Ischemic stroke in Greyhounds: 21 cases (2007–2013)

Marc Kent, DVM; Eric N. Glass, MS, DVM; Allison C. Haley, DVM; Phillip March, MS, DVM; Elizabeth A. Rozanski, DVM; Evelyn M. Galban, MS, DVM; Abagail Bertalan, VMD; Simon R. Platt, BVMS

**Objective**—To determine the prevalence of ischemic stroke in Greyhounds and determine whether affected dogs had coagulation abnormalities and hypertension.

**Design**—Multi-institutional, retrospective study.

**Animals**—21 dogs.

**Procedures**—Medical records (including diagnostic testing results) and MRI images of the brain were reviewed for Greyhounds with ischemic stroke that had been evaluated at 4 institutions. The proportion of Greyhounds with ischemic stroke was compared with the proportion of non-Greyhound dogs with ischemic stroke. Demographic information for dogs evaluated at each institution was obtained to determine the proportion of Greyhounds in the hospital populations.

**Results**—21 Greyhounds with ischemic stroke were identified. Abnormalities in coagulation were not identified in the 14 Greyhounds that underwent such testing. Systemic hypertension was identified in 6 of 14 Greyhounds that underwent such testing. No other abnormalities were identified by means of other routine diagnostic tests for Greyhounds. For all institutions combined, the prevalence of ischemic stroke in Greyhounds was 0.66% (21/3,161 Greyhounds). Greyhounds were significantly more likely to be evaluated because of ischemic stroke, compared with all other dog breeds combined (OR, 6.6; 95% confidence interval, 4.2 to 10.2).

**Conclusions and Clinical Relevance**—Results of this study suggested that Greyhounds were predisposed to ischemic stroke, compared with all other breeds combined. Coagulation abnormalities did not seem to contribute to ischemic stroke. Hypertension may have contributed to the development of ischemic stroke. Greyhounds with ischemic stroke should undergo measurement of systolic arterial blood pressure. Antihypertensive treatments may be warranted for such dogs. (J Am Vet Med Assoc 2014;245:113–117)
breeds including mixed-breed dogs (non-Greyhounds); and determine whether affected Greyhounds have coagulation system abnormalities or systemic hypertension.

**Materials and Methods**

**Animals**—This was a retrospective, multi-institutional study. The medical records databases of 4 veterinary hospitals (University of Georgia Veterinary Teaching Hospital, Red Bank Veterinary Hospital, Tufts University Cummings School of Veterinary Medicine, and University of Pennsylvania Matthew J. Ryan Veterinary Hospital) were searched to identify dogs with a diagnosis of stroke, ischemic stroke, cerebrovascular accident, ischemic brain injury, or brain infarct between 2007 and 2013. The following inclusion criteria for Greyhounds were used: peracute to acute onset (<24 hours) of neurologic deficits, availability of physical and neurologic examination results, and availability of MRI images of the head. The MRI examinations were performed with a 3.0-T unit at the University of Georgia or a 1.0-T unit or 1.5-T unit at Red Bank Veterinary Hospital, Tufts University, and the University of Pennsylvania. All dogs underwent MRI within 24 hours after the onset of neurologic signs. Imaging was performed during anesthesia of dogs in ventral recumbency with an extremity coil or a head coil on the basis of hospital preference. At a minimum, all MRI examinations included the following routine sequences: T1W, T2W, and postcontrast T1W images of the head obtained in the transverse plane. Given the retrospective nature of the study, DWI and calculation of an ADC map were not performed for all dogs and therefore were not used as inclusion criteria. However, DWI images, ADC maps, and additional sequences were reviewed when available.

Published criteria for MRI characteristics consistent with stroke were used for evaluation of images. Briefly, criteria included a well-defined lesion that was hyperintense in T2W and T2W fluid-attenuated inversion recovery sequences, was hypointense in T1W sequences, had minimal to no enhancement after IV administration of paramagnetic contrast agents, resulted in minimal mass effect, and involved predominantly the gray matter in the vascular territory of main cerebral or cerebellar arteries or a perforating branch of such arteries. When DWI images and ADC maps were available, criteria compatible with a diagnosis of ischemic stroke were hyperintensity in DWI images and hypointensity in ADC maps.

