Canine & Feline Heart Markers – NT-proBNP + cTnI

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InSight V-IA®

Contents

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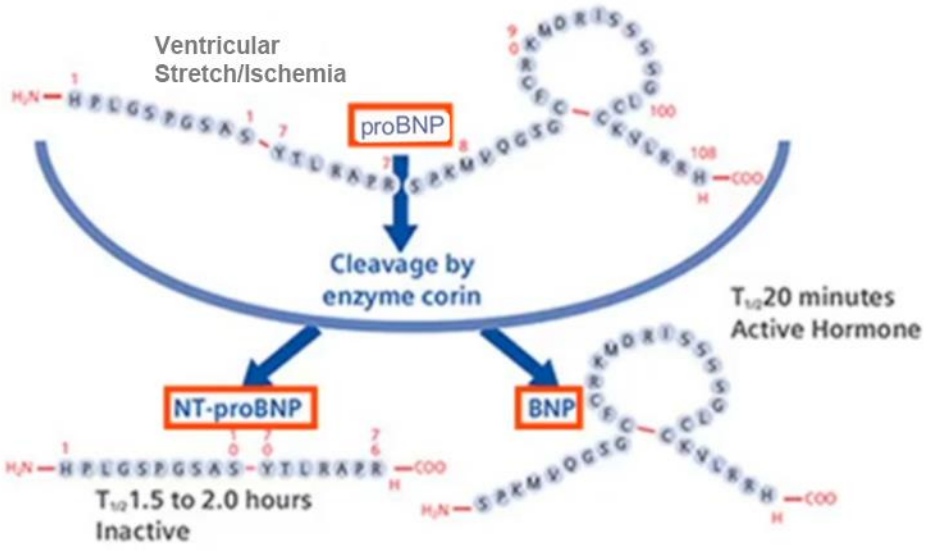
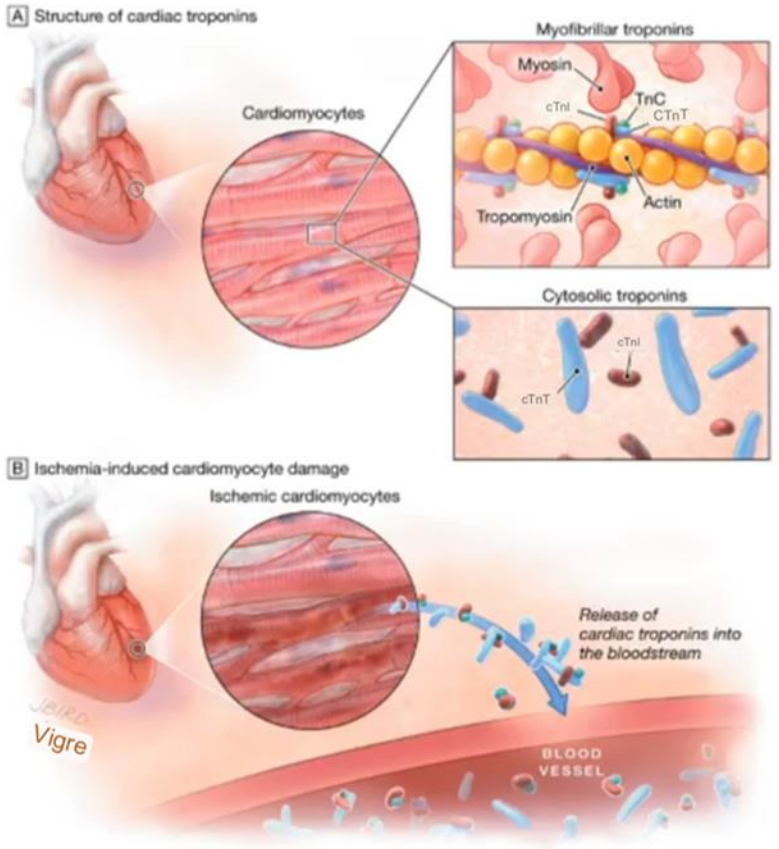
a. Cardiac Markers



NT-proBNP



Troponin I Cardiac Troponin I

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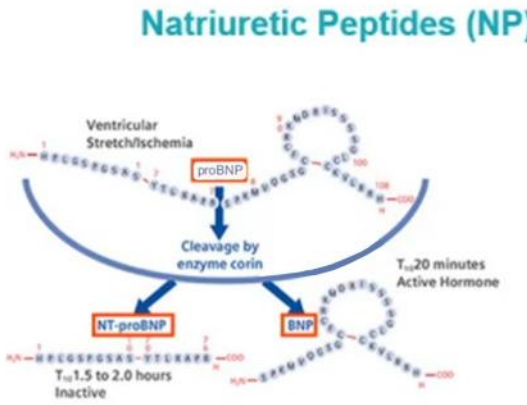
a. Biological Properties of Cardiac Markers

- NT-proBNP is secreted by the ventricle and enters the blood circulation through the stretching of myocardial cells. It is a polypeptide containing 76 amino acids.
- Straight-chain structure, biologically inactive, cleared by the kidneys.
- The half-life is 90 – 120 minutes, stable in vitro.
- The concentration in the blood is high (15 – 20 times that of BNP) and the concentration in the blood is positively correlated with the degree of cardiac dysfunction.
- The level of NT-proBNP is not affected by factors such as body position and daily activities, and there is no intraday or day-to-day fluctuation, with good repeatability.

a. Cardiac Markers



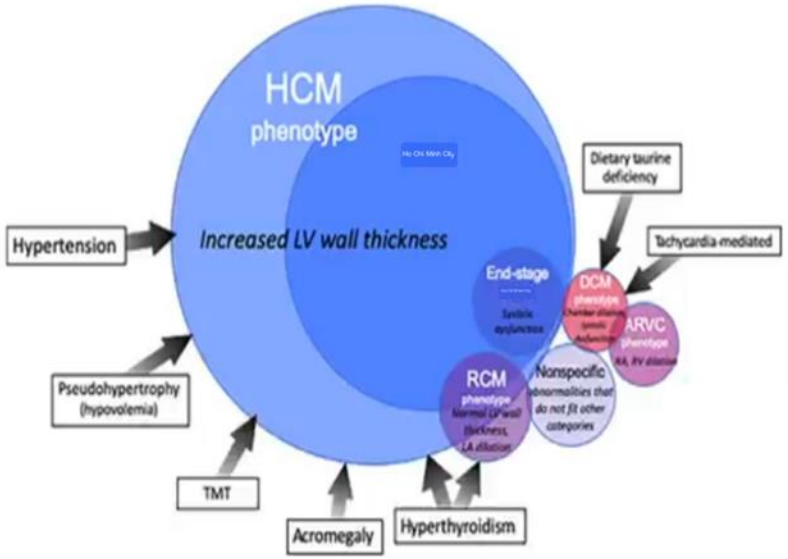
NP's

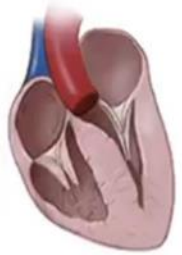
are produced and secreted (primarily) at specific cardiac sites in response to myocardial overload and cardiomyocyte strain

Table-1: Types of NP and release sites based on Baisan *et al.* [16].

NP types	Release
ANP	Atrial
BNP	Mainly ventricles
CNP	Brain, endothelium, kidney, chondrocytes, and pituitary gland
DNP	Venom gland of *Dendroaspis angusticeps* (eastern green mamba)
VNP	Primitive heart, normally in fish

b. Feline Heart Disease Markers – NT-proBNP





HCM hypertrophic cardiomyopathy :

increased left ventricular wall thickness (diffuse or regional)

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TABLE 3 Definitions of cardiomyopathy phenotypes. Cardiomyopathy is defined as a myocardial disorder in which the heart muscle is structurally and functionally abnormal in the absence of any other disease sufficient to cause the observed myocardial abnormality

Phenotype	Definition
Hypertrophic cardiomyopathy (HCM)	Diffuse or regional increased LV wall thickness with a nondilated LV chamber.
Restrictive cardiomyopathy (RCM)	
Endomyocardial form	Characterized macroscopically by prominent endocardial scar that usually bridges the interventricular septum and LV free wall, and may cause fixed, mid-LV obstruction and often apical LV thinning or aneurysm; LA or biatrial enlargement is generally present.
Myocardial form	Normal LV dimensions (including wall thickness) with LA or biatrial enlargement
Dilated cardiomyopathy (DCM)	LV systolic dysfunction characterized by progressive increase in ventricular dimensions, normal or reduced LV wall thickness, and atrial dilatation.
Arrhythmogenic cardiomyopathy (AC), also known as arrhythmogenic right ventricular cardiomyopathy (ARVC) or dysplasia (ARVD)	Severe RA and RV dilatation and often, RV systolic dysfunction and RV wall thinning. The left heart may also be affected. Arrhythmias and right-sided congestive heart failure are common.
Nonspecific phenotype	A cardiomyopathic phenotype that is not adequately described by the other categories; the cardiac morphology and function should be described in detail

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b. Feline Heart Disease Markers – NT-proBNP

What Cat NT-ProBNP Levels Can Tell Us

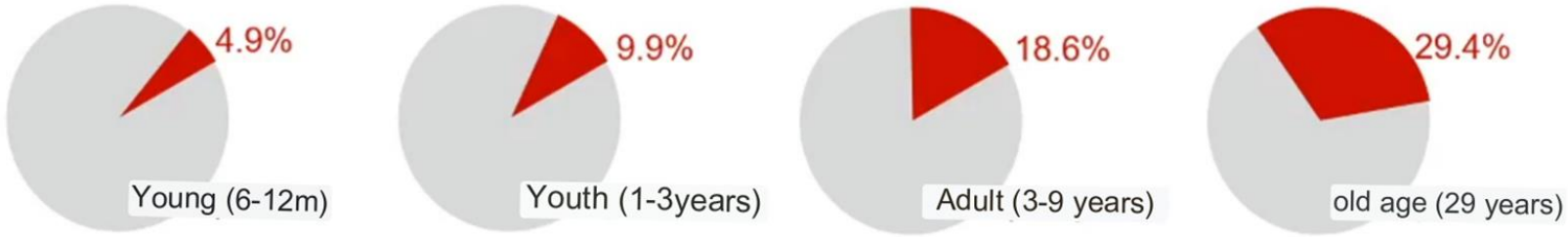
Cardiomyopathy prevalence in 780 apparently healthy cats in rehoming centres (the CatScan study)

