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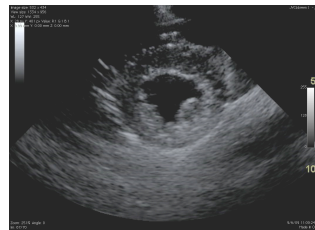


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## **NT-proBNP – CARDIAC BIOMARKERS – 3 PAGES**



B- type natriuretic peptide is released from the heart when ventricular filling pressure is increased. ProBNP is cleaved into NT-proBNP (inactive molecule) and BNP in a 1:1 ratio. BNP release results in vasodilation and diuresis to counteract the volume and pressure overload in the heart, which can occur with heart disease and/or heart failure secondary to both acquired and congenital heart disease. NT-proBNP is an inactive molecule but is more stable than BNP and is more easily measured.

NT-proBNP is a cardiac biomarker, which can aid in the differentiation of heart disease and respiratory disease in dyspneic patients and can also provide added information for early detection of cardiac disease in subclinical patients. In the future, we may be able to use it to monitor therapy or determine prognosis but this has not yet been fully determined or at least reported in the current literature.

Plasma NT-proANP was shown in dogs to have the highest sensitivity (95.5%) and specificity (84.6%) in a comparative study in 2007 by Solter et al. between Plasma NT-proAnp, BNP, ET-1 and c-TnI in 2007 but is currently only available for testing in Europe.

Biomarkers are still considered adjunctive tests and lead to further testing to differentiate respiratory versus cardiac origin of the clinical signs.

Indications for use:

-Small dogs: This can be used as a screening test in dogs with murmurs that are preclinical and can be used as a guide to recommend additional more expensive diagnostic tests. In one study, NT-proBNP increased in proportion with the grade of the murmur and with degree of cardiac disease. This would be especially useful in at- risk breeds such as Cavalier King Charles Spaniels, Cocker Spaniels, Dobermans, and Boxers for example.

- Congenital murmurs: Consider running an NT-proBNP in puppies with severe murmurs. This is most useful in the case of a PDA which results in cardiomegaly in very young dogs. An elevation in a young dog would indicate the need for further testing.

Cats: This test may be of most use in detecting subclinical heart disease in cats as our current screening test is not very sensitive (auscultation). If elevated, proceed with additional imaging such as radiographs and ultrasound. May provide better screening information than standard auscultation as cats without murmurs can have significant disease.

- Screening in cats with breed predispositions (Maine Coon); cats with murmurs and gallops
- Animals with dyspnea/ cough/ respiratory distress- this is perhaps the most important indication as there is a fairly good differentiation between animals with primary cardiac disease and pulmonary disease – although may be of increased use once bedside test is available. Reineke suggests the use of biomarkers is respiratory distress patients than cannot safely withstand manual restraint for thoracic radiographs or echocardiography.

Range of values

Dogs:

500 pmol/l – normal, clinically significant heart disease is not present, dyspnea is not due to CHF.

500-1100 pmol/l – elevated, heart disease may be present. Pursue additional diagnostics especially if signs are present.

1100-1725 pmol/l – elevated and consistent with heart disease and possibly CHF – strongly recommend additional work up.

>1725 pmol/l – significant elevation – CHF is likely and would likely be the cause of the dyspnea.

Cats:

< 45 – not elevated; heart disease is unlikely

45-70 – elevated, heart disease may be present – consider work up/ echocardiogram

70-180 elevated, heart disease is present +/- CHF – echo and radiographs if clinical

>180 significantly elevated, CHF likely

Submission - Idexx:

Request special submission kit from Idexx; collect blood into a purple top and spin immediately, transfer plasma to enclosed plastic tube or another purple top (if kit not immediately available) and freeze plasma immediately.

Follow submission directions - freeze the specialized cold packs and submit sample(s) in Styrofoam container and Fedex overnight. – \$60

Example of studies evaluating NT-proBNP:

Serum NT-proBNP levels were elevated in dogs with cardiac disease compared to healthy dogs and a level of >445 pmol/l can be used as the cut off with a sensitivity of 83% and specificity of 90%.

(Oyama et al 2008). In this study: NT-proBNP was significantly higher in dogs with class II and III heart disease compared with class I heart disease, and was significantly higher in dogs with a more severe murmur of grade V (median 2233 pmol/l) compared with grade III or IV (median 1010 pmol/l) or grade I or II murmur – median 646 pmol/l. Dogs with CHF had an increased level above 1725 pmol/l and less than 820 pmol/l in dogs without CHF (sensitivity 88% and specificity of 76%, PPV 77.5% and NPV of 87%). NT-proBNP levels also positively correlated with radiographic size/ cardiomegaly, heart rate, respiratory rate, LA/AO ratio, BUN and creatinine for examples.

Dogs with CHF had a much higher NT-proBNP level than dogs with primary respiratory disease (2554 pmol/l vs. 357 pmol/l) but interestingly in this study, NT-proBNP did not correlate with vertebral heart score or LA/Ao ratio (Fine et al, 2008).

NTproBNP was significantly elevated in dyspneic cats with cardiac failure compared to cats with primary respiratory disease when using a cut off of 180 pmol/L with a sensitivity of 94.1% and a

specificity of 86.4% (PPV of 91.4% and NPV of 90.5%) (Oyama NAVC 2008). In asymptomatic cats, NT-proBNP was able to differentiate cats with occult cardiac disease compared to healthy cats using a cut off of 40 pmol/L with a sensitivity of 100% and a specificity of 87.5% (Oyama NAVC 2008).

- 1) CardioPet proBNP Idexx test pamphlet 2008
- 2) Fine DM et al. Evaluation of circulating amino terminal-pro-B-type natriuretic peptide concentration in dogs with respiratory distress attributable to congestive heart failure or primary pulmonary disease. J AM Vet Med Assoc 2008;232:1674-1679.
- 3) Oyama MA Using BNP tests in dogs and cats with heart disease. ACVIM proceedings 2008. San Antonio.
- 4) Hori et al. Evaluation of NT-proBNP and CT-ANP as markers of concentric hypertrophy in dogs with a model of compensated aortic stenosis. J Vet Intern Med 2008; 22:1118-1123.
- 5) Tarnow et al. Predictive value of natriuretic peptides in dogs with mitral valve disease. Vet J. 2008; July 31.
- 6) Reineke E. A Diagnostic Approach to Respiratory Distress in ACVIM 2011 Proceedings.

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