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Questionnaire-based Analysis of Owner-reported Scratching and Pain Signs in Cavalier King Charles Spaniels Screened for Chiari-like Malformation and Syringomyelia

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Background: Chiari-like malformation (CM) and syringomyelia (SM) cause a pain syndrome in Cavalier King Charles spaniels (CKCS). Clinical signs are not consistently apparent on neurologic examination, and owner reporting of signs provides vital clinical history. However, owner questionnaires for this disease are not well developed.

Objectives: To develop a tool to capture owner-reported clinical signs for use in clinical trials and to compare owner-reported signs with the presence of pain on neurologic examination and SM on magnetic resonance imaging (MRI).

Animals: Fifty client-owned CKCS.

Methods: Owners completed a questionnaire and pain/scratch map. Each dog underwent a neurologic examination and craniocervical magnetic resonance imaging (MRI). Questionnaire responses were developed into scores, area of shading for pain/scratch maps was measured, and consistency of responses between these tools was assessed. Owner-reported findings were compared with neurologic examination findings and presence and severity of SM on MRI.

Results: Thirty-three dogs were symptomatic and 17 asymptomatic; 30 had SM. The most common sign of pain was crying out when lifted (n = 11). Extent of shaded areas on maps positively correlated with questionnaire scores for pain ($r^2 = 0.213$, $P = 0.006$) and scratch ($r^2 = 0.104$, $P = 0.089$). Owner-reported findings were not significantly associated with presence or severity of SM or neurologic examination findings. Owner-reported lateralization of signs was significantly associated with SM lateralization ($P < 0.0001$).

Conclusions: The questionnaire and maps may be useful for clinical trials. Lack of association of owner-reported signs with SM highlights our lack of understanding of the pathophysiology of pain in this disease.

Key words: Neuropathic pain; Paresthesia; Phantom scratch; Syrinx.

Cavalier King Charles Spaniels (CKCS) have an extremely high prevalence of Chiari-like malformations (CM) and syringomyelia (SM).[1–5] Chiari-like malformation results in a brain and skull mismatch that produces a relatively small caudal fossa with crowding of the foramen magnum, and stenosis of cranial venous sinuses and skull foraminae.[1,6,7] These changes conspire to produce turbulent flow of cerebrospinal fluid (CSF) and development of SM within the cervical, thoracic, and lumbar spinal cord.[8] This condition of dogs has

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Abbreviations:

CKCS	Cavalier King Charles Spaniels
CM	Chiari-like malformation
SM	syringomyelia
MRI	magnetic resonance imaging
NCSU	North Carolina State University
CSF	cerebrospinal fluid

similarities to Chiari-type 1 malformation in humans, characterized by caudal herniation of the cerebellar tonsils below the foramen magnum and also frequently associated with SM.[9] Clinical presentation in humans is variable but manifestations of neuropathic pain dominate including headaches, neck pain, and burning sensations of the upper extremities.[10]

Characterizing the signs of CMSM in dogs is challenging because of the difficulty of inferring signs of pain from behavior in dogs. Owners report that affected dogs cry out in pain; exhibit phantom scratching of the neck, flank, and ear (importantly, the paw does not make contact with the skin), rub their face, neck, or ear; and show other more insidious signs such as reluctance to play, jump, or lower their head to eat.[11–13] Findings on neurologic examination include neck and back pain, ability to induce phantom scratching, and, in severely affected dogs, ataxia and paresis. Thus far, studies have assigned a neurologic grade using the accumulation of data from questionnaires, history taking, and neurologic examinations and have reported a strong association between clinical signs and the presence and maximum diameter of SM.[14–16] However, the prevalence of apparently clinically normal CKCS with SM remains high with reported percentages ranging

from 25 to 70 percent,[3,17,18] raising questions about our ability to document clinical signs accurately and our understanding of the role of SM in pain in these dogs.

It is crucial to have quantitative measures of chronic pain that are valid and reliable in clinical patients to enable development and testing of interventions (such as drugs or surgical procedures) designed to decrease such pain. Given the importance of owner observations in describing and quantifying pain in their pets,[19] and the growing interest in identifying and treating neuropathic pain in dogs,[20] there is a need to better understand how to identify and quantify this pain using owner assessments. Limited data are available on the utility of owner questionnaires for this condition,[18,21,22] and none of the available questionnaires have been developed after recognized psychometric approaches.[23,24] In addition, there is limited information on the specific signs displayed, scratching versus pain, and how these signs relate to the presence or absence of SM. The aims of our study were to perform initial development of a tool to capture owner-reported clinical signs for use in clinical trials and to examine the relationship among owner-reported signs, presence of pain on neurologic examination, and presence and severity of SM on MRI. We hypothesized that owner-reported signs would correlate moderately or highly ($R^2 \geq 0.6$) with MRI findings.