To determine the prevalence of ischemic stroke in Greyhounds, medical records databases were searched to identify the total number of Greyhounds that were evaluated at each institution between 2007 and 2013. To determine whether Greyhounds were predisposed to ischemic stroke, the medical records databases for each institution were searched to identify non-Greyhound dogs with a diagnosis of stroke, ischemic stroke, cerebrovascular accident, ischemic brain injury, or brain infarct between 2007 and 2013. Additionally, the total number of dogs evaluated at each institution between 2007 and 2013 was determined.

**Medical records review**—For each Greyhound that met the study inclusion criteria, the following information was obtained from the medical records: age at the time MRI was performed, sex, neuter status, and body weight. For Greyhounds with ischemic stroke, ancillary diagnostic testing included a CBC (including platelet count), serum biochemical analyses, urinalysis, thoracic radiography, measurement of systolic arterial blood pressure by means of Doppler ultrasonography, a coagulation profile consisting of prothrombin time and activated partial thromboplastin time, and thromboelastography. Other testing was performed at the discretion of the clinicians.

**Statistical analysis**—Statistical analysis was performed with software. By means of a chi-squared test of independence, the proportion of Greyhounds with ischemic stroke was compared with the proportion of non-Greyhounds with ischemic stroke. The OR for evaluation of Greyhounds for ischemic stroke was calculated. Calculations were performed with data from all hospitals combined. Values of P < 0.05 were considered significant.

**Results**

In total, 21 Greyhounds (3 from the University of Georgia, 9 from Red Bank Veterinary Hospital, 5 from Tufts University, and 4 from the University of Pennsylvania) met the inclusion criteria. Mean age of affected Greyhounds was 8.2 years (median, 9 years; range, 2 to 12 years). Only 4 Greyhounds were ≤6 years old. There were 10 neutered male and 11 spayed female Greyhounds. Median body weight was 33 kg (72.6 lb; range, 29 to 45 kg [63.8 to 99.0 lb]).

For all 21 Greyhounds, ≥1 lesion satisfied study criteria for MRI characteristics consistent with an ischemic stroke. A single lesion (n = 19) or 2 anatomically distinct lesions (2) were observed in MRI images. In the Greyhounds with a single lesion, the lesion was observed in the cerebellum (n = 19), caudate and lentiform nuclei and the intervening internal capsule (3), thalamus (6), or piriform lobe of the cerebrum (1). On the basis of the anatomic location of the lesions, the arterial supply that was presumed disrupted included the rostral cerebellar artery (n = 9), lenticulostriate artery (3), another perforating artery (6), or distal branch of the middle cerebral artery (1). Both Greyhounds with 2 lesions had a lesion in the cerebellum; the second lesion was in the thalamus or the caudate and lentiform nuclei and the intervening internal capsule. In these dogs, the arterial supply that was presumed disrupted included the rostral cerebellar artery (n = 2), a perforating artery from the caudal communicating artery (1), and the lenticulostriate artery (1). Seven Greyhounds that underwent DWI had hyperintense lesions in DWI images and a corresponding signal void in the ADC map.

All 21 Greyhounds were evaluated within 24 hours after the onset of neurologic signs. Abnormalities identified during examination were limited to the nervous system in 20 Greyhounds. One Greyhound had concurrent signs of systemic disease; this dog had a history of polyuria and polydipsia. This dog was receiving prednisone (0.4 mg/kg [0.18 mg/lb], PO, q 24 h) for a presumptive diagnosis of inflammatory bowel disease and thyroxine (0.028 mg/kg [0.013 mg/lb], PO, q 24 h) for hypothyroidism.
In the 19 Greyhounds with a single lesion detected with MRI, the neurologic examination abnormalities were commensurate with the anatomic location of the lesion identified in the images. In the 2 Greyhounds with 2 lesions, the neurologic examination results were consistent with the lesion in the cerebellum. Signs related to the prosencephalic lesions in both of these dogs were not detected during neurologic examination.

