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Association between filum terminale internum length and pain in Cavalier King Charles spaniels with and without syringomyelia

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Abstract

Background: Lumbar syringomyelia (SM), lumbosacral pain, and more caudal spinal cord termination are reported in Cavalier King Charles spaniels (CKCS). Data are lacking on the clinical relevance of alterations in their spinal cord terminal structures.

Objectives: To compare spinal cord termination level and filum terminale internum length (FTIL) with presence of lumbar SM and clinical signs in CKCS.

Animals: Forty-eight CKCS.

Methods: In this prospective study, pain was quantified using owner and clinician assessments. Vertebral level of spinal cord and dural sac termination, presence of SM, and FTIL were determined from sagittal magnetic resonance imaging (MRI) sequences. Kappa and intraclass correlation (ICC) analyses determined interobserver reliability. The MRI findings were compared to owner and clinician-reported pain quantification.

Results: Interobserver reliability was good for spinal cord and dural sac termination (kappa = 0.61 and 0.64, respectively) and excellent for FTIL (ICC: 92% agreement). The spinal cord terminated at 6th lumbar vertebra in 1, 7th lumbar vertebra in 31, and the sacrum in 15 dogs, and termination level was associated with lumbar SM (P = .002) but not clinical signs. Mean FTIL was 2.9 ± 1.08 mm; it was associated with owner-reported pain (P = .033) and spinal palpation scores (P = .023). Painful CKCS without SM had shorter FTIL compared to normal CKCS and painful CKCS with SM (P = .02).

Conclusions: Painful CKCS without SM have decreased distance between the termination of the spinal cord and dural sac, suggesting a shorter FTIL. More caudal spinal cord termination is associated with development of lumbar SM.

KEYWORDS
Chiari-like malformation, conus medullaris, dural sac, morphometry, tethered cord

Abbreviations: Cd, caudal vertebrae; ChiMPS-T, Chiari-like malformation pain and scratch tool; CKCS, Cavalier King Charles spaniels; CM, Chiari-like malformation; CM1, Chiari-type 1 malformation; FTIL, filum terminale internum length; HASTE, half-Fourier acquisition single-shot turbo spin echo; ICC, intraclass correlation; L2, 2nd lumbar vertebra; L6, 6th lumbar vertebra; L7, 7th lumbar vertebra; LS, lumbosacral; MRI, magnetic resonance imaging; OTCS, occult tethered cord syndrome; Sa, sacrum; SM, syringomyelia; TCS, tethered cord syndrome; TL, thoracolumbar; TPS, total pain score; TSS, total scratch score.

1 | INTRODUCTION

Cavalier King Charles spaniels (CKCS) are affected by Chiari-like malformation (CM) and syringomyelia (SM) causing neuropathic pain and parasthesias of the head and neck region. Syringomyelia was first noted in the cervical spinal cord using magnetic resonance imaging (MRI) but more extensive imaging protocols identified its presence in the thoracic and lumbar spinal cord.[1-6] The etiology of clinical signs in CKCS with Chiari-like malformation with syringomelia (CMSM) is unclear. Many studies have found an association between the presence and the severity of SM with clinical signs.[7-10] However, there are many asymptomatic dogs with SM as well as symptomatic dogs that lack SM.[4,5,11-14] These discrepancies have led investigators to suggest that both CMSM and CM pain-only phenotypes occur in CKCS.[4,15,16]

In addition to the classical clinical signs of CMSM, we have noted severe lumbosacral (LS) pain in affected dogs. This finding, together with the presence of lumbar SM, led us to investigate the terminal structures of the spinal cord, and we found that the spinal cord and dural sac terminate more caudally in CKCS than in other size-matched breeds.[6] In addition, location of termination of these structures is associated with the presence of thoracolumbar (TL) SM.[6] However, we did not investigate the clinical relevance of this finding in our previous study.

A subset of people with Chiari-type 1 malformation (CM1) also suffer from a disorder known as tethered cord syndrome (TCS).[17-25] This syndrome is the consequence of abnormal anchoring of the caudal end of the spinal cord. The normal spinal cord tapers to a relatively elastic structure called the filum terminale internum, composed of ependymal, pial and glial cells and surrounded by the subarachnoid space and dural sac. Distally, the dural sac closes down onto the filum, creating a more fibrous tether, called the filum terminale externum. This structure fuses with the periosteum of the caudal (Cd) vertebrae, thus anchoring the meninges and spinal cord within the vertebral canal.[26,27] In patients with TCS, the attachment of the spinal cord is excessively tight, and they can suffer from back pain, numbness, ataxia, and shooting pain down their legs as well as bladder and bowel dysfunction.[28-35] This clinical scenario can occur in patients with spinal dysraphisms, a subset of which result from intradural changes that include thickened, shortened filum terminale, lipomas of the filum, or abnormal fibrous adhesions.[30] Diagnosis is established using a combination of clinical findings, urodynamic studies, MRI, and surgical findings.[20,30,36]