Materials and Methods

Dogs

Client-owned CKCS were recruited to North Carolina State University (NCSU) Veterinary Hospital between the years of 2015 and 2016 using an NCSU-hosted web page and through the CKCS Club of America. Dogs were required to be ≥15 months of age and healthy enough to be placed under general anesthesia for MRI based on laboratory results (CBC and serum biochemistry panel) performed within 2 weeks of anesthesia and on physical examination on the day of anesthesia. Before arrival, owners were asked to complete the study questionnaire (Fig S1) and pain/scratch map, termed ChiMPS-M (Chiari-like malformation pain and scratch maps; Fig S2). On arrival, dogs underwent physical and neurologic examinations by the study investigators. The presence and location of pain elicited by spinal palpation were recorded, and scratching in response to palpation was noted. All procedures were approved by the NCSU Animal Care and Use Committee (IACUC number 15-003-O; 20 January 2015).

Questionnaires

A preliminary questionnaire (Fig S1) and ChiMPS-M (Fig S2) were developed to capture information related to medical history and clinical signs observed in the household. During the initial stages of recruitment, we used a pre-existing questionnaire[1,14,15] that asked broad questions about signs that had been reported in the literature related to CMSM. The preliminary questionnaire captured information on the presence of episodic pain, scratching, and various signs of pain displayed. However, upon review of completed questionnaires and discussions with owners, it was evident that changes needed to be made to enhance the readability and reliability of responses. Open-ended questions on frequency of signs were commonly left blank; therefore, checkbox options on frequency seemed necessary. In addition, the overall level of discomfort for each clinical sign was not captured reliably in the preliminary questionnaire. A Likert-type scale was employed in the final questionnaire for each sign, and bold font was used to segregate pain and scratching for these questions to enhance readability and clarity (Fig S3).

The revised final questionnaire, named ChiMPS-T (Chiari-like malformation pain and scratch tool), was divided into 2 parts: medical history and clinical signs related to CMSM. The medical history portion consisted of 10 questions, 7 of which were binary (yes/no) questions that required further description if the "yes" box was chosen. The clinical signs portion of the ChiMPS-T consisted of 12 questions relating to frequency, location, lateralization of signs, severity, and types of clinical signs observed at home. The questions about frequency were allotted the following answer choices: more than twice daily, once or twice daily, once or twice a week, not at all. For severity of discomfort associated with scratching and, separately, to pain, an 11-point Likert-type scale was used and owners assigned a score between 0 and 10 (0—no discomfort; 10—extreme discomfort). These responses were used to categorize scratching and pain as present (1) or absent (0) and to generate ordinal scores that encompassed severity and frequency (Table 1).

In addition to the ChiMPS-T, owners completed separate maps for pain and scratching, ChiMPS-M, by outlining the areas on their pets that they considered affected by pain or scratching. All maps were scanned and analyzed using ImageJ software[a] to determine the area of the outlined regions for scratching and pain separately.

MRI Protocol

Anesthesia was induced with an IV bolus of fentanyl[b] as a premedication, followed by IV propofol.[c] After intubation, anesthesia was maintained with an inhaled isoflurane[d] and oxygen mixture. Temperature, heart rate, ventilatory rate, mean arterial blood pressure, and end tidal CO_2 were monitored and maintained within normal

Table 1. Total scratch and pain scores developed from ChiMPS-T responses encompassing frequency and severity of each clinical sign.

Question	Response (score)
Scratching	
Frequency of scratching (FS)	>2× daily (3); 1–2× daily (2); 1–2× week (1); not at all (0)
Frequency of rubbing face, neck or side (FR)	>2× daily (3); 1–2× daily (2); 1–2× week (1); not at all (0)
Discomfort related to scratching (DS)	0–10
Total scratch score (TS)	FS (0–3) + FR (0–3) + DS (0–10) = (0–16)
Pain	
Episodic pain (EP)	Yes (1); No (0)
Frequency of pain (FP)	>2× daily (3); 1–2× daily (2); 1–2× week (1); not at all (0)
Signs of pain (SP)	1 point for all boxes checked (0–6)
Discomfort related to pain (DP)	0–10
Total pain score (TP)	EP (0–1) + FP (0–3) + SP (0–6) + DP (1–10) = (0–20)

physiologic limits. Dogs were positioned in ventral recumbency with their necks extended during the MRI.[e] Acquired sequences of the brain and cervical spinal cord included T2 weighted and proton density (PD) sagittal images, and T2 weighted and PD axial images of the cervical and cranial thoracic spinal cord and brain.

