REVIEW

Cardiac biomarkers in cats

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Abstract Cardiac biomarkers have been used in cats as part of the clinical assessment of heart disease for over a decade. They are widely available to practitioners through commercial reference laboratories. The evidence base for the use of cardiac biomarkers (primarily N-terminal pro-B type natriuretic peptide and cardiac troponin I) in cats is comprehensively reviewed in this article, focusing on each of six specific areas: distinguishing cardiac from non-cardiac causes of respiratory distress; measurement of cardiac biomarkers in urine and pleural fluid; identification of occult cardiomyopathy; effects of systemic disease on circulating concentrations of cardiac biomarkers; point-of-care biomarker testing, and the possible prognostic utility of cardiac biomarker measurement.
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Introduction

For over a decade, the measurement of cardiac biomarkers has been reported in cats with a variety of cardiac and systemic diseases, and measurement of N-terminal pro-B type natriuretic peptide (NTproBNP) and cardiac troponin I (cTnI) has now become commonplace in general and referral practices. The diagnosis of cardiac disease in cats poses particular challenges to many practitioners, including: a high prevalence of sub-clinical (or 'occult') cardiomyopathy, the inconsistent implications of a heart murmur in asymptomatic cats of different ages, and a tendency for the first clinical signs of heart failure to be of sudden onset and severe. These assays offer a straightforward and accessible test, which often feature in the diagnostic investigation of feline cardiac disease by veterinarians in general and referral practice alike. However, understanding of the clinical utility of these laboratory tests is ever evolving.

This review was aimed at updating the reader on the published veterinary literature regarding

Abbreviations	
CHF	congestive heart failure
CKD	chronic kidney disease
cTnI	cardiac troponin I
cTnT	cardiac troponin T
HCM	hypertrophic cardiomyopathy
NPV	negative predictive value
NTproBNP	N-terminal pro-B type natriuretic peptide
PPV	positive predictive value

Table 1 Search terms used in combination to review electronic online databases for recent published literature on feline cardiac biomarkers.

Biomarker	Natriuretic
Cardiac	NTproANP
Cardiomyopathy	NT-proANP
Cat	NTproBNP
cTnI	NT-proBNP
cTnT	Peptide
Feline	Troponin

cardiac biomarkers in cats. The physiology of the natriuretic peptides and cardiac troponins has been reviewed in detail elsewhere. The focus of this review was on the role of cardiac biomarkers in clinical decision-making.

Review methods

Published literature was searched using Medline, Web of Science and Google Scholar electronic databases.[c,d,e] The terms used in various combinations are listed in Table 1. The reference lists of retrieved articles were also manually searched and the relevant citations were retrieved. Conference proceedings and research abstracts were not included as part of the formal review process, but the findings of two recent research abstracts were chosen for report because of their specific relevance to this area of study. Information recorded from each reviewed publication included: citation details; biomarkers measured; the assay used; the number of animals; and the hypothesis, findings, conclusions and limitations of each study. A second party then crosschecked this for errors.

Summaries of the studies reviewed in this manuscript were tabulated (Tables 2—5) for quick reference. This review initially considers biomarkers measured in reference laboratories. Some of the newer, point-of-care tests are considered later in this manuscript.

Distinguishing cardiac from non-cardiac causes of respiratory distress

Cats with respiratory distress are often unstable and frequently intolerant of any handling or

diagnostic interventions. Although echocardiography is useful for identifying cats with cardiogenic respiratory distress, it may not always be available. Measurement of a cardiac biomarker may be helpful if a blood sample can be obtained with minimal restraint, and this might be safer than thoracic radiography. Eight studies were identified that compared cardiac biomarker concentrations in cats with cardiac and non-cardiac causes of respiratory distress: four studies investigated cTnI[1—4] and four investigated natriuretic peptides (of which, all four featured NTproBNP and one also featured NTproANP)[5—8] (Table 2).

Of the cTnI studies, 75% reported a higher median cTnI concentration in the cardiac vs. the non-cardiac group and one failed to detect a statistically significant difference. The study in which no difference was detected[1] also had the smallest sample size, so this finding may reflect that the statistical comparison was under powered. All studies in which a difference was identified reported a considerable overlap in cTnI values between cardiac and non-cardiac groups, suggesting that a single cut-off value to identify cardiogenic dyspnea in cats is unlikely to be clinically useful.

In contrast, NTproBNP has shown greater accuracy in distinguishing cats with cardiac dyspnea from those with non-cardiac causes: all four studies reviewed reported higher median NTproBNP concentration in cats with cardiogenic respiratory distress.[5—8] The one study investigating NTproANP reported that the overall accuracy of this test was lower than NTproBNP, but despite this, the test was still useful for detecting cardiogenic dyspnea.[6] Published NTproBNP cut-off values for identifying cats with acute congestive heart failure (CHF) ranged from 214 to 277 pmol/L, with a sensitivity generally over 85% and a specificity of 84—88%. However, because these studies were published over a 5-year time frame and used three different commercially available assays, the cut-off values and sensitivity/specificity data should not be