Cervical spondylomyelopathy in Great Danes: A magnetic resonance imaging morphometric study

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A R T I C L E   I N F O

Article history:
Accepted 10 April 2014

Keywords:
Canine
Osseous-associated cervical spondylomyelopathy
Stenosis
Woberl syndrome

A B S T R A C T

Morphometric investigations comparing normal and affected animals increase our understanding of spinal diseases in dogs. The aim of this study was to generate morphometric data for osseous-associated cervical spondylomyelopathy (CSM) in Great Danes (GDs). Magnetic resonance imaging (MRI) morphometric features of the cervical vertebral column of GDs with and without clinical signs of CSM were characterized and compared. Thirty client-owned GDs were prospectively enrolled, including 15 clinically normal and 15 CSM-affected GDs. All dogs underwent MRI of the cervical to thoracic vertebral column (C2-C3 through T1-T2). Areas of the cranial and caudal articular processes, and the height, width and areas of the vertebral canal and spinal cord were determined. Middle foraminal heights were measured. Intervertebral disc width was measured before and after traction. Intraobserver and interobserver agreement were calculated. CSM-affected GDs had larger areas of the cranial articular processes from C2-C3 through T1-T2. In CSM-affected GDs, the vertebral canal and spinal cord areas were significantly smaller at C5-C6 and C6-C7, the vertebral canal width was significantly narrower at C6-C7 and C7-T1, and the spinal cord width was significantly narrower at C5-C6 and C6-C7. Middle foraminal height was smaller in CSM-affected GDs from C3-C4 through C7-T1. Neutral intervertebral disc widths were smaller in CSM-affected GDs. It was concluded that the cervical vertebral canal dimensions are significantly different between normal and CSM-affected GDs. Absolute vertebral canal stenosis and severe foraminal stenosis involving the cervical vertebrae distinguish CSM-affected from clinically normal GDs. These findings are relevant to the pathogenesis of osseous-associated CSM and should be taken into consideration when performing imaging studies and planning surgery.

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Introduction

Great Danes (GDs) with cervical spondylomyelopathy (CSM) are most frequently affected by the osseous-associated form, which is characterized by vertebral canal stenosis secondary to osseous proliferation of the vertebral arch, articular processes and/or pedicles (Trotter et al., 1976; Olsson et al., 1982; da Costa, 2010). Magnetic resonance imaging (MRI) is the imaging modality of choice for dogs with suspected CSM (Lipsitz et al., 2001; da Costa, 2010; Gutierrez-Quintana and Penderis, 2012).

The morphologic MRI features of GDs with osseous-associated CSM have been described retrospectively (Lipsitz et al., 2001; Gutierrez-Quintana and Penderis, 2012). These studies provided a qualitative description of MRI abnormalities in CSM-affected GDs with clinical signs, but no morphometric information was provided. Morphometric studies comparing anatomic measurements obtained from clinically normal and affected dogs help to establish normal values for healthy animals and increase the understanding of the pathologic changes associated with clinical signs (Herzog et al., 1991; da Costa et al., 2006).

Morphometry of the cervical vertebral column has been reported in asymptomatic human beings, as well as human patients with cervical spondylosis myelopathy, which is a chronic compressive myelopathy similar to canine CSM (Fujiwara et al., 1988; Boden et al., 1990; Sherman et al., 1990; Herzog et al., 1991; Okada et al., 1994; Tierney et al., 2002; Kato et al., 2012). Morphometric MRI studies of the cervical vertebral column have also been reported in Doberman dogs with and without signs of disc-associated CSM (da Costa et al., 2006; De Decker et al., 2012b). However, no equivalent studies are available for giant breed dogs with osseous-associated CSM. Despite some degree of overlap between disc-associated and osseous-associated CSM, the pathologic changes causing spinal cord compression in both forms of the disease are different, as well as the age and breed of the affected dogs.

The aim of this study was to prospectively characterize and compare the morphometric features of the cervical vertebral column of GDs with and without clinical signs of CSM using MRI. We hypothesized that the dimensions of the cervical vertebral canal structures would differ between clinically normal and CSM-affected GDs.
Materials and methods

Animals

The investigation was conducted in accordance with the guidelines and with approval of the Ohio State University Clinical Research Advisory Committee and the Institutional Animal Care and Use Committee (2011A00000027). Written owner consent was obtained prior to study enrolment.

