

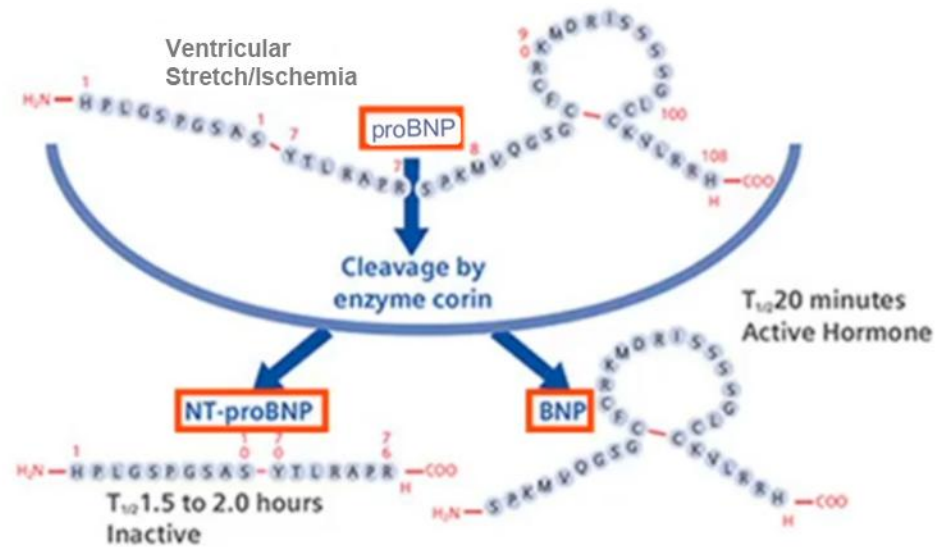


Canine Heart Markers – NT-proBNP + cTnI

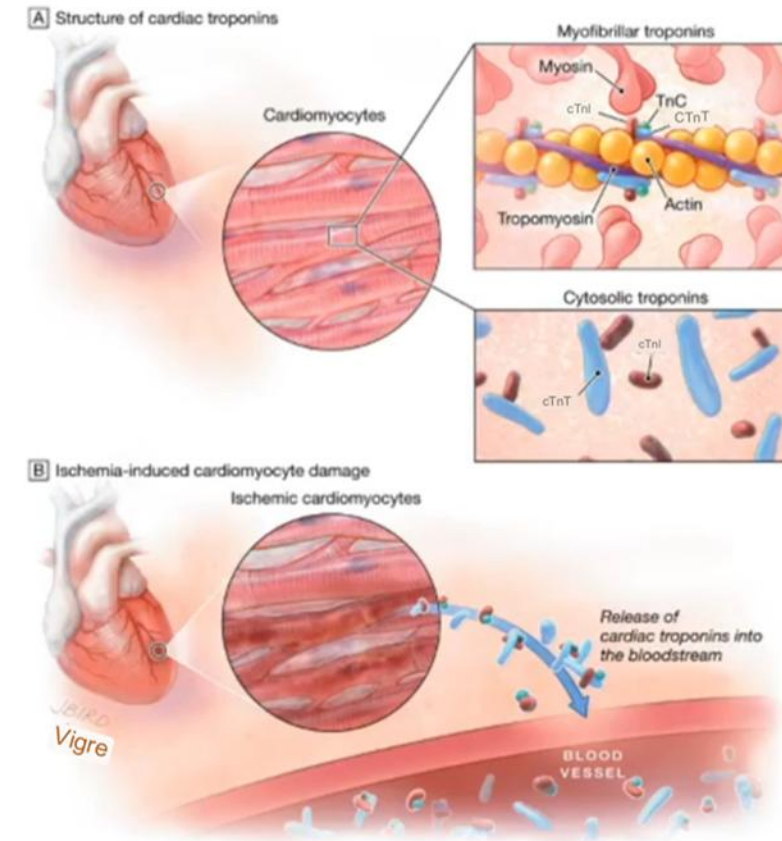
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a. Cardiac Markers



NT-proBNP



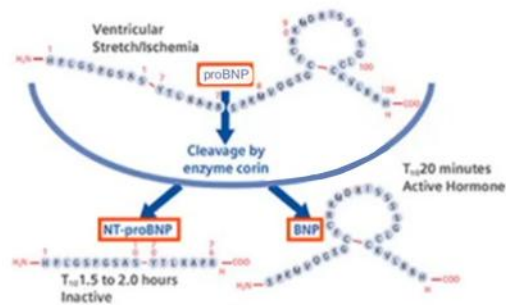
Troponin I Cardiac Troponin I

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

Natriuretic Peptides (NP)



