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Multicenter case-control study of signalment, diagnostic features, and outcome associated with cervical vertebral malformation-malarticulation in horses

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Objective—To compare signalment of horses with cervical vertebral malformation-malarticulation (CVM) with that of control horses and to describe results of clinical examination, diagnostic imaging and necropsy findings, and reported outcome in horses with CVM.

Design—Retrospective case-control study.

Animals—270 horses with CVM and 608 control horses admitted to 6 veterinary hospitals from 1992 through 2007.

Procedures—Medical records of participating hospitals were reviewed to identify horses with CVM (ie, case horses) and contemporaneous control (non–CVM-affected) horses that were admitted for treatment. Signalment was compared between case horses and control horses. Results of clinical examination, laboratory and diagnostic imaging findings, necropsy results, and outcome were assessed for horses with CVM.

Results—Case horses were younger (median age, 2 years) than were control horses (median age, 7 years). Thoroughbreds, warmbloods, and Tennessee Walking Horses were overrepresented in the CVM group. Gait asymmetry and cervical hyperesthesia were frequently detected in horses with CVM. Vertebral canal stenosis and articular process osteophytosis were commonly observed at necropsy; agreement between the results of radiographic or myelographic analysis and detection of lesions at necropsy was 65% to 71% and 67% to 78%, respectively. Of 263 horses with CVM for which outcome was recorded, 1 died and 172 (65.4%) were euthanatized.

Conclusions and Clinical Relevance—Odds of a diagnosis of CVM were greater in young horses and horses of specific breeds. Detection of gait asymmetry and cervical hyperesthesia were frequently reported in association with CVM. Accurate diagnosis of lesions associated with CVM by use of radiography and myelography can be challenging. (*J Am Vet Med Assoc* 2010;237:812–822)

Cervical vertebral malformation-malarticulation (also referred to as cervical vertebral compressive myelopathy, wobbler syndrome, cervical stenotic myelopathy, and cervical spondylotic myelopathy) is a common cause of extradural spinal cord compression in horses.[1–6] The causes of CVM are poorly understood, although malformation, nutritional factors, osteochondrosis of the articular processes, repeated microtrauma, sex, breed, and vertebral column malalignment may have roles in lesion development.[7–13] The physical sources of spinal cord compression in CVM are diverse and can develop alone or in combi-

Abbreviations

CC	Cerebellomedullary cistern
CI	Confidence interval
CVM	Cervical vertebral malformation-malarticulation
EPM	Equine protozoal myelitis
IQR	Interquartile range
IVR	Intravertebral ratio
LC	Lumbar cistern
OR	Odds ratio
QH	Quarter Horse

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nation; these include vertebral canal stenosis, vertebral column malarticulation, articular process hypertrophy, interarcuate ligament hypertrophy, physeal flaring, synovial cyst formation, and rarely, disk herniation.[3,11,14–17]

Most reports concerning diagnosis of CVM focus on radiographic, gross pathologic, or histopathologic findings. The sensitivity and specificity of radiography for the diagnosis of CVM are controversial.[9,18–21] In 1 report of 100 CVM-affected horses,[19] sensitivity and specificity of the IVR (defined as a ratio of the minimum height of the vertebral canal to the maximal height of the vertebral body measured on a lateral cervical radiograph) were both > 89%, whereas in another study of 22 affected horses,[9] sensitivity and specificity were 47% and 78%, respectively. Similarly, the diagnostic value of myelography for CVM in horses remains unclear. In a population of 38 horses with various neurologic diseases confirmed by necropsy, use of a decision criteria of ≥ 50% obstruction of the dorsal contrast column during myelography of the vertebral column was only 53% sensitive and 89% specific for the diagnosis of CVM.[22] Although the gross and histopathologic features of CVM have been defined, data concerning the relative frequency of various lesions associated with the disease are limited.

To our knowledge, few reports have detailed outcome for horses with CVM after medical and surgical intervention. A low-protein, low-carbohydrate diet combined with stall rest appeared to improve clinical signs in adolescent Thoroughbred foals with CVM.[7] Dorsal laminectomy or vertebral interbody fusion led to improvement of 51 of 71 (72%) horses in a single-center, retrospective study.[23] Cervical interbody fusion resulted in normal gait in 17 of 28 (61%) CVM-affected horses with long-term follow-up in 1 retrospective study.[24] Information concerning overall population-based outcome in horses admitted to veterinary hospitals for evaluation of CVM, such as survival to discharge from the hospital, is currently unavailable.

The relative lack of data available concerning CVM in horses prompted the multicenter, retrospective, case-control study reported here. The objectives of the study were to investigate previously identified associations of signalment with CVM in a population with relatively strict inclusion criteria for cases of CVM; to describe the clinical signs, laboratory diagnostic findings, imaging features, and lesions of horses with CVM; to compare findings prior to referral and at admission in horses with CVM that did or did not survive to discharge from the hospital; and to examine agreement between the results of image analysis and necropsy findings.

Materials and Methods

Case and control selection—Medical records of the following 6 veterinary hospitals were searched to identify horses with CVM (ie, case horses) and contemporaneous control (non–CVM-affected) horses admitted for treatment from 1992 through 2007: Texas A&M University Veterinary Medical Teaching Hospital, Cornell University Hospital for Animals, University of Georgia Large Animal Hospital, Marion DuPont Scott Equine Medical Center, University of Illinois Veterinary Teaching Hospital, and Rood and Riddle Equine Hospital.

Electronic medical records were searched for the following diagnoses: cervical compressive myelopathy, cervical vertebral malformation, cervical stenotic myelopathy, cervical static stenosis, cervical vertebral instability, ataxia, wobbler's, and wobbler's disease. All identified records were reviewed to satisfy criteria for confirmed or presumptive CVM to be included in this study. Confirmed CVM was defined as gross evidence during necropsy examination of cervical spinal cord compression due to vertebral column subluxation, articular process osteophytosis, or vertebral canal stenosis (alone or in combination), with microscopic evidence conforming to typical patterns of focal compression including secondary, ascending and descending white matter tract neuronal degeneration, as described by Mayhew et al.[2] Horses with other nervous system diseases diagnosed at necropsy were not enrolled in this study. Presumptive CVM was defined as diagnosis of CVM by a board-certified neurologist or large animal internist on the basis of appropriate neuroanatomical localization (ie, cervical spinal cord segments), findings during physical examination, and abnormal results (eg, detection of vertebral canal stenosis or vertebral column subluxation) of plain cervical vertebral column radiography or myelography according to radiology reports.

