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Utility of plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) to distinguish between congestive heart failure and non-cardiac causes of acute dyspnea in cats

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Abstract *Background:* Circulating plasma N-terminal pro-brain natriuretic peptide (NT-proBNP) concentration facilitates emergency diagnosis of congestive heart failure (CHF) in people. Its utility to discriminate between dyspneic cats with CHF vs. primary respiratory disease requires further assessment. Our objectives were to determine if NT-proBNP (1) differentiates dyspneic cats with CHF vs. primary respiratory disease; (2) increases with renal insufficiency; (3) correlates with left atrial dimension, radiographic cardiomegaly, and estimated left ventricular filling pressure (E/E_a).
Methods: NT-proBNP was measured in 167 dyspneic cats (66 primary respiratory disease, 101 CHF) to evaluate (1) relationship with clinical parameters; (2) ability to distinguish CHF from primary respiratory disease; (3) optimal cut-off values using receiver operating characteristic (ROC) curve analysis.
Results: NT-proBNP (1) was higher (median and inter-quartile [25th—75th] percentile) in CHF (754 pmol/L; 437, 1035 pmol/L) vs. primary respiratory disease (76.5 pmol/L; 24, 180 pmol/L) cohorts ($P < 0.001$); (2) positively correlated in CHF cats with increased inter-ventricular septal end-diastolic thickness ($\rho = 0.266$; $P = 0.007$) and LV free wall thickness ($\rho = 0.218$; $P = 0.027$), but not with radiographic heart size, left atrial size, left ventricular dimensions, E/E_a ratio, BUN, creatinine, or thyroxine; (3) distinguished dyspneic CHF cats from primary respiratory disease at 265 pmol/L cut-off value with 90.2% sensitivity, 87.9% specificity, 92% positive predictive value, and 85.3% negative predictive value (area under ROC curve, 0.94).
Conclusions: NT-proBNP accurately discriminated CHF from respiratory disease causes of dyspnea.

Introduction

Clinical interest in cardiac biomarkers has been stimulated by evidence that they facilitate cardiovascular diagnosis, risk stratification, and prognosis. In particular, the natriuretic peptides have become increasingly regarded as sensitive, specific, and reliable tools that are useful to help recognize and manage patients with heart failure.[1—3] The brain and atrial type natriuretic peptides are a family of important hormones that effect cardiovascular homeostasis. Brain natriuretic peptide (BNP) appears to provide greater diagnostic performance compared with atrial natriuretic peptide (ANP), leading to rigorous clinical investigation of this hormone.[4,5]

Brain natriuretic peptide is predominantly secreted from ventricular myocytes in response to myocardial stretch, volume, and pressure overload. It promotes natriuresis, diuresis, and vasodilatation — actions that oppose physiologic abnormalities that are activated during congestive heart failure (CHF).[6—8] The precursor molecule BNP is released into the circulation and becomes cleaved into the biologically active C-terminal BNP fragment and biologically inactive NT-proBNP fragment by serum proteases. Because plasma NT-proBNP concentration is raised in states of cardiac impairment[9,10] and has longer biological half-life, its measurement has provided a useful and effective adjunct to facilitate emergency diagnosis and treatment of CHF in people.[3,11—13]

Canine studies have also revealed that circulating natriuretic peptide concentrations vary in accordance with severity of heart disease and heart failure.[14—16] As such, measurement of circulating natriuretic peptides can provide a clinically useful adjunct test to distinguish between asymptomatic dogs with chronic acquired valve disease and dilated cardiomyopathy, from healthy dogs.[16] It can also help to discriminate CHF from primary pulmonary disease in dogs with dyspnea or cough.[16—18]

In the cat distinguishing dyspnea caused by CHF from primary respiratory conditions remains challenging. History is relatively insensitive, clinical signs are non-specific and variable, and substantial limitations are associated with physical examination, electrocardiography and thoracic radiography.[19—21] Echocardiography is the gold standard for assessing feline cardiac structure and function,[22] but has limited availability, and may not reflect with certainty the presence of acute diastolic dysfunction, or the exacerbation of heart failure. This underscores the need for a sensitive and specific cardiac biomarker to facilitate clinical diagnosis of CHF. Studies investigating natriuretic