Two groups of client-owned GDs were prospectively enrolled from April 2011 to October 2012. All dogs were examined by two of the investigators (PMV and RCdC). The first group included 15 GDs that were defined as clinically normal based on a normal neurologic examination and no prior history of neurologic disease. Only GDs 1 year of age or older were eligible for enrolment as normal dogs. The second group included 15 GDs with clinical signs and neurologic examination findings consistent with CSM. The time of onset of clinical signs was recorded.

Magnetic resonance imaging protocol

MRI of the cervical vertebral column was performed in all dogs under general anesthesia with a 3.0 T magnet (Achieva 3.0 Tesla, Philips Healthcare) and a surface coil. Dogs were positioned in dorsal recumbency, with the head and neck in a neutral position. Images were acquired using a turbo spin-echo technique. First, T1- and T2-weighted images (WI) were obtained in the dorsal, sagittal and transverse planes. After acquisition of all image sequences with the cervical area in the neutral position, T2-weighted sagittal images were acquired after applying linear traction by use of a neck harness and weight equivalent to 20% of the dog’s body weight.

Repetition time (TR) and time to echo (TE) were set for T1-WI sagittal images (TR 700 ms, TE 8 ms), transverse and dorsal T1-WI (TR 650 ms, TE 8 ms), sagittal T2-WI in neutral and traction positions (TR 5000 ms, TE 110 ms) and transverse and dorsal T2-WI (TR 4000 ms, TE 120 ms). The field of view was 30 cm in the sagittal and dorsal planes, and 20 cm in the transverse plane. Slice thickness was set at 3 mm, with no interslice interval.

Seven intervertebral spaces (C2-C3 to T1-T2) were imaged in each dog and five transverse slices were obtained for each intervertebral space. The transverse slices were aligned parallel to the intervertebral disc and arranged to pass through the center of each intervertebral space, as well as the cranial and caudal end plates of the adjacent vertebral bodies, as described previously (da Costa et al., 2006).

Morphometric analysis of magnetic resonance images

All MRI images were evaluated and measurements obtained by two investigators (PMV and CGL). Measurements were made using a software program for medical imaging analysis (ClearCanvas Workstation).

Transverse T1-WI at the center of the intervertebral space were used to measure the area of the caudal articular processes from the cranial vertebral body (dorsomedial position) and the area of the cranial articular processes from the caudal vertebral body (ventrolateral position) (Fig. 1). On transverse T2-WI, vertebral canal and spinal cord height, width and area were measured at three different levels for each intervertebral space, including the caudal aspect of the cranial vertebral body, the center of the intervertebral space and the cranial aspect of the caudal vertebral body (Fig. 2). The right and left middle foraminal heights were measured at the center of the intervertebral space also using transverse T2-WI (Fig. 2).

On mid-sagittal T2-WI, the spinal cord and vertebral canal height were measured at the caudal aspect of the cranial vertebral body, the center of the intervertebral space and the cranial aspect of the caudal vertebral body for each given space, as described previously (da Costa et al., 2006). Before and after application of traction, intervertebral disc width (VDW) was measured on mid-sagittal T2-WI. Mid-sagittal T1-WI images were used to measure vertebral body length and height.

Intraobserver agreement was tested by repeating all the measurements three times in four randomly selected dogs (two clinically normal and two CSM-affected) at least 1 week apart by one observer (PMV). To assess interobserver agreement, the same measurements were performed on all 30 dogs by a second observer (CGL), who was unaware of the clinical status of the dogs.

Statistical analysis

All measurements were compared for each intervertebral space between groups with a random-effects linear regression model using commercially available software (Stata version 12.1). Adjustments were made for age, sex, height and weight. Results were adjusted for multiple comparisons using the Sidak method to preserve the type I error at 0.05. Significance was set at a P value <0.05. Intraobserver agreement was estimated using the intraclass correlation (ρ, r) among the three replicates of measurements that were obtained for four dogs using a variance component model based on a random effect linear regression analysis (Searle et al., 1992). Interobserver agreement was also evaluated using the intraclass correlation (ρ) between the two sets of measurements obtained by the two observers. If ρ is close to 1.0, the agreement is excellent, whereas a value of ρ close to 0 indicates lack of agreement.
Clinical signs had been present for a mean of 1.9 years (range 0–5 years) before enrolment in the study.