A contemporaneous control group was generated by selecting 2 horses that were admitted on the same date for treatment of conditions not related to CVM, at the same institution and on the same clinical service as a case horse. In some instances, 2 control horses that met these criteria were not available. Also, some investigators provided more than 2 control horses for each case horse, and data were included for those control horses provided beyond the requested minimum of 2 per case horse.

Procedures—A standardized, survey-type data collection tool[a] was used to aid in data acquisition. The following were recorded for case horses and control horses: admitting institution, admission date, age, breed, sex, weight, and use or intended use. Breed was classified as Arabian, QH or QH type (eg, Paint and Appaloosa horses), Standardbred, Thoroughbred, warmblood (ie, Dutch Warmblood, Hanoverian, Holsteiner, Oldenburg, Swedish Warmblood, and Trakehner), or other (other breeds and mixed breeds). Intended use was classified as follows: breeding, English performance (dressage or other English riding), racing, Western-style or pleasure riding (eg, Western performance; ranch, farm, or trail riding; and other pleasure riding), or other use.

In horses with CVM, the duration of clinical signs in days, prior treatment history, detection of cervical hyperesthesia (ie, increased sensitivity to cervical palpation or manipulation), and neuroanatomical localization were recorded. The neuroanatomical localization was classified as C1 to C5 or C6 to T2; if the clinician of record was not able to classify the region of the cervical spinal cord affected, this was recorded as cervical spinal cord segments. When possible, the degree of ataxia was graded on a scale from I to IV by use of a standardized system described by Mayhew et al.[2] Horses that were assessed as between 2 grades (eg, between II and III) were scored as the midpoint of the range. Roman numerals from the Mayhew ataxia system were converted to the Arabic system within this manuscript to facilitate communication of range midpoints. Additionally, detection of asymmetric paresis or ataxia was recorded.

Data concerning diagnostic evaluations were also obtained from the records of CVM case horses. The methods of determining radiographic, myleographic, or gross lesions (at necropsy) were not standardized among institutions, and all assessments regarding lesion detection, type, and location were derived from medical records. Authors from all institutions indicated (on the basis of clinical experience) that although interindividual variation existed among radiologists or clinicians, with rare exception, the criterion used for determining CVM by use of myelography was a 50% reduction of the dorsal contrast column over a putative lesion site in the vertebral column, compared with the maximal dorsal contrast column over the cranial-adjacent vertebral body.[22] For each cervical vertebral articulation assessed via radiography, myelography, or necropsy, findings consistent with articular process osteophytosis, vertebral canal stenosis, vertebral column subluxation, disk herniation, ligamentous hypertrophy, or other lesions were recorded. Lesions were also classified as dynamic or static if necropsy or radiology reports contained this information. Data from radiology reports concerning intravertebral ratios were included when available. Intravertebral ratios were considered abnormal at C2, C3, C4, C5, and C6 if they were < 0.5 and abnormal at C7 if < 0.52.[19] The collection site for CSF was recorded, as were the WBC count, RBC count, and total protein concentration in each sample; for these variables, any value that exceeded the relevant upper laboratory reference limit was annotated. The cytologic appearance of WBCs in the CSF was characterized on the basis of clinical pathology reports as normal (ie, typical cell counts and morphology), neutrophilic pleocytosis, mononuclear pleocytosis, lymphocytic pleocytosis, mixed-cell pleocytosis, or other. Available data concerning serum titers of antibodies against *Sarcocystis neurona* (commonly associated with EPM; IgG), West Nile virus (IgM), equine herpesvirus (IgG), and Eastern equine encephalomyelitis virus (IgG) were recorded. Horses were classified as seronegative or seropositive on the basis of reference ranges provided by the testing laboratory, except for EPM where the descriptor of weak seropositive was permitted. Positive or negative results for antibody titers in the CSF were also recorded, if available. Descriptors used to qualify titer magnitude were obtained directly from laboratory reports.

Records of treatment prior to referral and after admission were reviewed, and data were obtained. Treatments were categorized as NSAID administration, glucocorticoid administration, pharmacological treatment for EPM, surgery (dorsal laminectomy or distraction and fusion of vertebral bodies), and rest. Response to treatment was determined from the medical records and graded as improvement, no change, or decline (ie, worsening condition). Outcome was based on whether the horse survived to discharge from the referral hospital (survivor) or was euthanatized for poor prognosis, was euthanatized for financial reasons, or died (nonsurvivor). Data concerning the insurance status of cases were also obtained from those institutions that would allow access to these materials.

Data analysis—Data were analyzed by use of descriptive and inferential methods. For descriptive analysis, medians and IQRs were reported for continuous data and categorical data were summarized as proportions. Overall agreement and relative sensitivities and specificities were reported for results of radiographic or myleographic analysis, compared with necropsy findings. These analyses were based on lesion type (eg, vertebral canal stenosis) regardless of specific anatomic location of the lesions. For inferential statistical analysis, random effects logistic regression models were fit for dichotomous outcomes (eg, case horse or control horse), with study center modeled as a random effect (to account for the lack of independence among observations arising from the same study center) and other variables (eg, age of the horse) modeled as fixed effects. Results were summarized as ORs with their 95% CIs derived from random-effects logistic regression analyses. Variables significantly associated with CVM in bivariate analysis were included in forward stepwise multivariate random-effects logistic regression analysis. A commercially available software package[b] was used for all analyses, and values of $P < 0.05$ were considered significant.

