

Use of magnetic resonance imaging for morphometric analysis of the caudal cranial fossa in Cavalier King Charles Spaniels

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Objective—To perform morphometric analysis of the caudal cranial fossa in Cavalier King Charles Spaniels (CKCSs), to assess the relationship between caudal fossa dimensions and the frequency of magnetic resonance imaging (MRI) features of occipital abnormalities in CKCSs (with and without syringomyelia), and to compare caudal cranial fossa measurements in CKCSs with measurements of 2 groups of mesaticephalic dogs.

Animals—70 CKCSs and 80 mesaticephalic (control) dogs.

Procedures—Dogs were placed into 4 groups as follows: Labrador Retrievers (n = 40), spaniel-type dogs (40; English Springer Spaniels and Cocker Spaniels), CKCSs with syringomyelia (55), and CKCSs without syringomyelia (15). Multiple morphometric measurements (linear, angular, and area) were obtained from cranial midsagittal T2-weighted magnetic resonance images including the brain and cervical portion of the spinal cord. Several specific MRI findings were also recorded for CKCSs that appeared to affect the occipital bone and cervicomedullary junction.

Results—No significant difference was identified among breeds in control groups and between sexes in any of the groups for all morphometric measurements. Significant differences were identified in CKCSs, compared with mesaticephalic dogs, in the area of the caudal cranial fossa and for several linear measurements that reflected the length of the ventral aspect of the occipital bone. These differences were greater in CKCSs with syringomyelia. All CKCSs had abnormalities in occipital bone shape.

Conclusions and Clinical Relevance—CKCSs had a shallower caudal cranial fossa and abnormalities of the occipital bone, compared with those of mesaticephalic dogs. These changes were more severe in CKCSs with syringomyelia. (*Am J Vet Res* 2009;70:340–345)

Type I CM in humans is a congenital disorder characterized by caudal herniation of the cerebellar tonsils through the foramen magnum into the spinal canal.^{1–6} In addition, type I CM in humans is an important cause of syringomyelia and frequently occurs in association with occipital dysplasia.⁷ There is accumulating evidence that this malformation in humans is attributable to overcrowding of the hind-brain because of an underdeveloped posterior cranial fossa, and findings in morphometric studies^{7–15} indicate that the posterior cranial fossa is small and shallow in comparison to the normal unaffected population.

A similar syndrome of cerebellar herniation and syringomyelia has been described in CKCSs, and the

ABBREVIATIONS

CKCS	Cavalier King Charles Spaniel
CM	Chiari malformation
MR	Magnetic resonance
MRI	Magnetic resonance imaging

term Chiari-like malformation has been applied.^{16–19} There is a consensus that the underlying cause of this syndrome in dogs is the presence of a shallow and small caudal cranial fossa.^{16,18–20} However, to date, only a few morphometric studies^{a–c} have been performed. A prerequisite for identifying dogs with an increased susceptibility of developing Chiari-like malformation and syringomyelia is understanding factors leading to the development of the condition, which may thereby enable effective breeding schemes and genetic eradication programs.

The purpose of the study reported here was to perform morphometric analysis of the caudal cranial fossa in CKCSs, to assess the relationship between these dimensions and the frequency of MRI features of occipital abnormalities in CKCSs (with and without syringomyelia), and to compare these measurements in CKCSs with those of 2 groups of mesaticephalic dogs.²¹

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Materials and Methods

Sample population—Searches (from 2001 to 2006) of MRI databases from the University of Glasgow Small Animal Hospital and the Animal Health Trust identified 70 CKCSs (36 males and 34 females) that had undergone MRI for which cranial midsagittal MR images that included the brain and the 3 first cervical vertebrae were available. The age range was from 0.66 to 9 years (median, 4.3 years). Dogs were placed into 2 groups depending on the presence or absence of evidence of syringomyelia on MR images. Fifty-five dogs had evidence of syringomyelia on MR images (28 males and 27 females; age range, 0.66 to 8 years [median, 4.1 years]), and 15 dogs did not have evidence of syringomyelia on MR images (8 males and 7 females; age range, 0.75 to 9 years [median, 4.4 years]).