In the CSM-affected group, 14/15 dogs exhibited ambulatory tetraparesis, with proprioceptive ataxia of all four limbs, and 1/15 showed a hypertonic thoracic limb gait, with ambulatory paraparesis and proprioceptive ataxia of the pelvic limbs. All CSM-affected GDs had delayed postural reactions involving all four limbs. Mild neck pain was elicited in 6/15 affected dogs at the time of examination. All clinically normal GDs had normal findings on neurological examination. The main site of spinal cord compression was recorded at C6-C7 for 8/15 CSM-affected GDs, with osseous-associated lateral and dorsolateral compressions being noted most frequently.

Morphometric data

A total of 7350 measurements was obtained in this study (245 measurements/dog) (Figs. 3–8 and Tables 1, 2). The areas of the caudal articular processes from the cranial vertebral bodies from C2-C3 through T1-T2, and the areas of the cranial articular processes of the caudal vertebral bodies at C6-C7, were significantly larger in CSM-affected GDs than clinically normal GDs (Fig. 3). The vertebral canal area (VCA) was significantly smaller at C5-C6 and C6-C7 in CSM-affected GDs for all three locations measured (Fig. 4). The VCA was also significantly smaller in CSM-affected GDs at C2-C3, C3-C4 and C4-C5 when measured at the center of the intervertebral space and at the cranial aspect of the caudal vertebral body. Similarly, the spinal cord area (SCA) was significantly smaller in CSM-affected GDs at C5-C6 and C6-C7 at the three levels measured (Fig. 5). The SCA obtained at the cranial aspect of the caudal vertebral body was also smaller at C4-C5 in CSM-affected GDs.

CSM-affected GDs had smaller vertebral canals at C2-C3 (mean 1.38 mm; 95% confidence interval, CI, 1.27–1.48 mm) than clinically normal GDs (mean 1.59 mm; 95% CI 1.48–1.70 mm) when this measurement was obtained at the cranial aspect of C3 (P < 0.0485); there was no significant difference in vertebral canal height in the transverse plane at other levels. There were no significant differences in transverse spinal cord height between CSM-affected and unaffected GDs (data not shown).

The mean vertebral canal width (VCW) was significantly narrower in CSM-affected GDs than unaffected GDs at C6-C7 and C7-T1 at all three levels measured, as well as C3-C4, C4-C5 and C5-C6 when measured at the center of the intervertebral space and at the cranial aspect of the caudal vertebral body (Fig. 6). Similarly, spinal cord width was significantly narrower in CSM-affected GDs at all three levels for the C5-C6 and C6-C7 intervertebral spaces, as well as at C4-C5 when this measurement was obtained at the cranial aspect of C5 (Fig. 7). Middle foraminal heights were significantly lower in CSM-affected GDs from C3-C4 through C7-T1 for both right and left sides, as well as T1-T2 on the left side (Fig. 8).

The vertebral canal height in the sagittal plane was significantly smaller in CSM-affected GDs at the caudal aspect of the cranial vertebral body at C3-C4, C4-C5 and C6-C7, at the center of the intervertebral space for C2-C3, C3-C4, C4-C5 and C6-C7, and at the cranial aspect of the caudal vertebral body for C2-C3 and C5-C6 (Table 1). No significant differences were found for the spinal cord height measured on sagittal images (Table 1). The mean IVDw was lower in CSM-affected GDs than unaffected GDs both before and after the application of traction. IVDw was significantly lower in the neutral position in CSM-affected GDs than unaffected GDs both before and after the application of traction. IVDw was significantly lower in the neutral position in CSM-affected GDs than unaffected GDs from C2-C3 through T1-T2 (Table 2). With application of traction, the mean IVDw remained significantly lower in CSM-affected GDs at C3-C4, C4-C5, C5-C6 and T1-T2. Vertebral body length and height data are summarized in Table 2.
Intraobserver agreement ($\rho$) ranged from 0.908 to 0.996 for all values, indicating excellent agreement. The best agreement was obtained for the area of the right cranial articular process ($\rho = 0.996$), while the least agreement was associated with the spinal cord height on sagittal T2-WI when measured at the cranial aspect of the caudal vertebral body ($\rho = 0.908$). The median interobserver agreement ($\rho$) was 0.73, ranging from 0.022 (vertebral canal height in the transverse plane at the caudal aspect of the cranial vertebral body) to 0.962 (vertebral body length) (Table 3).