Jessie Rose Payne, BVetMed, PhD ,
David Charles Brodbelt, MA, VetMB, PhD ,
Virginia Luis Fuentes, MA, VetMB, PhD*

Hypertrophic Cardiomyopathy (HCM) Hypertrophic Cardiomyopathy

: The most common heart disease and one of the 10 most common causes of death in cats

• Prevalence ranges from 15% in general cat population to as high as 29% in elderly cats (apparently healthy cats)



- Clinical symptoms: asymptomatic, dyspnea
- Diagnosis: echocardiography; left ventricular wall ≤ 6 mm

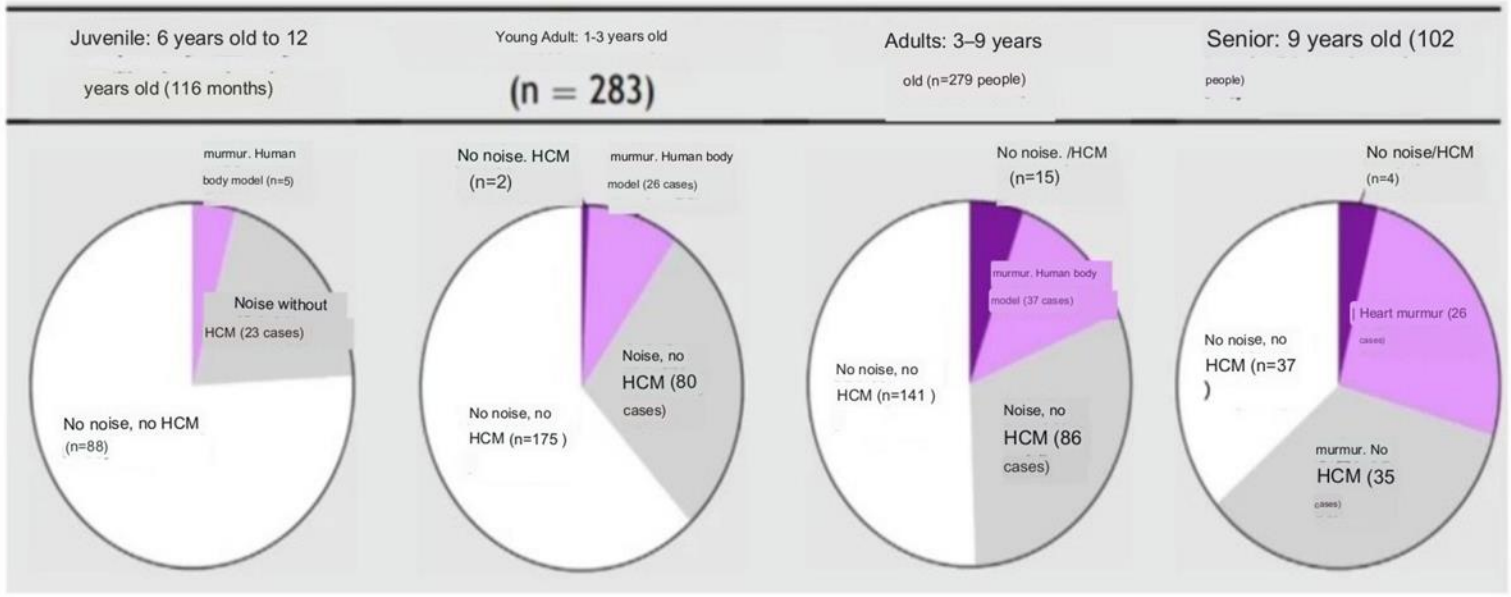
b. Feline Heart Disease Markers – NT-proBNP

What Cat NT-ProBNP Levels Can Tell Us

Heart murmur: 33.7% of cats without HCM, 81.7% of cats with HCM

Prevalence of Cardiomyopathy in 780 Apparently Healthy Cats at a Placement Center (CatScan Study)

Jessie Rose Payne, BVetMed, David Charles Brodbelt, MA, VetMB, Ph.D. Virginia Luis Fuentes, MA, VetMB, Ph.D.



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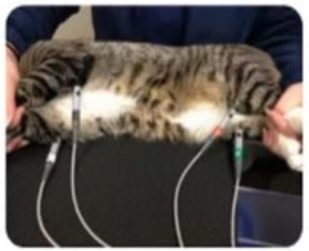
b. Feline Heart Disease Markers – NT-proBNP

What Cat NT-ProBNP Levels Can Tell Us

- Auscultation

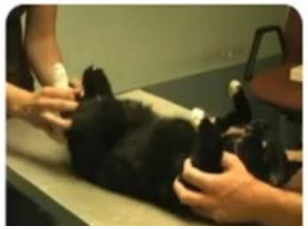
Insensitive and specific (up to 80% in HCM cats, up to 30-45% in healthy cats)

- ECG electrocardiogram



not recommended

- X-ray (Radiography) X-ray (Radiography)



Insensitive to mild or moderate HCM, but the gold standard for diagnosing CHF

- Echocardiography echocardiography

Gold standard test for diagnosing HCM but expensive ($200 to $400) and requires trained operators

b. Feline Heart Disease Markers – NT-proBNP

NT-proBNP: "ACVIM

- The measurement of NT-proBNP can be considered as an initial screening test for identifying advanced HCM. Cat NT-proBNP can be used for screening HCM (hypertrophic cardiomyopathy).
- When X-ray or echocardiography are unavailable, evaluation of NT-proBNP concentrations should be considered.


ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats

Virginia Luis Fuentes | Jonathan Abbott Valerie Chebu | ECO | Philo R. Fox Jens Hgl Mark D. Kitts Karen Schober Jesus A Stern

In apparently healthy cats, apparently healthy cats

The measurement of NT-proBNP can be considered as an initial screening test.

① NT-proBNP → ② Echocardiography → ③ diagnosed

≥100 pmol/L WE

HCM has high performance

East-West cooked

veterinarian 100 pmol/L

: HCM cannot be completely ruled out, the possibility is relatively small

In cats with respiratory signs, cats with respiratory signs

Point-of-care NT-proBNP test should be considered (high level of evidence).

① NT-proBNP → ② Echo and X-ray → ③ Definitive diagnosis

≥ 270 pmol/L: highly suspected heart disease

< 270 pmol/L :

Respiratory problems are more likely

BIONOTE

eference: 1. ACVIM consensus statement guidelines for the classification, diagnosis, and management of cardiomyopathies in cats. J Vet Intern Med. 2020;1–16.

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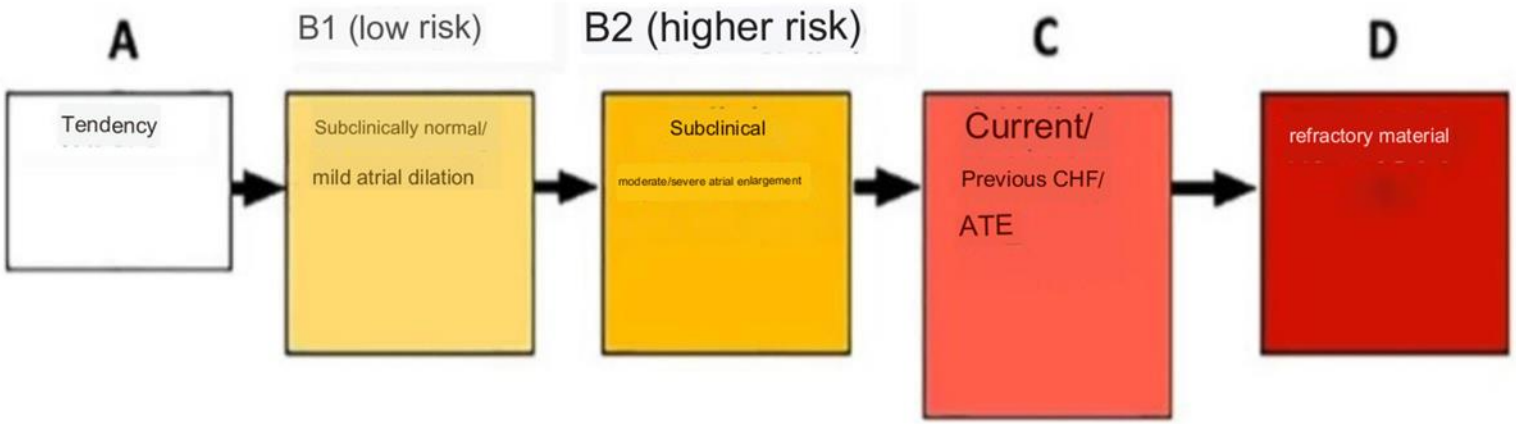
b. Feline Heart Disease Markers – NT-proBNP

American Academy of Internal Medicine

American College of Veterinary Internal Medicine Consensus

ACVIM Consensus Statement Guidelines for Classification, Diagnosis and Management of Feline Cardiomyopathy



Stages of cardiovascular disease In the second stage, additional risk factors include galloping sounds. Discordant left atrial hypofunction, extreme left ventricular hypertrophy, left ventricular systolic dysfunction

, spontaneous echo contrast/thrombosis, regional wall motion abnormalities. Arterial thromboembolism; congestive heart failure

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b. Feline Heart Disease Markers – NT-proBNP

Consensus Statement on Feline Cardiomyopathy

Date Received: January 8, 2020 Date Accepted: February 14,
2020 101111 / AM 15745

Journal of Veterinary Internal Medicine

consensus statement

The American College of Veterinary Medicine Consensus Statements in Internal Medicine (ACVIM) provide the veterinary community with the latest pathophysiological information. Diagnosis and Treatment of Clinically Important Animal Diseases The ACVIM Registration Committee oversees the delineation of relevant topics, identifying group members with expertise in drafting statements and other aspects to ensure the integrity of the process. Statements are drawn from evidence-based medicine wherever possible, and when evidence is insufficient or contradictory, explanatory commentary by expert panels. A draft was drawn up by a panel of experts for comments by ACVIM members and then incorporated into a statement, which was then submitted to the Journal of Veterinary Internal Medicine for editing prior to publication. The others are solely responsible for the refutation of the statement.