Tethered cord syndrome has been described in the veterinary literature most commonly in animals with coexisting anomalies such as spina bifida, but also in dogs with no other anomalies.[37-44] Our previous report of a more caudal spinal cord termination and presence of TL SM in CKCS, and the findings of another study in which a 3-dimensional computer model suggested that TL SM development in the canine spinal cord may be a consequence of spinal cord tethering led us to propose that TCS may coexist with CM SM in CKCS.[6,44] We hypothesized that symptomatic CKCS with CM with or without SM would have a significantly more caudal termination of their spinal cord than do asymptomatic dogs. Our aims were first to describe and compare the site of spinal cord and dural sac termination in symptomatic and asymptomatic CKCS, and second to quantify and compare the length of the filum terminale internum between these 2 groups of dogs.

2 | MATERIALS AND METHODS

2.1 | Dogs

Clinically affected and normal client-owned CKCS were prospectively recruited to North Carolina State University (NCSU) Veterinary Hospital. Inclusion criteria required dogs to be >11 months of age and healthy enough for general anesthesia. Physical examinations on the day of anesthesia and laboratory findings (hemogram and serum biochemistry profiles) performed within 2 weeks of anesthesia were used to determine health status. Dogs with comorbidities described by owners, identified on examination, or noted in patient records that could cause pain or scratching unrelated to CMSM, including osteoarthritis and allergic skin disease, were excluded from the study. Owners reviewed and signed informed consent forms and all procedures were approved by NCSU Animal Use and Care Committee (IACUC protocol number 18-163-O).

2.2 | Phenotypic evaluation

All dogs underwent neurological examinations, and pain elicited by spinal palpation was recorded as well as presence of scratching during the examination. Spinal pain was identified and recorded using categorical (presence of pain—yes or no) and ordinal assessments. Two authors (N.J.O., C.R.S.) evaluated each dog before MRI and agreed on palpation scores. Evaluations were separated by at least 15 minutes. Palpation scores for each anatomical location (cervical, TL, and LS) were assigned a value between 0 and 3 (Table 1). Ordinal pain scores for the cervical, TL, and LS spinal were summed to create a combined palpation score. Owners completed a previously developed clinical

TABLE 1 Criteria used to assign palpation scores for the cervical, thoracolumbar, and lumbosacral spine

Palpation score	Description
0	No pain
1	Mild pain—epaxial muscle tensing on palpation
1.5	Mild to moderate pain—epaxial muscle contraction and mild flinching
2	Moderate pain—muscle contraction and flinching, crouching
2.5	Moderate to severe pain—moves away from pressure, looking around
3	Severe pain—cries out, jumps away, tries to bite

metrology instrument, the Chiari-like malformation pain and scratch tool (ChiMPS-T).[4] The ChiMPS-T responses were converted to ordinal scores that capture frequency and severity of scratch and pain (total scratch score [TSS]; total pain score [TPS]).

2.3 | MRI protocol

All dogs were anesthetized and monitored using routine procedures. A 3.0 Tesla unit (Siemens Medical Solutions USA, Inc, Malvern, Pennsylvania) was used to evaluate the entire length of the spinal cord with dogs placed in sternal recumbency with their necks extended. Acquired sequences included T2-weighted sagittal and transverse as well as proton density transverse images of the brain and cervical spine, T2-weighted sagittal and transverse images of the TL and LS spine including transverse sequences through the conus medullaris, and sagittal half-Fourier acquisition single-shot turbo spin echo (HASTE) sequences of the TL and LS spinal cord.

