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Comparison of Glomerular Filtration Rate between Greyhounds and Non-Greyhound Dogs

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Greyhounds have significantly higher serum creatinine (SCr) concentration than do non-Greyhound dogs that may be attributable to differences in glomerular filtration rate (GFR). By means of plasma clearance of technetium Tc 99m diethylenetriaminepentaacetic acid, GFR was measured in 10 Greyhounds and 10 non-Greyhound dogs with normal findings of physical examination, CBC, serum biochemical analysis, and urinalysis. Dogs were fed the same diet for a minimum of 6 weeks before GFR data collection. Greyhounds had significantly higher mean ± SD GFR (3.0 ± 0.1 vs 2.5 ± 0.2 ml/min/kg; $P = .01$) and SCr concentration (1.8 ± 0.1 vs 1.5 ± 0.1 mg/dL; $P = .03$) than did non-Greyhound dogs, but the serum urea nitrogen (SUN) concentration was not significantly different (18 ± 1 vs 18 ± 2 mg/dL; $P = .8$). Therefore, the higher SCr concentration in Greyhounds is not attributable to decreased GFR, and may be associated with the high muscle mass in the breed. Healthy Greyhounds have higher GFR than do non-Greyhound dogs.

Key words: Blood urea nitrogen, Canine; Creatinine; Kidney; Nuclear medicine; Tc 99m pentetate.

Hematologic and biochemical differences between Greyhounds and non-Greyhound dogs are well documented.[1–5] In a study comparing 30 retired racing Greyhounds with age- and sex-matched non-Greyhound dogs, the serum creatinine (SCr) concentration of the Greyhounds was significantly higher (1.6 mg/dL vs 1.03 mg/dL), but the blood urea nitrogen (BUN) concentration was not.[2]

The increased SCr concentration in Greyhounds may be attributed to decreased glomerular filtration rate (GFR) and increased muscle mass or diet, or both.[2] In that study, the retired racing Greyhounds with significantly higher SCr concentration were not being fed high-protein diets typical of those fed to Greyhounds at the racetrack.[2,6] Determining whether there are differences in GFR between Greyhound and non-Greyhound dogs should help define the mechanism for the high SCr concentration in the breed.

Renal clearance of technetium Tc 99m diethylenetriaminepentaacetic acid (^{99m}Tc-DTPA) in dogs is an established method for estimating GFR.[7,8] By means of gamma camera-based methods for estimating GFR, global and split renal functions are determined; this correlates well with inulin clearance.[8,9] Split renal function, or individual renal function, can only be estimated with gamma camera-based methods, whereas global renal function, a combination of function from both kidneys, can be estimated with gamma camera-based or plasma clearance techniques. Plasma clearance of ^{99m}Tc-DTPA has the advantage of using lower doses of ^{99m}Tc-DTPA and being more accurate than are gamma camera-based methods, when each method is compared with inulin clearance.[10] Plasma clearance of ^{99m}Tc-DTPA has advantages over traditional inulin clearance because it does not require urine collection or complex assays to determine the amount of tracer in plasma.

The purpose of the study reported here was to determine whether Greyhounds have significantly lower GFR than that of non-Greyhound dogs; lower GFR might explain why Greyhounds have significantly higher SCr concentration than do non-Greyhound dogs.

Materials and Methods

Two groups of client-owned dogs (n = 10/group) were enrolled in the study. Group 1 consisted of 10 retired racing Greyhounds; group 2 included 10 size-matched non-Greyhound dogs, and excluded sight hound breeds. The study was approved by The Ohio State University, College of Veterinary Medicine, Veterinary Teaching Hospital Board; owner consent was obtained. Initial evaluation included physical examination, CBC determination, serum biochemical analysis, and urinalysis. Dogs with results within the laboratory's reference interval were enrolled in the study.