Control population—The control population comprised 40 Labrador Retrievers (20 females and 20 males) and 40 mesaticephalic spaniel-type dogs (English Springer Spaniels and Cocker Spaniels; 20 females and 20 males), which had undergone MRI of the brain but for which no cranial or intracranial pathologic findings were evident on MR images.

Morphometric study—Signed owner consent was obtained for all dogs undergoing MRI studies. Morphologic characteristics of the caudal fossa were determined on midsagittal T2-weighted MR images. The MRI was performed by use of a 1.5-Tesla scanner.^d All morphometric determinations were made by use of a commercial image analysis software package.^e In 8 dogs, midsagittal T1- and T2-weighted MR images were available. The accuracy of the linear, angle, and area measurements was compared between T1- and T2-weighted MR images in these 8 dogs to determine whether there were any significant differences in measurements.

Bony landmarks were used for the midsagittal plane measurements as follows: dorsal aspect of the cribriform plate, dorsal aspect of the dorsum sella turcica, caudal aspect of the most ventral part of the foramen magnum, rostral and caudal aspect of the most dorsal part of the foramen magnum, internal occipital protuberance, and tentorium cerebellum. Magnetic resonance images on which any of these landmarks were not clearly identified were rejected.

Measurements were made from midsagittal T2-weighted MR images from 70 CKCSs and 80 control dogs by use of image analysis software.^f Area measurements included the midline area of the caudal fossa (defined as the area limited cranially by the dorsum sella turcica and the most cranial part of the tentorium cerebellum and caudally by the foramen magnum), the total midline area of the braincase, and the midline area of the cerebellum. Regions lacking a boundary framed by bone were traced with a straight line (Figure 1).

Linear measurements included the following 9 measurements: linear measurement 1 = cribriform plate to dorsum sella turcica; 2 = cribriform plate to ventral margin of foramen magnum; 3 = cribriform plate to dorsal margin of foramen magnum; 4 = dorsum sella turcica to ventral margin of foramen magnum; 5 = ventral margin of foramen magnum to caudodorsal margin of

foramen magnum; 6 = ventral margin of foramen magnum to craniodorsal margin of foramen magnum; 7 = internal occipital protuberance to caudodorsal margin of foramen magnum; 8 = internal occipital protuberance to dorsum sella turcica; and 9 = most rostral aspect of tentorium cerebellum to dorsum sella turcica (Figure 2). An angle (angle $\alpha 1$) measurement was obtained between a line from the internal occipital protuberance to the dorsum sella turcica and a line to the tentorium of the cerebellum (Figure 3).

Description of specific MRI findings in CKCSs—Magnetic resonance images of CKCSs were evaluated for rostral indentation of the occipital bone, bony protuberance of the axis into the dorsal aspect of the vertebral canal, atlantoaxial subluxation, dorsal dens angulation, and spina bifida. Magnetic resonance images

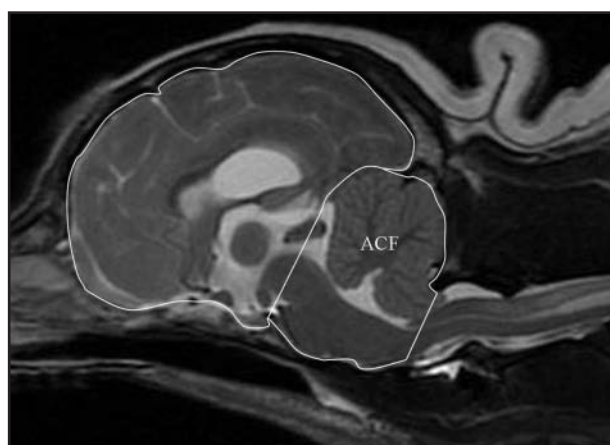


Figure 1—Cranial midsagittal T2-weighted MR image including the brain and cervical aspect of the spinal cord of a CKCS depicting area measurements of the midline total cranial area (peripheral boundary line) and area of the caudal fossa (ACF).

