Brief Communication

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Cardiac Troponin I in the Normal Dog and Cat

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Cardiac troponin I (cTnI) has proven to be a highly specific and sensitive marker for myocardial cellular damage in many mammalian species. The structure of cTnI is highly conserved across species, and assays for human cTnI (including the one used in the current study) have been validated in the dog. Blood concentrations of cTnI rise rapidly after cardiomyocyte damage, and assay of cTnI potentially may be valuable in many clinical diseases. The purpose of this study was to establish the normal range of cTnI in heparinized plasma of dogs and cats. Forty one clinically normal dogs and 21 cats were included in the study. One to 3 milliliters of blood were collected by venipuncture into lithium heparin vacutainers for analysis of cTnI (Stratus® CS). The range of plasma cTnI concentrations in dogs was <0.03 to 0.07 ng/mL with a mean of 0.02 ng/mL, with the upper tolerance limit (0.07 ng/mL) at the 90th percentile with 95% confidence. In cats, the range was <0.03 to 0.16 ng/mL with a mean of 0.04 ng/mL, and the upper tolerance limit (0.16 ng/mL) at the 90th percentile as well with 90% confidence. This study establishes preliminary normal ranges of plasma cTnI in normal dogs and cats for comparison to dogs and cats with myocardial injury or disease.

Key words: Cardiac disease; Cardiac troponin T; Creatine kinase; Diagnostics; Plasma cardiac markers.

Cardiac troponin I (cTnI) has been recognized as the most sensitive and specific marker of myocardial cell necrosis in humans, demonstrating a higher specificity than the cardiac isoenzyme creatine kinase (CK-MB) and better sensitivity and specificity than cardiac troponin T (cTnT).[1–3] Moreover, cTnI remains increased in blood samples longer than does CK-MB, with an increase above normal occurring within 5–7 hours after the onset of acute myocardial infarction and persisting for up to 8 days.[2] Although infarction is a very rare cause of myocardial cell disruption in the dog and cat, high concentrations of cTnI have been associated with many other cardiac diseases that are clinically relevant in these species. In several studies in humans, increased concentrations of cTnI and ongoing myofibrillar degradation were identified in patients with severe congestive heart failure.[4–6] Increased concentrations of cTnI also have been associated with myocarditis,[7,8] and increased concentrations after high dose chemotherapy have been correlated with future reductions in cardiac function.[9] In veterinary medicine, measurement of plasma cTnI concentrations has been utilized in a clinical report of a horse with a ruptured left ventricular outflow tract.[10] cTnT has been evaluated in canine patients receiving doxorubicin chemotherapy and those with congestive heart failure and extensive soft tissue trauma.[11] In a study of blunt chest trauma in dogs, cTnI concentrations were reported to be better correlated with myocardial damage than were ECG, cTnT, or CK-MB.[12] However, ECG analysis was brief (2–4 minutes), and the study was limited by lack of a ''gold standard'' to identify true myocardial cell damage. This study included normal canine plasma cTnI concentrations, but the assay used has since been modified to enhance specificity and sensitivity.[12] The purpose of the present study was to evaluate the normal range of plasma cTnI concentrations in dogs and cats using the Stratus® CS, an analyzer with improved sensitivity and specificity.

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Materials and Methods

Forty-one clinically normal dogs and 21 clinically normal cats were judged to be free of heart disease based on a complete physical examination. Echocardiograms, which were performed in approximately 25% of these animals (randomly chosen), were normal. The dogs and cats used in this study were owned by veterinarians and veterinary students at the University of Pennsylvania Veterinary School hospital. All animals still were clinically normal 6 months after collection of blood for the study. One to 3 milliliters of whole blood was collected by venipuncture into lithium heparin B-D vacutainers.[a] Samples were evaluated with a 2-site sandwich assay based on solid phase radial partition immunoassay technology by means of the Stratus® CS stat flourometric analyzer.[b] The analytical sensitivity of this machine is 0.03 ng/mL. All samples were evaluated within 2 hours of collection. Various dog breeds were represented in the population evaluated: 15 mixed-breed dogs, 6 Labrador Retrievers, 3 American Pit Bull Terriers, 3 German Shepherd Dogs, 2 Rottweilers, 1 Jack Russell Terrier, 1 Japanese Chin, 1 Pomeranian, 1 Toy Poodle, 1 German Short-Haired Pointer, 1 Cocker Spaniel, 1 Greyhound, 1 Boxer, 1 Rhodesian Ridgeback, 1 Whippet, 1 Belgian Malinois, and 1 Bichon Frise. The age range was 5 months to 10 years. All cats included in this study were domestic longhairs (n = 3) or domestic shorthairs (n = 18) ranging in age from 6 months to 10 years.