Results

Distribution of study population—Participating veterinarians from the 6 institutions contributed data from 878 horses (270 case horses [146 with confirmed CVM and 124 with presumptive CVM] and 608 control horses). The distribution of horses by institutions was as follows: 257 (82 case horses and 175 controls) were admitted to Cornell University, 118 (25 case horses and 93 controls) were admitted to the University of Georgia, 123 (27 case horses and 96 controls) were admitted to the University of Illinois, 34 (14 case horses and 20 controls) were admitted to Rood and Riddle Equine Hospital, 193 (67 case horses and 126 controls) were admitted to Texas A&M University, and 153 (55 case horses and 98 controls) were admitted to Virginia-Maryland Regional College of Veterinary Medicine. The category of primary health problem was recorded for all but 1 control horse. Control horses most commonly had a diagnosis of musculoskeletal disorder (230/607 [38%]) or gastrointestinal disorders (100/607 [16%]).

Associations of CVM with signalment and use or intended use of horses—The median age of case horses was 2 years (IQR, 1 to 3 years), whereas the median age of control horses was 7 years (IQR, 2 to 12 years). Horses with CVM were significantly ($P < 0.001$) younger than were control horses (**Table 1**). Because age data were not distributed normally, they were transformed by use of a natural logarithm for regression analysis. Eleven of 270 (4%) horses with CVM were ≥ 10 years old.

The majority of horses included in the study were QH and QH-type (n = 285 horses), followed by Thoroughbreds (224), Standardbreds (72), warmbloods (68), Arabians (44), and Tennessee Walking Horses (24); 161 horses were of other breeds (Table 1). The odds of a diagnosis of CVM were significantly greater for Thoroughbreds (OR, 3.4; $P < 0.001$), Tennessee Walking Horses (OR, 3.3; $P = 0.008$), and warmblood horses (OR, 4.9; $P < 0.001$) and significantly lower for Arabian horses (OR, 0.3; $P = 0.029$) relative to those for QH and QH-type horses.

Table 1—Results of bivariate random-effects logistic regression analysis of factors potentially associated with CVM in a retrospective case-control study of 878 horses examined and treated at 6 veterinary referral hospitals.

Variable	No. of horses with CVM	No. of control horses	OR	95% CI	*P* value
Log age (y)*	—	—	0.5	0.4–0.6	< 0.001
Breed					
QH or QH-type	65	220	1	—	—
Arabian	3	41	0.3	0.2–0.4	0.029
Standardbred	13	59	0.9	0.4–1.8	0.778
Thoroughbred	104	120	3.4	2.2–5.1	< 0.001
Tennessee Walking Horse	10	14	3.3	1.4–7.9	0.008
Warmblood†	38	30	4.9	2.8–8.7	< 0.001
Other	37	124	1.1	0.7–1.8	0.626
Sex					
Male	206	360	1	—	—
Female	64	248	0.4	0.3–0.6	< 0.001
Use					
Western-style or pleasure riding	23	73	1	—	—
Breeding	8	47	0.5	0.2–1.3	0.175
English performance	20	28	2.7	1.2–6.1	0.014
Racing	65	49	5.4	2.8–10.5	< 0.001
Other	60	77	2.8	1.5–5.2	0.002

Selected records included 270 case horses with confirmed (on the basis of clinical examination, diagnostic testing, and necropsy findings; n = 146) or presumptive (on the basis of clinical examination and diagnostic testing alone; 124) CVM and 608 contemporaneous control horses; a primary diagnosis was recorded for 607 of 608 control horses, and these typically had musculoskeletal (230/607 [38%]) or gastrointestinal disorders (100/607 [16%]). Values of $P < 0.05$ were considered significant.

*Age data were not distributed normally and were transformed by use of a natural logarithm to meet assumptions for regression analysis. †The warmblood breeds included Dutch Warmblood, Hanoverian, Holsteiner, Oldenburg, Swedish Warmblood, and Trakehner. ‡Use was not recorded for several horses.

— = Not applicable.

The proportion of female horses was significantly ($P < 0.001$) lower among case horses (64/270 [24%]) than among control horses (248/608 [41%]). The odds of a diagnosis of CVM were approximately 2× as great for male horses as they were for female horses (Table 1). The median weight of horses with CVM was 438 kg (963.6 lb; IQR, 345 to 500 kg [759 to 1,100 lb]) and that of control horses was 465 kg (1,023 lb; IQR, 380 to 523 kg [836 to 1,150.6 lb]). No significant ($P = 0.433$) association was detected between CVM and body weight.

The uses or intended uses of horses included breeding (n = 55 [8 case horses and 47 controls]), English performance (48 [20 case horses and 28 controls]), racing (114 [65 case horses and 49 controls]), and Western-style or pleasure riding (96 [23 case horses and 73 controls]); 137 horses (60 case horses and 77 controls) were designated as having other uses (eg, pasture horse or unspecified training). In bivariate analysis, the odds of a diagnosis of CVM were significantly greater for horses used for racing (OR, 5.4; $P < 0.001$), English performance (OR, 2.7; $P = 0.014$), and other use (OR, 2.8; $P = 0.002$) than for horses used for Western-style or pleasure riding (Table 1).

Multivariate random-effects logistic regression was performed to include variables for age, breed, sex, and use or intended use. After adjusting for effects of age, breed, and sex, no category of use of the horse remained significantly associated with CVM. Effects of age, most breeds, and sex remained significant after multivariate analysis (Table 2); the magnitudes of the ORs remained similar to those detected with bivariate analysis, which indicated that there was little or no confounding among variables. Only the significance of the association of CVM with Tennessee Walking Horses was altered after multivariate analysis, likely because of the relatively small number of horses of this breed that were included in the study.

Table 2—Results of multivariate random-effects logistic regression analysis of factors potentially associated with CVM in the 878 horses in Table 1.