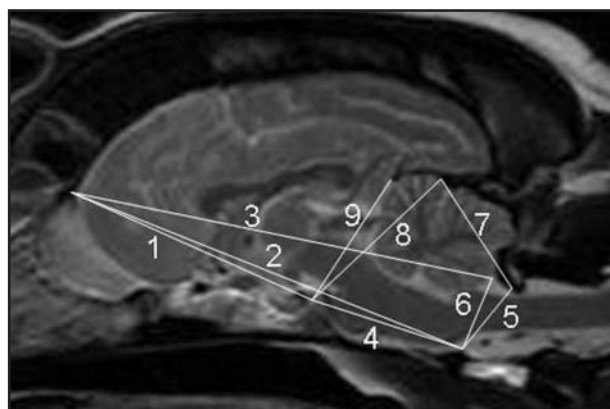


Figure 2—Cranial midsagittal T2-weighted MR image including the brain and cervical aspect of the spinal cord of a clinically normal mesaticephalic dog depicting the calculated linear measurements. 1 = Cribriform plate to dorsum sella turcica. 2 = Cribriform plate to ventral margin of foramen magnum. 3 = Cribriform plate to dorsal margin of foramen magnum. 4 = Dorsum sella turcica to ventral margin of foramen magnum. 5 = Ventral margin of foramen magnum to the caudodorsal margin of foramen magnum. 6 = Ventral margin of foramen magnum to craniodorsal margin of foramen magnum. 7 = Internal occipital protuberance to caudodorsal margin of foramen magnum. 8 = Internal occipital protuberance to dorsum sella turcica. 9 = Most rostral aspect of tentorium cerebellum to the dorsum sella turcica.

of CKCSs were also evaluated for displacement and abnormal shape of the cerebellum (herniation of the cerebellum was judged to be present when protrusion of the cerebellum was evident through the foramen magnum into the cervical spinal canal), kinked appearance of the brainstem or cervical portion of the spinal cord, attenuation of the subarachnoid space within the cervicomedullary region, syringomyelia, compression of the fourth ventricle, and ventriculomegaly (subjective assessment of enlargement of the lateral and third ventricles).

Statistical analysis—Commercially available software programs^{s,h} were used to perform analyses. In all instances, analyses were performed on ratio measurements or angles (collectively referred to as outcome measures) to account for the variation in size of study dogs. Exploratory data analysis was conducted, stratified by breed and sex, to derive summary statistics for the outcome measures. Analyses by use of 2-sample *t* tests and general linear models were used to verify differences in the outcome measures between control subgroups (Labrador Retrievers and spaniel-type dogs) and to verify the lack of differences between the sexes in all breed groups. Subsequently, study dogs were placed into 4 groups as follows: Labrador Retrievers, spaniel-type dogs, CKCSs without syringomyelia, and CKCSs with syringomyelia; a 1-way ANOVA was used to investigate differences in the outcome measure between these groups. In all instances, values of *P* < 0.05 were considered significant.

Results

Comparison of morphometric analysis in T1-weighted versus T2-weighted MR images—No significant difference was observed when comparing linear, area, and angle measurements taken from bony structures derived from T1-weighted MR images, compared with T2-weighted MR images.

Morphometric study—The general linear model revealed no significant difference between breeds in the control groups (ie, Labrador Retrievers and spaniel-type dogs). No significant differences were found between sexes in any of the breed groups.

The ratio of midline caudal fossa area to total midline braincase area was significantly smaller in CKCSs with syringomyelia, compared with control dogs (Figure 4). However, there were no significant differences in area measurements between CKCSs without syringomyelia, compared with control dogs. The midline area of the cerebellum was compared with the midline area of the caudal fossa and also to the midline area of the braincase among dogs; no significant differences were found between any of the groups or subgroups.

Ratios of linear measurements comparing the length of the cranium to the ventral aspect of the occipital bone (ratios of linear measurements 2 with 1, 2 with 4, 3 with 1, and 3 with 4; Figure 5) were significantly larger in CKCSs with or without syringomyelia, compared with control dogs. However, ratios of linear measurements comparing the length of the cranium to the dorsal aspect of the occipital bone (ratios of linear measurements 2 with 7, 3 with 7, and 7 with 4) were not significantly different from those of control dogs.