MRI Analysis

Images of all MRI sequences were imported into Horos[f] for analysis. Analysis was performed at least 3 months after the MRI was performed, and ChiMPS-T and ChiMPS-M were not reviewed at the time of image analysis. All measurements were performed by 1 investigator (CAR) and spot checks on consistency were performed for 10% of cases by another investigator (SCG). The presence or absence of SM was determined using a definition of SM as linear T2 hyperintensity on sagittal images >2 mm in diameter.[11] The maximum dorsoventral height of SM was measured and expressed as a percentage of the height of the spinal cord at that site as well as the absolute measurement of maximum syrinx diameter.[1,16] A vertical line was drawn on midline through the central canal using blood vessels as anatomical alignment markers, and SM was visually established as asymmetric or centered, and the side of lateralization was noted.

Statistical Analysis

Statistical analyses were performed using JMP software.[g] Summary data were generated on the pain and scratching scores and the area of scratching (mm^2), the presence of SM, maximum SM height, and asymmetry. Ordinal and continuous data were evaluated for normality of distribution by the Shapiro-Wilk test. If normally distributed, the mean and standard deviation were calculated, and if not, the data were represented by the median and range. The consistency of owner-reported observations between the ChiMPS-T and the ChiMPS-M was evaluated by summarizing the number of owners who indicated scratching/pain on the ChiMPS-T and ChiMPS-M as well as correlating the total pain or scratch score to the area shaded on the respective ChiMPS-M. The relationship between the presence (categorized as yes or no) and severity of SM (quantified by maximum SM height [%]) and clinical signs (scratching and pain, evaluated separately as binary data, as ordinal data from the ChiMPS-T generated score and as continuous data on area scratched), was examined. In addition, the presence of pain during neurologic examination (binary data) was compared with owner-reported findings as well as the presence or absence of SM. Finally, in order to compare our results with prior literature, the relationship between clinical signs (yes or no) and maximum SM diameter was examined in dogs with SM.[16] Associations between the presence or absence of SM with ordinal clinical sign data were investigated using Wilcoxon rank-sum tests. Likewise, the Wilcoxon rank-sum test was used to evaluate the presence of pain on neurologic examination and the total pain score. Linear regression was used to model the relationship between the maximum height of SM (%) as well as maximum diameter and nominal variables as well as the correlation between syrinx height and diameter measurements. All binary categorical data were compared using contingency tables and chi-square tests for association with Fisher's exact tests used when there were <5 observations in a category. Multiple comparisons were addressed using Holm's correction calculator to establish the appropriate P-value for significance.

Results

Fifty-two dogs were enrolled in the study, 30 of which had SM. Participation in the study was by the owner volunteering, and therefore, the population cannot be considered random. The ages of dogs involved ranged from 15 months to 11 years. There were 10 females, 15 spayed females, 7 males, and 20 neutered males. One patient was removed from analysis due to the discovery of a brain tumor on MRI. Failure of owner compliance (to complete the ChiMPS-T) resulted in removal of 1 patient, leaving the total number of dogs analyzed at 50. Of these 50 dogs, 6 dogs had historically suffered from allergies or recurrent ear infections (although they had no signs of these conditions at the time of evaluation) and were removed from analysis for scratching-related signs, but included for pain related signs. All other dogs had normal integument.