Discussion

In this study, we used objective measurements to show that, when compared to clinically normal GDs, the cervical vertebral columns of CSM-affected GDs had larger articular processes, an overall smaller and narrower vertebral canal and spinal cord, smaller intervertebral foramina and narrower intervertebral discs.

Degenerative or osteoarthritic changes of the articular processes are one of the most common causes of vertebral canal stenosis and secondary spinal cord compression in GDs with osseous-associated CSM (Rendano and Smith, 1981; Lipsitz et al., 2001; Gutierrez-Quintana and Penderis, 2012). In this study, the areas of the caudal articular processes at C5-C6 and C6-C7 were 45% and 37% larger in CSM-affected GDs than clinically normal GDs, respectively. The areas of the cranial articular processes at C6-C7 were also 26% larger in CSM-affected GDs than unaffected GDs.

The cause of the osteoarthritic changes affecting the articular processes in dogs with osseous-associated CSM is unknown. In humans, the vertebral articular processes are considered to be a component of a spinal ‘motion segment’ that also includes the intervertebral disc (Gellhorn et al., 2013). Most studies have shown that degeneration of articular processes is associated with and preceded by adjacent disc degeneration, where pathology begins in the intervertebral disc before the development of osteoarthritic changes in the articular processes (Jaumard et al., 2011; Maus, 2012; Gellhorn et al., 2013). In human beings, osteoarthrosis of the articular processes is strongly associated with age and is considered to be the result of a combination of genetic predisposition, previous injury, obesity, abnormal biomechanics and overload of the joint (Bogduk, 2012; Maus, 2012; Gelhorn et al., 2013). In canine osseous-associated CSM, the osteoarthritic changes of the articular processes usually
occur in young adult dogs that do not have obvious intervertebral disc degeneration.

An osteological study comparing the shape and orientation of the articular facets of the C3–C7 cervical vertebrae of various dog breeds, including cadavers of six neurologically normal GDs revealed that males and larger breeds had a higher frequency of concave caudal articular processes, indicating higher axial rotation ability (Breit and Künzel, 2002); this might be related to the increased incidence of CSM in large and giant breed dogs. A combination of articular process conformation and genetic predisposition might explain why GDs affected by CSM frequently have degeneration of articular processes; however, additional biomechanical and genetic studies are needed to investigate this possibility.

The mean VCA and VCW were consistently smaller in CSM-affected GDs than unaffected GDs, indicating absolute cervical vertebral canal stenosis throughout the cervical vertebral canal. In human beings, a developmentally narrow cervical vertebral canal relates well with the severity of clinical signs and histopathological spinal cord changes (Gutierrez-Quintana and Penderis, 2012). However, only six of the CSM-affected GDs had cervical pain on examination. The importance attributed to the presence of foraminal stenosis needs to be interpreted in the context of the clinical picture, since clinically normal human beings and dogs can also have foraminal stenosis (Fujiwara et al., 1988; Okada et al., 1994).

Marked foraminal stenosis was present in GDs affected by CSM. Although foraminal stenosis secondary to the abnormal bony proliferation is common in osseous-associated CSM (da Costa et al., 2012; Gutierrez-Quintana and Penderis, 2012), this is the first morphometric MRI study reporting intervertebral foraminal sizes in a giant dog breed. Foraminal stenosis can be a source of cervical pain (Humphreys et al., 1998; da Costa et al., 2006). However, only six of the CSM-affected GDs had cervical pain on examination.