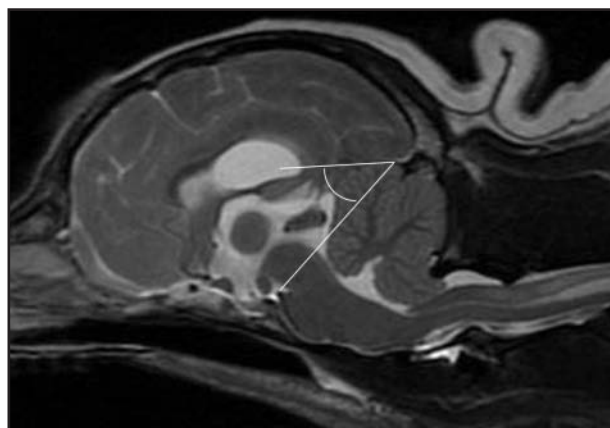


Figure 3—Cranial midsagittal T2-weighted MR image including the brain and cervical aspect of the spinal cord of a CKCS with syringomyelia depicting an angle made between a line from the internal occipital protuberance and dorsum sella (line 8 of linear measurements) and the tentorium of the cerebellum.

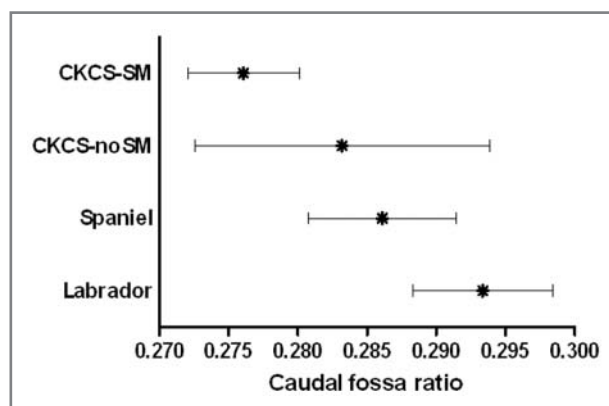


Figure 4—Mean \pm SD ratio of midline caudal fossa area to total midline braincase area for each type of dog. Notice that the ratio for CKCSs with syringomyelia has no overlap with ratios for spaniel-type dogs and Labrador Retrievers, reflecting the smaller caudal fossa in CKCSs with syringomyelia. CKCS-SM = CKCSs with syringomyelia. CKCS-no SM = CKCSs without syringomyelia. Spaniel = Spaniel-type dogs (ie, English Springer Spaniels and Cocker Spaniels). Labrador = Labrador Retrievers.

Ratios of linear measurements 6 with 8 and 6 with 9 correlated the most rostral part of the foramen magnum with the most rostral part of the caudal fossa and were significantly different between CKCSs and control dogs. Also, ratios of linear measurements 5 with 6, which reflected the rostral indentation of the most rostral part of the occipital bone, were significantly smaller in CKCSs, compared with those in control dogs.

The $\alpha 1$ angle measurement was significantly different between CKCSs and control dogs. The angle of the tentorium was considerably larger in CKCSs, which made the tentorium more horizontally orientated.

MRI findings in CKCSs—Rostral indentation of the dorsal aspect of the occipital bone was impinging on the cerebellum and associated with an abnormal shape and displacement of the cerebellum in all 70 CKCSs. Herniation of the cerebellum through the foramen magnum was observed in 5 of the 70 (7.1%) CKCSs. There was no evidence of atlantoaxial subluxation or spina bifida. A kinked appearance to the

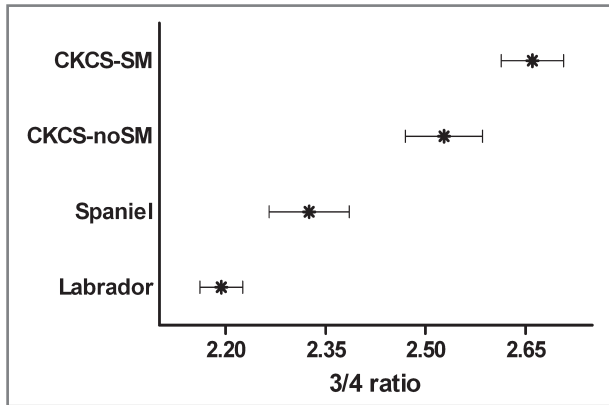


Figure 5—Mean \pm SD ratio of linear measurements 3 to 4, which highlights the length of the ventral aspect of the occipital bone, for each type of dog. Notice that ratios for CKCSs have no overlap with ratios for spaniel-type dogs and Labrador Retrievers. See Figure 4 for key.

