

T2-WEIGHTED MAGNETIC RESONANCE IMAGING MEASUREMENTS OF OPTIC NERVE SHEATH DIAMETER IN DOGS WITH AND WITHOUT PRESUMED INTRACRANIAL HYPERTENSION

PETER V. SCRIVANI, DANIEL J. FLETCHER, STACY D. COOLEY, ALANA J. ROSENBLATT, HOLLIS N. ERB

Intracranial hypertension is a cause of cerebral ischemia and neurologic deficits in dogs. Goals of this retrospective study were to test interobserver agreement for MRI measurements of optic nerve sheath diameter and associations between optic nerve sheath diameter, signalment data, and presumed intracranial hypertension status in a cohort of dogs. A veterinary radiologist interpreted scans of 100 dogs and dogs were assigned to groups based on presence or absence of at least two MRI characteristics of presumed intracranial hypertension. Two observers who were unaware of group status independently measured optic nerve diameter from transverse T2-weighted sequences. Mean optic nerve sheath diameter for all dogs was 3 mm (1–4 mm). The mean difference between observers was 0.3 mm (limits of agreement, –0.4 and 1.0 mm). There was no correlation between optic nerve sheath diameter and age for either observer ($r = -0.06$ to 0.00) but a moderate positive correlation was observed between optic nerve sheath diameter and body weight for both observers ($r = 0.70$ – 0.76). The 22 dogs with presumed intracranial hypertension weighed less than the 78 dogs without ($P = 0.02$) and were more often female ($P = 0.04$). Dogs with presumed intracranial hypertension had a larger ratio of optic nerve sheath diameter to body weight for each observer-side pair ($P = 0.01$ – 0.04) than dogs without. Findings indicated that the ratio of MRI optic nerve sheath diameter relative to body weight may be a repeatable predictor of intracranial hypertension in dogs. © 2013 *Veterinary Radiology & Ultrasound*.

Key words: dog, intracranial pressure, MRI, optic nerve sheath diameter.

Introduction

INCREASES IN INTRACRANIAL PRESSURE reduce cerebral blood flow and contribute to cerebral ischemia. Intracranial pressure monitors are commonly used in hospitalized human patients at risk of intracranial hypertension, such as those with head trauma, extra-axial bleeds, and other intracranial diseases. These monitors are rarely used in small animal veterinary medicine due to their invasiveness and expense. Therefore, veterinarians often rely on clinical signs such as progression of neurologic deficits or the Cushing's reflex to diagnose increased intracranial pressure. Because the duration of cerebral ischemia affects the severity and reversibility of brain injury, a noninvasive method of detecting elevated intracranial pressure in dogs at risk of in-

tracranial hypertension would allow earlier diagnosis and might reduce morbidity and mortality.

Enlargement of optic nerve sheath diameter might be an indicator of elevated intracranial pressure in dogs. The optic nerve sheath surrounds the optic nerve and is composed of external (*vagina externa n optici*) and internal (*vagina interna n optici*) layers.¹ The outer layer is a continuation of the dura mater of the brain and the inner layer, which is closely applied to the optic nerve, is continuous with the pia mater.¹ The intervaginal space (*spacia intervaginalis*) between the two layers is filled with cerebrospinal fluid (CSF) that is continuous with CSF in the cranial subarachnoid space.¹ The optic nerve sheath is distensible in the retrobulbar region. Clinical and experimental studies in people and monkeys have shown that increases in intracranial pressure cause measurable increases in the optic nerve sheath diameter.^{2–7} Furthermore, optic nerve sheath diameter measurements are highly reliable in people when using magnetic resonance imaging (MRI). Measurements >5.82 mm in adults are predictive of intracranial hypertension (intracranial pressure >20 mmHg) with a sensitivity of 90% and a specificity of 92%.⁸ Ultrasonography also has been used to measure optic nerve sheath diameter noninvasively in adults suspected of intracranial hypertension.^{9–36} An

From the Department of Clinical Sciences (Scrivani, Fletcher, Cooley, Rosenblatt) Department of Population Medicine and Diagnostic Sciences (Erb), College of Veterinary Medicine, Cornell University, Ithaca, NY 14853.

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of this paper.

Address correspondence and reprint requests to Peter V. Scrivani, DVM, at the above address. E-mail: pvs2@cornell.edu

Received September 8, 2012; accepted for publication January 27, 2013.

doi: 10.1111/vru.12023

Vet Radiol Ultrasound, Vol. 54, No. 3, 2013, pp 263–270.

optic nerve sheath diameter cutoff of 5.86 mm was 95% sensitive and 79% specific for elevated intracranial pressure.⁹ The ultrasound technique has been described as simple to perform, with novice operators learning to measure optic nerve sheath diameter in people reliably after a 4-h workshop.³⁷

Limiting factors for directly measuring intracranial pressure in small animal patients include cost, availability of necessary equipment, and invasiveness. Therefore, it would be helpful to have an indirect test for diagnosing elevated intracranial pressure in dogs that is accessible, accurate, repeatable, and noninvasive. Detecting enlargement of the optic nerve sheath diameter by ultrasonography or MRI might be such a test. Previous studies have demonstrated that both ultrasonography and MRI can be used to measure optic nerve sheath diameter in normal dogs, but the cited studies did not address whether the optic nerve sheath diameter changed with elevated intracranial pressure.^{38,39} In addition, clinical application for the tests could be limited if measurements were unreliable, variability in body weight made it impossible to establish an unambiguous threshold for defining the abnormal state, or the optic nerve sheath were not as distensible as in people. Therefore, our aims were to use archived medical data for a cohort of dogs to test repeatability of MRI measures of optic nerve sheath diameter; test associations between MRI optic nerve sheath diameter and age, sex, and body weight; and test associations between MRI optic nerve sheath diameter and other MRI characteristics of presumed intracranial hypertension.