The IVDw was significantly lower in GDs affected by CSM than in unaffected GDs. Studies measuring IVDw in clinically normal Dobermans and Dobermans affected by CSM have reported conflicting results (da Costa et al., 2006; De Decker et al., 2012a). In human beings, loss of disc height is significantly correlated with disc degeneration (Benneker et al., 2005). Due to the anatomic differences between human beings and dogs, the human intervertebral disc height is equivalent to the IVDw in dogs. Loss of T2-weighted hyperintensity is also a common sign of disc degeneration (Benneker et al., 2005). However, the majority of the intervertebral discs that were narrower in CSM-affected GDs maintained a hyperintense signal on T2-WI. The significance of lower IVDw in CSM-affected GDs is unknown and warrants further imaging and histological investigations to determine whether the differences in
IVDw are an indication of disc pathology and/or play a role in the pathogenesis of osseous-associated CSM.

A limitation of this study is that the measurements used to calculate intraobserver agreement were performed by one investigator, who was not blinded to the identity and clinical status of the dogs. However, intraobserver agreement was high for all measurements from both CSM-affected and clinically normal GDs, which reflects little variability of measurements when these are obtained by the same person, regardless of the clinical status of the dog. Similar studies in human beings have also reported high degree of intraobserver reliability for MRI-based measurements in patients with cervical myelopathy (Karpova et al., 2013). In addition, interobserver agreement was good for the majority of the measurements obtained.

An additional limitation of the present study is that some of the clinically normal dogs enrolled were relatively young and there remains a chance that they could develop signs consistent with CSM in the future. Another limitation is the lack of a sex-matched population, since the frequency of male dogs was higher in the CSM-affected group than in the unaffected group. To control for this, adjustments were made for sex in the random-effects linear regression model used to analyze the morphometric data.

Table 1
Morphometric magnetic resonance imaging (MRI) results (mid-sagittal plane) of the vertebral canal and spinal cord heights of Great Danes with clinical signs of cervical spondylomyelopathy (CSM) and unaffected (Normal) Great Danes.

<table>
<thead>
<tr>
<th>Level Dogs</th>
<th>Dogs IVDw (cm)</th>
<th>SCH (cm)</th>
<th>VCHIVD (cm)</th>
<th>SCHIVD (cm)</th>
<th>VCH (cm)</th>
<th>SCH (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C2-C3 Normal</td>
<td>0.52 (0.49–0.55)</td>
<td>0.46 (0.43–0.49)</td>
<td>0.54 (0.50–0.59)</td>
<td>3.80 (3.71–3.89)</td>
<td>1.35 (1.29–1.41)</td>
<td></td>
</tr>
<tr>
<td>C3-C4 Normal</td>
<td>0.52 (0.49–0.55)</td>
<td>0.46 (0.43–0.49)</td>
<td>0.54 (0.50–0.59)</td>
<td>3.80 (3.71–3.89)</td>
<td>1.35 (1.29–1.41)</td>
<td></td>
</tr>
<tr>
<td>C4-C5 Normal</td>
<td>0.55 (0.52–0.58)</td>
<td>0.44 (0.41–0.47)</td>
<td>0.54 (0.50–0.59)</td>
<td>3.80 (3.71–3.89)</td>
<td>1.35 (1.29–1.41)</td>
<td></td>
</tr>
<tr>
<td>C5-C6 Normal</td>
<td>0.56 (0.53–0.59)</td>
<td>0.49 (0.46–0.53)</td>
<td>0.56 (0.52–0.59)</td>
<td>3.80 (3.71–3.89)</td>
<td>1.35 (1.29–1.41)</td>
<td></td>
</tr>
<tr>
<td>C6-C7 Normal</td>
<td>0.60 (0.56–0.63)</td>
<td>0.54 (0.51–0.58)</td>
<td>0.60 (0.55–0.64)</td>
<td>3.80 (3.71–3.89)</td>
<td>1.35 (1.29–1.41)</td>
<td></td>
</tr>
<tr>
<td>C7-T1 Normal</td>
<td>0.61 (0.58–0.64)</td>
<td>0.54 (0.51–0.58)</td>
<td>0.65 (0.61–0.70)</td>
<td>3.80 (3.71–3.89)</td>
<td>1.35 (1.29–1.41)</td>
<td></td>
</tr>
<tr>
<td>T1-T2 Normal</td>
<td>0.60 (0.56–0.63)</td>
<td>0.49 (0.46–0.53)</td>
<td>0.65 (0.61–0.70)</td>
<td>3.80 (3.71–3.89)</td>
<td>1.35 (1.29–1.41)</td>
<td></td>
</tr>
</tbody>
</table>

Data are presented as mean (95% confidence interval).