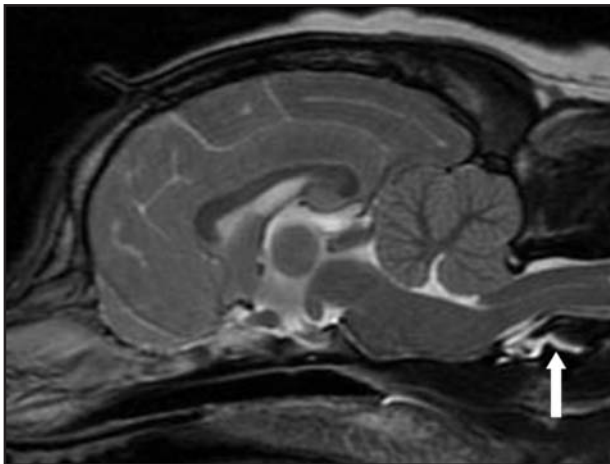


Figure 6—Cranial midsagittal T2-weighted MR image including the brain and cervical aspect of the spinal cord of a CKCS. The dorsal angulation of the dens is causing a kinked appearance of the cervicomedullary region and effacement of the ventral aspect of the subarachnoid space (arrow).

cervicomedullary junction was observed in 50 (71.4%) CKCSs, and attenuation of the subarachnoid space at this level was observed in 49 (70%) CKCSs. Dorsal displacement of the dens of the axis associated with severe cord compression was not seen in any CKCSs. However, a mild dorsal orientation of the dens was observed in 54 (77.1%) CKCSs at the same level as the kinked spinal cord (Figure 6). Bony protuberance of the axis associated with indentation into the dorsal aspect of the vertebral canal was seen in 24 (34.3%) CKCSs (Figure 7). This protuberance caused dorsal compression on the spinal cord in 21 (30%) CKCSs, whereas in the remaining 3 (4.3%) CKCSs, there was only obliteration of the dorsal subarachnoid space.

Syringomyelia was evident in 55 of 70 (78.6%) CKCSs, starting from the level of the axis in 48 of the 55 (87.3%) CKCSs, whereas in 7 of the 55 (12.7%) CKCSs, the syringomyelia was seen commencing cranial to the axis. In addition, 5 of these 7 CKCSs with more cranially located syringomyelia had concurrent dorsal compression of the spinal cord because of a bony impingement

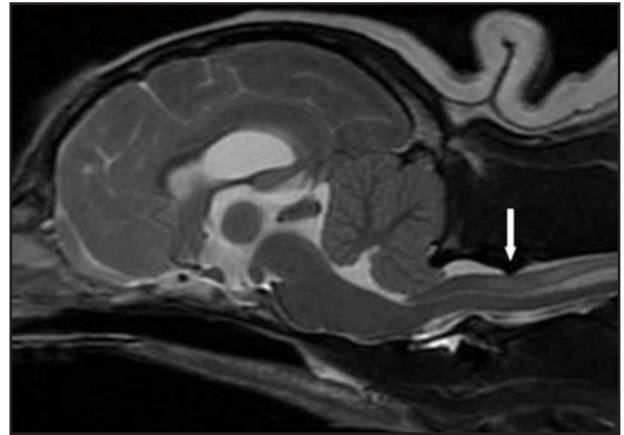


Figure 7—Cranial midsagittal T2-weighted MR image including the brain and cervical aspect of the spinal cord of a CKCS. Notice the bony protuberance of the axis causing indentation into the dorsal aspect of the vertebral canal (arrow).

of the axis. In 3 of these 5 CKCSs, there was also diffuse edema around the gray matter. Compression of the fourth ventricle was not evident in any CKCSs included in our study, and the presence of ventriculomegaly was seen in only 13 of 70 (18.6%) CKCSs.

