



STANDARD ARTICLE

Predictors of urinary or fecal incontinence in dogs with thoracolumbar acute non-compressive nucleus pulposus extrusion

Lorenzo Mari¹  | Sebastien Behr² | Anita Shea¹  | Elisabet Dominguez³ |
 Cristoforo Ricco² | Emili Alcoverro⁴ | Abel Ekiri⁵ | Daniel Sanchez-Masian⁴ |
 Luisa De Risio¹

¹Department of Neurology/Neurosurgery, Centre for Small Animal Studies, Animal Health Trust, Newmarket, Suffolk, UK

²Neurology/Neurosurgery Service, Willows Veterinary Centre and Referral Services, Solihull, UK

³Diagnostic Imaging Unit, Centre for Small Animal Studies, Animal Health Trust, Newmarket, Suffolk, UK

⁴Department of Small Animal Clinical Science, Institute of Veterinary Science, University of Liverpool, Neston, Cheshire, UK

⁵School of Veterinary Medicine, University of Surrey, Guildford, Surrey, UK

Correspondence

Lorenzo Mari, Department of Neurology/Neurosurgery, Centre for Small Animal Studies, Animal Health Trust, Newmarket, Newmarket, Suffolk, UK.
 Email: lorenzo.mari@hotmail.com

Present Addresses

Lorenzo Mari, Neurology and Neurosurgery Department, Wear Referrals Veterinary Hospital, Bradbury, Stockton-on-Tees, Durham, UK. Daniel Sanchez-Masian, Anderson Moores Veterinary Specialist, The Granary, Bunstead Barns, Poles Lane, Hursley, Winchester, Hampshire, UK. Elisabet Dominguez, ARS Veterinaria, Carrer del Cavallers 37, Barcelona, Spain.

Abstract

Background: Urinary (UI) and fecal (FI) incontinence occur in up to 7.5% and 32% of dogs, respectively, after thoracolumbar acute noncompressive nucleus pulposus extrusion (ANNPE).

Hypotheses/Objectives: To investigate clinical, diagnostic, and therapeutic predictors of UI and FI in dogs with ANNPE affecting the T3-L3 spinal cord segments.

Animals: Hundred and eighty-seven dogs with T3-L3 ANNPE diagnosed based on clinical and MRI findings.

Methods: Multicenter retrospective study. Data were obtained from medical records and telephone questionnaires and analyzed by logistic regression.

Results: UI and FI were reported in 17 (9.1%) and 44 (23.5%) dogs, respectively. Paraplegic dogs were 3 times (95% CI = 1.25, 10.87) more likely to develop UI ($P = .018$) and 4 times (95% CI = 1.94, 12.56) more likely to develop FI ($P = .001$) compared to nonparaplegic dogs. Dogs with an intramedullary hyperintensity greater than 40% of the cross-sectional area of the spinal cord at the same level on transverse T2-weighted MRI images were 4 times more likely to develop UI (95% CI = 1.04, 21.72; $P = .045$) and FI (95% CI = 1.56, 10.39; $P = .004$) compared to dogs with smaller lesions. FI was 3 times (95% CI = 1.41, 7.93) more likely in dogs that were not treated with nonsteroidal anti-inflammatory drugs (NSAIDs) after diagnosis compared to dogs administered NSAIDs ($P = .006$) and 2 times (95% CI = 1.12, 5.98) more likely in dogs presented with clinical signs compatible with spinal shock compared to dogs without ($P = .026$).

Abbreviations: ANNPE, acute non-compressive nucleus pulposus extrusion; COX2, cyclooxygenase-2; FI, fecal incontinence; LL:VL, ratio of the length of the intramedullary lesion to the length of the L2 vertebra; NSAIDs, nonsteroidal anti-inflammatory drugs; PCSAL, percentage of the cross-sectional spinal cord area occupied by the lesion; SCI, spinal cord injury; UI, urinary incontinence.

This article was published online on 31 October 2019. An Error was subsequently identified in Table 2. This notice is included in the online version to indicate that has been corrected 8 November 2019

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2019 The Authors. *Journal of Veterinary Internal Medicine* published by Wiley Periodicals, Inc. on behalf of the American College of Veterinary Internal Medicine.

Conclusion and Clinical Importance: The identification of clinical, diagnostic, and therapeutic predictors of UI and FI in dogs with T3-L3 ANNPE can help to approach these autonomic dysfunctions occurring after spinal cord injury.

KEYWORDS

high-velocity intervertebral disc extrusion, neurogenic bowel dysfunction, nonsteroidal anti-inflammatory drugs, spinal cord injury, spinal shock, traumatic intervertebral disc extrusion