2.4 | MRI analysis

All images were evaluated by 1 of the authors (C.R.S.). Twenty percent of the cases were reviewed by another author (C.W.) to determine interrater reliability. Patient name, history, and examination findings were masked at the time of image review. Images were viewed using eUnity software (version 6.3.0.1.4, Client Outlook Inc, Waterloo, Ontario). They were reviewed for sufficient image quality and appropriate sequences and were excluded if there were extradural lesions caudal to the 2nd lumbar vertebra (L2) that completely interrupted the HASTE signal and could potentially impact spinal cord termination. The vertebral level of spinal cord termination was determined using T2-weighted mid-sagittal images and was identified as the point at which the spinal cord was no longer tapered.[6,45] The termination site was recorded as the vertebral level (eg, 7th lumbar vertebra [L7]). The HASTE sequences and corresponding T2-weighted sagittal images were used to determine the vertebral level of dural sac termination.[6] Images were viewed in a side-by-side manner and the ending of the brightest HASTE signal was selected using the triangulation tool and the corresponding vertebral location was identified on T2-weighted sagittal views. Termination sites were recorded in the same manner as for spinal cord termination. For termination sites that occurred over a disc space, the more cranial vertebra was recorded (eg, 6th lumbar vertebra [L6]/L7 disc space was recorded as L6). The filum terminale internum length (FTIL) was measured as the distance from the end of the spinal cord to the end of the dural sac using sagittal HASTE sequences (Figure 1). Because the filum terminale internum itself could not be consistently visualized in all cases, this distance represents a presumptive FTIL in some cases. The FTIL was divided by the length of 2nd lumbar vertebra to account for dog size.[46] The FTIL could not be measured if images did not extend beyond the sacrum (Sa). If the HASTE signal continued beyond the end of the image in the Cd vertebrae, the measurement was obtained using the end of the image as the end point for the measurement. The angle of the LS curvature was measured using the angle measurement tool using T2 sagittal views. Angle measurements were taken by selecting the middle of the L6/L7 disc space, LS disc space, and sacrocaudal disc space. The presence and maximal diameter of SM, defined as linear hyperintensity >2 mm in diameter, in the cervical, thoracic, and lumbar spinal cord was measured using T2-weighted sagittal and transverse views.

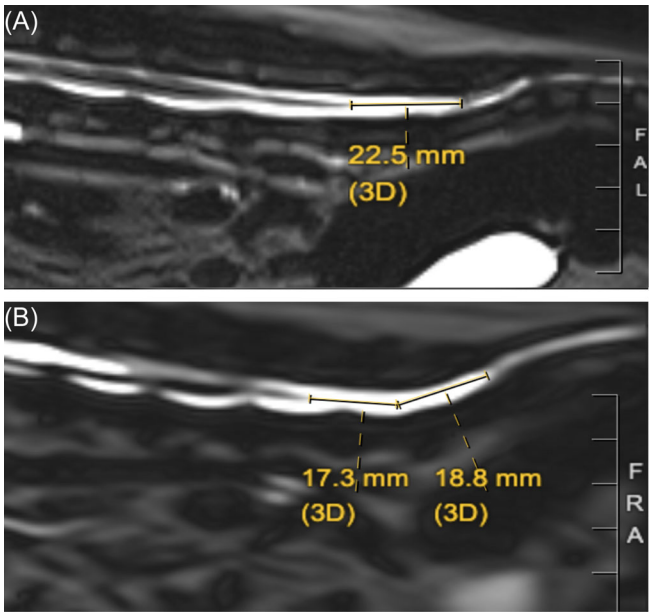

FIGURE 1 Determination of filum terminale internum length (FTIL) using half-Fourier acquisition single-shot turbo spin echo (HASTE) sequences. Panel A demonstrates a straight-line measurement from the end of the conus (hypointense signal) to the end of the dural sac (bright hyperintense signal). Panel B demonstrates the length measurements using multiple straight-line measurements due to the angle of the lumbosacral junction

2.5 | Statistical analysis

Analyses were performed using JMP (JMP Pro 14.1.0, SAS, Cary, North Carolina) and R Studio (version 1.1.456). Summary statistics were generated for the TSS and TPS, combined palpation scores, spinal cord and dural sac termination sites, FTIL, and the presence, location, and maximal diameter of SM. A Shapiro-Wilk *W* test was used to assess the normality of continuous data (termination distance and maximal diameter of SM). Normally distributed data were reported using mean and SD; median and range values were used to describe nonnormal data.

A reliability standard for ChiMPS-T responses was developed to account for owners who may have overexaggerated or underreported pain in their dogs compared to combined palpation scores. Exclusion of scores required an extreme discrepancy between TPS and palpation scores: (a) TPS ≥13 points above combined palpation scores or

TABLE 2 Missing data for study parameters

Variable	No analyzed	No excluded	Reason
ChiMPS-T	45	3	Owner noncompliance, n = 2 Failure to meet reliability criteria, n = 1
Spinal cord termination	47	1	Inadequate image quality
Dural sac termination	47	1	Inadequate image quality
FTIL	46	2	Truncation of images at sacrum

Abbreviations: ChiMPS-T, Chiari-like malformation pain and scratch tool; FTIL, filum terminale internum length.

(b) combined palpation score ≥7 points higher than TPS. Both cutoff values, 13 for TPS and 7 for combined palpation score, reflect severe pain for each scale.