Discussion

Results of our study indicate that a substantial degree of occipital hypoplasia is present in CKCSs, with hypoplasia being more pronounced in CKCSs with syringomyelia. Findings in morphometric studies^{2,7-15,22,23} in humans with type I CM have supported the hypothesis that hypoplasia of the bony structures of the calvarium is the main cause of CM in adults. Lower volume and midline area of the posterior cranial fossa sloping forward from the foramen magnum to the sella turcica, composed by the basioccipital and basisphenoid bones), reduced length of the basisphenoid bone, reduced length of the basioccipital bone, and steeper angle of the tentorium cerebellum were consistently found in studies^{2,7-15,22,23} in humans. All of these morphometric studies^{2,9,11,13,15,22,23} in humans used T1-weighted midsagittal MR images. Morphometric determinations performed in our study were based on T2-weighted midsagittal MR images because this is the most common sequence used in our hospitals. The T1-weighted sequences best reveal the anatomy and bony components, whereas T2-weighted sequences are normally used to reveal changes in signal intensity of the neural structures. When the measurements used in our study were compared between midsagittal T1- and T2-weighted MR images for the 8 dogs in which both image sequences were available, no significant differences were identified in measurements. All bony structures that were used as landmarks were clearly identifiable in both T1- and T2-weighted MR images.

In morphometric studies in humans, patients with CM are usually compared with the clinically normal population, which have a fairly homogenous skull shape. However, given that different breeds of dogs have radically different skull shapes, this approach would not

be valid for morphometric evaluation of dogs. The CKCSs are considered brachycephalic dogs (meaning short and wide-headed)²¹; it was decided to use dogs that were mesaticephalic as control dogs. The mesaticephalic dog breeds included in our study were considered to have a head of intermediate proportion for which CM has not been previously reported (Labrador Retrievers and spaniel-type dogs, with the latter subgroup including English Springer Spaniels and Cocker Spaniels). Because of the normal anatomic variations in skull shape and size in dogs, ratios rather than absolute values were used to achieve a more accurate comparison.

No attempt was made to measure the volume of the caudal cranial fossa; however, the midsagittal area and the dimensions of the supra- and infratentorial braincase were measured. The area of the midsagittal section only provides an estimate of the caudal cranial fossa volume, but it combines several of the linear and angular variables. Results of our study revealed that CKCSs with syringomyelia had a smaller caudal cranial fossa in comparison to mesaticephalic dogs. However, the hindbrain appeared to have a similar area in relation to the total braincase and the caudal cranial fossa in all breed groups. These findings may indicate a normally developed hindbrain, with an underdeveloped or shallower caudal cranial fossa. The orientation of the tentorium cerebellum was significantly more horizontal in CKCSs, compared with that of control dogs. In CKCSs with evidence of syringomyelia, this angle was even larger. This finding may indicate that overcrowding of the caudal cranial fossa can induce remodeling as the tentorium of the cerebellum shifts upward and that the caudal part of the cerebellum may herniate to accommodate the normally developed brain.

In addition, and supporting the results obtained for area measurements, several ratios of the linear measurements calculated to compare the length of the cranium with the depth of the caudal cranial fossa were significantly different in CKCSs, compared with control dogs; these differences were greatest for CKCSs with syringomyelia. This finding may indicate that the ventral part of the occipital bone is hypoplastic in CKCSs. In contrast, no significant differences were evident between CKCSs and control dog breeds for ratios comparing the length of the cranium with the most caudal part of the dorsal aspect of the occipital bone. However, ratios including the most rostral part of the foramen magnum were significantly different between CKCSs and control dogs. This may be explained by the rostral indentation of the most rostral part of the foramen magnum that is readily seen in all CKCSs on midline T2-weighted sagittal MR images, whereas the total length of the dorsal aspect of the occipital bone may remain within reference limits. Taken together, these findings support evidence found in studies^{2,7-12,14,15,24,25} that indicate that the fundamental problem in humans with type I CM is a small caudal fossa caused by an underdeveloped basioccipital bone, which results in varying degrees of hindbrain overcrowding.