A CBC, serum biochemical analyses, and urinalysis were performed for all Greyhounds. On the basis of published reference intervals, the only WBC count abnormalities were stress leukograms (ie, a neutrophilic leukocytosis and lymphopenia; n = 3). In one of these dogs, hemoconcentration (Hct, 82%; reference interval, 45% to 55%) was detected and the platelet count was qualitatively reported as low. In this dog, the low platelet count was considered spurious because clumps of platelets were observed in a blood smear. The platelet count was within the reference interval for the other dogs (n = 20). Serum biochemical analysis results were within reference intervals for 18 dogs and indicated azotemia for 3 dogs. Azotemia consisted of increased serum concentrations of creatinine (2.2, 2.0, and 1.9 mg/dL; reference interval, 0.8 to 1.6 mg/dL) and BUN (29, 56, and 33 mg/dL; reference interval, 10 to 22 mg/dL), along with various urine specific gravity values (1.027, 1.019, and 1.023). Results of urinalyses were unremarkable for 20 Greyhounds and indicated hyposthenuria for 1 Greyhound (value not reported). The dog with hyposthenuria was receiving prednisone and thyroxine. Findings for thoracic radiographs (n = 21) were unremarkable.

Cerebrospinal fluid sample WBC counts were within the reference interval for 8 Greyhounds and indicated mild pleocytosis for 1 Greyhound (WBC count, 10 cells/μL). Although a differential analysis was not performed for the dog with CSF sample pleocytosis, subjectively there was a mild increase in the number of neutrophils with low numbers of monocytes and rare lymphocytes. In Greyhounds with a WBC cell count within the reference interval for CSF samples, results of a differential analysis was not reported (n = 3) or the differential analysis (5) indicated neutrophils ranging from 4% to 83%, monocytes ranging from 5% to 62%, and lymphocytes ranging from 1% to 18% of the cells observed. The CSF sample protein content was within the reference interval (n = 5) or higher than the reference interval (range, 33 to 98 mg/dL; reference interval, <24 mg/dL; 4).

Fourteen Greyhounds underwent coagulation testing. Prothrombin and activated partial thromboplastin times (n = 14), thrombin time (2), D-dimer concentration (3), and antithrombin activity (3) were within reference ranges. Thromboelastography variables were measured for 4 Greyhounds, including R (reaction time), k (clotting time), α angle, maximum amplitude, G (clot strength), and a decrease in amplitude at 60 minutes after maximum amplitude; results were considered clinically normal for Greyhounds.

Within the first 24 hours after hospitalization, systolic arterial blood pressure was measured by means of Doppler ultrasonography for 14 Greyhounds; a single value was recorded for 13 dogs, and the result was reported as clinically normal for 1 dog (the blood pressure value was not recorded for this dog). Information regarding whether the recording was a mean of multiple measurements, positioning of the dog, testing environment, the limb that was used for blood pressure measurement, and cuff size was unavailable. For the 13 dogs with a recorded blood pressure value, the mean systolic arterial blood pressure was 177 mm Hg (median, 173 mm Hg; range, 110 to 220 mm Hg). On the basis of a conservative assessment of a physiologically normal systolic arterial blood pressure of 165 ± 17 mm Hg for retired racing Greyhounds measured in a cranial thial artery in a hospital environment, the systolic arterial blood pressure for these dogs was normal (n = 8) or hypertensive (6).

For all hospitals combined, Greyhounds represented 3,161 of 423,498 (0.07%) dogs evaluated from 2007 to 2013. Ischemic stroke was identified in 21 of 3,161 (0.66%) Greyhounds (University of Georgia, 3/117 [2.56%]; Red Bank Veterinary Hospital, 9/1,941 [0.46%]; Tufts University, 5/385 [1.29%]; and University of Pennsylvania, 4/718 [0.56%]) and 423 of 420,337 (0.10%) non-Greyhounds (University of Georgia, 15/293,130 [0.06%]; Red Bank Veterinary Hospital, 220/244,476 [0.09%]; Tufts University, 55/48,666 [0.11%]; and University of Pennsylvania, 135/102,065 [0.13%]). For all dogs combined (Greyhounds and non-Greyhounds), ischemic stroke was identified in 446 of 423,498 (0.11%) animals (University of Georgia, 18/25,247 [0.07%]; Red Bank Veterinary Hospital, 229/246,417 [0.09%]; Tufts University, 60/49,051 [0.12%]; and University of Pennsylvania, 139/102,783 [0.14%]). For all institutions combined, Greyhounds were significantly (P < 0.001) more likely to be evaluated because of ischemic stroke, compared with non-Greyhounds (OR, 6.6; 95% confidence interval, 4.2 to 10.2).

