

Use of Bedside NT-proBNP in Primary Care Practice

presented by Clinician's Brief



with Chris Stauthammer, DVM, DACVIM (Cardiology)

Summary

In June of 2021 Chris Stauthammer, DVM, DACVIM (Cardiology) along with Clinician's Brief discussed how to incorporate NT-proBNP in a primary care setting. Interpretation of NT-proBNP results, case selection and additional diagnostic and therapy recommendations were also reviewed. Below is the outline of the webinar presentation.

NT-proBNP Outline

- Natriuretic Peptides
 - Function
 - Stimuli for release
 - Biomarker implications
- Respiratory distress
 - Between CHF and respiratory
 - Review of the diagnosis of CHF
- Feline heart disease
 - Screening patients
 - HCM staging
- Mitral valve disease
 - Staging
 - Prognosis
- Dilated cardiomyopathy
 - Screening
 - Prognosis
- Current limitations of NT-proBNP
- Bionote Vcheck NT-proBNP
 - Canine test
 - Feline test

Natriuretic Peptides

- Family of proteins that function in fluid homeostasis
- Produced predominately by myocardium
 - In response to:
 - Myocardial stretch/wall stress
 - Hypertrophy
 - Hypoxia
 - Function to decrease vascular volume
 - Natriuresis
 - Diuresis
 - Vasodilation
- Congestive heart failure

Cardiac Biomarker

- Substance that can be objectively measured within blood
 - Assessment of biological or pathological process
 - Response to therapy
 - Prognosis
- Provide clinical information that is not easily obtainable
- Does not replace advanced diagnostic imaging

NT-proBNP

- **B-type natriuretic peptide (proBNP)**
 - Produced by the myocardium
 - Excessive stretching of the cells
 - **Correlated to the severity of the underlying heart disease**
- **proBNP is cleaved into BNP and NT-proBNP**
 - Amino-terminal pro-B type natriuretic peptide
- **NT-proBNP is stable and has a long half-life, making it a more desirable biomarker.**
 - **Used to assess the magnitude of cardiac muscle stretching**
 - **Proportionate to the severity of cardiac disease**

Table 1 Potential indications for BNP or NT-proBNP testing in humans and dogs		
Indication	Evidence in Humans ^{4,5}	Evidence in Dogs
Diagnosis of heart failure	Strong	Moderately strong ²¹⁻²⁴
Patients with ambiguous signs	Strong	Moderately strong
Patients with suspicious signs	Moderately strong	Moderately strong
Patients with obvious heart failure signs	Not useful	Not useful
Detection of occult left ventricular dysfunction	Moderate	
High-risk populations	Moderate	Moderate ³⁰⁻³²
General population screening	Not useful	Likely not useful
Risk stratification and prognostication	Strong	Moderately strong ³⁷⁻³⁹
Biomarker-guided therapy	Unknown	Few data available ⁴⁰

Oyama et al. Vet Clinics Small Animal 2010;40:545-558.

What NT-proBNP Levels Tell Us

- Congestive heart failure
 - Patients are often critical
 - Limited diagnostics available
 - Diagnostic imaging ≠ 100%
- NT-proBNP levels
 - Differentiates CHF vs respiratory disease
 - High diagnostic accuracy
- Measure in patients with respiratory signs

Diagnosis of Congestive Heart Failure

- Dogs presenting with respiratory signs
 - NT-proBNP is significantly higher in CHF
 - High sensitivity and specificity values
- Cats presenting with respiratory signs
 - NT-proBNP is substantially higher in CHF
 - Even higher sensitivity and specificity values
 - Improve our diagnostic accuracy of CHF
 - Used in conjunction with other diagnostic modalities

Bella

- 12 yr FS Chihuahua
- Elevated NT-proBNP
 - 2052 pmol/L (Normal < 900)
 - What is the probability of heart failure?

