Using Cardiac Biomarkers in Veterinary Practice

Mark A. Oyama, DVM

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

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Section of Cardiology, Department of Clinical Studies-Philadelphia, School of Veterinary Medicine, University of Pennsylvania, 3900 Delancey Street, Philadelphia, PA 19104, USA
E-mail address: maoyama@vet.upenn.edu

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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

significantly with age; additional studies establishing age-related reference ranges are needed (**Box 1**).[5]

NATRIURETIC PEPTIDES

BNP and its parent protein proBNP along with A-type natriuretic peptide (ANP) and its parent protein proANP are the main natriuretic hormones produced by myocardial tissue. Both proBNP and proANP are constitutively produced by atrial and to a lesser extent ventricular myocardiocytes. Stress or stretch of the myocardium (for instance, in response to volume overload) increases the production of proBNP and proANP, particularly within ventricular myocardiocytes. On release, these substances are quickly cleaved into separate N-terminal and C-terminal fragments. C-BNP and C-terminal ANP (C-ANP) elicit vasodilation and diuresis through binding of specific natriuretic receptors found in vascular and renal tissue. Their actions provide a counterbalance to those of the renin-angiotensin-aldosterone system. In humans, C-BNP and NT-proBNP assays are primarily used to help discriminate between cardiac causes (ie, congestive heart failure [CHF]) and noncardiac causes of respiratory clinical signs as well as to help estimate the risk of morbidity and mortality in patients with chronic heart disease. C-BNP and C-ANP have short half-lives, whereas NT-proBNP and NT-proANP are more stable and make more attractive targets for assay detection. There are 3 commercially available assays in the United States for natriuretic peptides, all involving various plasma forms of BNP: one for C-BNP in dogs (Cardio-BNP, Antech Diagnostics, Chesterfield, MO) and 2 for NT-proBNP, one each for dogs (CardioPet proBNP-Canine, IDEXX Laboratories, Westbrook, ME) and cats (CardioPet proBNP-Feline, IDEXX Laboratories, Westbrook, ME). Both the C-BNP and NT-proBNP assays require special blood-collection techniques to slow degradation during collection and transport to the reference laboratory. C-BNP and NT-proBNP are elevated in a variety of cardiac conditions, including MMVD, DCM, and HCM.[6–8] Increased concentrations also are present in noncardiac disease conditions that secondarily affect the heart, such as hyperthyroidism and systemic and pulmonary hypertension.[9,10] In both dogs and cats, concentrations are positively correlated with radiographic and echocardiographic measures of disease severity, and the ability of C-BNP and NT-proBNP assays to provide diagnostic and prognostic information is a subject of considerable interest. Most of the studies investigating the clinical utility of BNP in veterinary patients involve testing for NT-proBNP, and comparatively little is known about specific guidelines and cut points using the C-BNP assay (**Box 2**).

INDICATIONS FOR C-BNP AND NT-PROBNP TESTING

There are several indications for C-BNP or NT-proBNP testing, including differentiating cardiac versus noncardiac causes of respiratory signs, detection of occult

Box 1
Key points regarding cTnI

- Marker of myocardial cell injury and necrosis.
- Specific for cardiac muscle injury but not specific as to the underlying cause.
- Elevated in dogs and cats with a variety of heart and systemic diseases.

Box 2
Key points regarding C-BNP and NT-proBNP

- Parent molecule, proBNP, is produced in myocardiocytes in response to mechanical stress.
- Both are formed from the cleavage of the parent molecule proBNP.
- Both are released into circulation in a variety of heart diseases in dogs and cats.
- Both are positively correlated to clinical, radiographic, and echocardiographic measures of disease severity.

DCM in Doberman pinschers and occult HCM in cats, and as a prognostic tool in dogs with MMVD or DCM.