Interobserver reliability for the location of spinal cord and dural sac termination was determined by kappa analysis. Intraclass correlation (ICC) coefficient was calculated for interrater reliability determination for FTIL measurements. Our first objective was to compare spinal cord termination morphometry to owner and clinician-reported clinical signs. To do this, Wilcoxon rank sum tests were used to compare spinal cord and dural sac termination sites to TPS, TSS, and combined palpation scores. Linear regression was used to compare FTIL to TPS, TSS, and combined palpation scores. Next, we compared termination sites and FTIL to the presence of lumbar SM using chi-squared tests for association and logistic regression, respectively. Lastly, we placed dogs into groups based on the presence of SM and owner-reported clinical signs. The 4 phenotypes were as follows: normal dogs, asymptomatic dogs with SM, symptomatic dogs without SM (CM-pain dogs), and symptomatic dogs with SM (CMSM-pain dogs). We then compared FTIL (logistic regression) across all 4 phenotypes. The angle of the LS junction was compared with the presence of lumbar SM, owner-reported pain, and presence of pain on palpation using logistic regression. For all chi-squared tests for association, Fisher's exact tests were used when there were <5 observations in a category. The Holm-Bonferonni method was used to correct for multiple comparisons. A P value of <.05 was considered statistically significant.

3 | RESULTS

Fifty dogs were enrolled but 2 dogs were removed from the study because of comorbidities (degenerative myelopathy and intervertebral disc disease). Participation in the study was voluntary, and therefore, the population was not considered random and included predominantly owners of affected dogs and breeders screening their breeding dogs. Forty-eight dogs were analyzed, missing data are detailed in Table 2. The median age of dogs in the study was 3 years (range, 11 months to 12 years). There were 17 females, 12 spayed females, 6 males, and 13 neutered males. Of the 48 dogs, 20 (42%) were reported to be painful by their owners and 30 (63%) were painful on palpation. Summary statistics for TPS, TSS, and combined palpation scores are shown in Table 3.

Twenty-three of 48 dogs (48%) did not have SM, 2 dogs had cervical SM only (4%), 1 dog had lumbar SM only (2%), and 22 dogs had both cervical and lumbar SM (46%). All dogs with lumbar SM also had thoracic SM. The cohort consisted of 16 (33%) normal dogs, 12 (25%) asymptomatic dogs with SM, 7 (15%) symptomatic dogs without SM (CM-pain), and 13 (27%) symptomatic dogs with SM.

Kappa analysis indicated good interobserver agreement with a kappa value of 0.61 for spinal cord termination and 0.64 for dural sac termination. Interobserver agreement for the FTIL, determined using ICC coefficient, was 0.92. The spinal cord of 1/47 (2%) dogs terminated at L6, 31/47 (66%) at L7, and 15/47 (32%) in the Sa. Dural sac termination occurred at L7 in 3/47 (6%) dogs, the Sa in 24/47 (51%) dogs, and Cd vertebrae in 20/47 (43%) dogs, with continuation of the signal beyond the end of imaging of the Cd in 4 dogs. The FTIL measurements were normally distributed with a mean ± SD of 2.91 mm ± 1.08 mm.

Level of spinal cord termination did not correlate with TPS (P = .55), TSS (P = .37), or combined palpation scores (P = .20). Similarly, dural sac termination was not correlated with TPS (P_{adj} = .11), TSS (P_{adj} = .31), and combined palpation scores (P_{adj} = .31). However, FTIL correlated with TPS (P_{adj} = .03) and combined palpation score (P_{adj} = .02); but not TSS (P = .31)(Figure 2). Next, we investigated the relationship between the ending of the spinal cord and presence of SM. We found that the presence of lumbar SM correlated with spinal cord termination (Padj = .002) but not dural sac termination (P_{adj} = .41; Figure 3). The FTIL measurement did not correlate with the presence of lumbar SM (P = .21). Finally, when dogs were grouped by presence of signs and SM, symptomatic CKCS without SM had significantly shorter FTIL than did normal dogs as well as symptomatic and asymptomatic dogs with SM (P = .02; Figure 4). The angle of the LS junction was not associated with lumbar SM or the presence of owner and clinician-reported pain (Table 4).