1 | INTRODUCTION

Acute non-compressive nucleus pulposus extrusion (ANNPE) is a relatively common disease in dogs characterized by traumatic herniation of hydrated nucleus pulposus from an intervertebral disc, causing a contusive non-compressive or minimally compressive injury to the overlying spinal cord.^{1,2} Currently, the diagnosis of ANNPE is based on detection of specific MRI features in dogs presented with peracute, nonprogressive, and most often lateralized clinical signs of spinal cord dysfunction. The MRI features suggestive of ANNPE include (a) the presence of a narrowed intervertebral disc with reduced volume of nucleus pulposus located below a focal T2-weighted hyperintense intramedullary spinal cord lesion; (b) the presence of extradural material compatible with hydrated nucleus pulposus at the same level, causing no or minimal spinal cord compression; (c) the presence of a cleft in the dorsal part of the anulus fibrosus; (d) the presence of meningeal or epidural contrast enhancement in postcontrast T1-weighted fat-suppressed images.³⁻⁸ Considering the nonsurgical nature of the disease, histological confirmation of the diagnosis is rarely obtained; however, the MRI signal characteristics of extradural hydrated nucleus pulposus have been histopathologically validated in 2 studies and can support the diagnosis together with history and clinical signs.^{9,10} Successful functional recovery, defined as recovery of unassisted ambulation and complete urinary and fecal continence, occurs in 66% to 81% of dogs with a MRI- or myelography-based diagnosis of ANNPE.^{4,11-13} However, in cases with unsuccessful outcome, this was mainly related to persistently impaired micturition or defecation rather than inability to walk unassisted.^{4,11-13} In a large study including 157 dogs with MRI consensus diagnosis of T3-L3 ANNPE 99% of cases recovered ambulatory function (although most often with a degree of persistent motor deficits), 92.5% were urinary continent and 77% were fecally continent at long-term follow-up.¹² More specifically, fecal incontinence (FI) occurred in 100% of dogs that were paraplegic without nociception, 61% of dogs paraplegic with nociception, 20% of nonambulatory paraparetic or monoplegic dogs and in 9% of dogs that were ambulatory without assistance at the time of presentation.¹²

In humans with spinal cord injury (SCI), the level (cervical or thoracic compared to lumbar), duration (≥ 10 years compared to less), and severity of the lesion (complete compared to incomplete SCI) are predictors of the severity of neurogenic bowel dysfunction.¹⁴

Although the overall clinical improvement in dogs with ANNPE is generally dramatic with recovery of acceptable to good quality of life in most cases,¹¹ persistent urinary incontinence (UI) or FI can represent a challenge for owners to deal with. The aim of this study was to investigate clinical, diagnostic or treatment predictors of persistent UI or FI in dogs with T3-L3 ANNPE.

2 | MATERIALS AND METHODS

Ethics approval was provided by the ethics committee of the institution in which the study was designed and data analysis and manuscript preparation occurred. Medical records of dogs presented at 3 referral veterinary hospitals between July 2006 and July 2017 with peracute nonprogressive T3-L3 myelopathy, that underwent high field MRI (1.5 Tesla Signa EchoSpeed or Signa HD; GE Healthcare, Milwaukee, Wisconsin; 1.5 Tesla Ingenia CX; Philips Healthcare, Best, the Netherlands; 1.0 Tesla Magnetom; Siemens, Erlangen, Germany) of the T3-S3 spinal cord segments within 7 days of onset of clinical signs were retrospectively reviewed. To be considered for inclusion in the study, sagittal and transverse T2-weighted were the minimum MRI sequences required. Further sequences including pre and postcontrast (Gadolinium: Gadovist-gadobutrol, Bayer Pharma AG, Berlin, Germany or Omniscan-gadodiamide, Nycomed, Oslo, Norway or Multihance-gadobenate dimeglumine, Bracco, Milan, Italy) T1-weighted and/or fat-suppressed T1-weighted, precontrast and postcontrast 3D SPGR, 3D FIESTA C, gradient echo, MERGE, and STIR sequences were obtained at the imager's discretion. The MRI studies were reviewed by a single board-certified specialist in diagnostic imaging (ED). The diagnosis of T3-L3 ANNPE was confirmed when all the following MRI criteria were fulfilled: the presence of a focal T2-weighted intramedullary hyperintensity overlying an intervertebral disc; reduction in the size of the residual nucleus pulposus; the presence of extradural material compatible with hydrated nucleus pulposus without significant spinal cord compression. Dogs with no evidence of extradural material compatible with nucleus pulposus were excluded from the study. Dogs with ANNPE of the L3-L4 intervertebral disc were included only if patellar reflexes were clearly defined as normal in the clinical records. A minimum follow-up of 16 weeks was necessary for dogs to be included in the study.

Data pertaining to signalment, general, and neurological examination findings, diagnostic findings, and treatment were retrieved from the medical records of the included dogs. Variables investigated