Once enrolled in the study, dogs were fed an identical diet[a] for a minimum of 6 weeks. Some dogs were already consuming this diet, so the 6-week diet normalization was not needed. Daily feed intake was controlled by each owner; feed intake was not normalized for all dogs of the study. Owners were asked not to feed treats to their dog, especially 3 days before data collection. The feeding routine was meant to mimic feeding routines of animals referred to veterinary practices. Body condition scores were not obtained. Food was withheld from the dogs from midnight of the day of GFR data collection until the last blood sample was drawn. Dogs were allowed ad libitum access to water during this time and during GFR data collection. On the day of GFR data collection, CBC acquisition, serum biochemical analysis, and urinalysis were repeated. Only GFR data from dogs with results within the laboratory's reference interval on the day of GFR measurement were included.

Two dedicated intravenous catheters were placed: one for administration of ^{99m}Tc–DTPA, and one for blood sample collection. A dose standard was created by injecting 3.70 MBq (100 μCi) of ^{99m}Tc-DTPA into 500 ml of saline. The net amount of radioactivity injected was determined by subtracting the amount of radioactivity in the syringe after injection from the amount of radioactivity in the syringe before injection, as measured in a dose

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calibrator.[b] A 0.5-ml sample of the dose standard was pipetted[c] into a test tube for analysis.

A dose of 3.70 MBq (100 μCi) of ^{99m}Tc-DTPA was administered intravenously to each dog. The net amount of radioactivity given was determined by subtracting the amount of radioactivity in the syringe after injection from the amount of radioactivity in the syringe before injection, as measured in a dose calibrator. Heparinized blood samples (2 ml) were collected 5, 10, 30, 60, 150, and 240 minutes after injection.[11] Blood samples were centrifuged[d] at 3,100 rpm for 15 minutes, and plasma (0.5 ml) from each sample time was pipetted into a test tube. The plasma samples and dose standard were counted for 1 minute in a NaI well counter.[e] All data were decay-corrected to the time of sample counting. The dose standard was used to determine the well-counter detector efficiency and to convert activity in MBq to counts per minute.

A time-activity curve was created by plotting the counts per milliliter versus minutes. By means of mathematical software,[f] a double exponential curve was fit to the data in the following form:

$$y = ae^{-\alpha x} + be^{-\beta x}$$

where a is the y-axis intercept of the fast component of the plasma disappearance curve, e is the natural logarithm, -α is the slope of the fast component of the plasma disappearance curve, b is the y-axis intercept of the slow component of the plasma disappearance curve, -β is the slope of the slow component of the plasma disappearance curve and x is time in minutes. The area under the curve (AUC) was calculated by the formula[12]:

$$AUC = a/\alpha + b/\beta$$

where a is the y-axis intercept of the fast component of the plasma disappearance curve, -α is the slope of the fast component of the plasma disappearance curve, b is the y-axis intercept of the slow component of the plasma disappearance curve and -β is the slope of the slow component of the plasma disappearance curve. Plasma clearance of ^{99m}Tc-DTPA was calculated by dividing the injected dose by the AUC, then by body weight (kg). Because of the low dose of radiation injected, the reading in all dogs was <2 mR/hr at the body surface, as detected with a Geiger-Muller counter at the conclusion of blood sample collection; therefore, radiation isolation was not needed.

Mean and SD for GFR and SUN and SCr concentrations were calculated for Greyhounds and non-Greyhound dogs. Comparisons between Greyhounds and non-Greyhound dogs were made by means of an unpaired, 2-tailed Student's t-test with statistical software.[g] Significance was set at $P < .05$. Pearson's correlation for age versus GFR was made for all 20 dogs and for each group.

Results

Ten retired racing Greyhounds (4 spayed females; 6 neutered males) were 4.97 ± 0.58 years old and weighed 32 ± 1 kg. The 10 non-Greyhound dogs (5 spayed females; 5 neutered males) were 2.6 ± 0.5 years old and weighed 30.0 ± 2.6 kg. The 10 non-Greyhound dogs included the following breeds: 8 mixed-breed dogs, 1 Doberman Pinscher, and 1 Golden Retriever.