4 | DISCUSSION

We compared the location of spinal cord and dural sac termination and the FTIL with the presence of clinical signs and SM in CKCS. The locations of spinal cord and dural sac termination were not related to clinical signs (pain or scratch). However, FTIL was associated with both owner-reported pain (TPS) and spinal pain assessed by palpation. Location of spinal cord termination had a significant relationship with presence of lumbar SM, confirming the findings of our previous study.[6] Dural sac termination and FTIL did not correlate with the presence of SM. Importantly, scratch was not associated with any

TABLE 3 Summary statistics for owner-reported clinical signs and combined palpation scores

		Syringomyelia		Symptomatic per owner	
	Whole Cohort (n = 48)	Yes (n = 25)	No (n = 23)	Yes (n = 29)	No (n = 19)
Combined palpation score (median, range)	3.75, 0-9	4.5, 0.5-8	3, 0-9	5, 0.5-9	2, 0-7
TPS (median, range)	2, 0-16	2.25, 0-15.5	0, 0-16	4.75, 0-16	0, 0-2
TSS (median, range)	3, 0-14	7.75, 0-14	2, 0-12	9, 1-14	0, 0-3

Abbreviations: TPS: total pain score; TSS: total scratch score

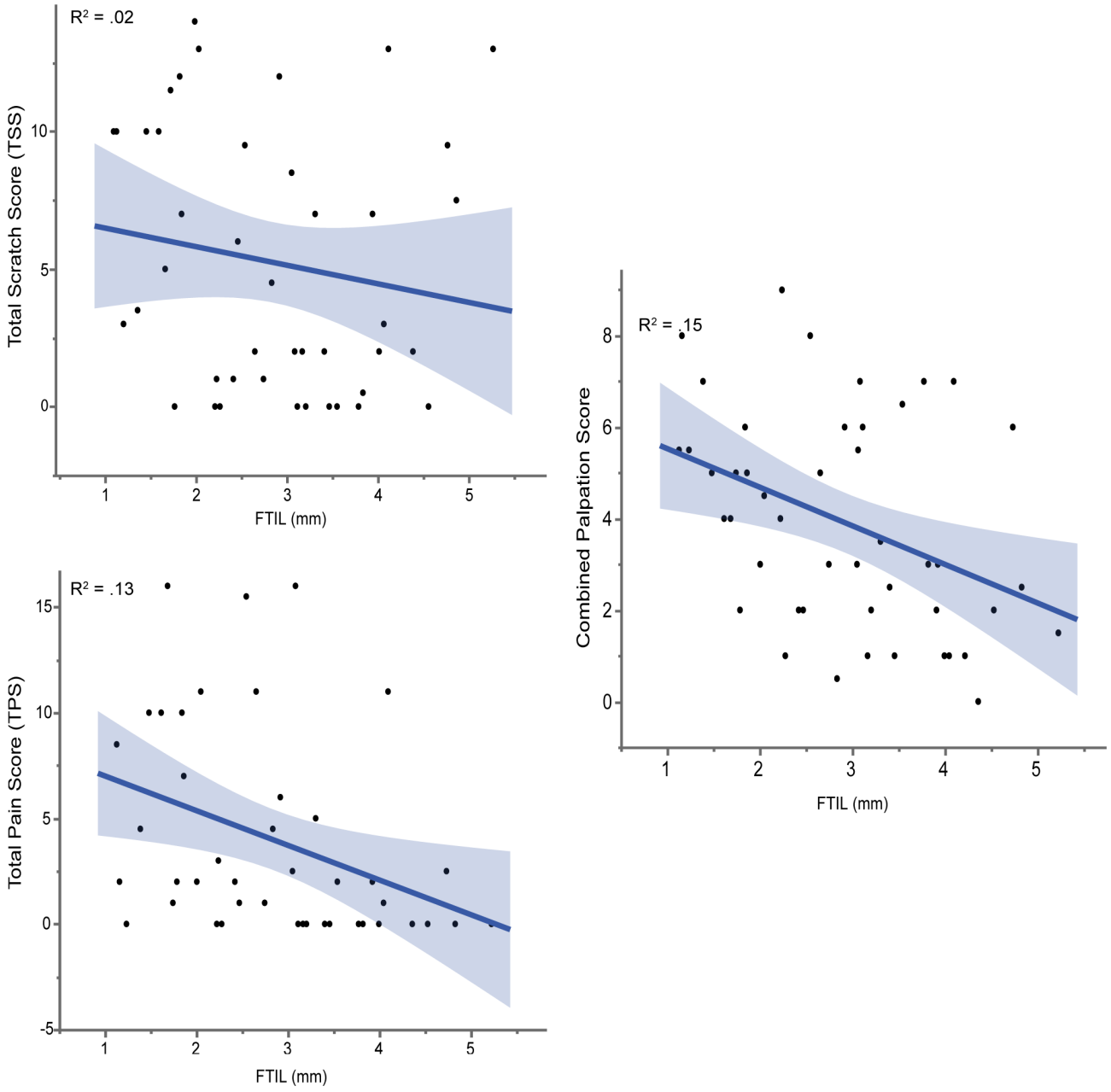

FIGURE 2 Scatterplots of the correlation among filum terminale internum length (FTIL) and, A, total scratch score (TSS) (P = .79), B, total pain score (TPS) (P_{adj} = .034), and, C, combined palpation score (P_{adj} = .015). The blue line reflects the linear fit of the data and the light blue shaded region is the 95% confidence region for the fitted line