ACVIM Consensus Statement Guidelines for the Classification, Diagnosis, and Management of Feline Cardiomyopathy

Virginia Luis Fuentes | Jonathan Abbott 2 Valerie Chable Etienne Cote '| Philippe Fox $© | Jens Hagstrom | Mark D. Kittle Carsten Schober* | Joshua A. Stim'

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American Academy of Veterinary Internal Medicine

Table 1 Level of evidence

level of evidence	
High	Randomized Controlled Trials in Cats
	forward-looking. Nonrandomized controlled trials in cats with adequate sample size and lack of major methodological flaws
medium	Cat Lab Tests
	Retrospective clinical study of intervention and control groups
low	Case series of cats with no control group
	Research on other species
	Expert Opinion

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b. Feline Heart Disease Markers – NT-proBNP

1) Screening in apparently healthy cats

5.10|Diagnostic approach to subclinical cardiomyopathy

Cats with subclinical cardiomyopathy can be difficult to recognize. Pacemaker evaluation should be considered in cats with suspicious tissue or physical examination findings, including honking, murmurs, or cardiac arrhythmias, and in cats judged to be at high risk for CHF if receiving interventions such as anesthesia or intravenous fluid therapy (Low LOE Table 4). Echocardiography is currently the most accurate clinical test for diagnosing cardiovascular disease in cats and the best technique for estimating prognosis, but is highly user dependent. "However, with appropriate training and experience, focused bedside echocardiography is feasible in first opinion (general) practice and can be used to improve the accuracy of non-specialist physicians in diagnosing cardiomyopathy, especially in cats with more advanced disease. It is recommended to perform focused bedside echocardiography 4299 (high LOE) only after appropriate training and practice, and should be followed by bedside testing with standard echocardiography to characterize the phenotype.

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When echocardiography is not available, assessment of NT-proBNP concentration may be considered. Circulating NT-proBNP concentrations increased in cat populations with increasing clinical severity of cardiomyopathy, but the overlap precluded the use of NT-proBNP to classify individual cats into mild, moderate, and severe groups. NT-proBNP detection can be used as a preliminary screening test for the diagnosis of advanced cardiomyopathy. A normal NT-proBNP result does not guarantee that a cat does not have cardiomyopathy. They also cannot guarantee that the cat will not develop cardiomyopathy later in life, especially when mild heart disease is present. However, they do suggest that there is a low probability that cardiomyopathy is immediately, dlinically deleterious. Therefore, in cats with suspected cardiomyopathy, follow-up echocardiography should be considered even if the initial NT-proBNP result is within the normal reference interval (low LOE). Echocardiography is recommended after a positive NT-proBNP test.

In elderly cats with heart murmurs, gallops, or arrhythmias, measurement of serum T4 concentration and blood pressure is recommended (high LOE). Echocardiography should also be considered (low LOE).

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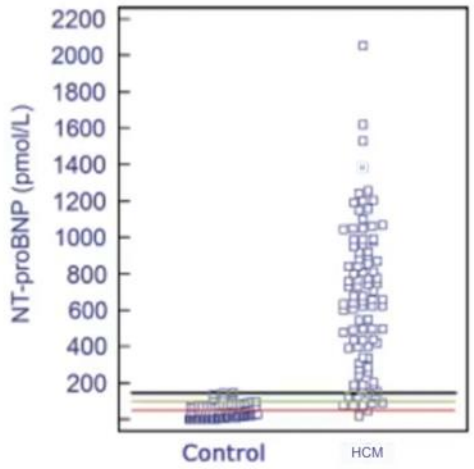
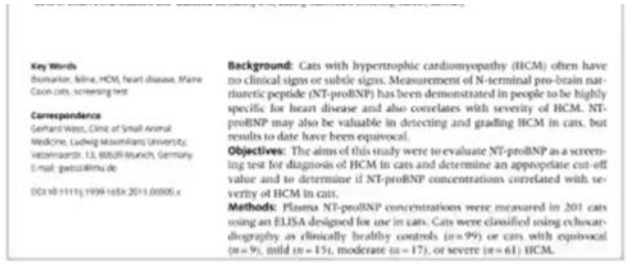
b. Feline Heart Disease Markers – NT-proBNP

1) Screening in apparently healthy cats

- High-risk cats should be re-evaluated annually.
- Assessing an Asymptomatic Cat for Possibility of Underlying Heart Disease
- Reference Range <100pmol/L





Key Words
Biomarker, feline, HCM, heart disease, Maine Coon cats, screening test

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DOI: 10.1111/j.1939-165X.2011.00305.x

Background: Cats with hypertrophic cardiomyopathy (HCM) often have no clinical signs or subtle signs. Measurement of N-terminal pro-brain natriuretic peptide (NT-proBNP) has been demonstrated in people to be highly specific for heart disease and also correlates with severity of HCM. NT-proBNP may also be valuable in detecting and grading HCM in cats, but results to date have been equivocal.
Objectives: The aims of this study were to evaluate NT-proBNP as a screening test for diagnosis of HCM in cats and determine an appropriate cut-off value and to determine if NT-proBNP concentrations correlated with severity of HCM in cats.
Methods: Plasma NT-proBNP concentrations were measured in 201 cats using an ELISA designed for use in cats. Cats were classified using echocardiography as clinically healthy controls ($n = 99$) or cats with equivocal ($n = 9$), mild ($n = 15$), moderate ($n = 17$), or severe ($n = 61$) HCM.

Cut-off cut point	Sensitivity Sensitivity	**Specificity** specificity
> 49 pmol/L	97.8%	66.7%
> 100 pmol/L	92.4%	93.9%
> 150 pmol/L	88%	100%

Vet Clin Pathol. 2011 Jun;40(2):237-44. doi: 10.1111/j.1939-165X.2011.00305.x

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b. Feline Heart Disease Markers – NT-proBNP

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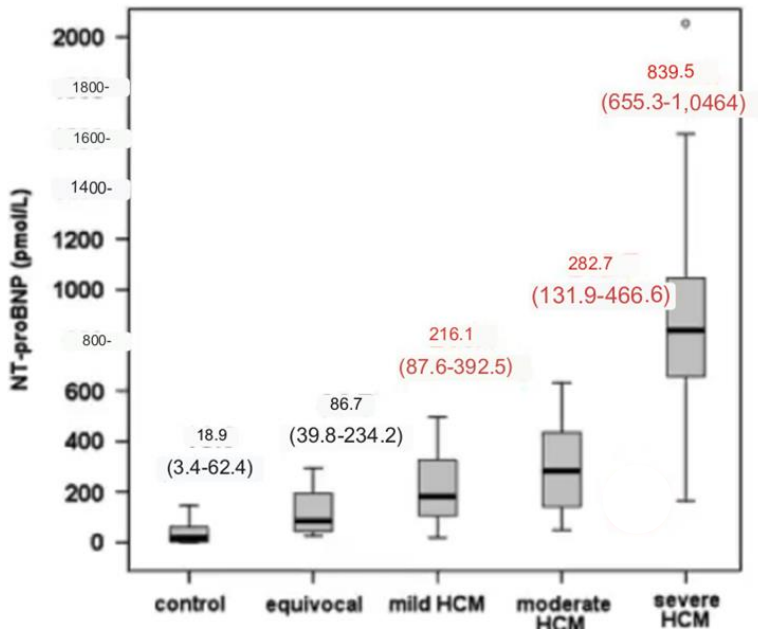

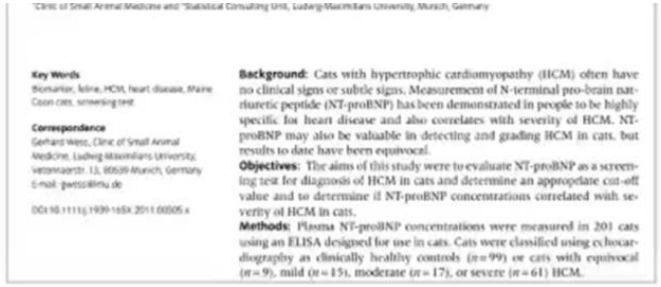

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The concentration of NT-proBNP was the highest in severe cats, but those in mild and moderate HCM groups

NT-proBNP concentrations also increased.

Echocardiography should be performed in cats with elevated NT-proBNP concentrations.

- (LVPWDIVSd<5.5mm; LA/AO<1.5)
- (LVPWd IVSd5.5-6.0; LA/AO<1.5)
- HCM (LA/AO<1.5 , LVPWd IVSD6.0-6.5mm)
- PHCM (LVPWD/IVSd 6.5-7.0 mm, LA/AO<1.8; LVPWd IVSd6.0-6.5 mm, LA/AO 1.5-1.8)
- Severe HCM (focal or systemic hypertrophy, left ventricular hypertrophy and/or venous density >7.0 mm; or left ventricular hypertrophy and/or venous density >6.0 mm and LA/AO >1.8).

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b. Feline Heart Disease Markers – NT-proBNP

2) Feline Respiratory Symptoms Determine why cats have respiratory symptoms

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American Academy of Internal Medicine

5.11|Diagnostic approach to cats with suspected CHF

Physical examination findings for dyspnea and tachypnea. Ruptured breaths, hypothermia, and galloping sounds are all very suggestive of CHF,47 but in some cats, shortness of breath with dyspnea may be the only abnormality. While this kind of racing photography is traditionally considered Kingstein. The DARD test, used to detect cardiogenic pulmonary edema, should take care to minimize stress when performing radiographs in cats with respiratory distress. Pulmonary infiltrates and cardiac enlargement are the main manifestations of CHF, but typical radiographic signs of chronic heart failure such as LA enlargement and dilated pulmonary vessels are not consistent in affected cats.

If radiographs cannot be obtained safely, bedside chest ultrasonography or bedside NT-proBNP testing should be considered (high LOE). On point-of-care ultrasonography, the presence of effusion or B-lines associated with severe LA enlargement is highly suggestive 58,115 CHF. Negative results of NT-proBNP testing at the point of care indicated that respiratory disease was a more likely cause of respiratory distress than cardiac disease. Once a cat with HF is stabilized, standard of care or best practice echocardiography should be considered (Table 5, low LOE).