Clinical Signs

All owners were asked to complete the ChiMPS-T, but 16 owners failed to do so, and thus, categorical and descriptive data are presented for all 50 dogs and scratch and pain scores were generated from the ChiMPS-T for 34 dogs. All participants completed the ChiMPS-M. Of the 50 dogs, owners reported signs in 33 dogs, whereas 17 reported no signs. Of the 33 symptomatic dogs, scratching was reported in 32 dogs and signs of pain were reported in 23 dogs. A range of different signs of pain was reported (Fig 1) with crying out when lifted reported most frequently. Lateralization of clinical signs was reported in 13 dogs in both the ChiMPS-T and the ChiMPS-M. Summary data for the ChiMPS-T, ChiMPS-M, and clinical findings are provided in Table 2. On neurologic examination, 36 dogs were found to have neck pain, thoracolumbar spinal pain on palpation, or both and 14 were not painful. Seven of 33 dogs with owner-reported signs were not found to be painful on neurologic examination. Twelve dogs displayed scratching behaviors
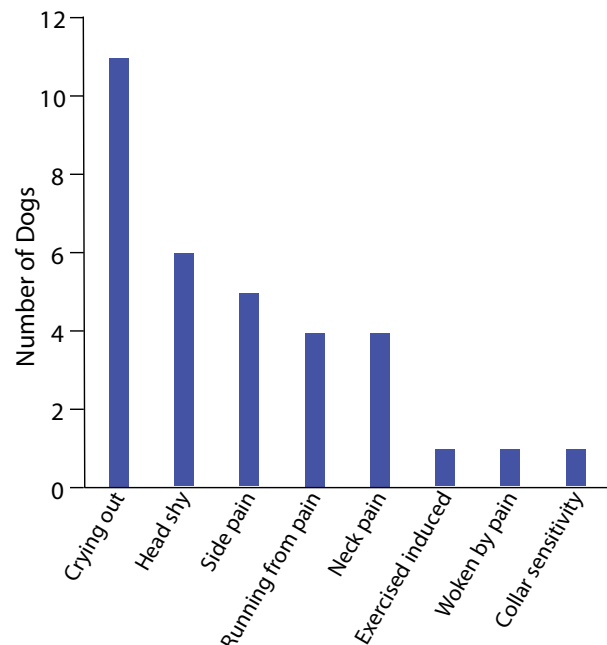

Fig. 1. The range and frequency of pain signs reported by owners of dogs with CMSM. N = 50 dogs.

Table 2. Cohort characteristics of dogs with and without SM and summary statistics for owner-reported clinical signs and neurologic examination findings.

	No SM (n = 20)	SM (n = 30)	P_{raw}	P_{adj}
Age (median, range)	3, 1–8	4, 1–11	—	
Sex (M, MN, F, FS)	3, 9, 4, 3	4, 10, 5, 12	—	
Allergies/Ear infections (n, %)	4, 20	2, 6.66	—	
Scratching reported on ChiMPS-T (n, %)	10, 50	22, 73.3	0.134	1.000
Scratch map (ChiMPS-M) completion (n, %)	7, 35	22, 73.3	0.026	0.312
Total area shaded scratch (ChiMPS-M) (mm^2) (median, range)	20.6, 0–646	78.5, 0–1,856	0.286	1.000
Pain reported on ChiMPS-T (n, %)	8, 40	15, 50	0.569	1.000
Pain map (ChiMPS-M) completion (n, %)	7, 35	16, 53.3	0.254	1.000
Total area shaded pain (ChiMPS-M) (mm^2) (median, range)	0, 0–961	20.1, 0–2,174	0.267	1.000
Pain and Scratching present (n, %)	9, 45	19, 63.3	0.251	1.000
Pain only (n, %)	0, 0	1, 3.33	0.444	1.000
Scratch only (n, %)	2, 10	8, 26.6	0.107	1.000
Neck pain on neurologic examination present (n, %)	10, 50	24, 80	0.034	0.374
Total scratch score (median, range)[a]	2.5, 0–14.5	4, 0–11.5	0.612	1.000
Total pain score (median, range)[a]	0, 0–10	2, 0–12	0.207	1.000

[a]Total scratch and pain score were analyzed from 34 dogs whose owners completed the more detailed questionnaire. P_{raw} represents the raw P values, and P_{adj} is the adjusted P values accounting for multiple comparisons. ChiMPS-T (Chiari-like malformation pain and scratch tool); ChiMPS-M (Chiari-like malformation pain and scratch Map).
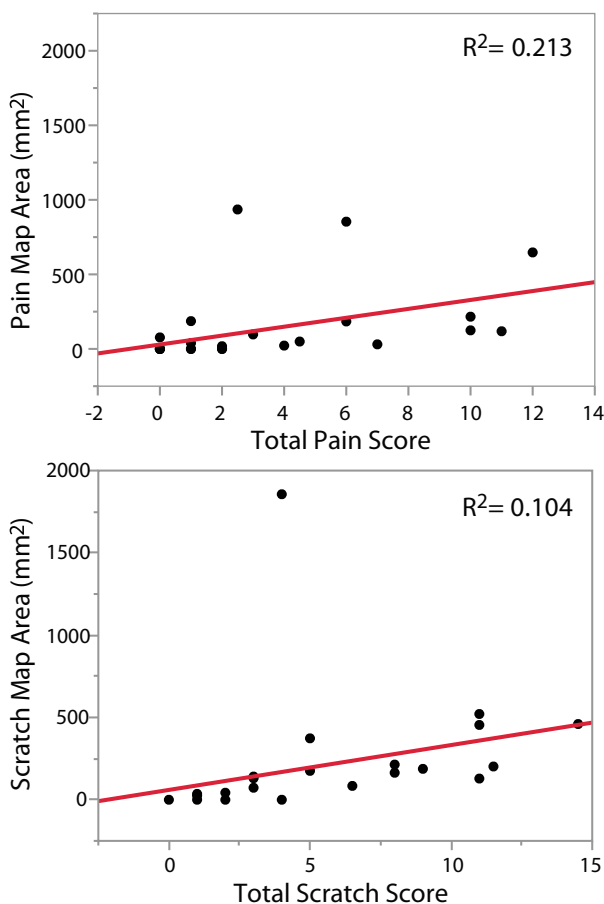
Fig. 2. Correlation of the total pain and scratch scores, developed from ChiMPS-T responses, with the area shaded on the corresponding ChiMPS-M. Area measured in mm^2.

