEDURES**

Caudocranial views of femorotibial joints were acquired in the proximodistal plane at 5°, 10°, and 15° (caudo-5°-proximal-craniodistal oblique, 10°, and 15°) and lateromedial plane (caudo-10°-proximo-5°-medial-craniodistomedial oblique and caudo-10°-proximo-5°-medial-craniodistolateral oblique). The mJSWs of medial and lateral femorotibial joint compartments were measured manually by 2 evaluators and automatically by a digital analysis software program. Interevaluator reproducibility was assessed. Post hoc tests were used to identify the projection angle that provided the largest measurements. Validation of mJSW measurements was performed by evaluation of 6 stifle joints ex vivo.

**RESULTS**

Excellent agreement was achieved between the 2 evaluators and between the veterinary radiologist and the analysis software for the medial and lateral compartments of femorotibial joints. Angle of caudocranial view in the proximodistal but not lateromedial plane had a significant effect on the medial compartment mJSW measurements. Mean mJSW for the medial compartment was significantly higher for the caudoproximal-craniodistal oblique projection made at 10° from the horizontal than for other angles. Angle had no significant effect on mean mJSW for the lateral compartment. Agreement between automated measurements of mJSW in the medial compartment and thickness of nonmineralized cartilage in histologic preparations of associated tissues was excellent.

**CONCLUSIONS AND CLINICAL RELEVANCE**

Measurements of mJSW in the medial compartment of femorotibial joints, the most common site of osteoarthritis in horses, were reproducible and optimal with a caudoproximal-craniodistal oblique radiographic projection made at 10° from the horizontal. (*Am J Vet Res* 2016;77:127–136)