Materials and Methods

The study design was blinded, observational, cross-sectional, and retrospective. Dogs were included in this study if they underwent MRI of the neurocranium at our institution between July 1, 2011 and August 2, 2012. All MRI examinations were performed using the same 1.5 T scanner (Vantage Atlas, Toshiba America Medical Systems, Tustin, CA). Dogs were excluded if the MRI examination did not include diagnostic scans of the entire brain in a minimum of fast spin echo sequences with T2 weighting in sagittal and transverse planes, T1 weighting in a transverse plane (before and after administration of contrast material [OmniscanTM; GE Health Care, Oslo, Norway]) and T2-weighted fluid attenuation inversion recovery (FLAIR) in a transverse plane (Table 1). Dogs also were excluded if the T2-weighted transverse scans did not include both orbits. One dog had a repeat MRI during that time; only the first examination was used. All images were stored in a commercially available picture archiving communication system (PACS) and this system also was used for viewing images and making measurements (Carestream, Rochester, NY).

TABLE 1. Technical Parameters for the 100 Dog MRI Scans used in This Study. There was No Gap and No Phase Wrap; the Frequency Direction was Left-to-Right for Transverse and Dorsal Planes; Rostral-to-Caudal for the Sagittal Plane

	FSE*-T1	FSE-T2	FSE-FLAIR†
Repetition time (ms)	450–750	4000–5500	8100–9500
Echo time (ms)	10–15	90–100	90–100
Inversion time (ms)	—	—	2105–2130
Echo train length	4	17	17
Number of acquisitions	3	3	2–3
Thickness (mm)	3.0–3.5	3.0–3.5	3.0–3.5
Field of view (mm)	18–21 × 20–21	18–20 × 19–20	18–22 × 20–22
Matrix (frequency × phase)	352 × 512	352 × 512	288 × 384

*Fast spin echo.

†Fluid attenuation inversion recovery.

The medical record of each dog was reviewed and age, sex, breed, and body weight data were recorded. The entire MRI examination was reviewed by a board-certified veterinary radiologist (P.V.S) and presence or absence of other MRI characteristics of presumed intracranial hypertension were recorded. These characteristics included mass effect (i.e., a lesion that compressed or displaced adjacent structures); substantial edema (i.e., >3-mm thick); effacement of sulci; midline shift of ≥ 3 mm; or collapse of the ventricles or cisterns. Dogs were assigned to the “presumed intracranial hypertension” group when at least two of these MRI characteristics were detected. Dogs with severe ventriculomegaly and no mass lesion also were assigned to the presumed intracranial hypertension group when there was concurrent deformation of the skull or periventricular edema.

The T2-weighted transverse scans for all dogs were reviewed independently by two first-year veterinary-radiology residents (S.D.C., A.J.R.) who were unaware of clinical data, results of the board-certified veterinary radiologist interpretation, and the study objectives. The residents measured the maximum optic nerve sheath diameter by identifying the scans between the eye and optic canal that best displayed the optic nerve sheath. Measurements were made perpendicular to the long axis of the nerve (Fig. 1) using electronic calipers included in the PACS software. The left and right sides for any one dog were measured at the same time, but the measurements could be made on different images at the reader’s discretion.

Statistical analyses were selected and performed by two of the authors (H.N.E., P.V.S.) using commercially available software (Microsoft Excel 2007, Microsoft Corporation, Redmond, WA; MedCalc 8.2.1.0, MedCalc Software, Mariakerke, Belgium; Statistix, version 7, Analytical Software, Tallahassee, FL). The frequencies of observations were reported for categorical data by group. The distributions of numerical data were assessed for Normality by group

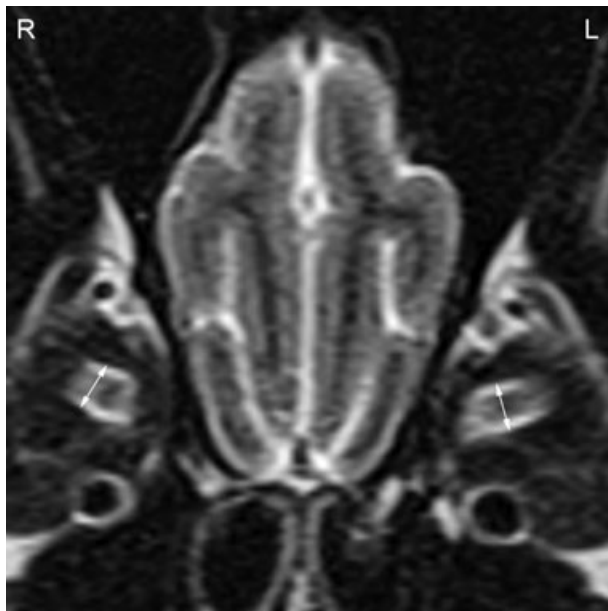


FIG. 1. Transverse T2-weighted MRI scan of the head of a 2-year-old, neutered female, mixed-breed dog depicting measurement of left (L) and right (R) optic nerve sheath diameter (double-headed arrows).

using the Kolmogorov–Smirnov test, and summarized using mean, standard deviation (SD), and range. Box-and-whiskers or scatter plots were made to illustrate selected relationships. We hypothesized that optic nerve sheath diameter measurements would have acceptable agreement (repeatability) between two novice observers, have a correlation with age, and have a positive correlation with body weight. In addition, we hypothesized that dogs with presumed intracranial hypertension would have a larger mean optic nerve sheath diameter but no association with age, body weight, or sex. Agreement between observers was assessed using scatter plots and Bland–Altman plot analysis for the left and right optic nerve sheath diameter in all dogs. Agreement arbitrarily was considered acceptable when the range of the limits of agreement for optic nerve sheath diameter was within ± 1 mm. Relationships between normally distributed variables in all dogs were investigated using Pearson's correlation and in groups of dogs by using two-tailed *t*-tests or a Yates' corrected χ^2 test (for categorical data). Statistical significance was set at 5% (two-sided, and without correction for multiplicity because study aims were to determine whether there are any relationships that we reasonably might examine in future prospective studies). We also tested associations for the ratio of optic nerve sheath diameter to body weight. We tested this variable for interobserver variation (in Bland–Altman analyses) and compared this variable between presumed intracranial hypertension groups by the Wilcoxon rank-sum test (two-sided significance again declared at 5%).