included breed, age, weight, sex, time from onset to presentation (less than 24 hours; 25-48 hours; 49-72 hours; more than 72 hours), grade of neurological dysfunction at presentation, the presence of clinical signs compatible with spinal shock, site of the lesion on MRI, longitudinal and cross-sectional size of the intramedullary lesion on T2-weighted MRI sequences, the presence of intramedullary signal void in gradient echo sequences, administration of corticosteroids or nonsteroidal anti-inflammatory drugs (NSAIDs) before referral or after diagnosis and requirement for pharmacological bladder management after diagnosis or removal of the indwelling urinary catheter. The placement of an indwelling urinary catheter after diagnosis was not an investigated variable as in some institutions this is a standard procedure in nonambulatory severely paraparetic or paraplegic dogs independent of their urinary function. The grade of neurological dysfunction at presentation was scored as grade 1: neurologically normal with spinal discomfort; grade 2: ambulatory monoparesis or paraparesis; grade 3: nonambulatory paraparesis or monoplegia; grade 4: paraplegia with preserved nociception; grade 5: paraplegia without nociception.^{4,12} Clinical signs were considered compatible with spinal shock when temporary reduced spinal reflexes, including withdrawal reflex, were detected in 1 or both pelvic limbs in the absence of any identifiable lesion in the L4-S3 spinal cord segments or nerves on MRI. To investigate the effect of the site of the spinal cord lesion on MRI on the outcome, the lesion localization was divided into "prehypogastric" (including ANNPE of T11-T12, T12-T13, and T13-L1 intervertebral discs), and "hypogastric" (including ANNPE of L1-L2, L2-L3 or L3-L4 intervertebral discs). This was based on the described location of the soma of the neurons of the hypogastric nerve between the L1 and L4 spinal cord segments¹⁵ and the anatomical correlation between spinal cord segments and vertebrae.¹⁶ The longitudinal extension of the spinal cord lesion in relation to the length of L2 vertebral body (LL:VL), and its cross-sectional area compared to the area of the spinal cord at the same level (PCSAL) were measured as previously described⁴ using a commercial software application (functions Ruler and Polygonal ROI, respectively, ClearCanvas Workstation 2.0, ClearCanvas Inc., Toronto, Canada). Regarding the anti-inflammatory treatment, paracetamol was not considered in the NSAIDs group because of the different mechanism of action and the lack of relevant anti-inflammatory function.¹⁷

The ability of the dogs to urinate and defecate during hospitalization and after discharge was evaluated based on details available in the medical records and a follow-up telephone questionnaire with the owners performed at the time of the study. Long-term UI or FI were defined as the presence of any persistent deficit in micturition or defecation reported from the time of the injury to the time of the questionnaire or death (with a minimum follow-up of 16 weeks).

2.1 | Statistical analysis

Descriptive statistics were performed for signalment (eg, breed, age, body weight, sex), clinical presentation (eg, neurological grade at presentation and the presence of signs of spinal shock), diagnostic (eg, site of the ANNPE, LL:VL, PCSAL, the presence of intramedullary

signal void in gradient echo MRI sequences) and treatment (eg, treatment with NSAIDs compared to without, treatment with corticosteroids compared to without, requirement for pharmacological bladder management) variables. Continuous variables were reported as medians (minimum, maximum), and categorical variables were reported as frequencies. Logistic regression was performed to assess predictors for UI and FI, using each of these variables (UI and FI) as separate dependent variables. In the univariate analysis, variables with a P value $\leq .20$ were considered eligible for multivariate analysis. Variables meeting this criterion were then examined for multicollinearity. For model selection, a backward stepwise approach using likelihood ratio statistic was used with probability of entry $\leq .05$ and probability of removal $> .1$. Explanatory variables retained in the model were examined for confounding by adding each of the variables to the model and assessing the changes in the odds ratios of the remaining variables in the model. Studentized residuals were examined for outliers, flagging any cases with residuals greater than 2 SD. The logistic regression model was assessed for goodness of fit using the Hosmer-Lemeshow test, whereas the ability to discriminate between the 2 options for each dependent variable (eg, FI: yes or no) was determined using receiver operating characteristic curves. Odds ratios were calculated to estimate magnitude of association between selective investigated factors. In the final model, adjusted OR and 95% confidence intervals (CI) were reported. For all analyses, a two-sided P value of $< .05$ was considered statistically significant, and all analyses were performed using the IBM SPSS statistical software (version 24).

3 | RESULTS

A total of 187 dogs were included in this study. One hundred and forty-four of these dogs were also included in a previous study¹² whereas the remaining 43 dogs were newly added. The most represented breeds included Labrador retriever (30), Border collie (22), Staffordshire bull terrier (22), Lurcher (10), Whippet (8), Greyhound (6), Golden retriever (5), Cocker spaniel (4), Siberian husky (4) and cross breed (31). All other breeds were only represented by 1 or 2 cases. Median age at presentation was 6.5 years (2-11). Median body weight was 23 kg (3-71). There were 122 males (85 neutered) and 65 females (48 neutered); the male to female ratio was 1.88. One hundred and fifty-two dogs were presented to the referral veterinary hospital within 24 hours from the onset of the clinical signs, 19 dogs between 25 and 48 hours, 10 dogs between 49 and 72 hours, and 6 dogs between 73 hours and 7 days. At presentation, 1 dog was neurologically normal with spinal discomfort (grade 1), 65 dogs were ambulatory monoparetic or paraparetic (grade 2), 90 dogs were nonambulatory paraparetic or monoplegic (grade 3), 28 dogs were paraplegic with preserved nociception (grade 4), and 3 dogs were paraplegic without nociception (grade 5). Clinical signs compatible with spinal shock were detected in 105 dogs. The presence of clinical signs compatible with spinal shock was significantly associated with a time from onset to presentation up to 24 hours compared to more than 24 hours ($P = .001$). The ANNPE was localized at the T11-T12 (11 dogs), T12-T13 (65 dogs), T13-L1 (57 dogs), L1-L2

(31 dogs), L2-L3 (21 dogs), and L3-L4 (2 dogs) intervertebral discs. The ANNPE was affecting the “prehypogastric” segments in 133 dogs and the “hypogastric” segments in 54 dogs. The mean LL:VL ratio was 0.7 (0.2-5.7). The mean PCSAL was 43.8% (11%-84%). Intramedullary signal void was detected in 17 of 133 cases (12.8%) in which gradient echo sequences were performed.