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b. Feline Heart Disease Markers – NT-proBNP

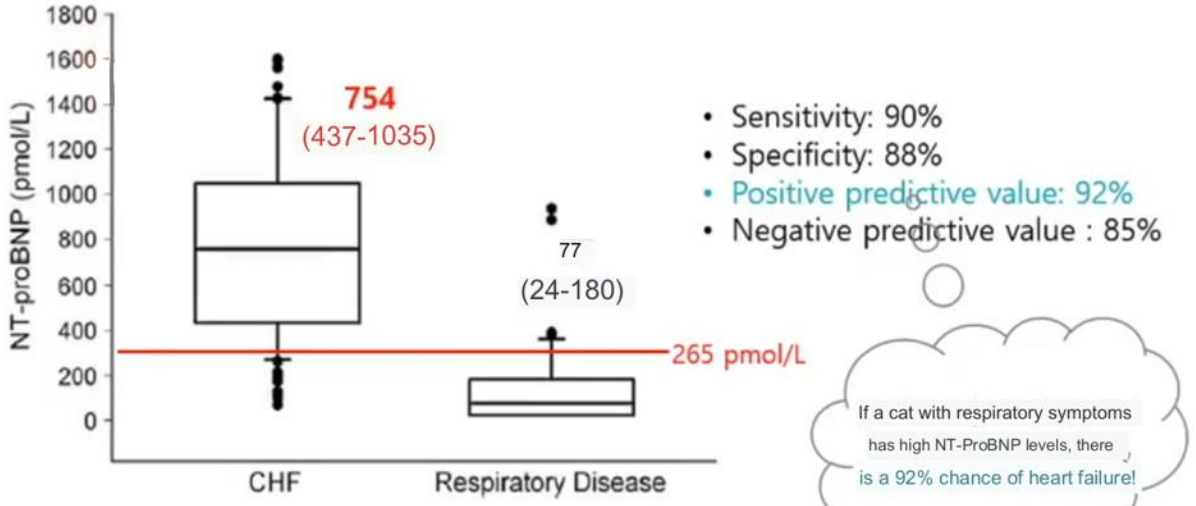
2) Determining the cause in cats with respiratory signs

Determining the Cause of Respiratory Symptoms in Cats

- Differentiate between cardiac and respiratory causes in cats with respiratory symptoms ② Cardiac causes: congestive heart failure ② Primary respiratory diseases: bronchitis, asthma, pneumonia, tumors
- Reference Range: <270pmol/L

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

Philip R. Fox, DVM [a,*], Mark A. Oyama, DVM [b], Caryn Reynolds, DVM [b], John E. Rush, DVM [c], Terri C. DeFrancesco, DVM [d], Bruce W. Keene, DVM [d], Clark E. Atkins, DVM [d], Kristin A. MacDonald, DVM, PhD [e], Karsten E. Schober, DVM, PhD [f], John D. Bonagura, DVM [f], Rebecca



- Sensitivity: 90%
- Specificity: 88%
- Positive predictive value: 92%
- Negative predictive value : 85%

If a cat with respiratory symptoms has high NT-ProBNP levels, there is a 92% chance of heart failure!

Quantitative cat-specific NT-proBNP assay

Good diagnostic accuracy for differentiating cats with cardiac and noncardiac causes of respiratory distress. ' '

(Level of Evidence: High)

InSight V-IA®

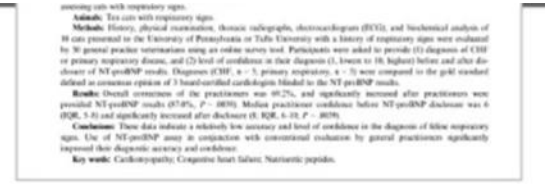
b. Feline Heart Disease Markers – NT-proBNP

Increasing diagnostic accuracy

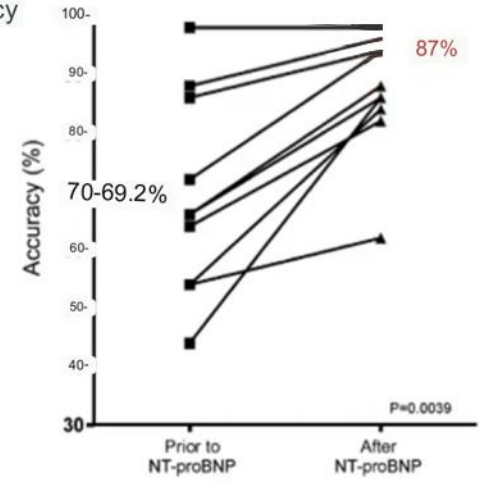
Improve diagnostic accuracy

In cats with respiratory symptoms,

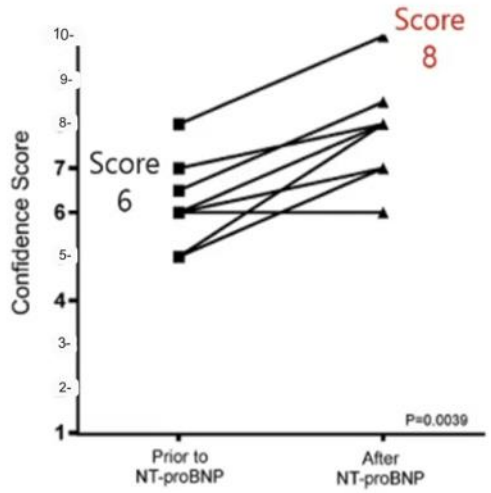
NT-proBNP determination combined with routine assessment by general practitioners significantly improved their diagnostic accuracy and confidence. (PE. X 1+/-NT proBNP)



GP diagnostic accuracy



Confidence in GP diagnosis



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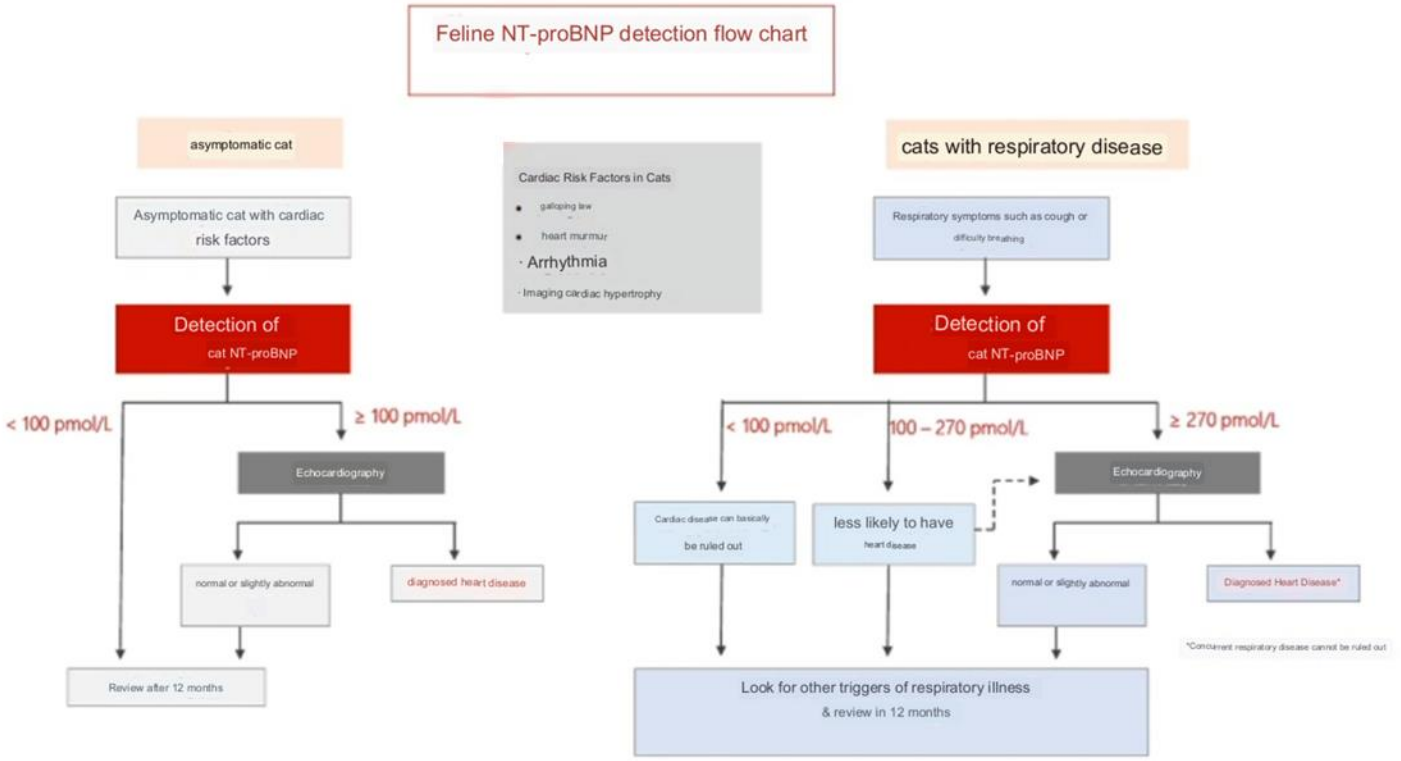
b. Feline Heart Disease Markers – NT-proBNP

Clinical AlgorithmClinical Guidelines



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c. Feline Heart Disease Markers – FcTnI

Most veterinarians know that Troponin I (TnI) is a protein present in cardiomyocytes, but when used as a cardiac biomarker, the concentration is lower than that of NT-proBNP.

However, in the guidelines issued by the American College of Veterinary Internal Medicine (ACVIM), TnI, a biomarker, was directed for use in feline cardiomyopathy and is very valuable in clinical practice.