Results

The sample population consisted of 100 dogs. The mean age was 6.6 years (SD, 3.6 years; range, 0.3–14.0 years) and the mean body weight was 23.1 kg (SD, 16.3; range, 1.4–72 kg). Intracranial hypertension was presumed to be present based on MRI signs in 22 of 100 dogs. In this group there were 1 intact male, 4 neutered males, 2 intact females, and 15 neutered females. In addition, this group was composed of the following breeds: beagle ($n = 2$), Cane Corso (1), English Springer spaniel (1), French bulldog (2), German Shorthaired pointer (1), Greyhound (1), Labrador retriever (3), Maltese (1), Miniature Dachshund (1), Miniature Doberman (1), mixed-breed (3), Pug (1), Standard Poodle (1), Toy Poodle (2), and Yorkshire terrier (1). Intracranial hypertension was presumed to be absent based on MRI signs in 78 of 100 dogs. In this group there were 7 intact males, 32 neutered males, 7 intact females, and 32 neutered females. In addition, this group was composed of the following breeds: Australian shepherd ($n = 1$), Bernese Mountain dog (1), Border collie (1), Boston terrier (1), Boxer (1), Bull mastiff (2), Bulldog (2), Chihuahua (2), Cocker spaniel (1), Dachshund (5), German shepherd (1), German Shorthaired pointer (1), Golden retriever (7), Great Dane (2), Greyhound (1), Havanese (2), Irish setter (1), Labrador retriever (6), Miniature Pinscher (1), mixed breed (19), Pekingese (1), Pomeranian (1), Poodle (2), Pug (2), Rhodesian Ridgeback (1), Rottweiler (3), Saint Bernard (1), Scottish terrier (1), Shetland sheepdog (1), Shih Tzu (1), Springer spaniel (1), Staffordshire terrier (1), Swiss Mountain dog (1), West Highland White terrier (1), Wire-haired Fox terrier (1), and Yorkshire terrier (1). Age and body weight by group are tabulated (Table 2).

Comparisons between observers and measurements of left and right optic nerve sheath diameter, by group and observer, are summarized in Table 2. Observer 1 was able to measure the left optic nerve sheath diameter in 96 of 100 dogs and the right optic nerve sheath diameter in 97 dogs. Observer 2 was able to measure the left optic nerve sheath diameter in 98 of 100 dogs and the right optic nerve sheath diameter in 99 dogs. Comparison of measures by the two observers is summarized in Fig. 2. Observer 1 frequently measured the optic nerve sheath diameter slightly larger than observer 2. For the left optic nerve sheath diameter, the mean difference between observers was 0.28 mm (limits of agreement, -0.47 and 1.04 mm). For the right optic nerve sheath diameter, the mean difference between observers was 0.28 mm (limits of agreement, between -0.40 and 0.96 mm). On the basis of Bland–Altman plot analyses for the first observer, the mean difference between sides was 0.01 mm (limits of agreement, -0.24 and 0.26 mm). For the second observer, the mean difference between sides was 0.01 mm (limits of agreement, -0.47 and 0.49 mm).

TABLE 2. Summary of Statistics by Dog Group Status. Groups of Dogs were Assigned Based on Presence or Absence of at Least Two MRI Characteristics of Presumed Intracranial Hypertension

Variable*	Presumed Intracranial Hypertension Group Status						P Value
	Present (n = 22 dogs)			Absent (n = 78 dogs)			
	Mean	SD	Range	Mean	SD	Range	
Age (years)	7.0	9.2	0.3–11.0	6.5	3.7	0.3–14.0	0.61
Body weight (kg)	16.1	9.7	2.0–31.4	25.2	17.3	1.4–72.0	0.02
Left optic nerve sheath diameter, O1 [†] (mm)	3.1	0.5	2.3–3.8	3.1	0.6	1.8–4.4	0.62
Left optic nerve sheath diameter, O2 [‡] (mm)	2.7	0.6	1.6–3.4	2.8	0.7	1.1–4.1	0.56
Right optic nerve sheath diameter, O1 (mm)	3.1	0.5	2.1–3.9	3.1	0.6	1.7–4.4	0.65
Right optic nerve sheath diameter, O2 (mm)	2.7	0.6	1.3–3.7	2.8	0.6	1.2–4.0	0.65
Left optic nerve sheath diameter:BW, O1 (mm/kg)	0.33	0.29	0.11–1.17	0.22	0.20	0.06–1.05	0.01
Left optic nerve sheath diameter:BW, O2 (mm/kg)	0.28	0.23	0.10–0.98	0.20	0.18	0.05–0.81	0.03
Right optic nerve sheath diameter:BW, O1 (mm/kg)	0.32	0.28	0.11–1.17	0.21	0.18	0.05–1.01	0.01
Right optic nerve sheath diameter:BW, O2 (mm/kg)	0.27	0.22	0.10–0.99	0.21	0.19	0.04–1.18	0.04

*BW, body weight; mm, millimeters; kg, kilogram.