during physical and neurologic examination (all had scratching behavior reported by the owner). None had paresis or ataxia.

Intertool Agreement

Twenty-six of 32 owners who reported presence of scratching on the ChiMPS-T indicated a region on the respective ChiMPS-M, and 18 of 23 of those who reported pain on the ChiMPS-T also indicated a site on the respective ChiMPS-M. Owners who did not complete the ChiMPS-M noted difficulty in localizing signs to specific regions. The total shaded area of the ChiMPS-M was positively correlated with the total pain score ($P = 0.006$, $r^2 = 0.213$) and total scratch score ($P = 0.089$, $r^2 = 0.104$), respectively (Fig 2).

Findings

Syringomyelia was present in 30 of 50 dogs, and lateralization of SM was present in 15 dogs. All dogs with SM had SM located in the cervical spinal cord, and 24 also had SM in the cranial thoracic spinal cord. Four dogs did not have MR images that extended into the thoracic spinal cord far enough to determine presence of SM in this region. The maximum height of SM expressed as a percentage of the height of the spinal cord ranged from 50 to 83% (median, 67%) in dogs with SM (Table 3). Syringomyelia was present in 23 of 33 owner-reported symptomatic dogs and 7 of 17 owner-reported asymptomatic dogs, and in 24 of 36 dogs with pain on neurologic examination and 6 of 14 dogs with no pain on neurologic examination. Cohort characteristics of dogs with and without SM and summary statistics for owner-reported clinical signs and neurologic examination findings are presented in Table 2.

Statistical Analysis

There was no relationship between the presence of owner-reported pain (yes or no) or scratching (yes or no) and the presence of SM. Likewise, the total scratch score and pain score were not significantly associated

Table 3. Comparison of owner-reported presence of pain or scratching compared with maximum SM height (measured as a percentage of spinal cord height). Values are expressed as median (range). P_{raw} represents the raw P values, and P_{adj} is the adjusted P values accounting for multiple comparisons.

	Presence of Pain				Presence of Scratching			
	Yes	No	P_{raw}	P_{adj}	Yes	No	P_{raw}	P_{adj}
Maximum height of syrinx (% of cord)	62.0 (0–80)	51.0 (0–82)	0.355	0.355	62.5 (0–82)	34.0 (0–77)	0.062	0.124

with the presence of SM (Table 2). Similarly, the presence of pain and scratching (Table 3), their total scores (Fig 3), and ChiMPS-M area (Fig 4) were not associated with the maximum SM height (%). Owner-reported presence of pain, total pain score, and area shaded on the pain ChiMPS-M did not correlate with the presence of pain on neurologic examination (Table 4). In order to compare our findings with previous literature, dogs without SM were excluded and the relationship between presence of pain and maximum SM diameter was examined, but no significant association was identified ($P = 0.37$). In order to determine whether location of SM was critical, we evaluated whether there was a relationship between regions
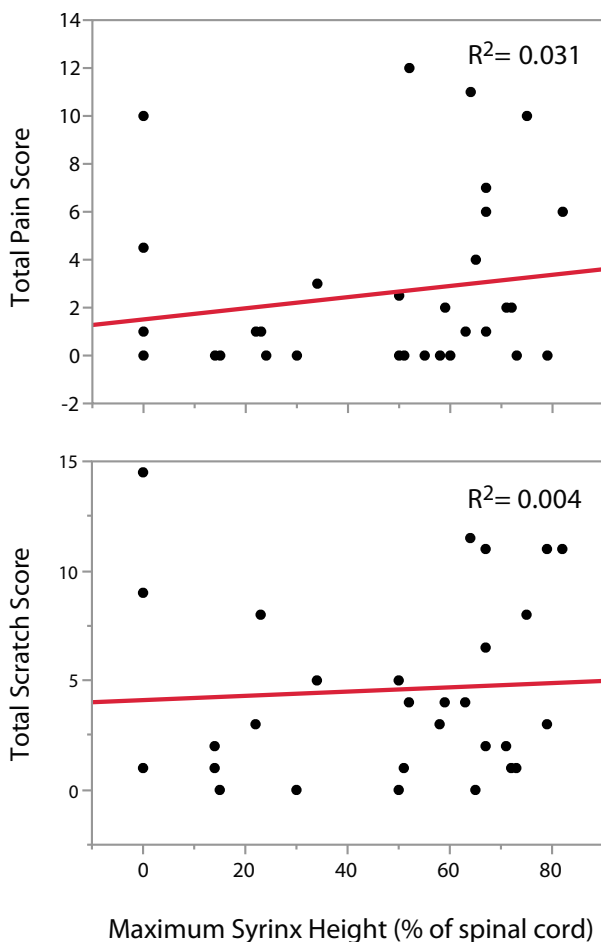

