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Serum Cardiac Troponin I Concentration in Retired Racing Greyhounds

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Background: Cardiac troponin I (cTnI) is a polypeptide found specifically in cardiac muscle tissue that has been used as a diagnostic and prognostic indicator of cardiomyopathy. Increases in cTnI are associated with myocardial pathologic processes. However, high serum cTnI concentrations have been observed in normal Greyhounds.

Hypothesis: We hypothesized that Greyhounds have cTnI concentrations higher than non-Greyhound dogs, and that a separate reference range should be established for Greyhounds.

Animals: Blood samples were collected from the jugular vein from a group of 20 healthy Greyhound blood donors.

Methods: Analysis of serum cTnI was performed with an immunoassay system with a detection level of 0.01 ng/mL, as described previously. The Greyhound values were compared with 2 groups of Boxers with and without arrhythmogenic right ventricular cardiomyopathy (ARVC), and to a group of non-Boxer control dogs from a previous study.

Results: The mean cTnI concentration in Greyhounds was significantly higher ($P < .0001$) than that in non-Greyhound control dogs, although not significantly different from normal Boxers ($P = .50$), or Boxers with ARVC ($P = .58$). Greyhound serum cTnI concentrations were in the range found in Boxers with ARVC. The proposed reference range for cTnI in Greyhounds is 0.05–0.16 ng/mL.

Conclusions and Clinical Importance: Greyhounds have a reference range for serum cTnI concentrations that differs from that of other previously published reference ranges for dogs of other breeds. Until a broader database and more precise reference range can be established, caution should be exercised in interpreting serum cTnI concentrations in Greyhounds with suspected cardiac disease.

Key words: Cardiac biomarkers; Cardiac reference ranges; Cardiology; Cardiomyopathy; Cardiovascular.

Retired racing Greyhounds have increased in popularity as pets over the last several years, there is some evidence that many of their physiological and clinicopathologic variables differ from those of other breeds. Red blood cell (RBC) count; packed cell volume; mean corpuscular hemoglobin concentration; sodium, chloride, bilirubin, and creatinine concentrations; and aspartate aminotransferase activity are higher in Greyhounds than in non-Greyhound breeds.[1,2] Platelet counts, total protein, globulin, α- and β-globulin,[3] and thyroid hormone concentrations are also lower in Greyhounds than in non-Greyhounds.[4,5] These findings have led to interest in defining normal reference ranges for other variables in Greyhounds.

Cardiac troponin I (cTnI) is a polypeptide found specifically in cardiac muscle tissue.[6] Serum concentrations of this protein have been used as a diagnostic and prognostic indicator of heart disease in humans, and more recently, in dogs. High concentrations of cTnI have been observed in association with several pathologic conditions, including babesiosis, doxorubicin cardiotoxicity, mitral valve disease, subaortic stenosis (SAS), dilated cardiomyopathy (DCM), pericardial effusion, gastric dilatation-volvulus (GDV), cardiac contusions,[7–14] and arrhythmogenic right ventricular cardiomyopathy (ARVC) in Boxers.[15] In human patients with acute myocardial injury or infarction, the concentration of cTnI has been shown to correlate positively with the size of the infarct.[6] In people, initial increases in cTnI occur 3–12 hours postinfarction, and peak at 24 hours.[6] Once the inciting cause is stabilized, concentrations return to normal in 5–10 days. Chronic increases in cTnI are associated with a chronic or ongoing pathologic process.[6] However, we occasionally have observed high serum cTnI concentrations in normal Greyhounds examined at the Ohio State University Veterinary Teaching Hospital (OSU-VTH).

Studies of cardiovascular anatomy and physiology have shown that Greyhounds have a higher heart weight-to-body weight ratio than non-Greyhounds, as well as higher left ventricular free wall thickness; many Greyhounds have functional murmurs with no detectable structural or physiologic abnormalities.[16–20] We recently reported that Greyhounds have significantly higher vertebral heart scores (VHS) than other dogs.[21] Considering these data, we hypothesized that Greyhounds have cTnI concentrations higher than those in non-Greyhound dogs, and that a separate reference range should be established when evaluating cTnI in Greyhounds with potential cardiac disease.