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	<u>Mainly ventricles</u>
CNP	Brain, endothelium, kidney, chondrocytes, and pituitary gland
DNP	Venom gland of <i>Dendroaspis angusticeps</i> (eastern green mamba)
VNP	Primitive heart, normally in fish

b. Canine Heart Disease Markers

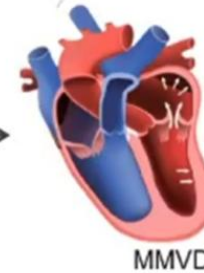
In Dogs,

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 Breeds at higher risk: Small to medium breeds (including Cavalier King Charles Spaniel) 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)

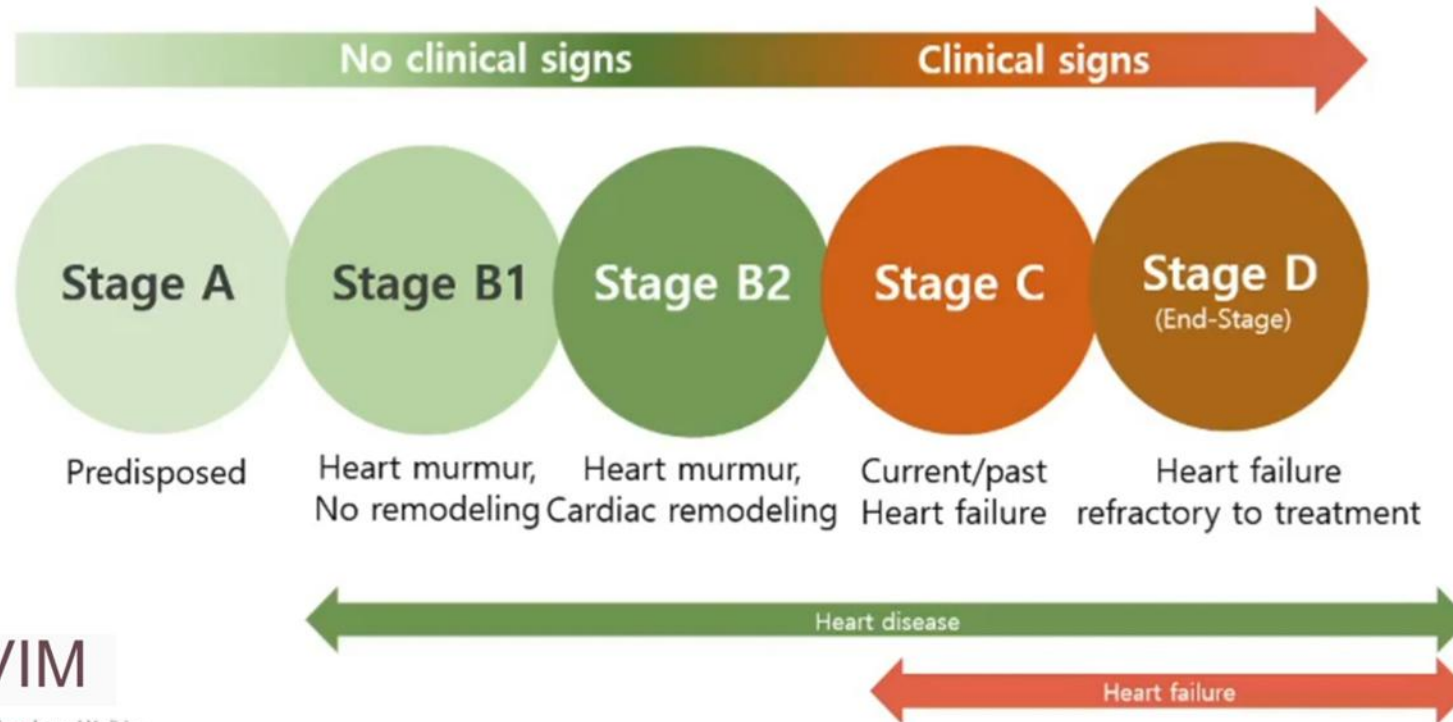
- Age: Older (9 years old)
- Condition: As dogs age, the valves thicken.
→ Blood leaks backwards

b. 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. Rush³ | Rebecca Stepien | Masami Uechi
isn't following anyone, Autodesk_new *