Fig. 4. Correlation of the maximum syrinx height (measured as a percent of spinal cord height) with the area shaded on the corresponding pain and scratch ChiMPS-M. Area measured in mm^2.

shaded on the ChiMPS-M and SM location, but there was not (Table 5). By contrast, owner-reported lateralization of signs was significantly associated with lateralization of the syrinx on MRI ($P < 0.0001$; Table 6).

Discussion

In our study, we initiated development of 2 subjective clinical metrology instruments (CMIs)—a questionnaire that included frequency and severity of signs (ChiMPS-T) and pain/scratch maps (ChiMPS-M) that outlined surface area affected, both designed to capture and quantify subjective owner evaluations of pain and

Fig. 3. Correlation of the maximum syrinx height (measured as a percent of spinal cord height) with the total pain and scratch scores developed from ChiMPS-T responses.
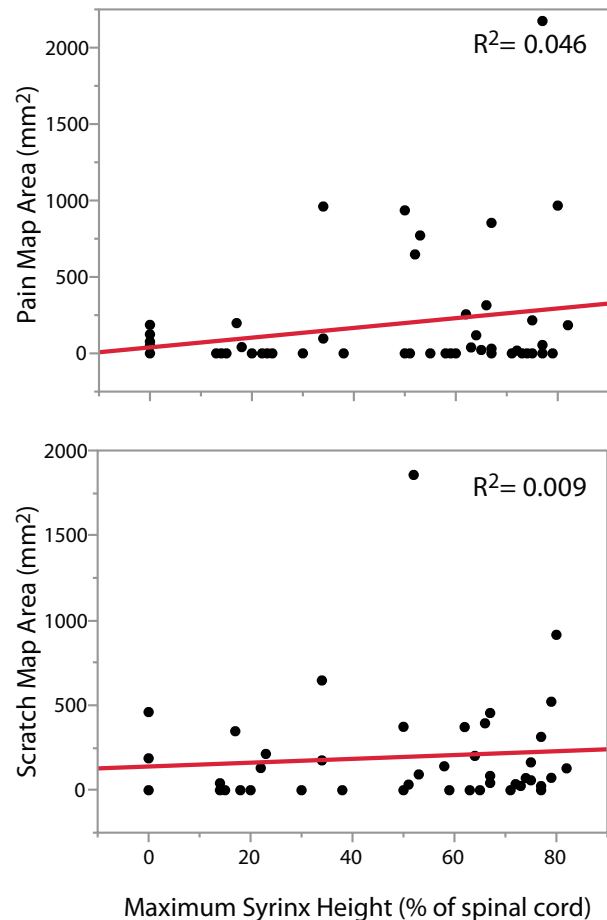
Table 4. Presence of pain on neurologic examination compared with owner-reported presence of pain, total pain score developed from ChiMPS-T responses, and the total area shaded on the pain ChiMPS-M. Total pain score and pain ChiMPS-M area are expressed as median values (range). P_{raw} represents the raw P values, and P_{adj} is the P values adjusted for multiple comparisons.