Ninety-four dogs received anti-inflammatory treatment after ANNPE diagnosis; 81 received NSAIDs (41 meloxicam, 36 carprofen, 2 cimicoxib, 1 firocoxib, 1 robenacoxib) and the other 13 received corticosteroids (12 prednisolone and 1 methylprednisolone). Considering the discrepancy in group sizes and the low number of dogs receiving corticosteroids, a direct comparison of outcome between dogs that received NSAIDs and dogs that received corticosteroids was not performed. For further analyses, the effect of the treatment on outcome was assessed comparing dogs that were administered NSAIDs to dogs that were not (including untreated dogs and dogs treated with corticosteroids), and comparing dogs that were administered corticosteroids to dogs that were not (including untreated dogs and dogs treated with NSAIDs). After diagnosis, 13 dogs required medication (including diazepam, prazosin, and phenoxybenzamine) to reduce internal/external urethral sphincter tone and enable micturition.

The median follow-up from initial presentation to the time of the telephone questionnaire or to death was 834 days (range: 115-2963 days). None of the dogs that were dead at the time of follow-up were euthanized for reasons related to the SCI.

All dogs recovered ambulatory status. Long-term UI was observed in 17 dogs (9.1%). More specifically UI occurred in 3.1% of dogs presented with neurological grade 2, 8.9% with grade 3, 17.9% with grade 4, and 66.7% with grade 5. The most commonly reported abnormalities were occasional dripping of urine (7 cases); losing urine overnight (4 cases); starting walking before completing micturition (3 cases); urinating when excited (3 cases); and being unable to control the urge to urinate (1 case).

Long-term FI was reported in 44 dogs (23.5%). More specifically FI was reported in 7.7% of dogs presented with neurological grade 2, 23.3% with grade 3, 53.6% with grade 4, and 100% with grade 5. Eleven of these FI cases (5.9% of the total) had both UI and FI. The most commonly reported abnormalities were being unable to control the urge to defecate (17 cases); starting walking before completing defecation (12 cases); losing feces overnight (11 cases); occasionally losing of feces while walking (8 cases); defecating when excited (6 cases), and being completely unaware of bowel motion (2 cases).

The owners of 2 dogs spontaneously reported that they were able to induce defecation by digital stimulation of the dog's anal region. By performing this maneuver at the last daily walk both owners reported reduced incidence of incontinence overnight.

3.1 | Analysis of predictors

After univariate analysis for predictors of UI, the following variables had P values $\leq .2$ and were considered for inclusion in the final multivariate analysis model: neurological grade at presentation, administration of NSAIDs before referral, site of the ANNPE, LL:VL, PCSAL, and requirement for pharmacological bladder management. In a follow-up multivariate analysis model, predictors of long-term UI included the neurological grade at presentation ($P = .018$) and a PCSAL higher than 40% ($P = .045$) (Table 1). Paraplegic dogs were 3 times (CI = 1.25, 10.87) more likely to develop UI compared to nonparaplegic dogs ($P = .018$). Dogs with a PCSAL higher than 40% were 4 times (CI = 1.04, 21.72) more likely to develop UI compared to dogs with lower PCSAL ($P = .045$). The Hosmer-Lemeshow goodness of fit test for the final model (chi-square = 5.04; df = 2; $P = .599$) indicated a good fit for the data. No confounding effect was observed when either neurological grade at presentation or PCSAL was added to the final model.

Variable	Urinary incontinence		OR (95% CI)	P value
	Yes n = 17 (%)	No n = 170 (%)		
Neurological grade at presentation				
1 to 3	10 (58.8)	146 (85.9)	Reference	.018
4 to 5	7 (41.2)	24 (14.1)	3.69 (1.25, 10.87)	
PCSAL				
10.9% to 40%	2 (11.8)	71 (41.8)	Reference	.045
>40%	15 (88.2)	99 (58.2)	4.75 (1.04, 21.72)	

TABLE 1 Multivariate unconditional logistic regression analysis of investigated variables associated with UI in dogs diagnosed with ANNPE

Note: Besides the above variables that were retained in the final multivariate model for UI (neurological grade at presentation and PCSAL), other variables with P values $\leq .2$ in the univariate analysis were considered for inclusion in the final multivariate analysis model including site of the ANNPE, LL:VL, administration of NSAIDs before referral, and requirement for pharmacological bladder management after diagnosis or removal of the indwelling urinary catheter. Other investigated variables that had P values $> .2$ in the univariate analysis were not considered for inclusion in the final multivariate analysis model and these included breed, age, weight, sex, time from onset to presentation, the presence of neurological signs compatible with spinal shock, the presence of intramedullary signal void in gradient echo sequences, and administration of corticosteroids before referral or after diagnosis or of NSAIDs after diagnosis.

Abbreviation: CI, confidence interval.