*Stage B2 criteria

- Murmur $\geq 3/6$
- LA: Ao ratio ≥ 1.6
- LVDDN ≥ 1.7
- VHS > 10.5

ACVIM

American College of Veterinary Internal Medicine

b. 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 N = 10	MMVD stage B1 N = 10	MMVD stage B2 N = 10	MMVD stage C-stable 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)

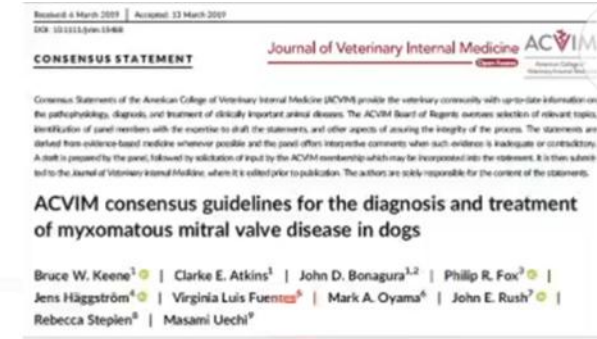
E/E', ratio of left ventricular filling velocity to myocardial motion velocity in early diastole; E/IVRT, ratio of early diastolic left ventricular filling velocity to isovolumic relaxation time; FS%, fractional shortening; NTproBNP, N-terminal pro-brain natriuretic peptide pmol/L; LA/Ao, ratio of left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

b. Canine Heart Disease Markers – NT-proBNP

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

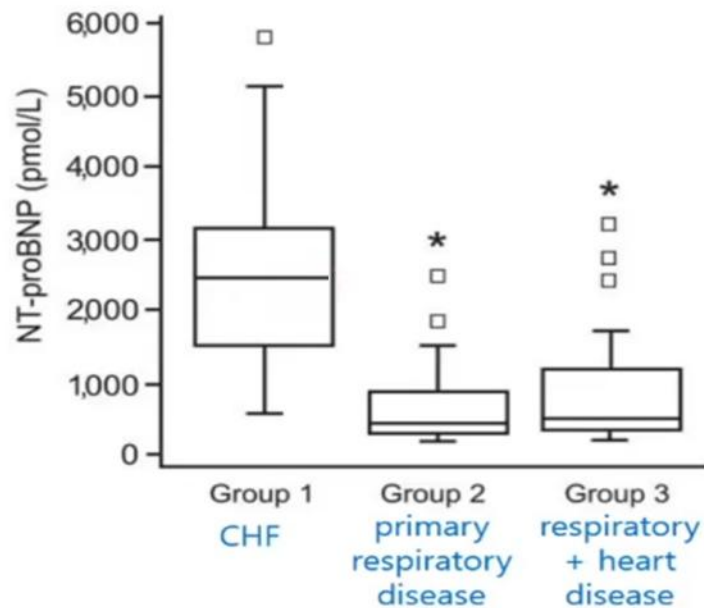
6.5.1 | Recommendations for stage C diagnosis

- 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.



b. 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.



- 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]

b. 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

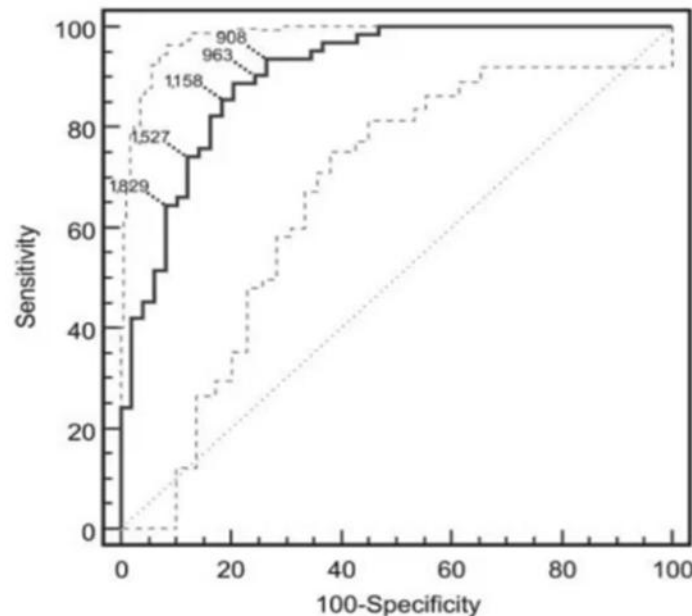
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Objective—To determine whether serum N-terminal pro-B-type natriuretic peptide (NT-proBNP) concentration is useful in discriminating between cardiac and noncardiac (ie, primary respiratory tract disease) causes of respiratory signs (ie, coughing, staccato stink, excessive panting, increased respiratory effort, tachypnea, or both) in dogs.