ACVIM
American College of Veterinary Internal Medicine

"ACVIM Consensus Statement Guidelines for the Classification, Diagnosis, and Treatment of Feline Cardiomyopathy"

(1 stroke | including 2) different, not outstation ACVI 1011)

Yes Society Outside 1(Open access)

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c. Feline Heart Disease Markers – FcTnI

1) Screening for HCM in apparently healthy cats

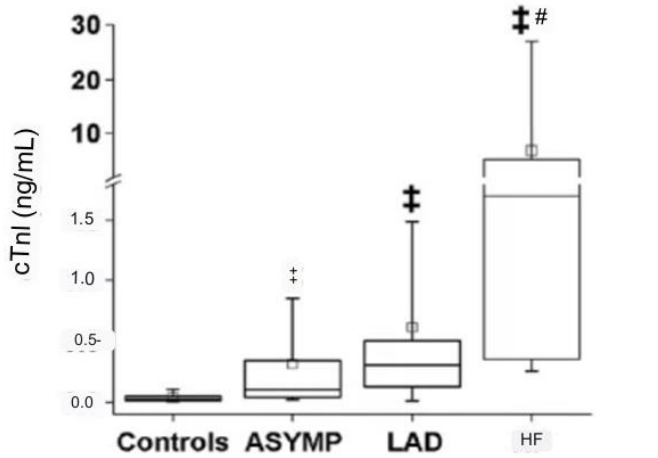
ACVIM

"Troponin I can be used to distinguish normal cats from cats with subclinical HCM when cardiac disease is suspected1 (evidence level: moderate)

- Troponin I reflects myocardial injury induced by HCM development.

If other causes of cardiac injury are ruled out, measurement of Tn1 may provide additional information useful in assessing the severity of HCM.

- TnI<0.163ng/ml: HCM may be ruled out
- TnI>0.234ng/ml: May identify severe HCM



ASYMP: asymptomatic HCM without LA dilatation, **LAD**: asymptomatic HCM with LA dilatation, **HF**: cats with heart failure

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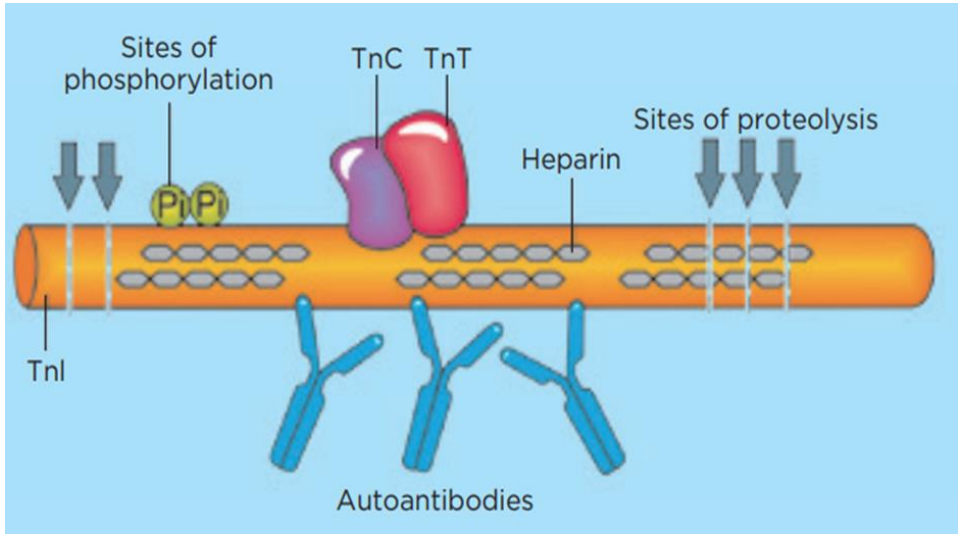
c. Biological Properties of cTnI

- Cardiac Troponin I is a contractile protein found only in the heart muscle. It is one of the three subunits of the troponin complex (I, T, C) and associates with tropomyosin in the filaments of myofibrils to form actin. Studies have found that cTnI is free Troponin I (free TnI), which can bind to Troponin C (binary IC), Troponin T (binary IT) or both with Troponin C and Troponin T (Triple ITC) compound.



c. Feline Heart Disease Markers – FcTnI

2) Predictor of cardiac death in cats with HCM

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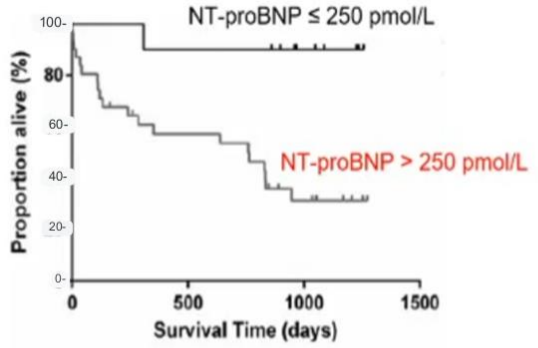
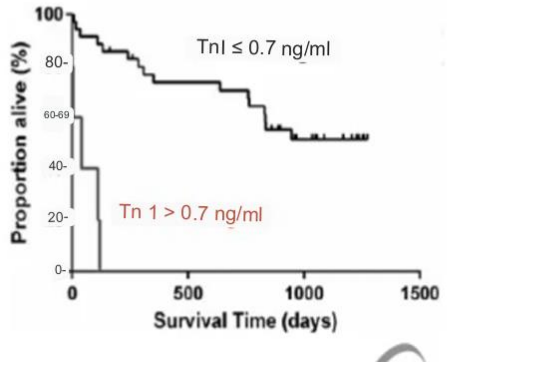
"Increased concentration of TnI
Associated with increased risk of cardiovascular death" (evidence level: high)

- Poor prognosis of cats with HCM: increased CHF, ATE, LA...
- A single measurement of NT-proBNP, TnI, or both (in humans) can be used as an independent predictor of adverse cardiovascular events.
- Study on Predictors of Cardiac Death in HCM Cats
  - NT-proBNP: cut-off value 250pmol/L risk factor: 10 times
  - Troponin I: cut-off 0.7 ng/ml → risk factor: 5-fold (compared to CHF or LA dilatation irrelevant)





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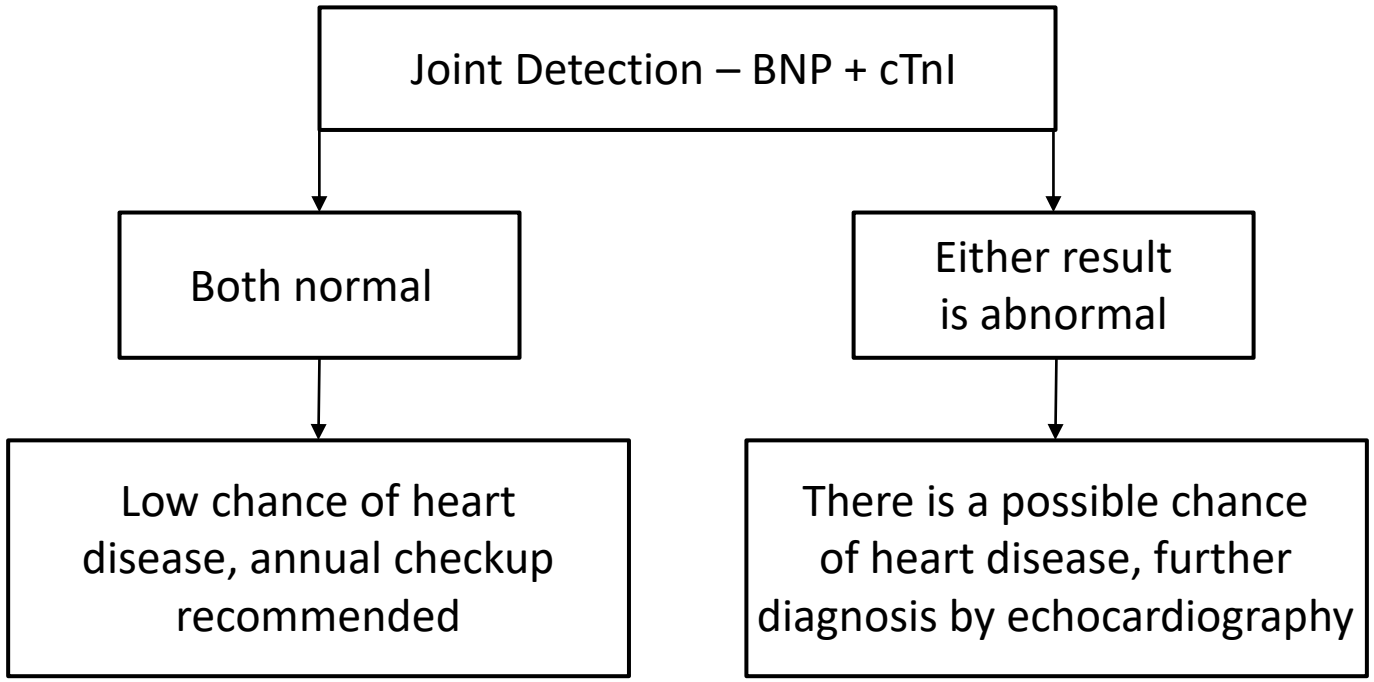
d. Application of fNT-proBNP + fcTnI



1. Screening for potential heart disease
2. Distinguish between causes of breathing problems
3. Assessing the risk of death
4. Differentiate the severity of heart disease

Remarks – In the early stages of HCM or RCM, when the pressure on the myocardial wall is not significantly generated, BNP may be normal but abnormal cTnI is a common phenomenon.

- BNP – According to the different stages of heart disease development, it reflects the degree of myocardial stretch.
- cTnI – According to the different stages of heart disease development, it reflects the degree of myocardial damage.

InSight V-IA®

d. Application of fNT-proBNP + fcTnI

Example 1

Symptom	NT-proBNP	cTnI
Difficulty breathing	65	8.7

Analysis – NT-proBNP is normal. When cTnI is abnormal, there are two situations:
Case 1 – It can be considered that it is not a heart disease that causes secondary myocardial damage, such as pneumonia.
Case 2 – Myocardium wall stress has not been stretched significantly, but the myocardium has caused damage.

Example 2

Symptom	NT-proBNP	cTnI
No symptom	315	1.2

Analysis – When NT-proBNP and cTnI are abnormal at the same time, it is recommended to further perform ultrasonography.

Example 3

Symptom	NT-proBNP	cTnI
Shortness of breath with both CKD & HCM	1500	2.5

Analysis – When NT-proBNP and cTnI are abnormal at the same time, there are two situations:
Case 1 – It is not necessarily a heart disease. It can be considered that CKD causes NT-proBNP and cTnI to increase at the same time.
Case 2 – The treatment plan needs to be adjusted.

