Clinical sheet - Cardiology

Clinical usefulness of the NT-proBNP test

BNP (B-type or brain natriuretic peptide) is a hormone produced by the atrial and ventricular myocytes in humans, dogs and cats. It is secreted during myocardial stretch, pressure overload, neurohormonal stimuli.1,2 The blood concentration of BNP increases during acute congestive heart failure,4,5 asymptomatic and minimally symptomatic systolic and diastolic dysfunction.6-8 Levels of BNP have been shown to discriminate dyspnea of non-cardiac origin from congestive heart failure (CHF) in dogs and cats with good specificity and sensitivity (both > 80%).3,5 Levels of BNP have also been shown to be correlated to disease severity in cats.11 However, studies in Maine Coon cats concluded that BNP levels could discriminate normal cats from cats with severe hypertrophic cardiomyopathy (HCM), but not normal cats from cats with mild to moderate disease.9 Several studies have shown a correlation between BNP levels and left atrial size in cats.4,11,12

There is a now a commercially available test to measure BNP (or to be more precise a fragment of the more stable N terminal of the prohormone: NT-proBNP) levels in dogs and cats (CardiopetTM by Idexx).

Guidelines for interpretation have been proposed as follows:

In cats:

- BNP levels < 100 pmol/l: presence of heart disease highly unlikely
- BNP levels between 100 and 270 pmol/l: heart disease is unlikely
- BNP levels > 270 pmol/l: clinically significant cardiomyopathy

In dogs:

- BNP levels < 900 pmol/l: Likelihood that symptoms are due to CHF is low
- BNP levels between 900 and 1800 pmol/l: not diagnostic
- BNP levels > 1800 pmol/l: Likelihood that symptoms are due to CHF is high

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A first draw-back of this test is the time required to get results: 2-3 days. This is hardly helpful in an emergency setting.

Therefore, its main application would be in the detection of heart disease in a stable patient. This would be particularly interesting in cats, in which other markers such as heart murmurs are not always present.

A recent study looked at the ability of NT-proBNP to distinguish normal cats from cats with occult HCM. 12 They found that a cut-off value of > 46 pmol/l had a specificity of 91.2%, and a sensitivity of 85.8%, and that a cut-off value > 100 pmol/l had a specificity of 100%, and a sensitivity of 70.8%.12 Similar cut-off values differentiating normal from cats with HCM have been identified in other studies.11

In the light of these studies, NT-proBNP appears to be a very good test to discriminate normal from abnormal. However, one has to take in account the prevalence of the disease in the overall population. If we look at the prevalence of HCM in the overall feline population, and that we assume that it is 2%, and if we take as an hypothesis a sensitivity of 95%, and a specificity of 96%, then 67% of the cats testing positive (NT-proBNP > 100 pmol/l) will be false positive. Conversely, 99.9% of the cats having a NT-proBNP < 100 pmol/l will be true negatives. Therefore, this test has an excellent negative predictive value (absence of disease), but a positive test may be a false positive. The lower the overall prevalence, the higher the proportion of false positive will be.

Let us apply the same reasoning to another population of cats: Ragdolls, where the prevalence of HCM has been estimated at around 30%. If we use the same test with the same sensitivity and specificity, then the number of false positive drops to 8.9%, and the number of true negative to 96.4%.

Finally if we look solely at cats with heart murmurs, where the prevalence of HCM climbs to roughly 50%, then the number of false positive drops to 4%, and the number of true negative to 95%.

I ran a small study to illustrate these points. The goal was to correlate BNP levels to echocardiographic findings and presence or absence of CHF in 9 cats and 6 dogs. The 9 cats included: 3 cats with no or minimal heart disease (2 normal, 1 trivial MR), 3 cats with asymptomatic heart disease (HCM or RCM), and 3 HCM/RCM with CHF. The conclusions were that no normal cats had a BNP > 270, no cats with heart disease had a BNP < 100, and all 3 cats in CHF had BNP > 270. There were 3 false positive (normal heart with elevated BNP). Two cats had an exaggerated BNP level (asymptomatic heart disease with BNP > 270)

The 6 dogs included: 2 dogs without heart disease, 3 dogs with asymptomatic heart disease, 1 dog with CHF. The conclusions were that no normal dogs had a BNP > 1800, no dogs in CHF had a BNP < 900. There was however 1 false negative (heart disease with a BNP < 900), 1 false positive (normal heart with a BNP > 900), and 1 exaggerated BNP level (asymptomatic heart disease with a BNP > 1800)

To summarize: high levels of BNP suggest the presence of heart disease. Symptoms and radiographic changes needed to confirm presence of CHF. Low BNP levels make heart disease unlikely. BNP in the mid-range are non-diagnostic, and false positives are to be expected. Further testing is necessary. Beware of kidney function that can affect BNP levels.

In the light of recent studies, NT-proBNP could be used as a useful screening test in cats with an excellent negative predictive value. Its effectiveness could be improved further if used in populations of cats at risk (specific breeds or cats with heart murmurs).

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1. References

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