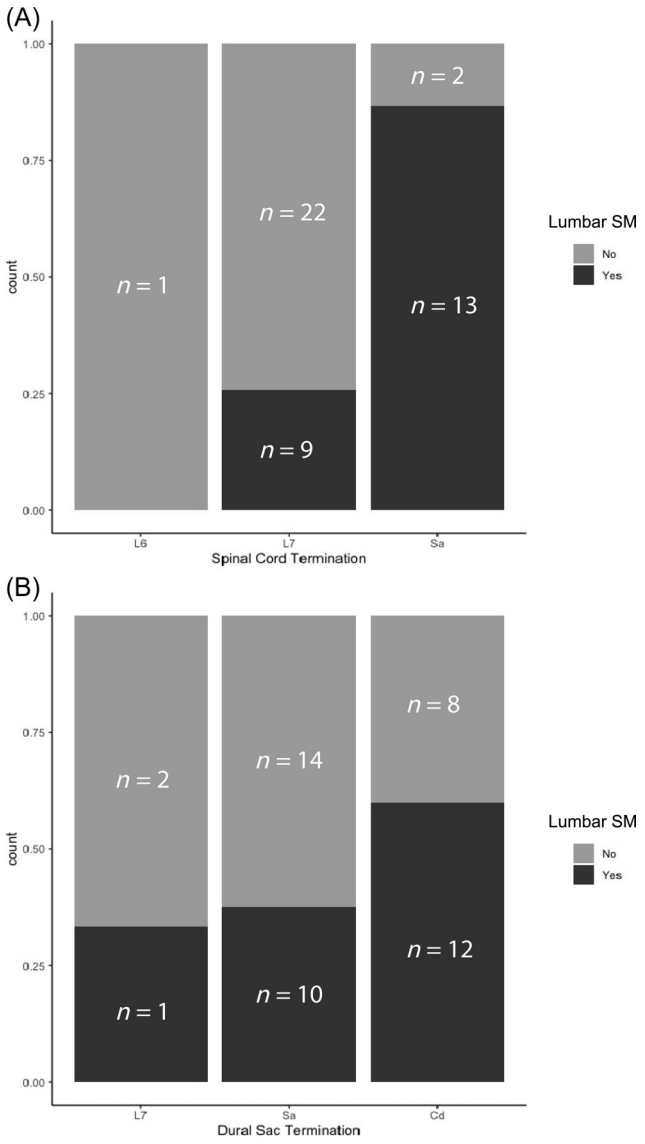

FIGURE 3 A, Spinal cord and, B, dural sac termination in Cavalier King Charles spaniels (CKCS) with and without lumbar syringomyelia (SM). Each stacked bar shows the relative count for each group terminating at every vertebral level. L6, lumbar vertebrae 6; L7, lumbar vertebrae 7; Sa, sacrum; Cd, caudal vertebrae

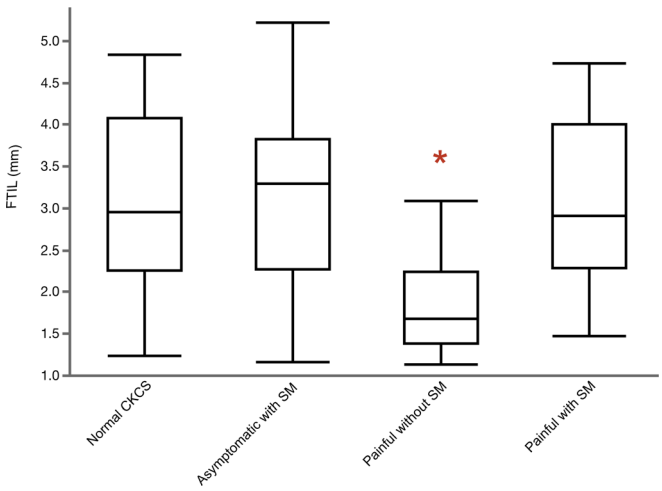

FIGURE 4 - Box plots showing filum terminale internum length (FTIL) measurements for normal Cavalier King Charles spaniels (CKCS), asymptomatic dogs with syringomyelia (SM), painful dogs without SM (Chiari-like malformation [CM] pain), and painful dogs with SM. The horizontal line within the boxplot represents the median, the ends of the box represent the interquartile range, the upper and lower whisker extend 1.5 × interquartile range from the top and bottom of the box.*P = .02

morphometric features of the terminal spinal cord and filum terminale. Lastly, symptomatic dogs without SM (CM pain dogs) had a shorter FTIL than did symptomatic CMSM dogs and asymptomatic dogs.