Clinical Reference	NT-proBNP	cTnI
Level A	65	<0.13
Level B1	300	0.13-0.25
Level B2	600	0.26-1
Level C	700	2.5+10 (PE, PLE)
Level D	1500	1.5+10 (PE, PLE)

Remarks – In the early stages of HCM or RCM: when the pressure on the myocardial wall is not significantly generated, BNP may be normal, but abnormal cTnI is a common phenomenon.

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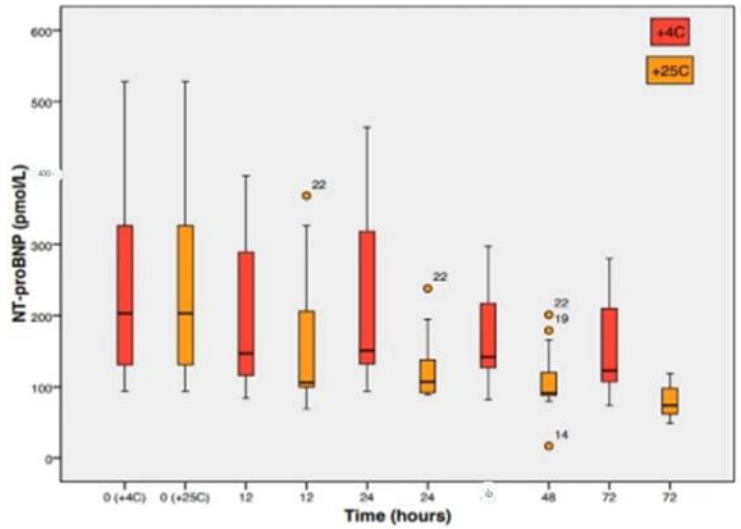
d. Application of fNT-proBNP + fcTnI

Precautions

NT-proBNP: peptide ⇒ protease (enzyme) degrades NT-ProBNP

- Enzyme activity is temperature dependent and decreases at lower temperatures.
- NT-proBNP degraded significantly at room temperature or under refrigeration.

Therefore, it should be tested as soon as possible after blood collection.



Changes of serum NT-proBNP concentration in cats at +4C and +25C for 72 hours

InSight V-IA®

d. Application of fNT-proBNP + fcTnI

NT-proBNP in Cats

Factors Contributing to NT-ProBNP False Positives

- feline hyperthyroidism
- Renal insufficiency or prerenal azoemia
  - ⇒ NT-proBNP levels should be interpreted in conjunction with renal function tests. (creatinine>2.8)
- systemic hypertension
- severe arrhythmia
- Pulmonary hypertension (rare)

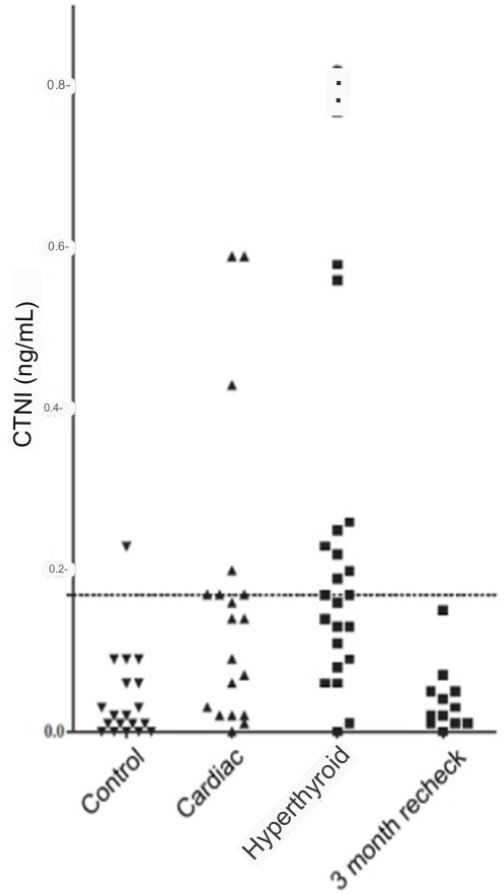
d. Application of fNT-proBNP + fcTnI

Conditions Affecting TnI Concentration

The troponin I assay only detects myocardial injury.

Noncardiac disease may also cause secondary myocardial injury.

- Hyperthyroidism (elderly cats)
- Kidney disease
- Respiratory diseases
- Anaemia
- Tumour



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d. Clinical Application of Feline Cardiac Markers

- Clinical screening for potential heart disease and differential diagnosis
  - Asymptomatic HCM Screening
- Differential diagnosis such as dyspnoea
  - Cardiac or pulmonary
- Estimation of prognosis of heart disease and monitoring of treatment effect
  - The prognosis evaluation of heart failure, prediction of re-morbidity and mortality
  - Prognostic assessment of acute myocardial injury, prediction of mortality
  - The concentration change of NT-proBNP is related to the curative effect and the drug dose can be adjusted according to the change to estimate the curative effect.
- Differentiate the severity of heart disease
  - Monitoring tool before, during and after surgery

After the diagnosis of heart disease, the level of BNP can also evaluate whether the symptoms of heart failure are relieved. Cat Troponin days can be used to predict the life expectancy of cats after heart disease. The expected life expectancy can be 1000-1200 days if it is controlled below 0.7. If it is above 0.7, the life expectancy can be 60-120 days. False positive results of BNP. Troponin in dogs and cats can be used to detect hyperthyroidism, CDK, pulmonary edema and tumours.

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e. Canine Heart Disease Markers

In Dogs,

DCM (Dilated Cardiomyopathy)

Dilated cardiomyopathy

: Most common heart disease in large dogs (10% of all dogs with heart disease)

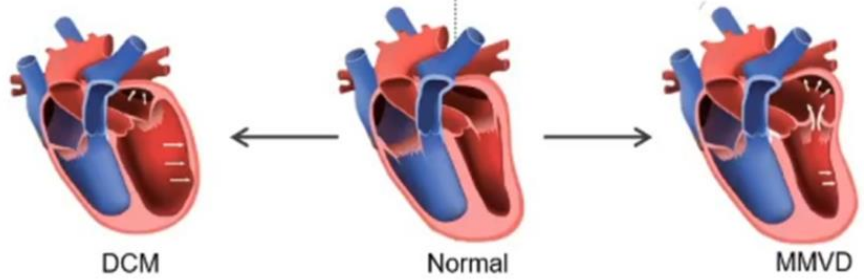
- Age: 3-7 years old
- High-risk breeds: Large breeds (Boxer, Doberman, Great Dane, Irish Wolfhound, Saint Bernard)
- Condition: Thinning of the ventricular walls
  - → Poor pumping capacity

MMVD (Mitral valve disease)

mitral valve disease

: Most common heart disease in small dogs (more than 70% of all dogs with heart disease)

- Age: Older (9 years old)
- Breeds at higher risk: Small to medium breeds (including Cavalier King Charles Spaniel)
- Condition: As dogs age, the valves thicken.
  - →Blood leaks backwards



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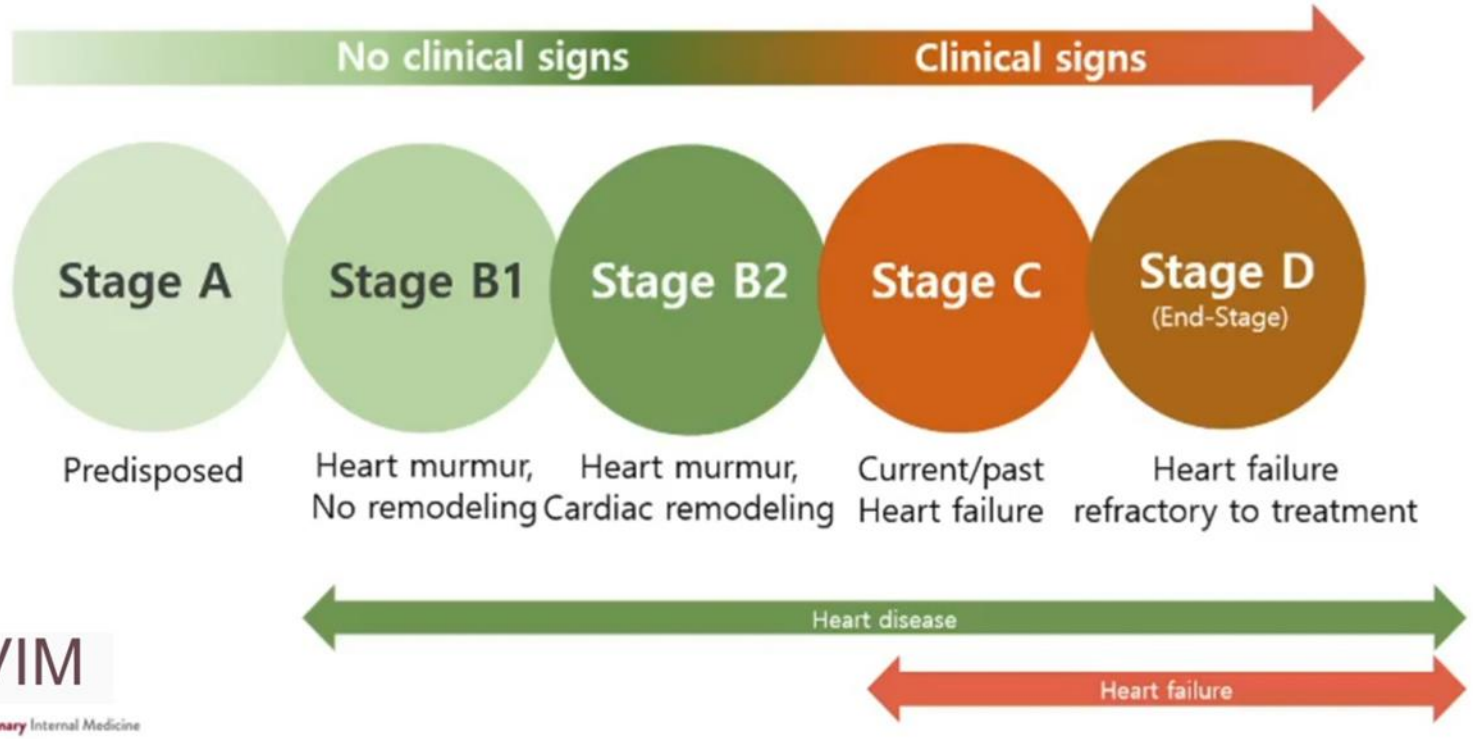
e. Canine Heart Disease Markers – NT-proBNP

ACVIM (American College of Veterinary Internal Medicine) consensus for dogs with MMVD

ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs

Bruce W. Keene1| Clarke E. Atkins | John D. Bonagura2 | Philip R. Fox | Jens Häggström | Virginia Luis Fountains | Mark A. Oyama | John E. Rush? | Rebecca Stepien | Masami Uechi
isn't following anyone. Autodesk_new



ACVIM
American College of Veterinary Internal Medicine

***Stage B2 criteria**

- Murmur ≥ 3/6
  - LA: Ao ratio ≥ 1.6
- LVIDDN ≥ 1.7
- VHS > 10.5

InSight V-IA®

e. Canine Heart Disease Markers – NT-proBNP

Table 2 Median and range of age, weight, echocardiographic measures and NTproBNP for healthy dogs and dogs with myxomatous mitral valve disease (272 observations on 38 dogs).