Results

The cTnI range for normal dogs was <0.03–0.07 ng/mL, with a mean of 0.02 ng/mL and a median of 0.02 ng/mL (SD = 0.0192 ng/mL). The cTnI range for normal cats was from <0.03 to 0.16 ng/mL, with a mean of 0.04 ng/mL and a median of 0.03 ng/mL (SD = 0.0387 ng/mL). Test results of <0.03 ng/mL are not accurate because of the sensitivity of the machine. Figure 1 shows the plasma cTnI concentrations for all dogs and cats included in this study. Table 1 summarizes the descriptive statistical data. We used

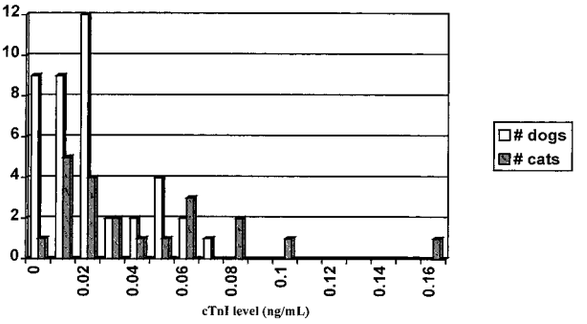

Fig 1. Plasma cTnI concentrations for all dogs and cats evaluated (*x* axis = cTnI concentration; *y* axis = number of individuals).

nonparametric tolerance intervals to determine the tolerance limits, which indicated that with a sample size of 41 dogs, we could accurately identify the 90th percentile with 95% confidence (an upper limit of 0.07 ng/mL cTnI).[13] For cats, with a sample size of 21, we could identify the 90th percentile with 90% confidence (an upper limit of 0.16 ng/mL cTnI).[13]

Discussion

The normal range of plasma cTnI in dogs is similar to that established for humans (0.0 to 0.04 ng/mL).[b] The mean for cats was higher than that for dogs, with a wider range as demonstrated by increased SD. These ranges suggest that the normal plasma cTnI concentration in peripheral blood of dogs and cats is similar to that of humans. cTnI appears to be a useful marker of myocardial cell damage in small animal species as in humans, and cTnI has proven to be a sensitive marker of myocardial damage in a canine model of infarction.[14] Clinical utility of this assay awaits more evaluations performed in animals with naturally occurring heart disease. Increases in plasma cTnI concentrations have been reported in a horse and in dogs with various myocardial complications.[10–12,14] Results from 1 study in dogs suggest that the plasma concentration of cTnI may be correlated with degree of myocardial injury.[12] Moreover, a study in humans indicated that blood cTnI concentration was correlated with myocardial infarct size and may therefore be useful for prognostic purposes.[15] Based on evidence from previous studies in humans and experimental animals, cTnI assays likely will be helpful in diagnosing myocarditis, myocardial contusion, early cardiotoxicity from chemotherapeutic agents such as doxorubicin, and response to therapy for congestive heart failure.

One appealing feature of cTnI evaluation is that it represents an objective way to measure severity of cardiac involvement and response to therapy. Monitoring plasma cTnI concentrations could be a sensitive, noninvasive, and cost-effective method for evaluating therapy in patients with congestive heart failure or myocardial diseases that cause cardiomyocyte damage. Although further studies are needed to evaluate cTnI in various forms of naturally occurring cardiovascular disease in small animal species, plasma concentrations >0.07 ng/mL in the dog and >0.16 ng/mL in the cat tentatively should be considered pathologic on the basis of these preliminary results. These observations are based on the established tolerance limits, which predict with the stated confidence the upper percentile given for the normal populations under consideration.