How to Diagnose Congestive Heart Failure

- Clinical signs
- Physical exam
- Thoracic radiographs
- TFAST/ECHO
 - Evidence of left atrial enlargement
 - B-lines
 - Limitations
 - Difficult
 - Subjective
 - Equipment needs
- Response to therapy
- NT-proBNP

Bella

- 12 yr FS Chihuahua
- Presenting for progressive respiratory distress over past two weeks
- Physical examination
 - Tachypnea with RR of 54 BPM
 - Grade 4/6 systolic murmur
 - Crackles bilateral pulmonary fields
- NT-proBNP = 2052 pmol/L (N < 900)

How to Diagnose Congestive Heart Failure

- Clinical signs
- Physical exam
- Thoracic radiographs
- TFAST/ECHO
 - Evidence of left atrial enlargement
 - B-lines
 - Limitations
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 - Equipment needs
- Response to therapy
- NT-proBNP
2052 pmol/L (> 1800 Abnormal) 3031 pmol/L

Tyke

- 5 year MN DMH
- Presenting to the ER
 - Increased respiratory effort and rate over past 24 hours
 - Previously diagnosed with hypertrophic cardiomyopathy 2 years ago
 - No medical therapy
 - Last recheck with Cardiology was 9 months ago
 - Remained an ACVIM Stage B1
 - Physical
 - Normal cardiac auscultation
 - Crackles bilateral pulmonary fields

What If?

- 50% of feline CHF manifested as pleural effusion
- NT-proBNP
 - Diagnostic sensitivity 93.9% (79.8-99.3%)
 - Specificity 72.2 % (46.5-90.3%)

- Previous studies
 - Sensitivity 90-93%
 - Specificity 80-87%

Feline Cardiomyopathy

- High prevalence
 - 1/7 asymptomatic cats have HCM
- Difficult to detect
 - Echo screening on annual basis?
- Morbidity/mortality

Meg

- 12 Yr FS Sphynx
- Presenting for annual exam
- Previously healthy
- Physical examination
 - Grade 2/6 left parasternal systolic murmur
 - What's the significance of the murmur?
 - Is an echo truly needed?

Feline Preclinical Heart Disease

- Preclinical heart disease is common in cats
 - 1/7 (14%) apparently healthy cats have HCM
- Often detected on physical exam
 - Murmur – 15% of apparently healthy cats have murmurs
 - Arrhythmia
 - Gallop sound
- NT-proBNP testing in cats with abnormal auscultation
 - Diagnostic accuracy of **83%** in detecting moderate to severe cardiomyopathy
 - **Elevated result = 5x risk of moderate to severe heart disease**
 - **Normal result = 94% probability of normal to mild heart disease**

Table 2 Summary of results of studies investigating the utility of NT-proBNP to identify cats with asymptomatic myocardial disease					
Echocardiographic Classification of Severity of HCM	Wess G et al ²³ Mean (±SD) Plasma NT-proBNP (pmol/l)	Hsu A et al ²⁰ Median (Range) Plasma NT-proBNP (pmol/l)	Clinical Classification	Connolly et al ¹⁸ Median (1 QR 25th and 75th Percentiles) Serum NT-proBNP (pmol/ml)	Fox et al ²² Median (IQ Range) Serum NT-proBNP (pmol/ml)
Control	58 ± 65	21 (10-79)	Control	33.6 (18.5, 11.5-30)	24 (24-45)
Mild/equivocal	333 ± 244	19 (5-53)	Cats with myocardial disease but not CHF	184.1 (217, 56-273)	283 (154-603)
Moderate	433 ± 299	22 (5-77)	Notes	NT-proBNP concentration was significantly greater in myocardial group compared with control group	NT-proBNP concentration was significantly greater in myocardial group compared with control group
Severe	835 ± 314	134 (12-252)	-		

- NT-proBNP did not detect mild forms of cardiomyopathy
- **Previous studies reported an even higher diagnostic accuracy with quantitative results**

Feline Preclinical Heart Disease - Hypertrophic Cardiomyopathy

- NT-proBNP progressively increases with HCM severity with the highest levels in CHF

What NT-proBNP Levels Tell Us

- Mitral Valve Degeneration (MMVD)
 - Most common form of heart disease
 - 65% dogs by age 9
 - 90% dogs by age 13
- Progressive elevations with every disease stage
- Differentiates CHF from preclinical stages
- Prognostic information
- Response to therapy
- What NT-proBNP Levels Tell Us
- Staging of Myxomatous Mitral Valve Degeneration (MMVD)
- Difference between classification scores

