Using Cardiac Biomarkers in Veterinary Practice

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KEYWORDS

• Natriuretic peptide • BNP • Troponin • Cardiac biomarkers • Heart disease

KEY POINTS

- Blood-based assays for cardiac biomarkers can assist in the diagnosis of heart disease in dogs and cats.
- The most established applications are differentiation of cardiac versus noncardiac causes of respiratory signs and the detection of preclinical cardiomyopathy.
- Cardiac biomarkers are best used as part of the overall clinical cardiac workup that includes the medical history, physical examination, electrocardiogram, thoracic radiographs, and echocardiography.
- The selection of proper patient populations in which to test is key to obtaining reliable results.
- Future applications might include the use of cardiac biomarkers to help guide therapy and improve patient outcomes.

INTRODUCTION: NATURE OF THE PROBLEM

The evaluation of cardiac disease in small animals can be challenging. The patient history is often nonspecific; the presence or intensity of a heart murmur on physical examination is not always a reliable measure of disease severity; concurrent pulmonary disease can confound the interpretation of thoracic radiographs; and other diagnostics, such as echocardiography, are relatively expensive and might not be readily available. For these reasons, blood-based biomarkers that are capable of detecting and staging cardiac disease are a subject of considerable interest.

A biomarker is a substance that is

- Specific to the organ or tissue under study
- Released in proportion to injury or disease

This article originally appeared in Veterinary Clinics of North America: Small Animal Practice, Volume 43, Issue 6, November 2013.
Disclosures: The author consults for and has received funding for clinical trials from IDEXX Laboratories, Westbrook, ME.
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Clin Lab Med 35 (2015) 555–566
http://dx.doi.org/10.1016/j.cll.2015.05.005 **labmed.theclinics.com**
0272-2712/15/$ – see front matter

In order to be clinically useful, the biomarker should provide information regarding diagnosis, prognosis, or response to treatment that is otherwise not readily available using conventional testing. The use of blood-based biomarkers for noncardiac organ systems, such as the use of gamma-glutamyl transferase to detect cholestasis or the use of creatinine to detect renal disease, is a familiar concept; cardiac biomarkers act in much the same fashion for the heart. The 2 cardiac biomarkers with the most extensive evaluation in small animals are cardiac troponin-I (cTnI) and 2 forms of B-type natriuretic peptide (BNP), namely, the C-terminal fragment (C-BNP) and the N-terminal fragment (NT-proBNP).

CARDIAC TROPONIN

The cardiac biomarker cTnI, along with troponin-T (cTnT) and troponin-C, form a conglomeration of 3 myocardial proteins that is bound to the actin backbone within myocardiocytes. The troponin complex regulates calcium binding and subsequent interaction between actin and myosin filaments. Damage to the myocardiocyte and to the sarcolemmal membrane dissociates troponin from the actin and allows leakage of troponin into the extracellular space where it then enters into the circulation. The cardiac isoforms of cTnI and cTnT are specific to cardiac tissue and are specific markers of myocardial cell injury or necrosis. In healthy patients, little to no cardiac troponin is detectable blood. Because of its high specificity for cardiac tissue, detection of either circulating cTnI or cTnT is one of the primary diagnostic tools used by emergency department clinicians to diagnose acute myocardial infarction in human patients. Cardiac troponin is also elevated in patients with chronic heart disease, although not to the extent that is seen in acute myocardial infarction; circulating concentrations of cTnI also are a fraction of those seen in acute myocardial infarction. There are 2 commercially available veterinary cardiac troponin assays (i-Stat Cardiac Troponin assay, Abaxis, Union City, CA; Troponin-I, IDEXX Laboratories, Westbrook, ME), both of which test for cTnI. Current veterinary tests are plagued by a relatively low limit of detection of approximately 0.2 ng/mL, whereas circulating cTnI concentrations in dogs with mild to moderate myxomatous mitral valve disease (MMVD) are often less than 0.03 ng/mL and can be detected only using newer high-sensitivity assays.[1] Despite these relatively modest elevations, cTnI concentrations are predictive of the outcome in human patients with chronic heart failure as well as in dogs with MMVD.[2] The troponin molecules are highly conserved across species, and many high-sensitivity assays designed for human testing can be used to detect canine and feline cTnI. Thus, cardiac troponin assays have the potential to provide both diagnostic and prognostic information. In a meta-analysis of more than 6800 human patients with stable chronic heart failure, patients with elevated cTnI or cTnT were 2.9 times more likely to die during the study follow-up period than those patients with lower values.[3] Acute myocardial infarction in dogs and cats is rare. However, chronic heart diseases, such as MMVD and dilated cardiomyopathy (DCM) in dogs and hypertrophic cardiomyopathy (HCM) in cats, are relatively common; the diagnostic and prognostic value of cardiac troponin is a subject of interest. There are several factors that potentially limit the usefulness of cardiac troponin in veterinary patients. Although elevated cardiac troponin is sensitive for the presence of myocardial injury, it is not specific to any one underlying cause. Moreover, animals with mild disease can have normal cTnI concentrations. Thus, the utility of the test to screen for specific heart diseases in various populations is limited. Cardiac troponin is partially excreted through renal mechanisms, and cardiac injury in the presence of chronic or acute kidney disease can result in false elevations.[4] Finally, cTnI concentrations increase slightly but