TABLE 2 Multivariate unconditional logistic regression analysis of investigated variables associated with FI in dogs diagnosed with ANNPE

Variable	Fecal incontinence		OR (95% CI)	P value
	Yes n = 44 (%)	No n = 143 (%)		
Neurological grade at presentation				
1 to 3	26 (59.1)	130 (90.9)	Reference	.001
4 to 5	18 (40.9)	13 (9.1)	4.93 (1.94, 12.56)	
Site of the lesion				
Hypogastric	6 (13.6)	48 (33.6)	Reference	.051
Pre-hypogastric	38 (86.4)	95 (66.4)	2.76 (0.99, 7.66)	
Presence of spinal shock				
No	12 (27.3)	70 (49)	Reference	.026
Yes	32 (72.7)	73 (51)	2.58 (1.12, 5.98)	
NSAIDs following diagnosis				
Yes	11 (25)	70 (49)	Reference	.006
No	33 (75)	73 (51)	3.34 (1.41, 7.93)	
PCSAL				
10.9% to 40%	7 (15.9)	66 (46.2)	Reference	.004
>40%	37 (84.1)	77 (53.8)	4.03 (1.56, 10.39)	

Note: Besides the above variables that were retained in the final multivariate model for FI (neurological grade at presentation, site of the ANNPE, PCSAL, not receiving NSAIDs following diagnosis and having signs of spinal shock at the time of presentation), other variables that had P values $\leq .2$ in the univariate analysis were considered for inclusion in the final multivariate analysis model including requirement for pharmacological bladder management after diagnosis or removal of the indwelling urinary catheter. Other investigated variables that had P values $> .2$ in the univariate analysis were not considered for inclusion in the final multivariate analysis model and these included breed, age, weight, sex, time from onset to presentation, LL:VL, the presence of intramedullary signal void in gradient echo sequences, administration of corticosteroids or NSAIDs before referral or of corticosteroids after diagnosis. Abbreviations: CI, confidence interval; FI, fecal incontinence; UI, urinary incontinence.

After univariate analysis for predictors of FI, the following variables had P values $\leq .2$ and were considered for inclusion in the final multivariate analysis model: neurological grade at presentation, the presence of spinal shock, administration of NSAIDs after diagnosis, site of the ANNPE, PCSAL, and requirement for pharmacological bladder management. Significant predictors of long-term FI in a multivariate analysis model included the neurological grade at presentation ($P = .001$), a PCSAL higher than 40% ($P = .004$), not receiving NSAIDs after diagnosis ($P = .006$), and having signs of spinal shock at the time of presentation ($P = .026$) (Table 2). The time interval between onset of neurologic deficits and initial presentation at the referral hospital was not significantly different between dogs that developed FI and dogs that did not ($P = .89$). Paraplegic dogs were 4 times (CI = 1.94, 12.56) more likely to develop FI compared to nonparaplegic dogs ($P = .001$). Dogs with a PCSAL $>40\%$ were 4 times (CI = 1.56, 10.39) more likely to develop FI compared to dogs with smaller lesions ($P = .004$). Dogs that were not administered NSAIDs following diagnosis were 3 times (CI = 1.41, 7.93) more likely to develop FI compared to dogs that received NSAIDs ($P = .006$). Dogs that presented with signs of spinal shock were 2 times (CI = 1.12, 5.98) more likely to develop FI compared to dogs presented without signs of spinal shock ($P = .026$). Dogs with a lesion at T11-12, T12-13, or T13-L1 ("prehypogastric" segments) were 2 times (CI = 0.99, 7.66) more likely to develop FI compared to dogs with lesions at L1-L2, L2-L3 or L3-L4

("hypogastric" segments); however, this variable did not reach statistical significance ($P = .051$). The Hosmer-Lemeshow goodness of fit test for the final model (chi-square = 5.66; df = 7; $P = .58$) indicated a good fit for the data. No confounding effect was observed when each of the retained variables was added to the final model: neurological grade at presentation, PCSAL, not receiving NSAIDs following diagnosis and having signs of spinal shock at the time of presentation.

4 | DISCUSSION

This study investigated clinical, diagnostic, and therapeutic predictors of UI and FI in dogs with T3-L3 ANNPE. The neurological grade at presentation and the PCSAL were significant predictors of both UI and FI. Clinical signs compatible with spinal shock at initial presentation and not receiving NSAIDs after diagnosis were also significantly associated with FI but not UI. However, the results obtained regarding predictors of UI might have been affected by the low number of cases experiencing this outcome.

The association between severity of the neurological signs at initial presentation and functional recovery is in agreement with findings in a smaller population of dogs with ANNPE.⁴ The same is true for the association between PCSAL and functional recovery.⁴ However, the longitudinal extension of the lesion was not associated with the risk

of incontinence, which might suggest that what is relevant for the occurrence of UI or FI is the involvement of specific spinal cord tracts. This assumption can be supported by the fact that the disruption of specific spinal cord tracts would become more likely in association with a higher PCSAL and remain less influenced by the longitudinal extension of the lesion. Spinal cord tracts involved in urinary and fecal control run in dorsal, ventral, and lateral funiculi.^{18,19} The influence of the location of the T2W hyperintensity in transverse MRI sections in terms of the affected funiculi (dorsal, ventral, lateral, or combinations of them) on the outcome was technically challenging to be investigated. The reasons behind this difficulty included not only limitations because of resolution of the MRI signal within the spinal cord but also the frequently oblique pattern of the T2W hyperintensity in longitudinal sections, which caused changes in the location of the lesion in transverse images according to the level of the section.⁷