Owner-reported Findings	Pain on Neurologic Examination			
	Yes (n = 36)	No (n = 14)	P_{raw}	P_{adj}
Pain present (n)	20	3	0.056	0.168
Total pain score	2 (0–11)	0 (0–12)	0.073	0.168
Pain ChiMPS-M area (mm^2)	20.11 (0–966.7)	0 (0–2,174.3)	0.477	0.477

scratching in CKCS. The most common presenting sign was phantom scratching, occurring in 32 dogs, and the most common sign of pain was crying out when being lifted, occurring in 11 dogs. There was a moderate association between owners who reported scratching or pain on the ChiMPS-T and the area shaded on the corresponding ChiMPS-M potentially validating use of a map to quantify signs. However, we found that neither the presence nor severity of SM correlated with owner-reported signs (ChiMPS-T or ChiMPS-M) or neurologic examination findings.

Owner observations are extremely important in CMSM because clinical signs of neuropathic pain can be difficult to elicit and quantify on neurologic examination, and the full spectrum may not be seen in the veterinary clinic. Phantom scratching, the primary presenting sign of dogs with CMSM, suggests these dogs are experiencing paresthesia and allodynia and there are many other signs of pain described by owners that are episodic in nature. One group has reported use of a questionnaire to capture the effect of CMSM on quality of life and behavioral variables[21] but did not attempt to capture more information on the signs shown at home. Previous scoring systems combined owner-reported signs of pain and scratching and neurologic examination findings to establish a broad grade for clinically affected dogs.[1,14,15] Such approaches, however, have failed to address the fact that owner and board-certified neurologist assessments use very different experiences,

Table 6. Contingency table comparing lateralized SM with the presence of lateralized owner-reported signs. Chi-square analysis gives $P < 0.0001$.

Lateralized SM (Y/N)	Lateralized Signs (Y/N)		
	No	Yes	Total
No	32	3	35
Yes	5	10	15
Total	37	13	50

tools, and knowledge to draw conclusions on observations. One study demonstrated the usefulness of owner assessments, but, highlighted the lack of correlation with surgeon assessments after cruciate treatment in dogs.[23] Although the CMSM complex may cause scratch and pain through a common pathway, it is possible that different pathways may be involved.[25–27] We therefore decided to examine whether a more detailed reporting of clinical signs would uncover new relationships within this complex syndrome. When reporting signs, owners allude to the severity of signs in terms of both their intensity and their frequency, as well as the extent of their distribution. Thus, we considered several factors when attempting quantification. In our preliminary questionnaire, the frequencies of each sign were self-reported, and as a result, there was a wide range of different ways of responding. We used these preliminary data to create check box options based on subjective assessment of clustering of responses, allowing us to generate scores for each response. The ordinal scores produced from ChiMPS-T responses were utilized to capture severity and frequency of clinical signs. There is no gold standard against which we can compare these scores to determine whether they accurately estimate severity.

The area shaded by owners on the ChiMPS-M was a novel approach to assessing dogs with CMSM. This ChiMPS-M was adapted from human literature on pain in humans with Chiari I malformations in which patients are asked to shade regions of the body that were painful, and scores were based on total area shaded and number of painful sites.[28] While capturing different aspects of signs (area versus intensity versus frequency), there was a moderate, statistically significant correlation between ChiMPS-M areas and the scores we

Table 5. Location of area shaded on ChiMPS-M and pain on neurologic examination in dogs with and without syrinxes located in the cervical and thoracic. P_{raw} represents the raw P values, and P_{adj} is the P values adjusted for multiple comparisons.

	Cervical Syrinx				Thoracic Syrinx			
	Yes (n = 30)	No (n = 20)	P_{raw}	P_{adj}	Yes (n = 24)	No (n = 22)	P_{raw}	P_{adj}
Head/neck/ears shaded—scratch ChiMPS-M	20	6	0.054	0.270	15	8	0.200	0.985
Head/neck/ears shaded—pain ChiMPS-M	11	4	0.345	1.000	9	4	0.197	0.985
Shoulder/side shaded—scratch ChiMPS-M	9	4	0.739	1.000	6	5	1.00	1.000
Shoulder/side shaded—pain ChiMPS-M	11	5	0.538	1.000	8	6	0.754	1.000
Neck pain neuroexamination	24	10	0.034	0.204	19	12	0.116	0.696
Back pain neuroexamination	11	6	0.764	1.000	7	7	1.00	1.000

generated from the ChiMPS-T. This finding suggests there is a correlation between intensity of clinical signs and the area affected, but currently, the mechanisms resulting in a particular area being affected are unknown. However, because owners completed the ChiMPS-T first, there may have been a tendency for them to relate the shaded areas to the severity indicated on the ChiMPS-T. Future work should randomize the order of presentation of the ChiMPS-M and ChiMPS-T, or divide up the timing of completion.