Variable	Healthy	MMVD stage B1	MMVD stage B2	MMVD stage C-stable
	N = 10	N = 10	N = 10	N = 8
Age (years)	2.27 (1.32–11.30)	8.18 (4.07–11.38)	8.16 (6.02–12.32)	11.77 (8.99–14.87)
Weight (kg)	10.65 (5.10–13.6)	7.40 (5.60–9.10)	8.95 (6.70–11.80)	9.15 (5.00–10.70)
Echo				
LA/Ao	1.25 (1.13–1.42)	1.32 (1.13–1.49)	1.79 (1.35–1.89)	1.73 (1.61–2.40)
LVIDdN	1.39 (1.15–1.59)	1.46 (1.14–1.64)	1.82 (1.70–2.31)	1.86 (1.20–2.26)
FS%	41.0 (27.3–50.5)	37.2 (29.4–49.0)	46.4 (37.1–51.3)	48.1 (39.2–64.1)
E/E′	8.54 (6.31–14.60)	8.63 (7.13–13.55)	9.71 (6.05–17.16)	12.42 (9.13–24.86)
E/IVRT	1.76 (0.86–2.50)	1.11 (0.77–1.61)	1.61 (1.21–2.67)	1.81 (1.02–3.90)
VHS		10.70 (9.20–11.10)	11.10 (10.80–12.80)	12.40 (9.80–12.70)
Biomarker	N = 160	N = 40	N = 40	N = 32
NTproBNP (pmol/L)	543 (16–1,558)	677 (24–1,344)	1,553 (531–3,010)	1,963 (424–4,086)

E/E′, ratio of left ventricular filling velocity to myocardial motion velocity in early diastole; E/IVRT, ratio of early diastolic left ventricular filling velocity to isovolumic relaxation time; FS%, fractional shortening; NTproBNP, N-terminal pro-brain natriuretic peptide pmol/L; LA/Ao, ratio of left atrial size in short axis to aortic diameter; LVIDdN, left ventricular internal dimension in diastole normalized to body weight; VHS, vertebral heart size.

InSight V-IA®

e. Canine Heart Disease Markers – NT-proBNP

Consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in village dogs"

6.5.1 | Recommendations for stage C diagnosis

- Serum NT-proBNP concentrations (obtained by commercial testing) can provide useful adjunct evidence in determining the cause of clinical symptoms in dogs with MMVD, especially when NT-proBNP concentrations are normal or near-normal. Dogs with clinical signs of heart failure have higher serum NT-proBNP concentrations than dogs with clinical signs of primary lung disease, but the positive predictive value of any one specific NT-proBNP concentrations has not been adequately characterised. A dog with normal or near-normal NT-proBNP concentrations accompanied by clinical signs of cough, dyspnoea, or exercise intolerance strongly suggests that heart failure is not the cause of the clinical signs.


CONSENSUS STATEMENT

Journal of Veterinary Internal Medicine ACVIM

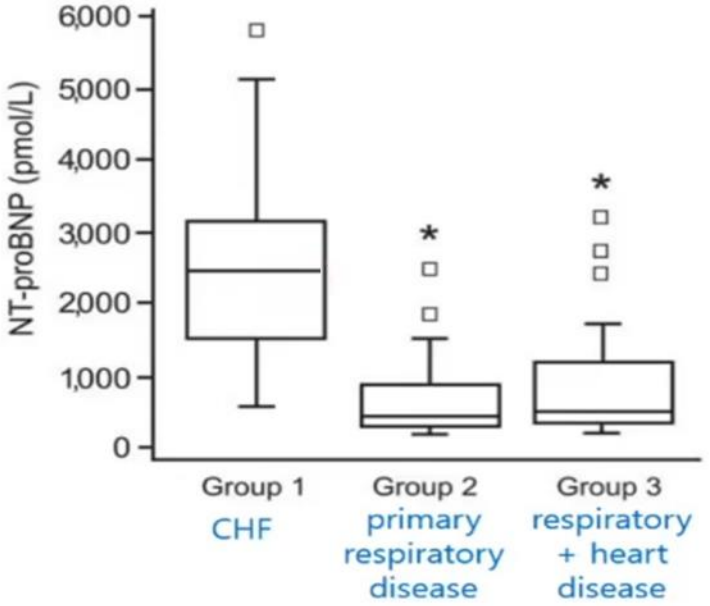
ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs

Bruce W. Keene | Clarke E. Atkins | John D. Bonagura | Philip R. Fox | Jens Häggström | Virginia Luis Fuentes | Mark A. Oyama | John E. Rush | Rebecca Stepien | Masami Uechi

e. Canine Heart Disease Markers – NT-proBNP

Measuring serum NT-proBNP concentrations in dogs with respiratory symptoms can help differentiate congestive heart failure from underlying causes of primary respiratory disease.

Assessment of serum N-terminal pro-B-type natriuretic peptide concentration for differentiation of congestive heart failure from primary respiratory tract disease as the cause of respiratory signs in dogs



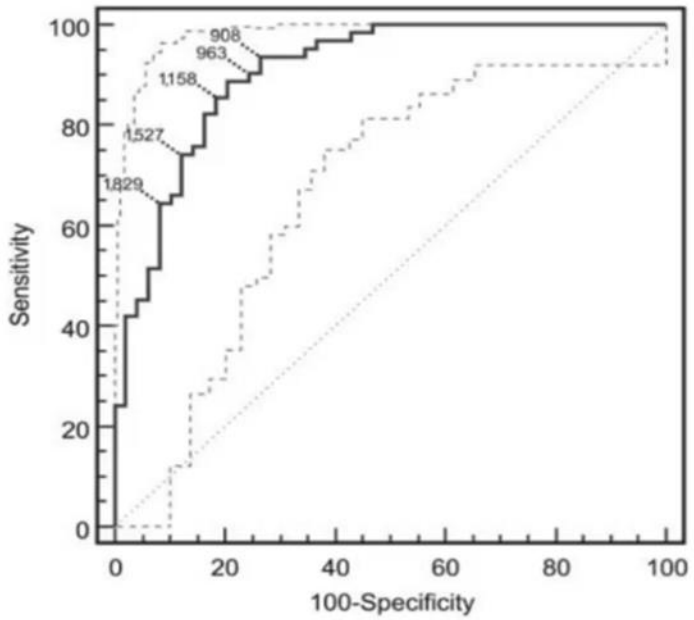
- 1 (CHF)
  - NT-proBNP : 2445 pmol/L[1499-3134 pmol/L]
- Group 2 (primary respiratory diseases)
  - NT-proBNP : 413 pmol/L[245-857 pmol/L]
- Group 3 (respiratory system + heart disease)
  - NT-proBNP : 478 pmol/L[323-1158 pmol/L]

InSight V-IA®

e. Canine Heart Disease Markers – NT-proBNP

Measuring serum NT-proBNP concentrations in dogs with respiratory symptoms helps differentiate congestive heart failure and underlying causes of primary respiratory disease.

Assessment of serum N-terminal pro-B-type natriuretic peptide concentration for differentiation of congestive heart failure from primary respiratory tract disease as the cause of respiratory signs in dogs



The AUC_{ROC} was **90.5%** (95% CI, 83.4% to 95.2%)

Cut-off	Sensitivity	Specificity
> 963 pmol/L	90.3%	73.5%
> 1,158 pmol/L	85.5%	81.3%
> 1,829 pmol/L	64.5%	91.7%

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e. Canine Heart Disease Markers – NT-proBNP

ACVIM (American College of Internal Medicine)

Journal of Veterinary Internal Medicine ACVIM

STANDARD ARTICLE

Factors associated with disease progression in dogs with presumed preclinical degenerative mitral valve disease attending primary care veterinary practices in the United Kingdom

Madeleine J. Mattin | David C. Brodbelt | David B. Church | Adrian Boswood

t Internal Med. 2019;33:445–454.