Differentiation of Cardiac Versus Noncardiac Causes of Respiratory Signs

Dogs and cats with respiratory signs represent a considerable diagnostic challenge because, for many cases, the cause of the clinical signs is not immediately clear. Most potential causes can be classified as either cardiac in origin (ie, CHF) or noncardiac (primary airway or parenchymal diseases, such as asthma, chronic bronchitis, pneumonia, and so forth). Studies have demonstrated the utility of C-BNP and NT-proBNP assay in distinguishing the cause of respiratory signs in dogs[6,11,12] and the utility of the NT-proBNP assay in distinguishing the cause of respiratory signs in cats.[13,14] A low NT-proBNP concentration is most consistent of a noncardiac cause, whereas an elevated concentration is more suggestive of CHF. In human medicine, NT-proBNP is best used as a test to help rule out CHF because patients with low or normal NT-proBNP are highly unlikely to have CHF. The diagnostic value of an elevated NT-proBNP concentration is less than that of a low concentration because patients with symptomatic respiratory disease and concurrent asymptomatic heart disease could have elevated concentrations. For this reason, the recommended cutoff values suggestive of a cardiac cause of respiratory signs in dogs and cats are more than the upper reference value for healthy animals. NT-proBNP and C-BNP assays are not stand-alone tests; their results should be evaluated in the context of the medical history, physical examination, and other diagnostic testing, such as radiography and echocardiography. In cases for which traditional diagnostic testing reveals the cause of the respiratory signs, BNP testing adds little additional value to the already apparent diagnosis. In cases for which the diagnosis is uncertain, the addition of the NT-proBNP assay to the diagnostic workup improved the accuracy and confidence of diagnosis in cats with respiratory signs (**Box 3**).[15]

Box 3
Guidelines for differentiation of cardiac versus noncardiac causes of respiratory signs in dogs and cats using NT-proBNP assay

- Low or normal NT-proBNP concentration is most consistent with a noncardiac cause of the current signs, whereas elevated NT-proBNP is more suggestive of a cardiac cause, such as CHF.
- In animals with asymptomatic heart disease, an increased NT-proBNP concentration can confound the diagnosis of a noncardiac cause of the respiratory signs.
- Results should be viewed in context of the medical history, physical examination, and traditional diagnostics, such as thoracic radiography.

Detection of Occult Cardiomyopathy in Doberman Pinschers and in Cats

Cardiomyopathy is common in particular breeds of dogs and cats. For instance, the lifetime incidence of DCM in Doberman pinschers is as high as 60%, and the Maine coon, ragdoll, and Persian breeds of cats, among others, are highly predisposed to HCM.[16,17] Both DCM and HCM are characterized by a long preclinical (occult) phase during which clinical signs of disease are absent despite the presence of underlying cardiac dysfunction. In animals with occult cardiomyopathy, the first clinical sign of disease can be sudden death or life-threatening CHF; thus, the detection of preclinical disease using preliminary tests is a subject of interest. The gold standard for the diagnosis of occult DCM in Doberman pinschers is the detection of ventricular premature beats via in-hospital electrocardiogram (ECG) or Holter monitoring and/or the detection of left ventricular systolic dysfunction via echocardiography. Some dogs with occult DCM will demonstrate both abnormalities, whereas others will have only one or the other. Three studies have investigated the ability to detect occult DCM in Doberman pinschers, 2 involving NT-proBNP[18,19] and one involving C-BNP.[20] C-BNP has a high sensitivity (95.2%) but a low specificity (61.9%), resulting in a high number of false-positive results. The studies involving NT-proBNP yielded similar results; the NT-proBNP assay was good at detecting dogs with systolic dysfunction whether or not they also had arrhythmias, but was poor at detecting dogs whose sole criterion for occult DCM was ventricular arrhythmias. Thus, NT-proBNP cannot be used as a stand-alone test to detect occult DCM. However, the combination of an NT-proBNP assay with Holter monitoring was 94.5% sensitive and 87.8% specific for detecting all dogs with occult disease.[19] From these studies, NT-proBNP assay does not replace the current gold standards for diagnosis. In instances when echocardiography is not immediately accessible, an elevated NT-proBNP or C-BNP concentration would support the pursuit of echocardiographic examination. Thus, BNP assesses the likelihood of finding significant abnormalities on gold standard testing rather than being a diagnostic test in and of itself. This distinction is subtle but important if the number of false-positive and negative results inherent in the BNP assays are to be avoided.