The strong significant association detected between not administering NSAIDs after diagnosis and a higher risk of FI suggests that further prospective randomized studies are warranted to investigate nonsteroidal anti-inflammatory treatment in dogs with ANNPE. In our analyses, dogs that were administered NSAIDs (81 cases) were compared to dogs that did not receive NSAIDs (106 cases), including in the latter group both dogs that did not receive any anti-inflammatory treatment (93 cases) and dogs that received corticosteroids (13 cases). Conversely, when comparing dogs that received corticosteroids to dogs that did not, no significant association with FI was found. However, the low number of cases receiving corticosteroids and the lack of randomization prevented us from attempting any direct comparison between the effect of these 2 classes of anti-inflammatory drugs on the occurrence of UI or FI. The use of NSAIDs after SCI in humans has been reviewed.²⁰ Overexpression of cyclooxygenase-2 (COX2) in secondary injury after spinal cord trauma was demonstrated in a rat model, therefore opening a therapeutic window for COX2 inhibitors in SCI.²¹ In the same model, the use of SC58125, a selective COX2 inhibitor, 15 minutes after SCI improved motor outcome based on Basso, Beattie, and Bresnahan score compared to controls.²¹ Similar results were obtained in rats with the administration of another selective COX2 inhibitor, NS-398, 15 minutes before the SCI,²² and with a single intraperitoneal injection of meloxicam 30 minutes after SCI.²³ On histopathologic examination, rats that were administered the above treatments had decreased disruption of axons and interstitial edema,²³ and a reduced extent of the spinal cord lesion compared to controls.²² In adjunction to their COX2 inhibitory effect, another mechanism of action related to their positive effects after SCI is the inhibitory action of some NSAIDs on Ras homology protein member A (RhoA), an intracellular GTPase protein.²⁴ Multiple molecules expressed in the spinal cord after SCI ultimately converge in activation and overexpression of RhoA, which induces cytoskeletal axonal cone collapse via RhoA-kinase proteins, consequently inhibiting axonal regeneration.^{24,25} The expression of RhoA is elevated for up to 28 days post-SCI in rats.²⁶ Some NSAIDs, primarily ibuprofen and indomethacin, reduce the activity of RhoA both in vitro and in vivo.^{24,25,27-29} Ibuprofen, specifically, improves axonal outgrowth and restoration of synapses, increases axonal myelination, and

reduces apoptosis via RhoA inhibition after SCI, with concurrent improvement of neurological function in rats.²⁹⁻³² Although meloxicam does not directly reduce RhoA activity in cell cultures,²⁷ an indirect modulatory effect of COX inhibitors in vivo limiting the molecular cascade and inflammatory cycle leading to the activation of RhoA, cannot be excluded.²⁸ To date, no information could be found in the literature regarding the effect of carprofen, cimicoxib, firocoxib or robenacoxib on RhoA protein.

This study identified the presence of clinical signs of spinal shock as a predictor of FI. Although the presence of spinal shock was significantly associated with the time interval between onset of clinical signs to presentation at the referral hospital, which is logical considering that it is a transient event, dogs that developed FI in this study were not presented significantly sooner than dogs that did not. Apart from its association with the rapidity of onset of the injury, a recent review on the clinical implications of spinal shock in humans highlighted the presence of a direct correlation between the severity of the spinal cord damage, the degree of spinal shock, and the prognosis.³³ In this study, it is possible that the presence of spinal shock as a prognostic factor for recovery reflects its potential correlation with the degree of anatomical injury; however, at this stage, this remains a purely speculative interpretation and would require histological studies to be proven. In human patients with spinal shock, autonomic activity is altered as well as somatic reflexes, and the recovery of bladder reflexes follows that of tendon reflexes.³³ The recovery of spinal reflexes after spinal shock follows a four-phase model including the transition to hyperreflexia in the latest phases. This could be because of formation of new excitatory synapses involving interneurons, sensory afferents, and lower motor neurons below the level of injury after the loss of supraspinal inputs.^{34,35} When applied to autonomic reflexes, this could lead to mechanisms of rectal hyperreflexia, which is one of the described mechanisms behind FI in humans after SCI.^{36,37}

The possible association between the site of the lesion within the T3-L3 spinal cord segments and the outcome in terms of autonomic function was not previously investigated in dogs. In this study, we attempted to divide these segments based on the reported location of the neuronal bodies of the hypogastric nerve and the spatial correlation between spinal cord segments and vertebrae. Although in multivariate analysis, the location of the lesion as defined above was technically not significantly associated with the outcome, the *P* value of .051 suggests that rejecting this correlation based only on this result might represent a type I error. With these results, it is indeed possible that even with a small change in sample size the association between a "prehypogastric" site of the lesion and a worse outcome might well become statistically significant.