ACVIM

American College of Veterinary Internal Medicine

Assess the likelihood of not reaching heart failure (or cardiac death) within 1 year

(asymptomatic dogs, non-CKCS)

1. Cough
2. Noise intensity (level 1~6)
3. NT proBNP test
4. Heart rate

Not CKCS, no cough

	NT-proBNP (pmol/L)	Heart rate (bpm) <110	Heart rate (bpm) 110 - 140	Heart rate (bpm) >140
Soft murmur Grade I/VI II/VI	<900	97.3 (95.1-98.5)	96.3	94.8
	900-1800	95.3	93.7	91.0
	>1800	87.8	83.9	77.6 (61.8-87.6)
Moderate murmur Grade III/VI	<900	93.7 (89.9-96.0)	91.5	88.1
	900-1800	89.1	85.6	79.9
	>1800	73.4	65.9	54.8 (36.9-69.4)
Loud murmur Grade IV/VI	<900	92.8 (87.9-95.8)	90.4	86.5
	900-1800	87.7	83.8	77.5
	>1800	70.3	62.2	50.5 (31.7-66.6)
Thrilling murmur Grade V/VI	<900	88.5 (78.5-94.0)	84.8	78.8
	900-1800	80.6	74.7	65.7
	>1800	56.1	45.8	32.5 (11.9-55.1)

Not CKCS, cough reported

	NT-proBNP (pmol/L)	Heart rate (bpm) <110	Heart rate (bpm) 110 - 140	Heart rate (bpm) >140
Soft murmur Grade I/VI II/VI	<900	95.4 (91.4-97.6)	93.8	91.2
	900-1800	92.0	91.2	85.1
	>1800	80.0	74.0	64.8 (43.8-79.6)
Moderate murmur Grade III/VI	Done			
	<900	89.4 (82.1-93.8)	85.9	80.4
	900-1800	82.1	76.67	68.1
	>1800	58.8	48.8	35.6 (17.7-54.1)
Loud murmur Grade IV/VI	<900	88.0 (79.4-93.2)	84.2	78.0
	900-1800	79.9	73.8	64.6
	>1800	54.7	44.3	30.9 (14.4-49.1)
Thrilling murmur Grade V/VI	<900	81.0 (66.1-89.9)	75.3	66.5
	900-1800	69.1	60.7	48.7
	>1800	37.0	26.2	14.5 (3.3-33.7)

Detection range: 5-10000pmol/L

significance	pg/mL	pmol/L
low heart failure risk	<9490	<900
Suspected MVD or DCM or cardiac hypertrophy	>9490	>900
high risk heart failure	>18981	>1800

InSight V-IA®

e. Canine Heart Disease Markers – NT-proBNP

4) Pre-analysis error

: NT-proBNP is significantly degraded when using the current method at refrigeration and room temperature, which may alter diagnostic and prognostic decision-making.

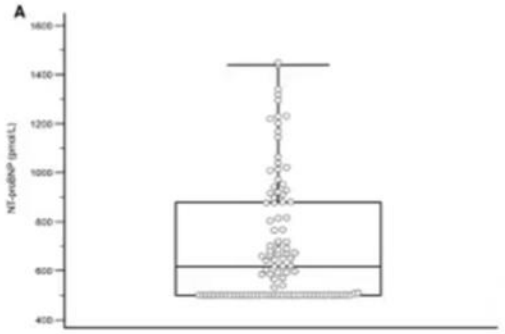
When 10 unaltered samples of raw canine serum were stored at 4°C, a loss of approximately 20% of the original mean concentration was recorded within 14 h, during which time sample losses ranged from 16% to 33%. Ten samples were then purposely left at room temperature (20°C) overnight. Measurements the next day showed a reduction in concentration of at least 50% in all samples, which would lead to significant differences in clinical interpretation for all samples.

5) Reference time interval

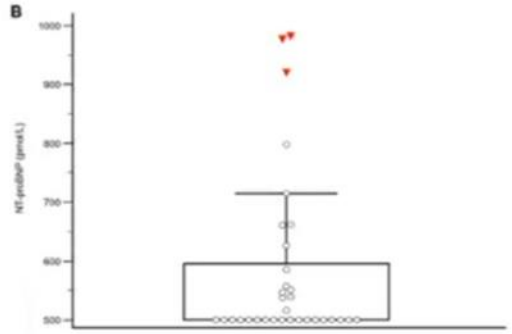
: The reference value of the age division reference interval for puppies and adult dogs

They are 750pmol/L and 1280pmol/L respectively.

Six outliers were removed from apparently healthy adult dogs (n=125) using Tukey's outlier analysis, resulting in a median ± SD of 119 remaining values with a min/max range of 617 ± 257, <500- 1450. Using the nonparametric percentile approach, the 95% medical reference interval was <500-1280 pmol/L, with a 90% CI for the upper reference limit of 1168-1440 pmol/L. From apparently healthy pups (n=36), three outliers were removed using Tukey's outlier analysis, resulting in a median standard deviation of the 33 remaining values, min/max range <500±142, <500- 982pmol/L. (Fig. 4B) 95% of the medical reference interval is <500-750 pmol/L, with a 90% confidence interval for the upper reference limit of 719-884 pmol/L



125 apparently healthy, **adult dogs** (between 2 years and geriatric ages)



36 apparently healthy, **juvenile** dogs (between 0 and 18 months)

InSight V-IA®

e. Canine Heart Disease Markers

Published in 2022

Research Articles

Assessment of Two New Commercial Rapid Tests for Canine N-terminal Pro-B-type Natriuretic Peptide to Distinguish the Severity of Mitral Valve Disease in Dogs

Nattapon Riengvirodkij[1] Walasinee Sukcamduang[2*]

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[2]Department of Clinical Sciences and Public Health, Faculty of Veterinary Science, Mahidol University, Salaya, Phutthamonthon, Nakhon Pathom, Thailand

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Abstract

N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) is a potential cardiac biomarker released primarily from ventricular myocytes. Previous studies in dogs suggest that the NT-proBNP assay can be used to distinguish dogs with respiratory signs between congestive heart failure and primary respiratory illnesses. The objective of this study is to determine and assess the clinical sensitivity and specificity of the two new NT-pro-BNP immunoassay tests for distinguishing dogs affected by myxomatous mitral valve disease (MMVD) between with and without congestive heart failure (CHF), as well as between dogs with MMVD and normal dogs. Thirty-seven dogs were enrolled in this study. Thirty-two dogs were measured by the NT-proBNP immunoassay test (Bionote®), including 11 healthy dogs, 11 dogs with MMVD stage B2 (absence of CHF) and 10 dogs with MMVD stage C (presence of CHF). Twenty-eight dogs were measured by the NT-proBNP rapid detection kit (Dianotech®), including 6 healthy dogs, 7 dogs with MMVD stage B2 and 15 dogs with MMVD stage C.

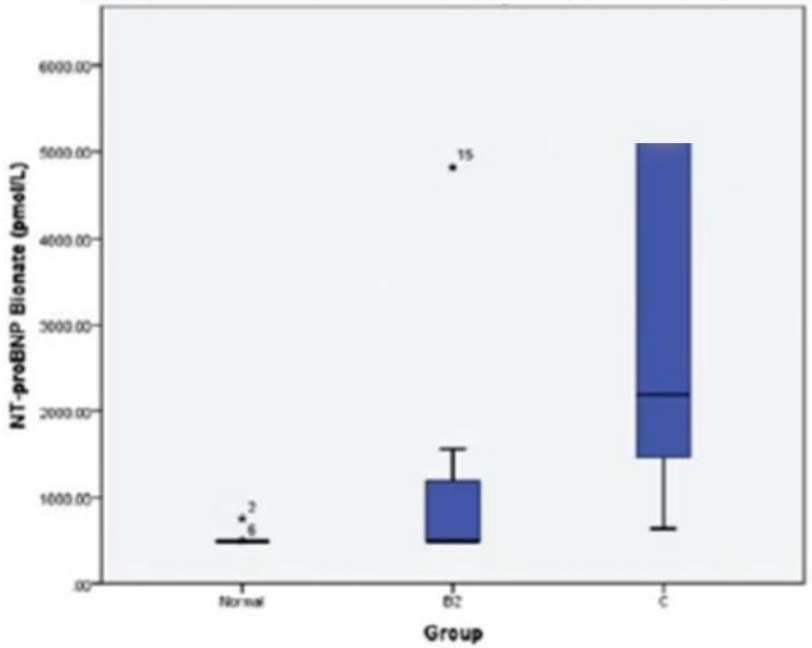
The median NT-proBNP concentration in dogs with MMVD stage C was significantly higher than the median NT-proBNP concentration in dogs with MMVD stage B2 and normal healthy dogs (p-value <0.001). The Receiver operating characteristic (ROC) curve analysis showed that serum NT-proBNP concentration could differentiate dogs with CHF signs (MMVD stage C) from dogs without CHF signs (normal healthy dogs and MMVD stage B2. The area under the curve (AUC) was 0.932 and 0.928 for NT-proBNP Bionote® and Dianotech® test, respectively. It also could discriminate dogs affected by MMVD with CHF (MMVD stage C2) from dogs affected by MMVD without CHF (MMVD stage B2) with AUC of 0.818 and 0.867 for NT-proBNP Bionote® and Dianotech® tests, respectively. In conclusion, the results suggested that serum NT-proBNP concentrations tests from both companies could discriminate between dogs affected by CHF from those without CHF and normal healthy dogs with reasonable accuracy.

Keywords: N-terminal pro-B-type natriuretic peptide, NT-pro-BNP, mitral valve disease, dogs

Journal of Applied Animal Science 2021; 14(2): 9-20.

Nattapon Riengvirodkij, Mahidol University, et al. .

- Elevated NT-proBNP in dogs with heart failure
  - NT-proBNP in dogs with MMVDC was significantly higher than in normal dogs and dogs with MMVD B2.



Conclusion

- BNP is used to detect the presence of heart failure and Troponin is used to detect the degree of myocardial damage, preferably combined interpretation.

- After a heart disease is diagnosed, the BNP value can also evaluate whether the symptoms of heart failure are relieved. Feline Troponin can be used to predict the life expectancy after heart disease. If the Feline Troponin is controlled below 0.7, the life expectancy will be 1000-1200 days, above 0.7 is expected to be 60-120 days.

InSight V-IA®

cNT-proBNP/ccTnI Rapid Quantitative Test

Woodley have developed a rapid, accurate, reliable and highly sensitive detection method for NT-proBNP/cTnI in dogs.

The InSight V-IA cNT-proBNP/ccTnI Rapid Quantitative Test is a fluorescence immunoassay used with the InSight V-IA Veterinary Immunoassay Analyser for the quantitative determination of cNT-proBNP and ccTnI concentration in canine serum or plasma.

The test is used to assist myocardial function diagnosis and diagnosis of cardiomyocyte injury.

It can be stored at room temperature.

InSight V-IA®

fNT-proBNP/fcTnI Rapid Quantitative Test

Woodley have developed a rapid, accurate, reliable and highly sensitive detection method for NT-proBNP/cTnI in cats.

The InSight V-IA fNT-proBNP/fcTnI Rapid Quantitative Test is a fluorescence immunoassay used with the InSight V-IA Veterinary Immunoassay Analyser for the quantitative determination of fNT-proBNP and fcTnI concentration in feline serum or plasma.

The test is used to assist myocardial function diagnosis and diagnosis of cardiomyocyte injury.

It can be stored at room temperature.

Thank You

WOODLEY
EQUIPMENT COMPANY LTD.

InSight V-IA®