One major study limitation that must be remembered when interpreting these results is the difficulty in determining with certainty on physical examination that small animals have normal hearts. In particular, it is difficult to diagnose on physical examination asymptomatic myocardial disease in cats, which could explain the wider range of plasma cTnI concentrations seen in cats as compared with dogs. The wider range in cats was due primarily to 1 outlier data point (see Fig 1); this cat was evaluated by echocardiography and was considered normal. However, early myocardial disease can be difficult to diagnose even with the benefit of echocardiography. Early myocardial disease in dogs, especially dilated cardiomyopathy (DCM), also can be difficult to detect on physical examination (or with echocardiography), and many of the dogs included in this study are from large breeds that are predisposed to the development of DCM. However, all the dogs and cats included in this study still were clinically normal 6 months after collection of blood for cTnI sample, suggesting that clinically relevant heart disease was not present. Until cTnI assays are performed on a larger number of dogs and cats and animals can be followed over a long period of time, it will be difficult to definitively determine the normal cTnI range. Therefore, it is important to evaluate the entire clinical picture and other diagnostic test results (eg, thoracic radiographs, echocardiography, and electrocardiography) to avoid overinterpretation of plasma cTnI concentrations in individual animals.

Footnotes

[a] Vacutainer Systems, Becton Dickinson, Franklin Lakes, NJ
[b] Stratus® CS stat flourometric analyzer, Dade Behring, Newark, DE

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Table 1. Statistical evaluation of plasma cTnI concentration (ng/mL) in normal dogs and cats.

Species	Sample Size	Mean	SD	Range	Median	25% Median	75% Median
Dog	41	0.0210	0.0192	0–0.07[a]	0.0200	0.01	0.03
Cat	21	0.0448	0.0387	0–0.16[a]	0.03	0.0175	0.0625

[a] The upper value is the tolerance limit for the 90th percentile (with 90% confidence in the cat and 95% confidence in the dog).

References

1. O'Brien PJ, Landt Y, Landenson JH. Differential reactivity of cardiac and skeletal muscle from various species in a cardiac troponin I immunoassay. Clin Chem 1997;43:2333–2338.

2. Adams JE, Bodor GS, Davila-Roman VC, et al. Cardiac troponin I: A marker with high specificity for cardiac injury. Circulation 1993; 88:101–106.

3. La Vecchia L, Mezzena G, Zanolla L, et al. Cardiac troponin I as diagnostic and prognostic marker in severe heart failure. J Heart Lung Transplant 2000;19:644–652.

4. Chen YN, Wei JR, Zeng LJ, et al. Monitoring of cardiac troponin I in patients with acute heart failure. Ann Clin Biochem 1999;36:433–437.

5. Briassoulis G, Papadopoulos G, Zavas N, et al. Cardiac troponin I in fulminant adenovirus myocarditis treated with a 24-hour infusion of high-dose intravenous immunoglobulin. Pediatr Cardiol 2000;21: 391–394.

6. Rice MS, MacDonald DC. Appropriate roles of cardiac troponins in evaluating patients with chest pain. J Am Board Fam Pract 1999; 12:214–218.

7. Missov E, Calzolari C, Pau B. Circulating cardiac troponin I in severe congestive heart failure. Circulation 1997;96:2953–2958.

8. Smith SC, Ladenson JH, Mason JW, Jaffe AS. Elevations of cardiac troponin I associated with myocarditis. Circulation 1997;95:163–168.

9. Cardinale D, Sandri MT, Martinoni A. Left ventricular dysfunction predicted by early troponin I release after high-dose chemotherapy. J Am Coll Cardiol 2000;19:644–652.

10. Cornelisse CJ, Schott HC, Olivier NB, et al. Concentration of cardiac troponin I in a horse with a ruptured aortic regurgitation jet lesion and ventricular tachycardia. J Am Vet Med Assoc 2000;217: 231–235.

11. DeFrancesco TC, Atkins CE, Keene BW, et al. Evaluation of cardiac troponin T as a potential predictor of doxorubicin cardiotoxicity in dogs. J Vet Intern Med 2000;14:335 (abstract).

12. Schober K, Kirbach B, Oechtering G. Noninvasive assessment of myocardial cell injury in dogs with suspected cardiac contusion. Eur J Vet Cardiol 2000;1:17–25.

13. Conover WJ. Practical Nonparametric Statistics. New York, NY: Wiley and Sons; 1980.

14. Cummings B, Cummings P. Cardiac specific troponin-I release in canine experimental myocardial infarction: Development of a sensitive enzyme-linked immunoassay. J Mol Cell Cardiol 1987;19:999–1010.

15. Mair J, Wagner I, Morass B, et al. Cardiac troponin I release correlates with myocardial infarction size. Eur J Clin Chem Clin Biochem 1995;33:869–872.