[†]Observer 1.

[‡]Observer 2.

Relationships between variables for optic nerve sheath diameter, by group for observer and side are depicted in Fig. 3A. Relationships by group for age and body weight are depicted in Fig. 3B. A Normal distribution was accepted for age, body weight, and all optic nerve sheath diameter measurements (for each observer-side pair) for all dogs and by group. No significant difference was detected between presumed intracranial hypertension status and left or right optic nerve sheath diameter for either observers ($P = 0.55$ – 0.65). However, dogs with presence of presumed intracranial hypertension weighed less than dogs with absence of presumed intracranial hypertension ($P = 0.02$) and were more often female ($P = 0.04$). Relationships between optic nerve sheath diameter and age are depicted in Fig. 4A and body weight in Fig. 4B. No correlation was observed between left optic nerve sheath diameter and age for observer 1 ($r, -0.05$; 95% confidence interval [CI], -0.25 to 0.15 ; $P = 0.63$) or observer 2 ($r, -0.06$; CI, -0.25 to 0.14 ; $P = 0.58$) nor between right optic nerve sheath diameter and age for observer 1 ($r, 0.00$; CI, -0.20 to 0.20 ; $P = 0.99$) or observer 2 ($r, -0.03$; CI, -0.23 to 0.17 ; $P = 0.75$). A moderate positive correlation was observed between left optic nerve sheath diameter and body weight for observer 1 ($r, 0.76$; CI, 0.66 – 0.84 ; $P < 0.0001$) and observer 2 ($r, 0.71$; CI, 0.59 – 0.79 ; $P < 0.0001$) and between right optic nerve sheath diameter and body weight for observer 1 ($r, 0.72$; CI, 0.61 – 0.80 ; $P < 0.0001$) and observer 2 ($r, 0.71$; CI, 0.60 – 0.80 ; $P < 0.0001$).

Associations between group status and the ratio variable of optic nerve sheath diameter:body weight are summarized for the left and right sides for both observers in

Table 2 and illustrated in Fig. 5. Because the distribution of the ratios was non-Gaussian in dogs without presumed intracranial hypertension, the differences were tested using Wilcoxon's rank-sum test. Dogs with presumed intracranial hypertension had a larger ratio than dogs without presumed intracranial hypertension on the left side for observer 1 ($P = 0.01$) and observer 2 ($P = 0.03$) and on the right side for observer 1 ($P = 0.01$) and observer 2 ($P = 0.04$). The median optic nerve sheath diameter:body weight ratio in dogs with presumed high intracranial pressure was 0.21 mm/kg (range, 0.10 – 1.17 mm/kg) and in dogs without presumed high intracranial pressure was 0.14 mm/kg (range, 0.04 – 1.18 mm/kg). For the left side, the mean optic nerve sheath diameter:body weight ratio difference between observers was 0.03 mm/kg (limits of agreement, -0.09 and 0.15 mm/kg). For the right side, the mean difference between observers was 0.03 mm/kg (limits of agreement, -0.07 and 0.13 mm/kg).

Discussion

The rationale for performing this study was to determine whether there was suitable preliminary evidence that enlargement of the optic nerve sheath diameter might be a clinically relevant test for diagnosing intracranial hypertension in dogs before prospectively evaluating the test in live animals. We observed reasonable agreement between the two observers, and did not find an association between optic nerve sheath diameter and age. In people, optic nerve sheath diameter is positively correlated with age in apparently healthy children due to growth and development.⁶ We