Results of our study differ from those of other studies^{a-c} in CKCSs. Disparities in our findings with those of other studies^{a-c} may be attributed to the lack of a suitable control population because comparison of CKCSs

was done with other small-breed dogs that also may have CM.²⁶ Results of our study indicate that differences in measurements became significant when those of CKCSs were compared with those of a control group of mesaticephalic dogs. Comparison of CKCSs with syringomyelia and without syringomyelia revealed that lower values were found in CKCSs with syringomyelia. These results indicate that, in general, brachycephalic dogs have shallower caudal cranial fossae, but this is more marked in dogs with syringomyelia. Therefore, the smaller caudal cranial fossa may be the underlying cause of syringomyelia.

In humans, type I CM has been described in conjunction with occipital dysplasia.^{7,8,24,25,27} Occipital dysplasia in dogs is defined as incomplete ossification of the supraoccipital bone, resulting in the widening of the foramen magnum.^{28,29} This varies from a small dorsal notch (resulting in a keyhole shaped foramen magnum) to a wide midline defect. Occipital dysplasia is reported as common in dogs with a rounded skull shape,²⁸ but in most instances, it does not appear to result in a functional problem because the overall size and shape of the caudal fossa remain unchanged. Occipital dysplasia has been described in conjunction with occipital hypoplasia in 2 CKCSs.³⁰ No CKCSs with abnormal ossification of the supraoccipital bone were identified in our study; however, this is not easy to appreciate on sagittal MR images and is better viewed by use of radiography²⁹ or computed tomography. However, a persistent finding in all CKCSs included in our study was rostral indentation of the dorsal aspect of the foramen magnum. This feature was not seen in any dogs of the control group, which had a straighter shape to the dorsal aspect of the occipital bone; therefore, this could be defined as another manifestation of occipital dysplasia. Associated with this abnormal rostral indentation of the dorsal aspect of the occipital bone was displacement and abnormally shaped cerebellum in all CKCSs. However, true herniation of the cerebellum through the foramen magnum was identified in only 5 CKCSs.

Dorsal dens angulation has been described in a CKCS with CM¹⁹ as well as in 1 dog with CM and syringomyelia.²⁶ In these 2 affected dogs, the dorsal angulation of the dens restricted the vertebral canal diameter, resulting in spinal cord compression. No evidence of dorsal angulation of the dens of the axis resulting in severe spinal cord compression was found in our study. However, a slightly more dorsal orientation of the dens was identified in 54 of 70 (77.1%) CKCSs, but not in any of the dogs in the control group. Dorsal to the abnormal alignment of the dens of the axis, obliteration of the subarachnoid space and a kinked appearance of the spinal cord were present in 50 (71.4%) CKCSs. Head position at the time MRI was performed may influence the position of the dens; however, given that this feature was only evident in CKCSs and not in the control group would make this explanation unlikely. Significant radiographic differences have been identified when the morphologic characteristics of the atlantoaxial region in CKCSs were compared with other breeds; however, these anomalies were not associated with excessive atlantoaxial movement.³¹ All of the MRI findings in our study are in broad agreement with results of other studies.^{16,18,19,26,32}

Common craniocervical bony abnormalities evident in humans with type I CM include platybasia and basilar invagination, with these abnormalities reported to occur to a varying degree among studies^{7,8,24,25,27} (ie, 23% to 88%). The difference in orientation of the nose in relation to the skull base in dogs means that these abnormalities are unlikely to occur in dogs and that they have not been described.

The presence of occipital hypoplasia, abnormal indentation of the dorsal aspect of the occipital bone, stepping of the tentorium of the cerebellum, mild dorsal angulation of the dens, kinked appearance of the cervicomedullary junction, obliteration of the subarachnoid space, and dorsal compression of the spinal cord at the level of the axis may all be factors that contribute to the formation of syringomyelia. Multiple explanatory theories have been advanced.²⁰ Despite the fact that the complete pathogenesis is not fully understood, the syringomyelia that accompanies caudal fossa abnormalities is considered to be a consequence of abnormal dynamics of the CSF.²⁰

In conclusion, overrepresentation of CM and syringomyelia in CKCSs indicates a heritable cause. All CKCSs included in our study had some degree of CM, and 55 of 70 (78.6%) CKCSs had evidence of syringomyelia. Comparison of CKCSs with syringomyelia to CKCSs without syringomyelia revealed that the latter had a smaller caudal fossa and that this may be related to the increased likelihood of developing syringomyelia.

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