Variable	OR	95% CI	*P* value
Log age (y)*	0.5	0.4–0.6	< 0.001
Breed			
QH or QH type	1	—	—
Arabian	0.3	0.1–0.9	0.040
Standardbred	0.7	0.3–1.4	0.273
Thoroughbred	3.1	2.0–4.8	< 0.001
Tennessee Walking Horse	2.3	0.9–5.9	0.091
Warmblood†	5.0	2.7–9.2	< 0.001
Other	1.2	0.7–2.0	0.445
Sex			
Male	1	—	—
Female	0.5	0.3–0.7	< 0.001

See Table 1 for key.

Clinical examination findings—The median duration of clinical signs prior to referral was 28 days (range, 1 to 730 days) for 217 of 270 (80%) case horses for which these data were reported. Physical examination–derived neuroanatomical localization was recorded for 246 of 270 (91%) horses with CVM. Many case horses (116/246 [47%]) had lesions localized to cervical spinal cord segments; 90 horses had lesions localized to C1 to C5, 24 had lesions localized to C6 to T2, and 16 were recorded as having lesions in other locations. Thoracic limb ataxia grades were recorded in 173 of 270 (64%) case horses. The median thoracic limb ataxia grade was 2 (range, 0 to 4). Pelvic limb ataxia grades were reported for 176 of 270 case horses with the median value being 3 (range, 0 to 4). Gait deficits were described as asymmetric for 71 of 166 case horses for

which these data were available. In 82 necropsied case horses for which gait symmetry had also been recorded, there was no association between asymmetric gait deficits and categories of gross lesions (ie, vertebral canal stenosis, vertebral column subluxation, articular process osteophytosis, ligamentous hypertrophy, disk herniation, and subchondral cysts). Cervical hyperesthesia was detected in 44 of 91 (48%) case horses for which medical record comments were available concerning the response to paraspinal manipulation or palpation. The proportion of horses with articular process osteophytosis identified at necropsy that had cervical hyperesthesia (11/17) was significantly greater ($P = 0.009$) than the proportion of horses with this lesion that did not show signs of hyperesthesia (5/25). Cervical hyperesthesia was not associated with any other category of gross lesion identified during necropsy examination. There were no significant differences in age, breed, or sex of horses that had gait asymmetry or cervical hyperesthesia, compared with horses that did not have signs of these conditions.

CSF evaluation and serologic analysis data— Cerebrospinal fluid was collected from 110 horses with CVM. The site of CSF collection was reported for 81 case horses; samples were obtained from the CC in 52 (64%) and from the LC in 29 (36%). The median RBC count in CSF was 2 cells/µL (range, 0 to 9,360 cells/µL) in 99 horses with CVM for which these data were available. The median WBC count in CSF was 1 cell/µL (range, 0 to 13 cells/µL) in 103 horses with CVM for which these data were available. There were no significant differences in RBC and WBC counts in CSF samples acquired at the CC site (median RBC count, 2.0 cells/µL [range, 0 to 9,360 cells/µL]; median WBC count, 1 cells/µL [range, 0 to 13 cells/µL]), compared with samples acquired at the LC site (RBC median, 3 cells/µL [range, 0 to 1,725 cells/µL]; median WBC count, 1 cells/µL [range, 0 to 11 cells/µL]).

The median CSF protein concentration was 56 mg/dL (range, 7.5 to 129 mg/dL) for 101 case horses that had these data recorded. Although protein concentrations were somewhat higher in samples obtained from the LC site (median, 65 mg/dL; range, 7 to 129 mg/dL) than those collected from the CC site (median, 51 mg/dL; range, 10 to 118 mg/dL), the difference was not significant ($P = 0.10$). Cytologic examination of the CSF was performed for 101 case horses. No abnormalities were detected in samples from 77 horses; reports were consistent with albuminocytologic dissociation in 8 horses and were indicative of inflammation with a predominance of mononuclear cells in 3 horses. The cytologic samples for another 3 horses were contaminated with blood, and other abnormalities (unspecified) were reported for samples from the remaining 10 horses.

Serologic analysis for *S neurona* IgG was performed for 53 horses with CVM, with 25 reported as seronegative (14 necropsied horses), 5 as weakly seropositive (1 necropsied horse), and 23 as seropositive (13 necropsied horses). Titers for *S neurona* in the CSF were evaluated in 64 case horses (32 of which had results for *S neurona* serologic analysis), with 29 reported as having negative results (12 necropsied horses), 13 as having weakly positive results (5 necropsied horses), and 22 as having positive results (13 necropsied horses). Anti-West Nile virus IgM was measured in serum of 15 horses with CVM; 1 was reported as seropositive. Serologic analysis for antiequine herpes virus 1 antibodies was performed for 11 horses, of which 2 were seropositive; only 4 horses were tested for antibodies against Eastern equine encephalitis virus, and all were described as seronegative.

Necropsy findings—One horse with CVM died, and 172 were euthanized; of the 173 horses that did not survive until discharge from the hospital, 146 (84%) were necropsied **(Table 3)**. The incidence of lesions in any segment of the cervical vertebral column was recorded: of the 146 case horses, 74 (51%) had evidence of vertebral canal stenosis, 47 (32%) had articular process osteophytosis, 28 (19%) had vertebral column subluxation, 6 (4%) had ligamentous hypertrophy, 4 (3%) had synovial cysts, 4 (3%) had CVM-associated compression of unspecified type, and 3 (2%) had disk herniation within the vertebral canal (1 at C2-3 and 2 at C6-7). Additionally, 2 horses had epidural hematomas and 1 horse had dural erythema associated with other CVM lesions. The most common combinations of paired lesions were articular process osteophytosis with vertebral canal stenosis (n = 29 horses), vertebral canal stenosis with vertebral column subluxation (13), and articular process osteophytosis with vertebral column subluxation (9).

Table 3—Number and anatomic location of each of 6 types of lesions identified during necropsy in 146 of 173 horses with CVM that were euthanized (n = 172) or died (1) prior to discharge from the hospital.

	Lesion					
Location	**Articular process osteophytosis**	**Disk herniation**	**Ligamentous hypertrophy**	**Vertebral canal stenosis**	**Vertebral column subluxation**	**Synovial cyst**
C2-3	10	1	1	15	8	0
C3-4	25	0	1	27	16	1
C4-5	17	0	0	27	10	1
C5-6	15	0	1	16	2	0
C6-7	23	2	3	20	6	2
C7-T1	0	0	0	1	2	0
Total No. of lesions*	**90**	**3**	**6**	**106**	**44**	**4**

*Some horses had > 1 type of lesion.
See Table 1 for remainder of key.