< ACVIM Consensus Classification >

A	B1	B2	C	D
At Risk	Murmur & No Enlargement	Murmur & Enlargement	CHF Signals	Refractory
535 pmol/L (373-723)	665 pmol/L (401-1,024)	1,405 pmol/L (789-2,375)	3,922 pmol/L (2,091-7,111)	

NT-proBNP

What NT-proBNP Levels Tell Us

- Staging of Myxomatous Mitral Valve Degeneration (MMVD)
- Detects dogs with MMVD
- NT-proBNP values of all disease stages (MMVD B1-D) were significantly higher than the control group
- Not able to differentiate B1 vs B2

Staging of Myxomatous Mitral Valve Degeneration (MMVD)

- NT-proBNP is useful to discriminate between asymptomatic dogs and dogs with CHF
- NT-proBNP does not reliably discriminate
 - Between stages B1 and B2
 - Between healthy and stages B1 and B2

Prognosis of Myxomatous Mitral Valve Degeneration (MMVD)

- Baseline NT-proBNP predictive of survival
- Higher concentrations equate to cardiac mortality
 - Shorter survival times
 - Increased OR death
 - Sudden cardiac death
- Serial monitoring of NT-proBNP
 - Monitoring the effectiveness of medical treatment
 - Response to therapy predictive of survival

What NT-proBNP Levels Tell Us

- Detects Dilated Cardiomyopathy (DCM)
 - Detects all stages of DCM
 - Increases diagnostic accuracy with Holter
 - Evaluates survival time
- Detects all stages of DCM in Dobermans
 - Recommend annual screening tests to determine if DCM is present even if apparently healthy
 - Elevated results highly predictive of developing disease
 - Most common in large breeds
 - Doberman Pinscher: Very high risk of developing cardiomyopathy
 - Recommendation: Echocardiogram + ECG (Holter) Annually from 3-4 years of age
- Evaluates the Survival Time
 - In asymptomatic Dobermans with DCM
 - With low NT-proBNP survival is much longer
 - The median survival time of Dobermans:
 - NT-proBNP > 900 pmol/L: 284 days (6.1 times shorter)
 - NT-proBNP < 900 pmol/L: 1743 days

Limitations

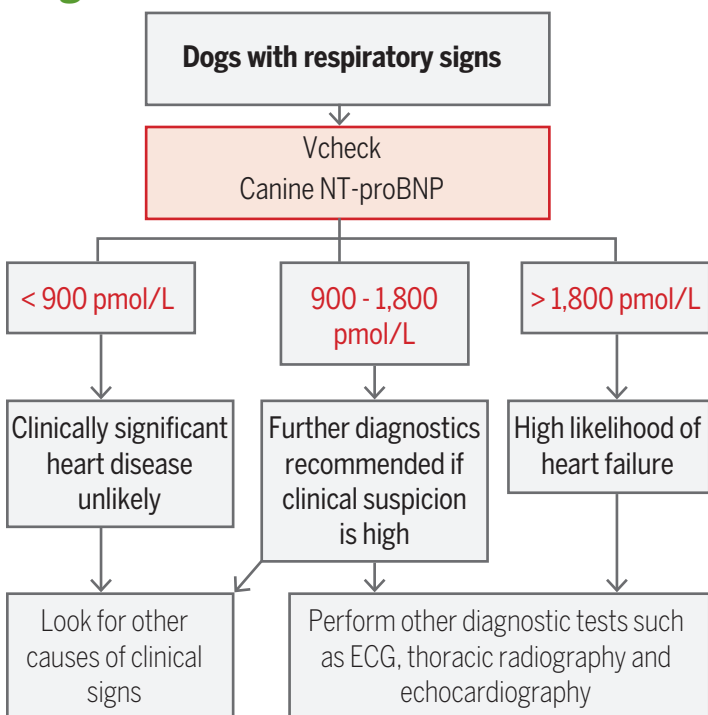
- Pulmonary hypertension
 - Significant cardiac and pulmonary dysfunction
 - NT-proBNP guide therapy