As mentioned in the results, 2 owners independently reported that they were able to induce defecation in fecally incontinent dogs by applying digital pressure to the dog's anal region. This was reported to be helpful in reducing overnight incontinence by inducing defecation at the last daily walk, in this way at least partially emptying the rectum before bed time. Digital anorectal stimulation (DARS) is a well-described technique to induce defecation in humans with neurogenic

bowel dysfunction after SCI. DARS does not only cause relaxation of the anal canal but also increases rectal pressure and induces colonic peristalsis during and up to 5 minutes after the procedure, with consequent rectal emptying by the fifth stimulation.^{38,39} This anorectal reflex is suggested to be induced by stretching of mechanoreceptors of the internal anal sphincter causing reflex parasympathetic stimulation of colon and rectum mediated by the S2-S4 spinal cord segments.^{38,39} Based on the anecdotal effectiveness in dogs, the described effectiveness in humans and the possible physiological explanation behind it, a clinician could consider mentioning this maneuver to owners of dogs with persistent FI after SCI, in order to possibly help with the management of this inconvenient complication.

Limitations of this study are mainly because of its retrospective nature leading to nonstandardized and nonrandomized treatments, uneven size of treatment groups and the use of telephone questionnaire to assess outcome.

In conclusion, this study on dogs with T3-L3 ANNPE identified the neurological grade at presentation and the PCSAL as predictors of both UI and FI. The presence of neurological signs compatible with spinal shock at presentation and the lack of administration of NSAIDs after diagnosis were predictors of FI only. The role of the specific site of the lesion within the T3-L3 spinal cord segments as predictor of FI might also deserve further investigation. Taking into consideration these variables at the time of diagnosis will help the clinician to predict the risk of UI and FI in dogs with T3-L3 ANNPE.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Ethics approval was obtained from the Animal Health Trust Clinical Research Ethics Committee (AHT 47_2016).

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

ORCID

Lorenzo Mari  <https://orcid.org/0000-0002-5732-1011>

Anita Shea  <https://orcid.org/0000-0003-2353-9028>

REFERENCES

- De Decker S, Fenn J. Acute herniation of nondegenerate nucleus pulposus: acute noncompressive nucleus pulposus extrusion and compressive hydrated nucleus Pulposus extrusion. *Vet Clin North Am Small Anim Pract.* 2018;48:95-109.
- De Risio L. A review of fibrocartilaginous embolic myelopathy and different types of peracute non-compressive intervertebral disk extrusions in dogs and cats. *Front Vet Sci.* 2015;2:24.
- Chang Y, Dennis R, Platt SR, Penderis J. Magnetic resonance imaging of traumatic intervertebral disc extrusion in dogs. *Vet Rec.* 2007;160:795-799.
- De Risio L, Adams V, Dennis R, et al. Association of clinical and magnetic resonance imaging findings with outcome in dogs with presumptive acute noncompressive nucleus pulposus extrusion: 42 cases (2000-2007). *J Am Vet Med Assoc.* 2009;234:495-504.
- Henke D, Gorgas D, Flegel T, et al. Magnetic resonance imaging findings in dogs with traumatic intervertebral disk extrusion with or without spinal cord compression: 31 cases (2006-2010). *J Am Vet Med Assoc.* 2013;242:217-222.
- Ros C, de la Fuente C, Rodenas S, Novellas R, Viu J, AÃ Or S. Myelographic and low-field magnetic resonance imaging findings in dogs with presumptive acute hydrated non-compressive nucleus pulposus extrusion. *Vet Rec.* 2017;181:594-599.
- Specchi S, Johnson P, Beauchamp G, Masseur I, Pey P. Assessment of interobserver agreement and use of selected magnetic resonance imaging variables for differentiation of acute noncompressive nucleus pulposus extrusion and ischemic myelopathy in dogs. *J Am Vet Med Assoc.* 2016;248:1013-1021.
- Fenn J, Drees R, Volk HA, Decker SD. Inter- and intraobserver agreement for diagnosing presumptive ischemic myelopathy and acute noncompressive nucleus pulposus extrusion in dogs using magnetic resonance imaging. *Vet Radiol Ultrasound.* 2016;57:33-40.
- Falzone C. Canine acute cervical myelopathy: hydrated nucleus pulposus extrusion or intraspinal discal cysts? *Vet Surg.* 2017;46:376-380.
- Manunta ML, Evangelisti MA, Bergknot N, Grinwis GCM, Ballocco I, Meij BP. Hydrated nucleus pulposus herniation in seven dogs. *Vet J.* 2015;203:342-344.
- Fenn J, Drees R, Volk HA, de Decker S. Comparison of clinical signs and outcomes between dogs with presumptive ischemic myelopathy and dogs with acute noncompressive nucleus pulposus extrusion. *J Am Vet Med Assoc.* 2016;249:767-775.
- Mari L, Behr S, Shea A, et al. Outcome comparison in dogs with a presumptive diagnosis of thoracolumbar fibrocartilaginous embolic myelopathy and acute non-compressive nucleus pulposus extrusion. *Vet Rec.* 2017;181:293.
- McKee WM, Downes CJ, Pink JJ, et al. Presumptive exercise-associated peracute thoracolumbar disc extrusion in 48 dogs. *Vet Rec.* 2010;166:523-528.
- Liu CW, Huang CC, Chen CH, Yang YH, Chen TW, Huang MH. Prediction of severe neurogenic bowel dysfunction in persons with spinal cord injury. *Spinal Cord.* 2010;48:554-559.
- Purinton PT, Oliver JE Jr. Spinal cord origin of innervation to the bladder and urethra of the dog. *Exp Neurol.* 1979;65:422-434.
- Evans HE, de Lahunta A. *Miller's Anatomy of the Dog.* 4th ed. St. Louis, MI: Elsevier Saunders; 2013.
- Plumb DC. *Plumb's Veterinary Drug Handbook.* 7th ed. Stockholm, WI: PharmaVet Inc.; 2011.
- de Lahunta A, Glass E, Kent M. *Veterinary Neuroanatomy and Clinical Neurology.* 4th ed. St. Louis, MI: Elsevier Saunders; 2015.
- Benarroch EE. Neural control of the bladder: recent advances and neurologic implications. *Neurology.* 2010;75:1839-1846.
- Hayta E, Elden H. Acute spinal cord injury: a review of pathophysiology and potential of non-steroidal anti-inflammatory drugs for pharmacological intervention. *J Chem Neuroanat.* 2018;87:25-31.
- Resnick DK, Graham SH, Dixon CE, et al. Role of cyclooxygenase 2 in acute spinal cord injury. *J Neurotrauma.* 1998;15:1005-1013.