Radiographic and myelographic findings—Of 270 case horses, 239 (89%) underwent radiographic examination of the cervical vertebral column (**Table 4**). The IVRs were recorded for 59 (25%) horses for which cervical radiography was performed; 31 of these had ≥ 1 abnormal IVR. The most frequently reported lesions were articular process osteophytosis (98/239 [41%]), vertebral canal stenosis (76/239 [32%]), and vertebral column subluxation (61/239 [26%]).

Of the 239 horses that underwent radiography, 116 (49%) were also necropsied. Overall agreement between the results of radiography and necropsy was 66% (76/116), 61% (71/116), and 78% (91/116) for the diagnosis of articular process osteophytosis, vertebral canal stenosis, and vertebral column subluxation, respectively. The relative sensitivity for detection via radiography for articular process osteophytosis, vertebral canal stenosis, and vertebral column subluxation was 63%, 42%, and 56%, respectively. The relative specificity for detection via radiography for articular process osteophytosis, vertebral canal stenosis, and vertebral column subluxation was 67%, 83%, and 85%, respectively. Only 16 horses with CVM for which IVRs were determined were necropsied; the relative sensitivity and relative specificity for detection of vertebral canal stenosis at any specific site via this method were 50% and 70%, respectively.

Of the 270 cases of CVM, 134 (50%) underwent myelography (**Table 5**). The most frequently detected lesions were vertebral canal stenosis (67/134 [50%]), dynamic compression (53/134 [40%]), vertebral column subluxation (47/134 [35%]), and articular process osteophytosis (24/134 [18%]).

Sixty-eight of 134 (51%) horses that had myelography performed also had necropsy data available for analysis. Overall agreement between results of myelography and necropsy for the detection of articular process osteophytosis, vertebral canal stenosis, and vertebral column subluxation was 78% (53/68), 68% (46/68), and 76% (52/68), respectively. The relative sensitivity for detection via myelography of articular process osteophytosis, vertebral canal stenosis, and vertebral column subluxation was 43%, 71%, and 85%, respectively. The relative specificity for detection via myelography of articular process osteophytosis, vertebral canal stenosis, and vertebral column subluxation was 96%, 65%, and 75%, respectively.

Outcome—Outcome was reported for 263 of 270 (97%) horses with CVM. Among horses with known outcome, 173 of 263 (66%) died or were euthanatized prior to discharge from the hospital and 90 (34%) survived to discharge from the hospital. Of the 173 nonsurviving horses, 1 died (< 1%) and 6 (3%) were euthanatized for financial reasons. The remaining 166 horses were euthanatized due to poor prognosis. Age, breed, body weight, use or intended use, and treatments prior to referral (ie, any history of rest, duration of rest, and administration of glucocorticoids, NSAIDs, or EPM treatments) were not related to outcome (**Table 6**). Only 2 case horses that did not survive until discharge from the hospital underwent vertebral column surgery. Horses that survived until discharge from the hospital had significantly lower grades of thoracic limb ataxia (median, 1; IQR, 0 to 4; $P < 0.001$) and pelvic limb ataxia (median, 2.5; IQR, 0 to 4; $P < 0.001$) at admission than did nonsurvivors (thoracic limb median, 2; IQR, 0 to 4; pelvic limb median, 3; IQR, 0 to 4).

Table 4—Number and anatomic location of each of 4 types of lesions identified by use of radiography in 239 horses with CVM.

Variable	Abnormal IVR†	Articular process osteophytosis	Vertebral canal stenosis	Vertebral column subluxation
Location				
C2	1	6	4	9
C3	9	17	25	39
C4	16	26	41	33
C5	23	48	38	12
C6	19	78	32	17
C7	17	69	23	19
Total No. of lesions*	**85**	**244**	**163**	**129**
No. of horses with lesion*	31	98	76	61

†IVRs were considered abnormal at C2, C3, C4, C5, and C6 if < 0.5; IVRs were considered abnormal at C7 if < 0.52.
See Table 3 for remainder of key.

Table 5—Number and anatomic location of each of 4 types of lesions detected by use of myelography in 134 horses with CVM.

Variable	Dynamic lesion osteophytosis	Articular process	Vertebral canal stenosis	Vertebral column subluxation
Location				
C2-3	0	0	2	1
C3-4	29	3	31	15
C4-5	27	3	23	12
C5-6	18	11	12	25
C6-7	18	18	14	46
Total No. of lesions*	**92**	**35**	**82**	**99**
No. of horses with lesion*	53	24	47	67

See Table 3 for key.

Twenty-seven of 90 (30%) horses that survived to discharge from the hospital were treated surgically after referral; vertebral distraction and fusion (n = 17) was the most commonly reported procedure. Medical treatments included rest (n = 59; median duration, 60 days; range, 7 to 360 days), NSAID administration (29), retirement (18), and glucocorticoid administration (3). Intra-articular administration of glucocorticoids or NSAIDs into the joint space between articular processes was not reported for any horse.

Insurance status—Two of the 6 participating hospitals did not permit access to records concerning insurance status. Of 197 case horses that were referred to the other 4 institutions for treatment, 32 (16%) were described as insured at the time of admission. Although the proportion of insured horses that survived to discharge from the hospital (7/32 [22%]) was smaller than that of uninsured horses (58/165 [35%]), this difference was not significant ($P = 0.20$). Data concerning

Table 6—Prereferral- and physical examination–based outcome determinants for 270 horses with CVM that did or did not survive to discharge from the hospital.