Table 2
Morphometric magnetic resonance imaging (MRI) results (mid-sagittal plane) of the intervertebral disc width in neutral position (IVDwn) and after the application of traction (IVDwt), vertebral body length (VBL) and vertebral body height (VBH) of Great Danes (GD) with clinical signs of cervical spondylomyelopathy (CSM) and unaffected (Normal) GD.

<table>
<thead>
<tr>
<th>Level Dogs</th>
<th>Dogs IVDwn (cm)</th>
<th>IVDwt (cm)</th>
<th>VBL (cm)</th>
<th>VBH (cm)</th>
</tr>
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<tbody>
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<td>0.54 (0.50–0.59)</td>
<td>3.80 (3.71–3.89)</td>
</tr>
<tr>
<td>C3-C4 Normal</td>
<td>0.52 (0.49–0.55)</td>
<td>0.46 (0.43–0.49)</td>
<td>0.54 (0.50–0.59)</td>
<td>3.80 (3.71–3.89)</td>
</tr>
<tr>
<td>C4-C5 Normal</td>
<td>0.55 (0.52–0.58)</td>
<td>0.44 (0.41–0.47)</td>
<td>0.54 (0.50–0.59)</td>
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<tr>
<td>C5-C6 Normal</td>
<td>0.56 (0.53–0.59)</td>
<td>0.49 (0.46–0.53)</td>
<td>0.56 (0.52–0.59)</td>
<td>3.80 (3.71–3.89)</td>
</tr>
<tr>
<td>C6-C7 Normal</td>
<td>0.60 (0.56–0.63)</td>
<td>0.54 (0.51–0.58)</td>
<td>0.60 (0.55–0.64)</td>
<td>3.80 (3.71–3.89)</td>
</tr>
<tr>
<td>C7-T1 Normal</td>
<td>0.61 (0.58–0.64)</td>
<td>0.54 (0.51–0.58)</td>
<td>0.65 (0.61–0.70)</td>
<td>3.80 (3.71–3.89)</td>
</tr>
<tr>
<td>T1-T2 Normal</td>
<td>0.60 (0.56–0.63)</td>
<td>0.49 (0.46–0.53)</td>
<td>0.65 (0.61–0.70)</td>
<td>3.80 (3.71–3.89)</td>
</tr>
</tbody>
</table>

Data are presented as mean (95% confidence interval).

* P < 0.05 is considered to be significant.
Cau Pro, caudal articular process of the cranial vertebral body for a given intervertebral disc level; Cpa Pro, cranial articular process of the caudal vertebral body; MFH, mid-foraminal height; IVDa, intervertebral disc width in neutral position; IVDw, intervertebral disc width after traction; VBL, vertebral body length; VBH, vertebral body height; VCH, vertebral canal height; VCW, vertebral canal width; VCA, vertebral canal area; SCH, spinal cord height; SCW, spinal cord width; SCA, spinal cord area; cra, caudal aspect of the cranial vertebral body for a given intervertebral disc level; cau, cranial aspect of the caudal vertebral body for a given intervertebral disc level; vch, center of the vertebral disc level.

Conflict of interest statement

None of the authors has any financial or personal relationship that could inappropriately influence or bias the content of the paper.

Acknowledgements

This study was supported by a grant provided by the Great Dane Club of America, an Intramural Canine grant from the Ohio State University College of Veterinary Medicine and the Award Number Grant UL1TR000090 to the Ohio State University Center for Clinical and Translational Science (CCTS) from the National Center for Advancing Translational Sciences. We wish to thank Tim Vojt for assistance with illustrations, Gary Phillips for assistance with statistical analysis and Dr Sara Zaldivar-Lopez for assistance with graphs. Preliminary results were presented as an Abstract at the American College of Veterinary Internal Medicine Forum, Seattle, WA, USA, 12–15 June 2013.

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