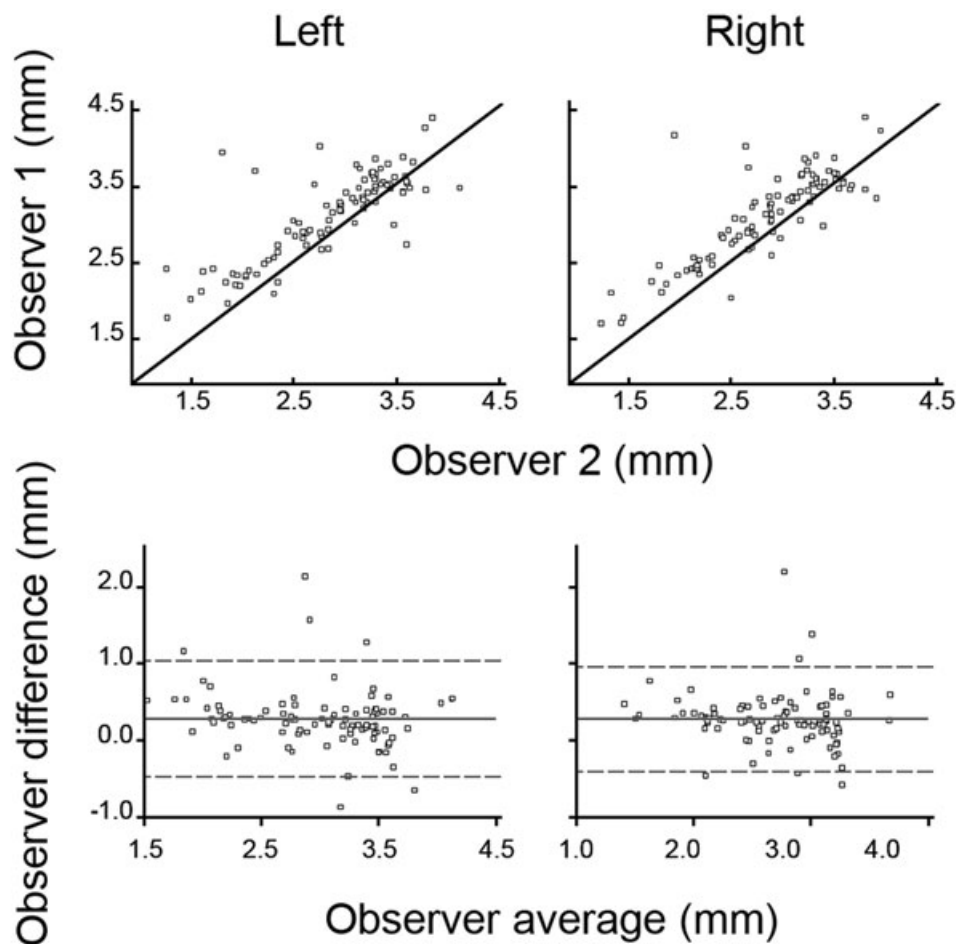


FIG. 2. Scatter plots (top row) comparing optic nerve sheath diameter between observers for the left and right sides. If there were perfect agreement, then the dots (top row) would fall along the line drawn from the lower left-hand corner of the graph to the upper right-hand corner. Observer 1 frequently measured optic nerve sheath diameter slightly larger than observer 2. The solid horizontal line in each Bland–Altman plots (bottom row) indicates the mean difference between each observer’s measure and the dashed horizontal lines depict the limits of agreement (equivalent to ± 1.96 SD). For both sides, the mean difference between observers was 0.28 mm with the limits of agreement ranging approximately between -0.4 and 1.0 mm.

identified associations between body weight and optic nerve sheath diameter, between optic nerve sheath diameter:body weight ratios and presumed intracranial hypertension, and between sex and presumed intracranial hypertension. It is reasonable to suspect that larger dogs would have a larger optic nerve sheath diameter and that optic nerve sheath diameter would be larger in dogs with presumed intracranial hypertension when accounting for body weight, but we are uncertain why presumed intracranial hypertension was detected more frequently in female dogs. We did not perform a Bonferroni correction; therefore some or all of the significant differences might be an artifact of multiple comparisons, but we are optimistic because of the consistency of the sets of P values for the alternative tests of the same hypotheses.

We first assessed interobserver agreement because we knew that making optic nerve sheath diameter measurements from archived MRI scans would be challenging.

There was no way to standardize the measurement location or to always obtain a scan in plane with the optic nerve sheath. However, the aim of this project was not to determine the actual size of the optic nerve sheath diameter but rather to assess how well two observers produced the same measurement and to look for associations between diameter measurements, signalment data, and presence or absence of presumed intracranial hypertension. Because the transverse images were acquired in a routine manner for all dogs and interobserver agreement was reasonable for novice readers (especially when accounting for body weight in the optic nerve sheath diameter:body weight ratio) we were comfortable performing additional statistical analyses. Our definition of acceptable agreement was arbitrary and stricter or more lenient criteria could have been used. We reported the results of the two observers separately to demonstrate the differences between observers. Averaging their measures likely would have reduced the standard

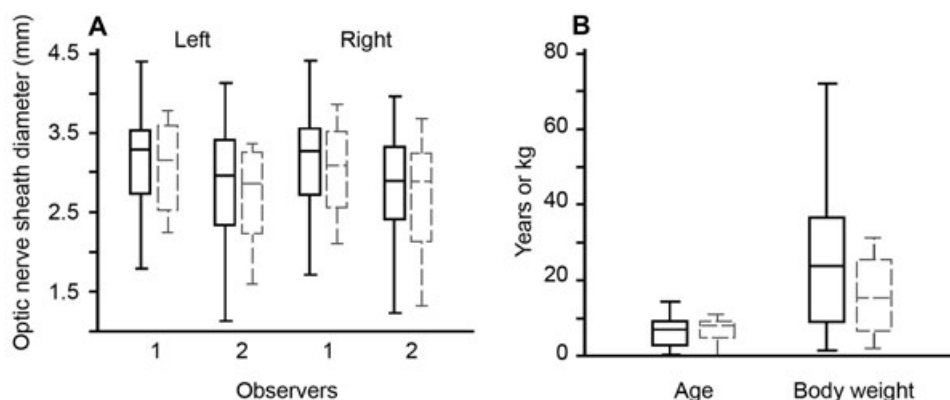


FIG. 3. Box and whiskers plots for left and right optic nerve sheath diameters by group and observer (A) and for age and body weight by group (B). Groups are indicated by the solid black and dashed gray lines. The solid-lines indicate dogs without presumed intracranial hypertension; the dashed-lines indicate dogs with presumed intracranial hypertension. No difference is detected in optic nerve sheath diameter between dogs with or without presumed intracranial hypertension by side, observer, or age. Presumed intracranial hypertension was observed more frequently in smaller dogs.

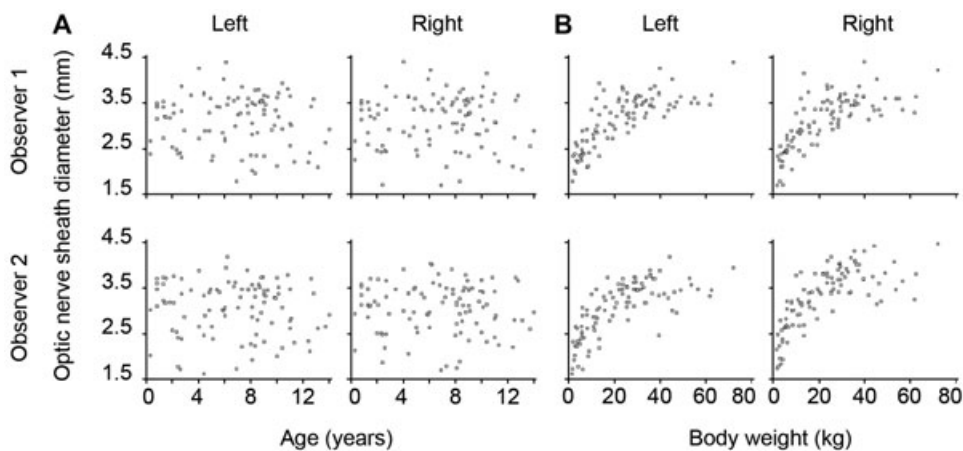


FIG. 4. Scatter plots for each observer comparing left and right optic nerve sheath diameters to age (A) and body weight (B) in all dogs. No correlation is detected between optic nerve sheath diameter and age. A moderate positive correlation is detected between optic nerve sheath diameter and body weight.