22. Hains BC, Yucra JA, Hulsebosch CE. Reduction of pathological and behavioral deficits following spinal cord contusion injury with the selective cyclooxygenase-2 inhibitor NS-398. *J Neurotrauma*. 2001;18:409-423.
23. Hakan T, Toklu HZ, Biber N, et al. Meloxicam exerts neuroprotection on spinal cord trauma in rats. *Int J Neurosci*. 2011;121:142-148.
24. Kopp MA, Liebscher T, Niedeggen A, et al. Small-molecule-induced rho-inhibition: NSAIDs after spinal cord injury. *Cell Tissue Res*. 2012;349:119-132.
25. Wu X, Xu XM. RhoA/Rho kinase in spinal cord injury. *Neural Regen Res*. 2016;11:23-27.
26. Conrad S, Schluesener HJ, Trautmann K, Joannin N, Meyermann R, Schwab JM. Prolonged lesional expression of RhoA and RhoB following spinal cord injury. *J Comp Neurol*. 2005;487:166-175.
27. Zhou Y, Su Y, Li B, et al. Nonsteroidal anti-inflammatory drugs can lower amyloidogenic Abeta42 by inhibiting Rho. *Science*. 2003;302:1215-1217.
28. Schwab JM, Conrad S, Elbert T, Trautmann K, Meyermann R, Schluesener HJ. Lesional RhoA+ cell numbers are suppressed by anti-inflammatory, cyclooxygenase-inhibiting treatment following subacute spinal cord injury. *Glia*. 2004;47:377-386.
29. Wang X, Budel S, Baughman K, Gould G, Song KH, Strittmatter SM. Ibuprofen enhances recovery from spinal cord injury by limiting tissue loss and stimulating axonal growth. *J Neurotrauma*. 2009;26:81-95.
30. Fu Q, Hue J, Li S. Nonsteroidal anti-inflammatory drugs promote axon regeneration via RhoA inhibition. *J Neurosci*. 2007;27:4154-4164.
31. Xing B, Li H, Wang H, et al. RhoA-inhibiting NSAIDs promote axonal myelination after spinal cord injury. *Exp Neurol*. 2011;231:247-260.
32. Devaux S, Cizkova D, Mallah K, et al. RhoA inhibitor treatment at acute phase of spinal cord injury may induce neurite outgrowth and synaptogenesis. *Mol Cell Proteomics*. 2017;16:1394-1415.
33. Ko HY. Revisit spinal shock: pattern of reflex evolution during spinal shock. *Korean J Neurotrauma*. 2018;14:47-54.
34. Ditunno JF, Little JW, Tessler A, Burns AS. Spinal shock revisited: a four-phase model. *Spinal Cord*. 2004;42:383-395.
35. Smith PM, Jeffery ND. Spinal shock—comparative aspects and clinical relevance. *J Vet Intern Med*. 2005;19:788-793.
36. Preziosi G, Emmanuel A. Neurogenic bowel dysfunction: pathophysiology, clinical manifestations and treatment. *Expert Rev Gastroenterol Hepatol*. 2009;3:417-423.
37. Valles M, Mearin F. Pathophysiology of bowel dysfunction in patients with motor incomplete spinal cord injury: comparison with patients with motor complete spinal cord injury. *Dis Colon Rectum*. 2009;52:1589-1597.
38. Korsten MA, Singal AK, Monga A, et al. Anorectal stimulation causes increased colonic motor activity in subjects with spinal cord injury. *J Spinal Cord Med*. 2007;30:31-35.
39. Shafik A, El-Sibai O, Shafik IA. Physiologic basis of digital-rectal stimulation for bowel evacuation in patients with spinal cord injury: identification of an anorectal excitatory reflex. *J Spinal Cord Med*. 2000;23:270-275.

How to cite this article: Mari L, Behr S, Shea A, et al. Predictors of urinary or fecal incontinence in dogs with thoracolumbar acute non-compressive nucleus pulposus extrusion. *J Vet Intern Med*. 2019;33:2693-2700. <https://doi.org/10.1111/jvim.15626>