Materials and Methods

The Greyhounds used in this study were blood donors from the OSU-VTH Blood Donor Program or participated in a student driven spay and neuter program, both of which are approved by the Laboratory Animal Care and Use Committee. In addition, signed owner consent was obtained for the study. All Greyhounds were retired healthy racers fostered in homes for at least 1 year. They were current on vaccinations, and were receiving either milbemycin[a] or ivermectin[b] monthly for heartworm prophylaxis, and

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fipronyl,[c] or imidacloprid and permethrin[d] for flea control. All were serologically negative for *Dirofilaria immitis* and *Ehrlichia canis*, and were free of external and intestinal parasites. The blood donors also tested serologically negative for *Babesia canis*. During their initial physical examination, blood samples were obtained from the jugular vein by a 21 G butterfly catheter and Vacutainer tubes,[e] or 20-G needle and a 12-cc syringe. Samples were allowed to clot in serum separator Vacutainer tubes. Samples were centrifuged and serum removed. Serum was aliquoted into 0.5 mL amounts, placed in storage at −80 °C for 3–10 months, and thawed only once at the time of analysis.

Twenty healthy Greyhounds were selected for this study; on cardiac examination, most Greyhounds had normal blood pressure and the previously described murmur,[21] but had no arrhythmias, gallop rhythms, pulse deficits, or jugular vein distention or pulsation. Their age range was 5–9 years, with an average age of 6.6 years. There were 3 intact males, 5 castrated males, 7 intact females, and 5 spayed females. The control dogs were part of a previously reported study comparing cTnI concentrations in Boxers with and without cardiomyopathy.[15] None of the normal dogs in the previous study had evidence of cardiac abnormalities on echocardiogram or electrocardiography (ECG), and had an age range of 3–7 years (reference range, 5.6 years). They included the following breeds: Australian Shepherd (n = 1), Labrador Retriever (n = 2), Collie (n = 1), and mixed (n = 6). In addition, we compared our results to the other 2 groups of Boxers with and without ARVC from the previous study.[15]

Analysis of serum cTnI concentrations in all samples from Greyhounds and from the previous study[15] was performed with an immunoassay system with a detection limit of 0.01 ng/mL, as described previously.[f,15]

Normality was evaluated with the D'Agostino method. A Welch's *t*-test assuming unequal variances[g] was used to compare the concentration of cTnI between Greyhounds and non-Greyhound controls, Greyhounds and normal Boxers, and Greyhounds and Boxers with ARVC. A test also was used to compare the cTnI concentrations in male versus female Greyhounds and in blood donors versus Greyhounds in the spay and neuter clinic. Significance was set as $P < .05$.

Results

The mean cTnI concentration in Greyhounds was significantly higher ($P < .005$) than that in non-Greyhound control dogs (Fig 1). The mean cTnI concentration was not significantly different between Greyhounds and normal Boxers ($P = .36$), or Greyhounds and Boxers with ARVC ($P = .48$) (Fig 1). The mean cTnI concentration in the Greyhounds was 0.10 ng/mL (median 0.08 ng/mL; range, 0.03–0.57 ng/mL). The reference range for cTnI in our population of Greyhounds calculated by 25 and 75% percentiles was 0.06–0.1 ng/mL.

There were no significant differences in cTnI concentration between male and female Greyhounds ($P = .42$), nor between the blood donor Greyhounds and those in the spay and neuter program ($P = .55$). The mean cTnI concentrations were 0.02 ng/mL (median, 0.02 ng/mL; range, <0.01–0.05 ng/mL) in non-Greyhound control dogs, 0.08 ng/mL (median, 0.085; range, 0.02–0.11 ng/mL) in normal Boxers, and 0.12 ng/mL (median, 0.13; range, 0.04–0.19 ng/mL) in Boxers with ARVC. Twelve of the 20 Greyhound cTnI concentrations (60%) were within or above the range of the Boxers with ARVC (ie 0.08–0.16 ng/mL) (Fig 1).

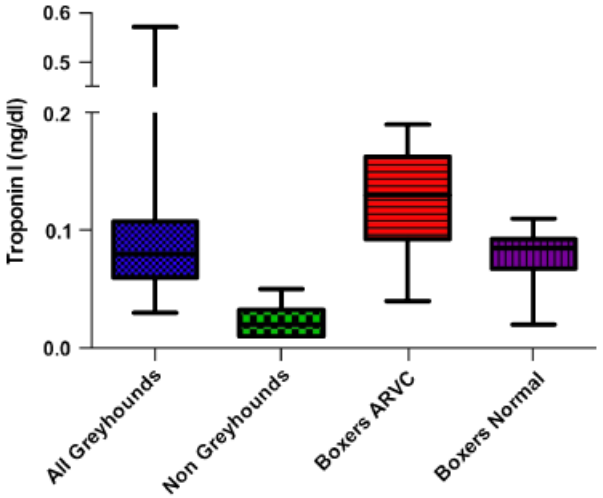

Fig 1. Box-and-whisker plot depicting the cTnI concentrations in normal Greyhounds, non-Greyhound dogs, Boxers with arrhythmogenic right ventricular cardiomyopathy (ARVC), and normal Boxers. Whiskers represent the 2.5% and 97.5 percentiles.