**Discussion**

Stroke is the third most common cause of death for humans in the United States. For dogs, the incidence of stroke and breed dispositions are unknown. Results of another study suggest Greyhounds have a higher incidence of ischemic stroke versus other breeds. In the present study involving 4 referral hospitals, the prevalence of ischemic stroke in Greyhounds was 0.66%. Greyhounds were 6.6 times as likely to be evaluated because of ischemic stroke as were non-Greyhounds.

Various etiologies have been associated with ischemic stroke in dogs, including sepsis, atherosclerosis, parasite migration, thromboembolic disease, and neoplasia. Metabolic disorders such as hyperadrenocorticism, kidney disease, hypothyroidism, and hypertension have also been detected in dogs with ischemic stroke, even though definitive causal relationships between these disorders and ischemic stroke have not been identified. Although the dogs of the present study did not undergo extensive diagnostic testing to exclude all known causes of ischemic stroke, most etiologies were either excluded from consideration or considered unlikely on the basis of physical examination results and results of CBCs, serum biochemical analyses, and urinalyses. Consequently, with the exception of hypertension in 6 dogs, a definitive predisposing cause of ischemic
stroke was not identified for dogs of the present study. One dog that was receiving prednisone and thyroxine may have had a systemic disorder leading to ischemic stroke. However, as in other studies, a cause-and-effect relationship could not be identified.

Physiologic differences between Greyhounds and non-Greyhounds could be a priori risk factors for ischemic stroke. Two such differences could be risk factors for ischemic stroke in Greyhounds are alterations in coagulation and blood pressure.

For Greyhounds in this study, prothrombin and partial thromboplastin times and results of various other coagulation tests were within reference intervals. Likewise, results of thromboelastography were unremarkable; unfortunately, thromboelastography was performed for only 4 dogs. However, compared with results for non-Greyhounds, results of thromboelastography for Greyhounds were compatible with slower clotting kinetics and weaker clot strength, suggesting a potential for bleeding. On the basis of the thromboelastography results, it seemed more likely that affected dogs would develop hemorrhagic stroke rather than ischemic stroke. However, the MRI characteristics were more consistent with ischemic stroke.

In the present study, hypertension was detected in 6 of 14 dogs for which blood pressure was measured. To be conservative, we used a high reported11 mean systolic arterial blood pressure to identify dogs with hypertension. Other authors17 have proposed that systolic arterial blood pressure in Greyhounds is only 10 to 20 mm Hg higher than it is in non-Greyhounds; by use of these values, more dogs would have been classified as hypertensive. Hypertension in humans results in changes in the cerebral vasculature, including hypertrophy and remodeling of arterial wall smooth muscle and increased arterial wall stiffness.18 As a consequence, there is a reduction in the luminal size of the arterial vasculature.19 In addition, alterations in vascular autoregulation resulting in reduced cerebral blood flow during periods of hypertension have been identified in hypertensive humans.20 Ultimately, these changes increase the susceptibility of the brain to ischemic stroke.18 Similar pathophysiologic changes may contribute to ischemic stroke in Greyhounds. Compared with non-Greyhounds, racing Greyhounds have higher cardiac output and systolic arterial blood pressure.21 Even months after cessation of racing, altered hemodynamic values and anatomic differences such as heart weight and heart weight-to-body weight ratio are detected in Greyhounds.22 However, hemodynamic values for Greyhounds that have never raced or been trained to race are not significantly different from such values for non-Greyhounds.23 None of the dogs in the present study were actively used as racing dogs at the time of ischemic stroke. Whether the Greyhounds in the present study had raced or been trained to race and the time between cessation of racing and the occurrence of ischemic stroke were unknown. If Greyhounds in this study had raced or been trained to race, further studies in which more extensive testing is used may allow identification of a predisposing dis-
order. Similarly, microscopic evaluation of the cerebral vasculature of Greyhounds with ischemic stroke would be needed to determine whether pathological changes to that vasculature are similar to changes in hypertensive humans. In addition, on the basis of the findings of this study, antihypertensive treatment should be considered for Greyhounds with ischemic stroke in which hypertension is detected. Long-term studies would be needed to determine the efficacy of antihypertensive treatments for the prevention of an initial stroke or recurrent strokes in hypertensive Greyhounds.

References