In previous work, we found that TL but not cervical SM was significantly associated with the location of dural sac termination in CKCS.[6] In the current study, we were unable to draw statistical comparisons for dogs with cervical SM because only 2/48 dogs (4%) had cervical SM only. Dural sac termination appeared to be located more caudally in dogs with lumbar SM, but this relationship was not significant (Figure 3). By contrast, spinal cord termination site was significantly more caudal in dogs with lumbar SM in this cohort of CKCS, confirming the findings of the previous study and suggesting that this finding is a robust observation. Furthermore, a recent study demonstrated that conus medullaris position, not dural sac position, is dependent on size in dogs.[45] The study reported that the most commonly observed conus medullaris termination in dogs weighing 5 to 10 kg is cranial L7 and the dural sac terminated in the cranial Sa most frequently for all sizes. In comparison, approximately 32% of CKCS in our cohort had their spinal cords end in the Sa and 43% had dural sac termination in the Cd vertebrae. These findings further corroborate our previous finding that CKCS have a more caudal spinal cord termination when compared to size-matched dogs of other breeds.[6]

Filum terminale internum length was measured based on authors observing considerable variation in this distance across the cohort of CKCS being evaluated. The distance was easily and reliably measured, as reflected by 92% agreement among observers. Dogs with shorter FTIL had considerably higher pain scores that were reported in 2 independent manners: from owners and from observations in the clinic that were recorded before the MRI procedure. The shortened FTIL reflects a rapid closure of the subarachnoid space altering the normal structure. A study of human cadavers indicated that the filum terminale internum is markedly elastic and has greater capacity to withstand strain than do the conus medullaris and filum terminal externum.[47] A thickened filum terminale has been extensively described as a cause of TCS in people.[21,22,29,47,48] Although we have not identified a thickened filumn terminale internum in these dogs, it is possible that shortening of the filum terminale internum results in altered mechanical properties and places stress on the spinal cord and meninges. Conversely, the shorter FTIL may be the result of a longer spinal cord. However, a study in cats has shown that tension on the filum terminale internum during growth results in lengthening of the caudal spinal cord.[49]

TABLE 4 Comparison of lumbosacral (LS) junction curvature and the presence of lumbar syringomyelia (SM) and pain

	Lumbar SM			Owner-reported pain			Pain on neurological examination		
	Yes	No	*P*	Yes	No	*P*	Yes	No	*P*
LS junction curvature (degrees) (mean, SD)	151.1, 5.93	152.8, 5.41	0.30	152.4, 7.0	151.8, 4.7	.72	151.9, 5.7	152.2, 5.8	.83

An important finding of our study is the observation that symptomatic dogs with and without SM could be differentiated based on their FTIL. Several studies have described the relationship between SM and clinical signs, but an increasing body of work highlights the prevalence of asymptomatic dogs with SM and those that have classical clinical signs but lack SM (CM-pain dogs).[4,5,7,11-13,15] Few studies have reported differences in CKCS with clinical signs of pain with and without SM. A skull morphometric study, using machine learning, identified skull changes associated with SM development and CM pain.[50] Although skull abnormalities are likely to cause pain of the head and neck, it is less likely that these skull changes also cause LS pain. Our work highlights alterations in the filum terminale as another possible contributing factor to development of diffuse spinal pain.

Diagnosis of TCS in people, in the absence of other spinal anomalies, relies on clinical presentation, urodynamic profiles, and MRI findings. The most common MRI findings in people with TCS are a low-lying (more caudal) conus medullaris and a thickened filum terminale.[30,34,36] However, another form of TCS, albeit controversial, has been described in which symptoms are consistent with TCS but the conus medullaris is located in a normal position and is referred to as occult tethered cord syndrome (OTCS).[51,52] In some cases of OTCS, the main presenting complaint is lower back pain.[48,53] Although the decision to operate on patients with OTCS is controversial,[54] many studies have shown postoperative improvements in pain and urodynamic and bowel dysfunction.[48,53,55] Furthermore, the coexistence of TCS and CM1 has been discussed.[17-23] Traction-based hypotheses have been advanced as the mechanism to explain CM1 occurring alongside TCS.[21,22,30,56-59] A genetic basis also has been described.[18,20,60]