Discussion

Greyhounds have developed many adaptational physiologic traits that are different from other breeds and should give them an advantage as racing dogs. They have developed a unique musculoskeletal conformation, larger myocardial muscle mass, and higher concentrations of RBC and hemoglobin to increase their exercise efficiency. Many of these adaptations have led to differences in their hematologic and biochemical variables, some of which are only now beginning to be understood.

Reference ranges for serum cTnI concentrations have been determined for humans and dogs[22,23]; but some of these studies were done by different instrumentation and reagents. Serum troponin concentrations have been evaluated in dogs with the following diseases: babesiosis, doxorubicin administration, mitral valve disease, SAS, DCM, pericardial effusion, gastric dilatation-volvulus (GDV), cardiac contusions, and ARVC in Boxers.[7–15] In humans, cTnI concentrations consistent with acute myocardial infarction have been reported after high-level exertion.[24] Although many of the Greyhounds in this study were serologically negative for *B. canis*, none had a history of chemotherapy administration, and all were healthy based on cardiac auscultation.

A limitation of this study is that only half of the Greyhounds had cardiac evaluations with ECG and blood pressure determinations. Interestingly, the female Greyhound with a serum cTnI concentration of 0.57 ng/dL, the only outlier in the group, had a normal physical examination, blood pressure, and ECG (data not shown). Because all of the Greyhounds used were retired racers, it is unlikely that persistently increased concentrations would be present because of their high-performance training. In addition, there were no significant differences in cTnI between the blood donor Greyhounds, that had lived in homes for over a year, and the Greyhounds in the spay and neuter clinic. The latter had raced more recently, but a detailed history was not available.

The cTnI concentration was above the upper limit of the reference range (0.11 ng/mL) in 5/20 Greyhounds (25%), and 12/20 Greyhounds (60%) had cTnI concentrations above the previously published reference range of 0–0.07 ng/mL.[22] We have shown that clinically normal Greyhounds have higher cTnI concentrations than other apparently normal dogs; their serum cTnI concentration is in the range found in Boxers with ARVC. This high concentration may be because of their larger heart weight-to-body weight ratios, an adaptational mechanism for high-stress physical performance. Despite the fact that none of these dogs were in racing condition or performing at the time, breeding would favor dogs with the capacity for high-stress performance, regardless of their actual activity level.

Although unlikely the fact, the cTnI concentration in normal Greyhounds was similar to that in Boxers with ARVC could indicate that these dogs have an as yet undetermined underlying myocardial pathology. However, all Greyhounds in this study were healthy, had no arrhythmias on auscultation, and remained asymptomatic months after completing the study. Myocardial histopathology (ie, endomyocardial biopsies) would have specifically addressed this issue. However, in a study of necropsies in 230 former racing Greyhounds, only 4% had histologic evidence of myocardial pathology (eg, infarcts).[25] Additional studies to compare serum cTnI concentrations in racing Greyhounds versus noncompeting or show Greyhounds may identify other differences in reference ranges among Greyhounds, as occur in people.[24]

Currently, practicing veterinarians frequently obtain plain thoracic radiographs in dogs with heart murmurs. In Greyhounds, those radiographs may lead to an inaccurate interpretation of cardiomegaly, if nonbreed-specific canine reference ranges for VHS are used.[26] Occasionally, serum cTnI concentration will be used to ascertain whether or not a dog with a heart murmur and cardiomegaly has myocardial disease. Consequently, a variable proportion of normal Greyhounds could be erroneously diagnosed as having myocardial disease based on the presence of a heart murmur, an apparently higher than normal VHS, and high serum cTnI concentration. The reference range for serum cTnI concentrations in Greyhounds differs from that of other breeds. Until a larger database can be established and a more precise reference range is widely available, caution should be exercised in interpreting serum cTnI concentrations in Greyhounds with suspected cardiac disease.

Footnotes

[a] Interceptor, Novartis, Greensboro, NC
[b] Heartgard, Merial, Iselin, NJ
[c] Frontline, Merial Duluth, GA
[d] K9 Advantix, Bayer, Shawnee Mission, KS
[e] BD Vacutainer, Franklin Lakes, NJ
[f] Unicel DXI, Beckman Coulter, Fullerton, CA
[g] Graph Pad Software, San Diego, CA

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