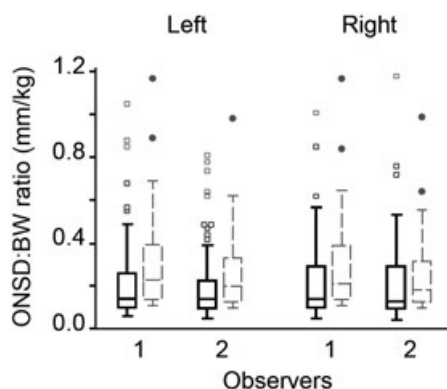


FIG. 5. Box and whiskers plots for left and right optic nerve sheath diameters (ONSD):body weight (BW) ratios by observer and group. Groups are indicated by the solid black and dashed gray lines. The solid line indicates dogs without presumed intracranial hypertension; dashed line, with presumed intracranial hypertension. Note that the median optic nerve sheath diameter:body weight ratio is higher in dogs with presumed intracranial hypertension but that there is substantial overlap between groups.

deviation and could have yielded more statistically significant differences, but averaging would not imitate how these measures would be performed clinically (i.e., one would not likely average the optic nerve sheath diameter measured by two observers). In addition, even though one might expect that raised intracranial pressure would be distributed uniformly throughout the cranial subarachnoid space and intervaginal spaces, we reported the left optic nerve sheath diameter and right optic nerve sheath diameter separately. It is possible for a dog to have a malformation that affects the optic nerve sheath on only one side or a mass that obstructs CSF flow into only one of the intervaginal spaces. That is, there is no a priori reason to expect that a dog must have the same optic nerve sheath diameter on both sides; an “important difference” (which we cannot yet define) between a dog’s two optic nerve sheath diameters might (in theory) indicate unilateral disease. This point is in contrast to the expectation that measurements by two different observers of the optic nerve sheath diameter on the same

MRI should be “the same.” Concerns about differences between sides might be less important in target populations that only have inflammatory conditions and/or vascular-occlusive diseases as these conditions are more apt to affect the CSF volume uniformly. We did not attempt to discover (and group separately) dogs with only unilateral diseases in this limited data set. We also reported the left and right side separately because there could be technical differences in measuring the optic nerve sheath diameter by side. Nevertheless, we observed only small differences between left and right sides within an observer. Although no association was detected between unscaled optic nerve sheath diameter and other MRI signs of presumed intracranial hypertension, our observation that the optic nerve sheath diameter:body weight was higher in dogs with MRI signs of high intracranial pressure across all four combinations of sides and observers supports the conclusion that optic nerve sheath diameter may vary with changes in intracranial pressure in dogs.

A limitation of this retrospective study was that there was no reference standard measure of actual intracranial pressure. If our goal was to measure the accuracy of MRI measurements of optic nerve sheath diameter for diagnosing intracranial hypertension (i.e., sensitivity, specificity, or ROC curve analysis), then a reference standard test would have been necessary. We used MRI signs of substantial space-occupying disease to categorize dogs as having presumed high intracranial pressure because this method was noninvasive and feasible in this type of study. Also, increased optic nerve sheath diameter has been compared to computed tomographic (CT) signs of presumed raised intracranial pressure in people—similar to the method used in our study.⁴⁰ Because direct intracranial pressure measurement was not available retrospectively, we do not recommend measuring the optic nerve sheath diameter in clinical practice on T2-weighted MRI for distinguishing dogs with intracranial hypertension until further work validates this approach in dogs. In addition, although the differences in weight-scaled optic nerve sheath diameter between groups were statistically significant, further refinement of this technique will be necessary before potential clinical application is considered. For example, additional analysis showed that using a cut-point of 0.3 mm/kg for the optic nerve sheath diameter:body weight ratio, the false-negative rate would have been approximately 70% and the false-positive rate approximately 25%. False-negative results can be encountered when intracranial hypertension is not associated with space-occupying disease, when masses obstruct CSF flow into the intervaginal spaces, or CSF hypovolemia occurs.⁴¹ In some dogs it was challenging to identify the optic nerve sheath because of the scarcity of CSF around the optic nerve. Possible causes of false-positive results include normal anatomic variability, measurement error, and diseases of the optic nerve itself. In people, intracerebral hemor-

rhage or glaucoma can cause an increase in the optic nerve sheath diameter.^{42,43}