Feline cardiomyopathy has a long preclinical phase similar to canine DCM, and detection of underlying heart disease in apparently healthy cats can be challenging. Unlike the situation in the dog, wherein the presence of a heart murmur is a reliable sign of underlying heart disease, cats commonly have heart murmurs of benign origin. Moreover, not all cats with cardiomyopathy will have a heart murmur; this further confounds the ability to readily detect heart disease on physical examination. The gold standard for the diagnosis of feline cardiomyopathy is echocardiography. In instances when heart disease is suspected because of a murmur, gallop, or arrhythmia, NT-proBNP has a sensitivity of 70% to 100% and a specificity of 67% to 100% to indicate the presence of significant echocardiographic abnormalities.[8,21–23] The exact sensitivity and specificity depends on the cutoff values used, with lower cutoff values resulting in higher sensitivity but lower specificity, and higher cutoff values resulting in lower sensitivity but higher specificity (**Table 1**). The NT-proBNP assay is best suited to identify cats with moderate to severe echocardiographic changes, and it is these cats that likely benefit from additional monitoring or treatment. NT-proBNP testing has been studied only in cats that have risk factors for cardiomyopathy (ie, murmur, gallop, arrhythmia, and so forth), and the clinical usefulness of NT-proBNP assay to detect cardiomyopathy in the general population is unknown (**Box 4**). For this reason, indiscriminate testing of cats is not recommended, particularly in instances when the likelihood of significant disease is very low (ie, young cats undergoing neutering). The

Table 1
Diagnostic uses of cardiac biomarker tests in dogs and cats

Indication	Marker	Cutoff Values	Sensitivity (%)	Specificity (%)	Comments
Differentiating cardiac vs noncardiac causes of respiratory signs in cats	NT-proBNP[13,14]	220, 265 (pmol/L)	90–94	88	Low values indicate cardiac causes are unlikely, high values suggest CHF
Differentiating cardiac vs noncardiac causes of respiratory signs in dogs	NT-proBNP[12,38]	1158, 1400 (pmol/L)	86–92	81	Low values indicate cardiac causes are unlikely, high values suggest CHF
	C-BNP[6,11]	17.4, 6.0 (pg/mL)	86–90	78–81	Low values indicate cardiac causes are unlikely, high values suggest CHF
Detection of cardiomyopathy in at-risk cats	cTnI[33,34]	0.157, 0.20 (ng/mL)	85–87	84–97	Elevated values not specific for primary heart disease
	NT-proBNP[21–23]	95, 99, 100 (pmol/L)	71–92	94–100	Studies were performed in populations with clinical suspicion for heart disease (ie, those with murmur, gallop, arrhythmias, and so forth)
Detection of cardiomyopathy in Doberman pinschers	NT-proBNP[18,19]	457, 550 (pmol/L)	70–79	81–90	NT-proBNP poor at detecting dogs with arrhythmias only, sensitivity and specificity improved if used in tandem with Holter monitoring
	C-BNP[20]	6.2 (pg/mL)	95	62	Low specificity results in large number of false positives

The reported cutoff values and range of respective sensitivities and specificities for various indications are presented. Cardiac biomarker assays indicate risk of a particular condition being present, and additional diagnostics are often needed to obtain a definitive diagnosis. Cardiac biomarker assays are not stand-alone diagnostic assays. When interpreting results, values that far exceed cutoff values provide more reliable information than those at or near the cutoff value.

Box 4
Guidelines for detection of occult cardiomyopathy in Doberman pinschers and in cats using NT-proBNP assay

- Testing should be done on selected patients that are at high risk for cardiac disease, such as adult Doberman pinschers and Maine coon cats and cats with a heart murmur or arrhythmia.
- Elevated concentrations increase the likelihood of clinically significant echocardiographic abnormalities, and further diagnostics should be pursued.
- Elevated concentrations could help assess the need or urgency to pursue more costly or time-consuming diagnostic tests if the presence of clinically significant disease is initially unclear.
- Elevated concentrations are not diagnostic of any one particular disease, and results should be interpreted in the context of the medical history, physical examination, and traditional diagnostic testing.

likelihood of a test result being either false positive or false negative is partly dependent on the prevalence of the disease condition in the population being tested. The less prevalent the disease, the less likely a patient has the disease, even if a test result is positive. As an example, in a dog living in Alaska, there is a high likelihood that a positive heartworm antigen test is actually a false-positive result simply because of the very low prevalence of disease in this region, whereas a positive heartworm antigen test from a dog living in the Mississippi River Valley is almost certainly a true positive. Thus, clinicians must select the appropriate patient population in which to test in order to optimize the reliability of the assay.