Using these tools, we did not find any relationship among SM and pain, scratching or neurologic examination findings. This finding contrasts with other studies that report a strong association between presence and width of SM with clinical signs.[1,16,29,30] A previous study found maximum syrinx diameter to be the strongest predictor of pain in dogs with SM, with 95% of dogs with maximum SM width >0.64 cm showing signs of pain.[16] To allow comparison with this literature, we performed the same analysis but maximum diameter was not associated with the presence of pain in our case cohort. Although this lack of association may reflect the pitfalls of owners quantifying pain, they are not completely unexpected given that the occurrence of asymptomatic SM has been reported to be as high as 70% in older CKCS and was estimated at 46% across a group of 555 asymptomatic dogs.[3] It is possible that the mechanism of pain production by SM includes a complicated mixture of factors such as CSF flow, pressure, and turbulence,[8,13,16,31,32] dynamic features that we cannot capture with measurements of SM size. However, it is also possible that the pain is originating elsewhere in the pathways[13] and SM is purely a surrogate. Indeed, a recent paper has discussed the potential interaction of morphological variables that might produce SM and pain.[33] Additionally, neuropathic-type pain results from changes in the functioning of the nervous system, and there is variability in the response of individuals to the same type of insult.

Given that neither part of our ChiMPS-T was associated with MRI findings, it could be argued that our questionnaire is not valid, or that our more refined approach to owner assessment has uncovered a mismatch between clinical signs and MRI findings. In order to further assess the validity of the ChiMPS-T, several other avenues of research are needed. Future work should assess the discriminatory validity of this questionnaire (diseased versus not diseased), test-retest validity, and also test responsiveness validity (using a drug reported to produce an improvement[34] to see whether it is detected). The test-retest validity method for this tool may not be useful because CMSM is a progressive disease with signs frequently changing and worsening. Ideally, it would be tested for criterion validity, but there currently is no gold standard objective method of evaluating neuropathic pain in dogs; however, techniques such as quantitative sensory thresholds and nociceptive withdrawal reflex may have utility.[35–39] The use of the words "pain" and "scratching" in the ChiMPS-T questions could introduce respondent bias; therefore, wording may need to be altered to increase validity of this tool. With further evaluation of our proposed ChiMPS-T, it is likely to undergo modification as we learn more about this condition and how to measure the clinical signs.

In contrast, we did see lateralization of clinical signs in dogs with asymmetrical SM. Previous studies have shown that painful dogs are more likely to have an asymmetrical syrinx.[16,29] It is possible that SM develops asymmetrically when there is asymmetric compression at the level of the foramen magnum, producing both lateralized signs and coincidentally lateralized SM. Asymmetric SM appears to impact the dorsal horn more significantly, potentially producing pain[16,29] but also may reflect dynamic variables not evaluated here such as turbulent CSF flow. Because CMSM signs tend to be insidious or resemble normal dog behavior (scratching), it is also possible that owners are more able to recognize the signs to be abnormal when they are unilateral.

The conclusion that SM causes pain in CKCS is complicated by the finding that dogs with CM but no SM can show classic signs of neuropathic pain, as illustrated by 10 dogs in our study. Inconsistencies have been described in prior studies as well.[1,3,17,18,40] These data emphasize the uncertainty surrounding the role of SM in producing signs in these dogs. Indeed, other breeds, such as Yorkshire terriers, commonly have SM yet do not display the same signs. Alternative sources of pain have been proposed for people with CM but no SM, including compression of cranial and cervical nerve roots and dysfunction of sensory processing at the level of the medulla.[28,41,42]

To conclude, the full range of signs reported by owners of CKCS includes a variety of manifestations of pain, with phantom scratching as the most commonly reported sign followed by crying out when being lifted. Owner reporting of pain and scratch frequency and severity captured by the ChiMPS-T correlates with the owner-reported surface area affected by these signs in their dogs. Neither the scores nor the surface area reported correlated with the presence or severity of SM, highlighting uncertainty on the source of pain in these dogs. Further validation of these tools including responsiveness, test-retest, and discriminatory validity needs to be assessed. The relationship among CM, SM, and pain and scratch in this population of dogs deserves further examination.

Footnotes

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Conflict of Interest Declaration: Dr. Olby was invited to give a presentation on proposed work at the Cavalier King Charles Spaniel Club of America in 2015. Her accommodation and travel costs were covered by the group.

Off-label Antimicrobial Declaration: Authors declare no off-label use of antimicrobials.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Figure S1. Preliminary Questionnaire.
Figure S2. ChiMPS-M.
Figure S3. ChiMPS-T.