It might be possible to address some of the limitations of this method in future studies. Some of the noise (i.e., overlap between groups) might be mitigated by optimizing image acquisition of the optic nerve sheath and using a standard location for measurement. For example, the measurement routinely is made 3 mm posterior to the eye in people.^{8,9} A standard location for measurement also might further reduce interobserver variation. Furthermore, one might use only the larger measure from the left and right side as the test result if the suspicion is only of diffuse (not unilateral) disease or that both sides must be enlarged to consider the test result positive for high intracranial pressure. Nevertheless, we consider our results realistic because the optic nerve sheath diameter in the 78 dogs without other MRI signs of presumed intracranial hypertension were similar to previous reports of optic nerve sheath diameter in normal dogs.^{38,39} However, we do not intend that the statistical analyses in this study be used to predict what the normal optic nerve sheath diameter should be for a particular body weight. We used a simple scaling technique to address the potential variation in optic nerve sheath diameter due to differences in weight between patients. Given the dramatic variation in size between different breeds of dogs (the weights of the dogs in this study ranged from 1.4 to 72.0 kg) different reference ranges for specific weight classes or an allometric scaling approach might be more appropriate; such an approach would require studying a diverse population of dogs with normal intracranial pressure. Because all dogs in this study underwent MRI for presumed intracranial disease, we suspect that even dogs in this data set without MRI evidence of intracranial hypertension could have had elevated intracranial pressure.

In conclusion, purposes of this study were to test whether measuring optic nerve sheath diameter using T2-weighted MRI was repeatable, describe relationships between the optic nerve sheath diameter and variables such as age and bodyweight, and determine whether optic nerve sheath diameter would be larger in dogs with MRI signs of presumed intracranial hypertension. Our results justified further studies exploring potential clinical applications of MRI optic nerve sheath diameter in dogs with confirmed intracranial hypertension. Our results also will be useful for estimating sample size, documenting feasibility, and avoiding potential complications when proceeding to prospective investigations in live animals. We elected to measure optic nerve sheath diameter on MRI because a large number of archived scans included the optic nerve sheath and because previous human studies describe this as a valid predictor of intracranial hypertension. Future studies likely will need to modify the method by which optic nerve sheath diameter measurements are obtained to improve measurement reliability and practicality. Future comparisons to the resistive

index of a cerebral artery or direct measures of intracranial pressure would be advantageous. Future studies in dogs likely will need to investigate methods for interpreting optic nerve sheath diameter measurements in relation to body

weight. Use of a ratio proved helpful in the current study. Application of this technique to other populations (e.g., cats, neonatal foals) with substantially less individual size variation could also be beneficial.