Predicting Morbidity and Mortality in Dogs with Heart Disease

Aside from their role in the diagnosis of heart disease, whether BNP assays can predict the risk of CHF in dogs with preclinical disease or predict the risk of cardiovascular mortality is a subject of interest. The use of the NT-proBNP assay to predict the first-onset of CHF in dogs with preclinical MMVD has been studied. In one study, baseline NT-proBNP concentration was 80% sensitive and 76% specific for identifying dogs that developed CHF within the subsequent 12 months.[24] Another study in dogs with preclinical MMVD reported that those with NT-proBNP greater than 1500 pmol/L were approximately 6 times more likely to develop CHF over the subsequent 3 to 6 months than dogs with lower values.[25] The predictive value of NT-proBNP was best when combined with measures of radiographic or echocardiographic left side of the heart size, and NT-proBNP should be used alongside traditional diagnostic methods.

Several studies have revealed an association between NT-proBNP and survival in dogs with MMVD.[2,24,26] In the most recent studies, increases in NT-proBNP, high sensitivity cTnI, and echocardiographic heart size were negatively associated with survival.[2] For each incremental increase of 100 pmol/L in NT-proBNP, the risk of death caused by cardiac disease increased by 7%. Two studies have investigated NT-proBNP and the survival of dogs with DCM. In one study, Doberman pinschers with DCM and elevated NT-proBNP had a median survival time that was 6 times shorter than those with lower values[19]; in another study, NT-proBNP predicted the survival of dogs with DCM 60 days after the initial examination.[27]

The use of the NT-proBNP assay to help predict the risk of either CHF or survival has several important limitations, and further studies are needed before the assay becomes part of the standard workup for dogs with MMVD (**Box 5**). Firstly, sensitivity and specificity are performance indices that apply to populations of individuals; the

Box 5
Guidelines for stratification of risk in dogs with MMVD

- Dogs with preclinical MMVD, radiographic or echocardiographic heart enlargement, and NT-proBNP greater than 1500 pmol/L are likely at an increased risk for the development of CHF.
- In dogs at an increased risk of morbidity or mortality, increased vigilance for subtle signs of heart failure and more frequent monitoring is recommended.
- There are no clinical studies assessing the value of treatment decisions based on NT-proBNP concentrations.

accuracy of the diagnostic test in any one individual is not 100%. Secondly, elevated NT-proBNP concentrations specify the risk, not the certainty, of morbidity or mortality. Elevated NT-proBNP, especially in dogs with radiographic or echocardiographic cardiomegaly, likely warrants heightened vigilance for early signs of CHF. In animals at high risk for CHF, owners can be counseled about how to obtain the animal's resting respiratory rate. In healthy dogs, the average sleeping respiratory rate is 13 breaths per minute and rarely exceeds 30 breaths per minute.[28] Respiratory rates of more than 41 breaths per minute have been shown to be a sensitive indicator for the detection of CHF.[29] Finally, there are no data indicating that NT-proBNP concentrations can be used to guide therapy decisions, such as when to initiate or alter existing drugs, such as diuretics or angiotensin converting enzyme inhibitor. In human patients with heart failure, 2 meta-analyses[30,31] indicated that BNP-guided therapy resulted in better outcomes, although these results are controversial. In one study of dogs being treated for CHF, dogs with NT-proBNP less than 965 pmol/L following therapy survived longer than those dogs with NT-proBNP concentrations more than 965 pmol/L,[32] suggesting the possibility that therapeutic targets of NT-proBNP could be useful. These data require specifically designed prospective studies for validation.

INDICATIONS FOR CARDIAC TROPONIN TESTING

Specific guidelines for cardiac troponin testing are not well established. Circumstances that might warrant testing include suspected myocarditis or cardiomyopathy or as a prognostic tool in dogs with MMVD or DCM. Troponin testing has also been used to detect myocardial injury in babesiosis, gastric dilatation and volvulus, brachycephalic airway syndrome, sepsis, racing and sled-dog athletes, heartworm disease, dogs receiving doxorubicin, and cases of respiratory distress with unknown cause. In general, cardiac troponin concentrations reflect the severity of cardiac injury and are inversely associated with morbidity and mortality[1,2,5]; however, more studies are needed before specific treatment guidelines can be made using specific concentrations.