Tethered spinal cord has been reported in the veterinary literature, most commonly in animals with coexisting anomalies.[39-43] One case report identified a dog with paraparesis, LS pain, paraparesis, and lameness to have subtle MRI findings of a caudodorsal displaced conus medullaris.[38] Surgical exploration identified caudal traction of the conus medullaris and a thickened filum terminale.[38] The MRI findings in the aforementioned case were mild, but the clinical presentation was consistent with TCS. The correlation of decreased FTIL to presence of spinal pain in our study may reflect a tight, and possibly thickened, filum terminale that more closely mirrors the occult form of TCS in people. However, a major difference is that this population of dogs shows no apparent bladder or bowel dysfunction. Urodynamic studies could be considered in the future to further evaluate bladder function. As a consequence of tension on the caudal spinal cord, decreased blood flow and regional hypoxemia develop as well as compression of nerve roots. In addition, CKCS with CM-pain have alterations in their cranial development,[50] but it is plausible that these changes, in conjunction with altered biomechanics within the filum terminale, combine to produce spinal pain. The lack of correlation between caudal spinal cord morphology and scratch suggests that TCS does not play a role in phantom scratch. This conclusion is not surprising with the recent postulation of syrinx damage causing disinhibition of descending projections to scratching central pattern generators.[61]

Our study had some limitations including the subjective nature of pain assessment by owners and investigators, which was unavoidable. Our cohort was mostly comprised of pet owners with affected dogs and breeders with asymptomatic dogs. We recognize the different biases associated with these distinct groups of owners. To account for under- and over-reporting of clinical signs, we developed a reliability standard for owner questionnaires. The reliability standard allowed comparison of owner-reported scores to combined palpation scores, and although these palpation scores are subjective, they lack owner- and breeder-related biases. To minimize subjectivity, the combined palpation scores were agreed upon by 2 authors (C.R.S., N.J.O.) who palpated each dog independently, and all observations were made before MRI to avoid bias. Using our reliability standard, only 1 ChiMPS-T score was removed from analysis. This owner described extremely severe pain whereas the dog showed minimal discomfort in the hospital on multiple visits. Nonetheless, this discrepancy highlights the occasional pitfalls in owner reporting of clinical signs and the need to incorporate standards against which to compare their responses in clinical trials.

Another limitation was the difficulty in differentiating structures on MRI. As was mentioned previously, the dural sac ending that was identified using HASTE signal was variable with either an abrupt ending, a trailing off signal, or an interruption and reappearance of hyperintense signal.[6] To account for this variability, we deemed the ending of the dural sac as the termination of the brightest HASTE signal and this approach also was applied for our FTIL observations. Uncommonly (n = 4), the HASTE signal still was present in the Cd and extended beyond the image window. In these cases, we most likely underestimated the FTIL. Of the 4 images with extended HASTE signal, 2 dogs were painful and 2 were not. Thus, we do not believe this finding had a substantial effect on our results, but must be considered for future use of this measurement. We used transverse sequences in combination with sagittal images to determine the end of the spinal cord, but found that the sagittal sequences alone adequately indicated the site at which the spinal cord stopped tapering, as described by others.[45] Interobserver reliability was good (kappa = 0.61) using sagittal scoring methods. In future work, other imaging sequences such as

construction interference steady state that delineate small structures such as nerves in the presence of high CSF-to-soft tissue contrast may be considered for better visualization of these terminal structures.

In summary, the purpose of our work was to determine if caudal spinal abnormalities in CKCS were associated with clinical signs of pain and scratch. We disproved our hypothesis that a more caudal location of spinal cord termination would be associated with clinical signs. However, we found that FTIL is associated with pain, not scratch, and our work supported previous findings that the vertebral level of the spinal cord termination is associated with lumbar SM. In addition, we found that painful dogs without SM were differentiated from other phenotypes by a decreased FTIL. These findings show that location of the filum terminale is associated with development of lumbar SM and FTIL is associated with spinal pain in CKCS. Future work is warranted to characterize other caudal clinical and functional abnormalities, potentially by use of gait analysis, electrophysiological evaluation of the conus medullaris, and urodynamic studies in these dogs. Also, because of limited time and financial restrictions, we were unable to perform dynamic view MRI on this cohort of dogs. Additional work to compare FTIL and termination sites using dynamic view MRI would be beneficial to further investigate TCS in CKCS. Finally, necropsy examination and histological studies of the filum terminale and associated structures are warranted.

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CONFLICT OF INTEREST DECLARATION

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

All procedures performed on dogs were a part of an imaging research study were covered by an approved IACUC protocol.

HUMAN ETHICS APPROVAL DECLARATION

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

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