REFERENCES

- Constantinescu GM, Shaller O. Illustrated veterinary anatomical nomenclature, 3rd ed. Stuttgart: Enke Verlag, 2012;510.
- Hayreh S. Pathogenesis of oedema of the optic disc (papilloedema). A preliminary report. *Br J Ophthalmol* 1964;48:522–543.
- Takeuchi N, Horikoshi T, Kinouchi H, et al. Diagnostic value of the optic nerve sheath subarachnoid space in patients with intracranial hypotension syndrome. *J Neurosurg* 2012;117:372–377.
- Watanabe A, Kinouchi H, Horikoshi T, Uchida M, Ishigame K. Effect of intracranial pressure on the diameter of the optic nerve sheath. *J Neurosurg* 2008;109:255–258.
- Kimberly HH, Shah S, Marill K, Noble V. Correlation of optic nerve sheath diameter with direct measurement of intracranial pressure. *Acad Emerg Med* 2008;15:201–204.
- Shofty B, Ben-Sira L, Constantini S, Freedman S, Kesler A. Optic nerve sheath diameter on MR imaging: establishment of norms and comparison of pediatric patients with idiopathic intracranial hypertension with healthy controls. *Am J Neuroradiol* 2012;33:366–369.
- Kimberly HH, Noble VE. Using MRI of the optic nerve sheath to detect elevated intracranial pressure. *Crit Care* 2008;12:R181.
- Geeraerts T, Newcombe VF, Coles JP, et al. Use of T2-weighted magnetic resonance imaging of the optic nerve sheath to detect raised intracranial pressure. *Crit Care* 2008;12:R114.
- Geeraerts T, Merceron S, Benhamou D, Vigué B, Duranteau J. Non-invasive assessment of intracranial pressure using ocular sonography in neurocritical care patients. *Intensive Care Med* 2008;34:2062–2067.
- Potgieter DW, Kippin A, Ngu F, McKean C. Can accurate ultrasonographic measurement of the optic nerve sheath diameter (a non-invasive measure of intracranial pressure) be taught to novice operators in a single training session? *Anaesth Intensive Care* 2011;39:95–100.
- Lee HC, Choi HJ, Yoon JH. Ultrasonographic measurement of optic nerve sheath diameter in normal dogs. *J Vet Sci* 2003;4:265–268.
- Boroffka SA, Görig C, Auriemma E, Passon-Vastenburg MH, Voorhout G, Barthez PY. Magnetic resonance imaging of the canine optic nerve. *Vet Radiol Ultrasound* 2008;49:540–544.
- Goel RS, Goyal NK, Dharap SB, Kumar M, Gore MA. Utility of optic nerve ultrasonography in head injury. *Injury* 2008;39:519–524.
- Watanabe A, Horikoshi T, Uchida M, Ishigame K, Kinouchi H. Decreased diameter of the optic nerve sheath associated with CSF hypovolemia. *Am J Neuroradiol* 2008;29:863–864.
- Skoloudik D, Herzig R, Fadrná T, et al. Distal enlargement of the optic nerve sheath in the hyperacute stage of intracerebral haemorrhage. *Br J Ophthalmol* 2011;95:217–221.
- Abegão Pinto L, Vandewalle E, Pronk A, Stalmans I. Intraocular pressure correlates with optic nerve sheath diameter in patients with normal tension glaucoma. *Graefes Arch Clin Exp Ophthalmol* 2012;250:1075–1080.
- Major R, Girling S, Boyle A. Ultrasound measurement of optic nerve sheath diameter in patients with a clinical suspicion of raised intracranial pressure. *Emerg Med J* 2011;28:679–681.
- Dubost C, Le Gouez A, Jouffroy V, et al. Optic nerve sheath diameter used as ultrasonographic assessment of the incidence of raised intracranial pressure in preeclampsia: a pilot study. *Anesthesiology* 2012;116:1066–1071.
- Cammarata G, Ristagno G, Cammarata A, Mannanici G, Denaro C, Gullo A. Ocular ultrasound to detect intracranial hypertension in trauma patients. *J Trauma* 2011;71:779–781.
- Rajajee V, Vanaman M, Fletcher JJ, Jacobs TL. Optic nerve ultrasound for the detection of raised intracranial pressure. *Neurocrit Care* 2011;15:506–515.
- Strumwasser A, Kwan RO, Yeung L, et al. Sonographic optic nerve sheath diameter as an estimate of intracranial pressure in adult trauma. *J Surg Res* 2011;170:265–271.
- Hamilton DR, Sargsyan AE, Melton SL, et al. Sonography for determining the optic nerve sheath diameter with increasing intracranial pressure in a porcine model. *J Ultrasound Med* 2011;30:651–659.
- Bäuerle J, Nedelmann M. Sonographic assessment of the optic nerve sheath in idiopathic intracranial hypertension. *J Neurol* 2011;258:2014–2019.
- Hansen HC, Lagrèze W, Krueger O, Helmke K. Dependence of the optic nerve sheath diameter on acutely applied subarachnoid pressure—an experimental ultrasound study. *Acta Ophthalmol* 2011;89:e528–e532.
- Dubourg J, Javouhey E, Geeraerts T, Messerer M, Kassai B. Ultrasonography of optic nerve sheath diameter for detection of raised intracranial pressure: a systematic review and meta-analysis. *Intensive Care Med* 2011;37:1059–1068.
- Moretti R, Pizzi B. Ultrasonography of the optic nerve in neurocritically ill patients. *Acta Anaesthesiol Scand* 2011;55:644–652.
- Jaggi GP, Miller NR, Flammer J, Weinreb RN, Remonda L, Killer HE. Optic nerve sheath diameter in normal-tension glaucoma patients. *Br J Ophthalmol* 2012;96:53–56.
- Bäuerle J, Lochner P, Kaps M, Nedelmann M. Intra- and interobserver reliability of sonographic assessment of the optic nerve sheath diameter in healthy adults. *J Neuroimaging* 2012;22:42–45.
- Geeraerts T, Dubost C. Theme: neurology—optic nerve sheath diameter measurement as a risk marker for significant intracranial hypertension. *Biomark Med* 2009;3:129–137.
- Soldatos T, Chatzimichail K, Papathanasiou M, Gouliamos A. Optic nerve sonography: a new window for the non-invasive evaluation of intracranial pressure in brain injury. *Emerg Med J* 2009;26:630–634.
- Moretti R, Pizzi B, Cassini F, Vivaldi N. Reliability of optic nerve ultrasound for the evaluation of patients with spontaneous intracranial hemorrhage. *Neurocrit Care* 2009;11:406–410.
- Le A, Hoehn ME, Smith ME, Spentzas T, Schlappy D, Pershad J. Bedside sonographic measurement of optic nerve sheath diameter as a predictor of increased intracranial pressure in children. *Ann Emerg Med* 2009;53:785–791.
- Moretti R, Pizzi B. Optic nerve ultrasound for detection of intracranial hypertension in intracranial hemorrhage patients: confirmation of previous findings in a different patient population. *J Neurosurg Anesthesiol* 2009;21:16–20.
- Beare NA, Kampondeni S, Glover SJ, et al. Detection of raised intracranial pressure by ultrasound measurement of optic nerve sheath diameter in African children. *Trop Med Int Health* 2008;13:1400–1404.
- McAuley D, Paterson A, Sweeney L. Optic nerve sheath ultrasound in the assessment of paediatric hydrocephalus. *Childs Nerv Syst* 2009;25:87–90.
- Geeraerts T, Launey Y, Martin L, et al. Ultrasonography of the optic nerve sheath may be useful for detecting raised intracranial pressure after severe brain injury. *Intensive Care Med* 2007;33:1704–1711.
- Tayal VS, Neulander M, Norton HJ, Foster T, Saunders T, Blaivas M. Emergency department sonographic measurement of optic nerve sheath diameter to detect findings of increased intracranial pressure in adult head injury patients. *Ann Emerg Med* 2007;49:508–514.
- Blaivas M, Theodoro D, Sierzenski PR. Elevated intracranial pressure detected by bedside emergency ultrasonography of the optic nerve sheath. *Acad Emerg Med* 2003;10:376–381.
- Newman WD, Hollman AS, Dutton GN, Carachi R. Measurement of optic nerve sheath diameter by ultrasound: a means of detecting acute raised intracranial pressure in hydrocephalus. *Br J Ophthalmol* 2002;86:1109–1113.
- Hansen HC, Helmke K. Validation of the optic nerve sheath response to changing cerebrospinal fluid pressure: ultrasound findings during intrathecal infusion tests. *J Neurosurg* 1997;87:34–40.
- Helmke K, Hansen HC. Fundamentals of transorbital sonographic evaluation of optic nerve sheath expansion under intracranial hypertension II. Patient study. *Pediatr Radiol* 1996;26:706–710.
- Helmke K, Hansen HC. Fundamentals of transorbital sonographic evaluation of optic nerve sheath expansion under intracranial hypertension. I. Experimental study. *Pediatr Radiol* 1996;26:701–705.
- Hansen HC, Helmke K. The subarachnoid space surrounding the optic nerves. An ultrasound study of the optic nerve sheath. *Surg Radiol Anat* 1996;18:323–328.