- Systemic hypertension
 - NT-proBNP differential pathologic vs white coat
 - Therapy guide
- Azotemia
- Day to day variability
- Assay variability
- In house measuring ability
 - Poor specificity
 - False positives

Product Introduction- Canine NT-proBNP

- Species : Dog
- Sample : Serum 100 µl
- Testing Time : 15 minutes
- Measurement : Quantitative
- Measurement Range : 500 – 10,000 pmol/L
- Storage Condition : 2 - 8 °C
- Test Procedure:
 - Samples should be centrifuged and tested immediately after collection. Alternatively, refrigerate and use within 24 hours or freeze.
 - * Degradation of NT-proBNP may occur if stored at room temperature or refrigerated for more than 24 hours, causing false negative results

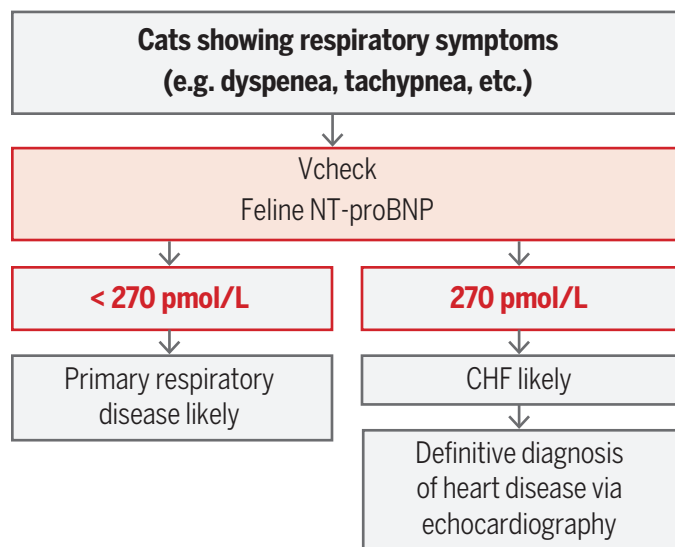
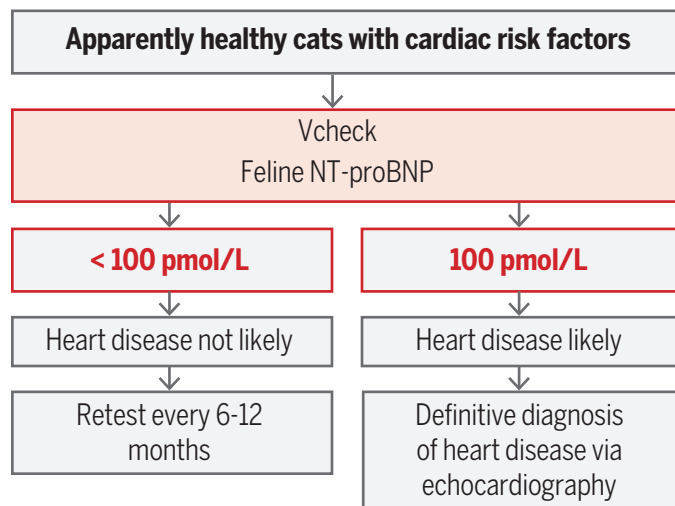
Algorithm: NT-proBNP Testing in Dogs



Product Introduction- Feline NT-proBNP

- Species : Cat
- Sample : Serum 100 µl
- Testing Time : 10 minutes
- Measurement : Quantitative
- Measurement Range : 50 – 1,500 pmol/L
- Storage Condition : Room temperature

Algorithm: NT-proBNP Testing in Cats



Summary

- Very useful in diagnosis of heart failure
 - Advise measuring all patients with respiratory signs
 - Provide complementary information on heart health

- Useful in screening cats with auscultation abnormalities
 - Cannot detect mild heart disease
 - Can detect disease progression
- Limited role with mitral valve disease
 - Detection of heart failure
 - Prognosis
- Dilated cardiomyopathy
 - Screening
 - Detection of CHF
 - Prognosis
- Vcheck NT-proBNP Tests
 - Provides rapid in house measurement of NT-proBNP in dogs and cats
 - Quantifiable result with improved specificity and reduced false positives
 - Validated assay
 - Game changer in veterinary cardiology