Variable	No. (%) or median (range) of survivors	No. (%) or median (range) of nonsurvivors	OR	95% CI	*P* value
Signalment*					
Breed					
QH or QH-type	25 (28)	39 (23)	1	—	—
Arabian	2 (1)	1 (1)	ND	ND	ND
Standardbred	5 (6)	8 (5)	0.9	0.2–3.1	0.826
Thoroughbred	28 (31)	72 (42)	0.5	0.2–1.0	0.065
Tennessee Walking Horse	4 (4)	6 (4)	0.8	0.2–3.5	0.823
Warmblood	16 (18)	21 (12)	1.1	0.5–2.6	0.814
Other	12 (13)	27 (16)	0.6	0.3–1.5	0.275
Sex or reproductive status					
Gelding	33 (37)	53 (31)	1	—	—
Mare	22 (24)	42 (24)	0.8	0.4–1.6	0.524
Colt or stallion	35 (39)	78 (45)	0.7	0.4–1.2	0.201
Age (y)	2 (0.3–22)	2 (0.3–23)	1	0.9–1.1	0.840
Body weight (kg)	443 (195–636)	436 (70–671)	1	< 1.0–> 1.0	0.548
Use or intended use†					
Western-style or pleasure riding	9 (16)	14 (12)	1	—	—
Breeding	6 (11)	2 (2)	4.7	0.7–29.4	0.099
English performance	9 (16)	9 (8)	1.5	0.4–5.4	0.550
Other	19 (33)	40 (35)	0.7	0.2–1.9	0.443
Racing	14 (25)	49 (43)	0.4	0.1–1.1	0.068
History					
Duration of signs (d)‡	30 (1–730)	24 (1–380)	1	0.8–1.3	0.662
Rest prior to referral§					
No	9 (43)	16 (32)	1	—	—
Yes	12 (57)	34 (68)	0.4	0.1–1.4	0.148
NSAIDs administered prior to referral‖					
No	9 (41)	23 (45)	1	—	—
Yes	13 (59)	28 (55)	1.2	0.4–3.5	0.753
Glucocorticoids administered prior to referral¶					
No	11 (79)	26 (58)	1	—	—
Yes	3 (21)	19 (42)	0.4	0.1–1.5	0.276
EPM medications administered prior to referral#					
No	12 (52)	22 (38)	1	—	—
Yes	11 (48)	36 (62)	0.7	0.2–2.5	0.4544
Thoracic limb ataxia score at admission**	1 (0–4)	2 (0–4)	0.4	0.3–0.6	< 0.001
Pelvic limb ataxia score at admission††	2.5 (0–4)	3 (0–4)	0.4	0.3–0.6	< 0.001

Ninety horses survived to be discharged from the hospital, 173 died or were euthanized prior to discharge, and outcomes for 7 horses were not recorded. Number of horses in each category indicates total for which this information was recorded. *n = 263 horses (90 survivors and 173 nonsurvivors). †n = 171 (57 survivors and 114 nonsurvivors). ‡n = 213 (67 survivors and 146 nonsurvivors). §n = 71 (21 survivors and 50 nonsurvivors). ‖n = 73 (22 survivors and 51 nonsurvivors). ¶n = 59 (14 survivors and 45 nonsurvivors). #n = 81 (23 survivors and 58 nonsurvivors). **n = 168 (64 survivors and 104 nonsurvivors). ††n = 171 (65 survivors and 106 nonsurvivors).

ND = Not determined.

See Table 1 for remainder of key.

insurance status and the choice of surgical treatment were available for 148 case horses. The proportion of horses with CVM that underwent surgery and were insured (5/22 [23%]) was higher than the proportion that underwent surgery and were not insured (10/121 [8%]), but this difference was also not significant ($P = 0.21$).

Discussion

Age, breed, and sex were significantly different between case horses and contemporaneous control horses. Similar to the results of other studies,[1,2,5,9,10,19] horses with CVM were significantly younger (median age, 2 years; IQR, 1 to 3 years) than control horses (median age, 7 years; IQR, 2 to 12 years). The relationship between onset of clinical signs and age supports a malformative, nutritional, or developmental etiopathogenesis or a combination of these causes. Thoroughbreds, warmbloods, and Tennessee Walking Horses were overrepresented in the CVM group. These results confirm the findings of a large retrospective study[10] that included horses with a diagnosis of CVM based on clinical evaluation, necropsy results, or both. The basis for breed predispositions in CVM remains unknown; as with many other diseases, it has been speculated to involve genetic, morphometric, and use-related factors.[5,9,10,25,26] Likewise, results of the study reported here substantiates a predisposition to CVM among male horses that was revealed in earlier studies[2,4,6,9,10] in horses; the mechanisms responsible for this finding may include direct effects of sex hormones, variability in the amount or intensity of activity between male

and female horses, and sex associations with use. Use has been speculated to influence the development of CVM, but the study reported here did not demonstrate an independent association. It has been previously suggested that vertebral column load (mechanical force applied to the vertebral column) and repeated vertebral microtrauma may have roles in the development of cervical spondylomyelopathy, a disease of humans and dogs that may be analogous to CVM.[25,27–29] Because athletic activities such as racing may result in frequent and intense vertebral loading, use has been speculated to have a directly causative role in the development of CVM lesions. However, breeds predisposed to development of CVM are frequently used in activities suggested to be associated with CVM (eg, Thoroughbreds used for racing). Indeed, the association of use with CVM in the study reported here was not significant after adjustments were made for age, breed, and sex in multivariate analysis.