Greyhounds had significantly higher GFR (3.0 ± 0.1 vs 2.5 ± 0.2 ml/min/kg; $P = .01$) and SCr concentration (1.8 ± 0.1 vs 1.5 ± 0.1 mg/dL; $P = .03$) than did non-Greyhound dogs, but the SUN concentration was not significantly different (18 ± 1 vs 18 ± 2 mg/dL; $P = 0.8$). Correlation between age and GFR was not observed for any of the 20 dogs ($r = .31$; P = .2), Greyhounds ($r = .04$; $P = .9$) or non-Greyhound dogs ($r = -.08$; $P = .8$).

Discussion

The significantly higher SCr concentration in Greyhounds[2] is not attributable to low GFR, because our results indicated that Greyhounds have significantly higher GFR than do non-Greyhound dogs. The Greyhounds of our study had significantly higher SCr concentration, compared with values for the control dogs, which was similar to results of another study.[2]

On the basis of our results, the higher SCr concentration in the Greyhound likely is the result of the large muscle mass. Serum creatinine originates endogenously from the metabolism of muscular creatine.[13,14] The creatine pool is influenced by muscle mass which, in turn, can be altered by disease, generalized muscle wasting, or muscle conditioning.[13] Serum creatinine concentration is not significantly affected by diet or catabolic factors.[13] The daily amount of creatine synthesis in rats is equal to the daily excretion of creatinine in urine.[14]

Increased dietary protein intake in dogs leads to increased GFR[15,16] and renal growth.[16] To control for this variable, all dogs of the study were fed the same diet for at minimum of 6 weeks before measurement of GFR. A lamb-and-rice diet was chosen because some of the Greyhounds had food allergies that were responsive to this diet. The amount of dietary protein was not normalized among the study dogs. Rather, feeding practices likely mimicked those of the average, client-owned dog.

In people, GFR decreases with age.[17] Renal size and volume decrease with age and result in decreased numbers of glomeruli and decreased mass of juxtamedullary nephrons. In turn, this leads to decreased filtration area of the glomerular basement membrane and decreased permeability.[17] Paradoxically, the Greyhounds of our study were older than the non-Greyhound dogs (4.97 years vs 2.64 years). Statistically, correlation was not found between age and GFR. However, the trend was toward a positive correlation of age and GFR. This likely reflects the fact that we selected healthy, nonazotemic dogs for our study. It was hoped that the non-Greyhound dogs would be age matched to the Greyhounds. However, the volunteer pool for the study was sufficiently small so that we could not control the age variable.

Healthy dogs have a wide range of GFR in response to their physiologic needs.[18] In a study of healthy Beagles, GFR was 3.97 ± 0.72 ml/min/kg (range, 2.66–5.67 ml/min/kg) by means of 99mTc-DTPA gamma camera-based scintigraphy.[18] In that study, there was a 95% probability that measurement of GFR for the same dog on different days would be within 1.06 ml/min/kg.[18] We chose not to make multiple GFR measurements in our dogs for two reasons: the volunteer rate for the study would have been lower with multiple data collection days; and single measurements of GFR more closely mimic the clinical use of GFR measurement.

In conclusion, higher SCr concentration in Greyhounds is not attributable to decreased GFR. Healthy Greyhounds have higher GFR than do non-Greyhound dogs.

Footnotes

[a] IAMS Lamb & Rice Diet, The Iams Company, Dayton, OH
[b] Radca Model 4050, Radcal Corporation, Monrovia, CA
[c] Pipetman P1000, Gilson, Middleton, WI
[d] Medispin, International Equipment Company, Needham Heights, MA
[e] Biodex, Medical Systems Inc, Shirley, NY
[f] Igor Pro 4.09A Carbon, Wavemetrics Inc, Lake Oswego, OR
[g] Prism 4, GraphPad Software Inc, San Diego, CA

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