Cats with HCM have higher cTnI concentrations than healthy cats; in 2 small studies, elevated cTnI was 85% to 87% sensitive and 84% to 97% specific for the detection of disease.[33,34] Comparatively, the diagnostic ability of cTnI to detect preclinical (occult) DCM in dogs is poor.[20] The cTnI concentrations are higher in cats and dogs with respiratory signs secondary to CHF, but the overlap between these animals and animals with respiratory signs caused by noncardiac causes is wide enough to limit clinical usefulness.[11,35] Elevated cTnI is not specific to primary cardiac disease because any systemic condition that causes hypoxemia and myocardial ischemia could result in elevated cTnI. In the author's experience, some of the highest cTnI

concentrations observed have been from dogs with severe pulmonary parenchymal disease and resultant hypoxemia.

In dogs with MMVD, a serum cTnI concentration more than 0.025 ng/mL was associated with a 1.9 times risk for death compared with lower concentrations.[2] Animals with elevated troponin concentrations might benefit from further diagnostic tests, such as ECG, thoracic radiography, and echocardiography (**Box 6**). Whether cardiac troponin concentrations can be used to help guide therapy is an intriguing possibility but requires well-designed prospective trials. In the author's experience, serial troponin measurements in dogs with suspected myocarditis offer some prognostic information; declining values often signify a one-time insult and myocardial recovery, whereas persistently elevated or increasing concentrations are a poor prognostic indicator.

LIMITATIONS OF CARDIAC BIOMARKERS

There are important limitations to the use of cardiac biomarkers in veterinary patients. These limitations involve technical issues, such as failure to properly collect and transport samples, as well as biologic issues, such as the effect of systemic disease on the production or excretion of cTnI and NT-proBNP. Both NT-proBNP and C-BNP assays require special sample collection procedures using manufacturer-supplied blood-collection tubes designed to prevent degradation of BNP during shipping. Improper collection techniques, extended storage at room temperature, or multiple freeze-thaw cycles likely produce inaccurate results. Both NT-proBNP and C-BNP are excreted via renal filtration and can be elevated in animals with acute or chronic kidney disease.[36,37] These elevations are relatively modest in patients with mild disease but increase as renal function worsens. Many clinical studies of NT-proBNP excluded patients with renal disease, highlighting the need to interpret cutoff values in these patients with caution. Other conditions associated with increased NT-proBNP include pulmonary hypertension[10] and feline hyperthyroidism,[9] and results from animals with these diseases should be interpreted with similar caution. Since the introduction of the canine NT-proBNP assay in 2006, there have been several revisions to the assay, the most recent involving the introduction of special blood-collection tubes in 2008. Earlier clinical studies, including those investigating the detection of occult DCM in Doberman pinschers and the discrimination of cardiac versus noncardiac causes of respiratory signs in dogs were performed using the pre-2008 version of the canine assay. Ideally, these studies should be repeated using the most current version of the assay.

Box 6
Guidelines for cardiac troponin testing

- Consider testing in animals with suspected myocarditis or myocardial injury.
- Concentrations generally reflect the magnitude of myocardial injury.
- Serial evaluations that reveal declining values suggest a one-time insult and myocardial recovery, whereas persistently elevated or increasing values suggest ongoing myocardial injury.
- Consider testing as an adjunctive diagnostic test to detect cats with a high likelihood for HCM.
- It is not useful as a test to differentiate cardiac versus noncardiac causes of respiratory signs in dogs and cats.

SUMMARY

Cardiac biomarkers are an exciting and growing science. Much data regarding their clinical use in dogs and cats have been generated; however, many questions remain unanswered. The most established applications involve use of cTnI to help detect myocarditis and feline cardiomyopathy and the use of NT-proBNP to help detect occult cardiomyopathy and differentiate cardiac versus noncardiac causes of respiratory signs. Compared with NT-proBNP, there is relatively little data regarding C-BNP. However, applications of the C-BNP assay are likely similar to those involving NT-proBNP. Both cTnI and NT-proBNP assays help predict the risk of cardiovascular mortality in dogs with MMVD, but additional study is needed to better understand how to use these data in everyday clinical practice. Cardiac biomarker tests are complementary to existing cardiac diagnostic testing and should be interpreted in the context of the overall clinical picture rather than being used as a stand-alone test. Future studies will help determine whether cardiac biomarker assays can help guide therapy and lead to improved outcomes in dogs and cats with cardiac disease.

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