Although the clinical signs associated with CVM have previously been described,[1,2,4–6] to the authors' knowledge, those reports were based on the analysis of small cohorts or on the experience of investigators. The cervical spinal cord (without localization to specific spinal cord segments) was the most commonly reported neuroanatomical location for CVM-associated lesions indicated in the medical records for 116 of 246 (47%) horses for which data was available in the present study. This suggested that veterinarians may have found sublocalization of lesions to the C1-C5 or C6-T2 segments challenging; only 24 of 246 (10%) horses had CVM localized to the C6-T2 segment. Most investigators have described gait deficits associated with CVM as typically symmetric, which is in contrast to gait deficits associated with EPM.[1,2,4–6] It has been suggested that asymmetric gait deficits are most frequently detected in older horses with CVM that have articular process osteophytosis.[5] Analysis of results of the present study indicated that asymmetric gait deficits were a relatively common clinical sign (detected in 71/166 [43%] horses for which these data were available) in horses with CVM and not related to age of affected horses. The authors speculate that asymmetric articular process osteophytosis and nonuniform vertebral canal stenosis may be potential mechanisms for asymmetric gait deficits in the study reported here; although no association was detected between asymmetric gait abnormalities and the identification of such lesions during necropsy, the extent of symmetry of gross lesions was not recorded and this might have masked a possible association. Additionally, intermittent vascular occlusion secondary to chronic spinal cord compression may result in asymmetric zones of ischemic myelopathy and thus contribute to gait asymmetry.[30] However, the results of the study reported here should be interpreted with caution because whether clinical signs were symmetric or asymmetric was recorded for only 166 of 270 (61%) horses with CVM, so the estimated proportion could have been biased by case selection.

Surprisingly little attention has been given to the incidence of detection of cervical hyperesthesia in horses with CVM. In other species with compressive myelopathies, hyperesthesia is frequently recognized and develops due to compression of dura or nerve roots, lesions within the dorsal horn, and other pathological processes. Investigators of a previous study[5] reported that hyperesthesia was rarely detected in young horses with CVM. In the study reported here, hyperesthesia was commonly recognized (44/91 [48%] case horses evaluated) when assessed by the attending clinicians and the detection of hyperesthesia was not significantly associated with age or breed. Cervical hyperesthesia was significantly associated with articular process osteophytosis identified at necropsy; although the authors believe this potential relationship is intriguing, only 42 horses with CVM for which hyperesthesia was assessed had necropsy data, which could have created a selection bias. Likewise, the frequency of detection of hyperesthesia in horses of the present study should be interpreted with caution because the hyperesthesia was evaluated in < 50% of the case horses.

Although CSF samples are often analyzed during assessment of equine neurologic disorders, limited data are available concerning the characteristics of CSF in horses with CVM. Samples of CSF collected from the LC of 18 horses in which CVM was diagnosed had a mean ± SD RBC count of 73 ± 145 cells/µL, WBC count of 2.2 ± 2.3 cells/µL, and protein concentration of 70.5 ± 32.7 mg/dL.[2] Another source provided qualitative information concerning the CSF of horses with CVM, indicating that the WBC and RBC counts and morphology are typically within accepted limits and the protein concentration may be mildly high.[4] Cerebrospinal fluid data were available from the medical records of approximately 100 horses in the study reported here; most of the CSF samples were collected from the CC. Most horses had CSF cell counts, cellular morphology, and protein concentrations within accepted limits; only 10 had albuminocytologic dissociation, and 3 had evidence of elevated WBC counts. Thus, an elevated WBC count in the CSF of a horse with clinical signs of neurologic disease may make a diagnosis of CVM less likely.

Twenty-eight of 53 (53%) horses with CVM that were tested for anti–*S neurona* antibodies were seropositive, and an additional 35 of 64 (55%) horses with CVM (of which 32 were evaluated for anti–*S neurona* antibodies in the serum) tested positive for anti–*S neurona* antibodies in the CSF. Fewer horses were seropositive for antibodies against West Nile virus (1/15) and equine herpesvirus (2/11). Although concurrent neurologic disease from an infectious agent is possible, it is likely that detection of antibodies in the horses of this study did not reflect active infection or was attributable to antigen cross-reactivity or to exposure that did not result in neurologic disease. The majority (146/270 [54%]) of case horses were necropsied, and none had lesions indicative of other CNS disease on the basis of exclusion criteria. These data underscore the challenges that result from the use of serologic tests for infectious disease in equine neurology. For example, it is recognized that a high proportion of healthy horses are seropositive for anti–*S neurona* antibodies, making interpretation of positive EPM test results challenging,[14,31–33] and that most horses infected with West Nile virus do not develop signs of neurologic disease.[34,35] Additionally, if the overall prevalence of a disease in a population is low,

the positive predictive value of detecting antibody in serum or CSF will be low; this was revealed in a study[36] of horses with and without EPM, in which investigators reported that the positive predictive value of a CSF antibody titer ≥ 20 was 56% when the prevalence of disease was 5% and was 91% when the prevalence of disease was 30%.

Information concerning the location and frequency of various gross necropsy lesions associated with CVM has been reported[2,11,17,19,22] in case series that comprised results of 30,[19] 19,[22] 13,[17] and 7[2] horses, with 1 report of 25 horses[11] limited to horses with static stenotic CVM. Only 2 of those reports[17,22] described the anatomic location of gross spinal cord compression. Van Biervliet et al[22] described the following distribution of lesions in 19 horses with CVM: C2-3 (n = 0), C4-5 (7), C5-6 (4), and C6-7 (3). Yovich et al[17] described the spinal cord segment compressed in 13 horses as follows: C4 (n = 8), C5 (0), C6 (2), and C7 (5). In the study reported here, 253 separate lesions were observed at necropsy in 146 horses and were localized to the following vertebral articulations: C2-3 (n = 35), C3-4 (70), C4-5 (55), C5-6 (34), C6-7 (56), and C7-T1 (3). The 3 most commonly detected lesions in the present study were vertebral canal stenosis (n = 106), articular process osteophytosis (90), and vertebral column subluxation (44). These results differ from those of smaller case series studies in which vertebral column subluxation[17] and articular process osteophytosis[19] were the most commonly observed lesions.

Calculations concerning the relative sensitivity and specificity of lesion detection via imaging techniques in the present study (ie, myelography and radiology) and agreement between the results of image analysis and necropsy findings were based on the detection of lesion types, regardless of vertebral localization. For example, a horse with single vertebral subluxation detected radiographically at C4-5 and a subluxation observed at necropsy that was limited to C3-4 would be considered to have agreement between assessments, even though the localization of the compression was different. For the purposes of calculating relative sensitivity and relative specificity of imaging for various lesion types, necropsy results were considered the standard for comparisons. However, the investigators understood that some lesions might not be detectable during necropsy, techniques would likely vary among clinicians, assessment of gross lesions could be somewhat subjective, and terminology used to describe lesions might vary among pathologists. The agreement between results of radiography and necropsy was considered moderate (65% to 71%), despite the use of methods that might bias results toward finding a positive correlation. The relative sensitivity of radiography was highest for detection of articular process osteophytosis (63%) and lowest for vertebral canal stenosis (42%). The relative specificity of radiography was highest for detection of vertebral column subluxation (85%) and lowest for articular process osteophytosis (67%). The moderate agreement between survey radiography and necropsy results and the low relative sensitivity and relative specificity of radiography for lesion detection were similar to results reported in various species for radiographic detection of vertebral column lesions; in dogs with cervical disk herniation, for example, assessment via radiography was only 35% accurate (22/64 dogs) for identification of the site of compression.[37] In a study[21] of foals, subjective impressions concerning radiography were suggested to only moderately correspond to the clinical diagnosis of CVM. Our dataset was too limited to assess whether the use of IVRs would have enhanced the relative sensitivity or relative specificity of radiography for detection of lesions in horses with CVM because IVRs were determined for only 16 of the necropsied horses. Additionally, during evaluation of the sensitivity and specificity of IVRs for detection of necropsy-confirmed stenosis in the present study, an abnormal IVR was considered to be a true positive if stenosis was detected at any vertebral location at necropsy (even if it was not the same anatomic site where the abnormality was detected during IVR assessment).

Agreement between the results of myelography and necropsy in 68 horses with CVM ranged from 67% to 78%, depending on lesion type. This range was similar to that for agreement between the results of radiography and necropsy. This finding is of interest because in other species, myelography is generally more accurate for detection of vertebral column lesions than is radiography.[37–39] Additionally, in a study of humans[40] with cervical spondylomyelopathy, interrater agreement as to the anatomic location of compressive lesions assessed by use of magnetic resonance imaging was only moderate (kappa statistic = 0.6) and agreement as to severity of lesions was poor (kappa statistic = 0.3), emphasizing the challenges associated with diagnosis of cervical compression in other species. The agreement assessed between results of myelography and necropsy in the study reported here should be interpreted cautiously because only 68 of 270 (25%) case horses underwent myelography and necropsy, which could introduce selection bias. The relative sensitivity of myelography in the present study was highest for the detection of vertebral column subluxation (85%) and lowest for the recognition of articular process osteophytosis (43%). These results supported the findings of Van Biervliet et al,[22] which suggested that the sensitivity of myelography for detection of CVM in 19 horses was 53%, even when strictly applied numerical limits were used as decision criteria to assess attenuation of the subarachnoid contrast column. The relative specificity of myelography in the present study was highest for detection of articular process osteophytosis (96%) and lowest for that of vertebral canal stenosis (65%). The increased relative specificity of myelography for detection of articular process osteophytosis, compared with that of radiography, may have been attributable to the use of contrast agents in the subarachnoid space; these may have enabled detection of spinal cord compression that could also be observed at necropsy. Additionally, the design of the present study did not include a group of control horses without CVM that underwent cervical radiography or myelography and were later necropsied. Therefore, the specificities reported reflect the false-positive rate of the 2 imaging methods relative to necropsy findings.

Outcome, determined on the basis of survival to discharge from the hospital, was reported in the records of

263 of 270 horses with CVM of the present study. One hundred seventy-three of the 263 (66%) horses did not survive; all but 1 of the deaths was due to euthanasia, and 96% of the nonsurviving horses were euthanatized as a result of perceived poor prognosis. Whether prognosis was truly poor may be debatable because the usual course and outcome of CVM have not been well characterized. Additionally, it is possible that insurance status may have influenced the selection of treatments and subsequent outcome. Among horses with a diagnosis of CVM, a higher percentage of those that were insured had surgical interventions and a higher percentage of those that were insured did not survive to discharge from the hospital, compared with uninsured horses. However, these differences were not significant. Thoracic limb or pelvic limb ataxia grade was the only prereferral or physical examination factor significantly ($P < 0.001$ for both) related to outcome. This was an expected finding because the severity of physical examination–based assessments has been linked to neurologic outcome after spinal cord injury in other species.[41–44]

Several limitations are associated with the study reported here, the most important of which was the retrospective nature of design. The retrospective design made it impossible to standardize certain aspects of data collection and record keeping, including physical examination findings, gross lesions observed at necropsy, imaging procedures used, and abnormalities detected. In particular, the lack of standardized diagnostic criteria for the interpretation of certain imaging data may have introduced a misclassification bias into the collected data. A multicenter approach was used to enhance the external validity of the findings and to improve study power. Although a prospective investigation of CVM in horses is needed, accrual of information for < 300 cases for this report required participation of 6 large referral institutions and use of data gathered during a 15-year time period. The study design, varying institutional policies concerning telephone contact, and extended duration of time in which horses with CVM were examined and treated made it challenging to evaluate outcome and difficult or impossible to perform long-term follow-up.

Previously recognized associations between CVM and signalment[2,4,10,22] were supported by results of the present study. Among horses for which data were recorded, the results of neurologic examination suggested asymmetric ataxia and cervical hyperesthesia were frequently detected. Anti-*S neurona* antibodies were detected in the serum and CSF of several horses that had CVM, including at least 18 horses that were necropsied and found to lack microscopic evidence of EPM. Agreement between the results of radiography or myelography and necropsy was moderate; in some instances, the relative sensitivity of these imaging techniques for detection of lesions observed grossly at necropsy was poor. Most of the horses in the present study that had a diagnosis of CVM did not survive to discharge from referral hospitals and were most often euthanatized for reasons related to perceived poor prognosis. Further studies are needed to better characterize the associations of physical examination findings, use, and genetic factors with the development and outcome of CVM and the accuracy of available imaging modalities for detection of CVM.

a. SelectSurvey.NET, version 3.0, Classapps, Overland Park, Kan.
b. S-PLUS, version 8.0, TIBCO Inc, Seattle, Wash.

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