Design—Multicenter cross-sectional study.

Animals—115 dogs with respiratory signs.

Procedures—Dogs with respiratory signs were selected for study. Physical examination, thoracic radiography, and echocardiography were used to determine whether respiratory signs were the result of cardiac (ie, congestive heart failure) or noncardiac (ie, primary respiratory tract disease) causes. Serum samples for NT-proBNP assay were obtained at time of admission for each dog. Receiver operating characteristic curves were constructed to determine the ability of serum NT-proBNP concentration to discriminate between cardiac and noncardiac causes of respiratory signs.



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%

b. Canine Heart Disease Markers – NT-proBNP

ACVIM (American College of Internal Medicine)

ACVIM

American College of **Veterinary** Internal Medicine



J. Intern. Med. 2019;33:445–454.

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

	NT proBNP (pmol/L)	Not CKCS, no cough			Not CKCS, cough reported		
		Heart rate (bpm)			Heart rate (bpm)		
Soft murmur Grade I/II	<900	97.3 (95.1–99.5)	96.3	94.8	<900	95.4 (91.4–97.6)	91.2
	900–1800	95.3	93.7	91.0	900–1800	92.0	85.1
	>1800	87.8	83.9	77.6 (85.8–87.8)	>1800	80.0	64.8 (73.8–79.8)
Moderate murmur Grade III/IV	<900	93.7 (89.9–96.0)	91.5	88.1	<900	89.4 (82.1–91.8)	80.4
	900–1800	89.1	85.6	79.9	900–1800	82.1	76.67
	>1800	73.8	65.9	54.8 (56.9–59.6)	>1800	58.8	48.6 (51.7–54.1)
Loud murmur Grade V/VI	<900	92.8 (87.9–95.8)	90.4	86.5	<900	88.0 (79.4–91.2)	78.0
	900–1800	87.7	83.8	77.5	900–1800	79.5	73.8
	>1800	70.3	62.2	50.5 (51.7–56.6)	>1800	54.7	48.3 (51.4–55.1)
Thrilling murmur Grade V/VI you/you	<900	88.5 (78.5–94.8)	84.8	78.8	<900	81.0 (68.1–89.5)	66.5
	900–1800	80.6	74.7	65.7	900–1800	69.1	60.7
	>1800	56.1	45.8	32.5 (33.9–38.1)	>1800	37.0	26.2 (31.3–33.7)

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

b. 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.

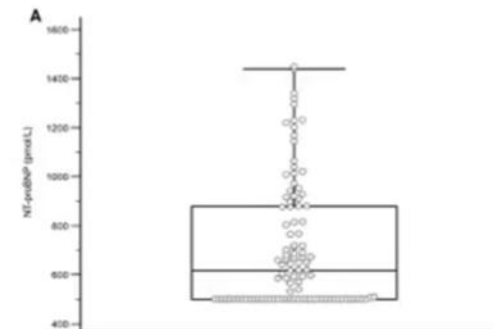
When 10 unaltered samples of raw canine serum were stored at 4°C, a loss of approximately 20% of the original mean concentration was recorded within 14 h, during which time sample losses ranged from 16% to 33%. Ten samples were then purposely left at room temperature (20°C) overnight. Measurements the 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

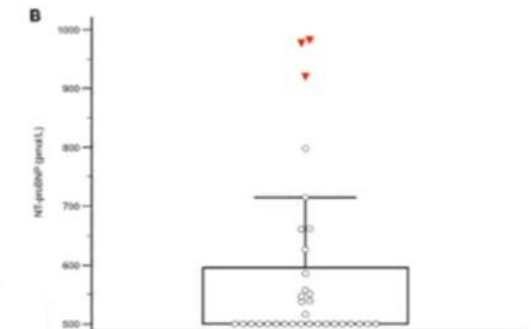
: The reference value of the age division reference interval for puppies and adult dogs

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 $\pm$ 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 $<500 \pm 142$, <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)

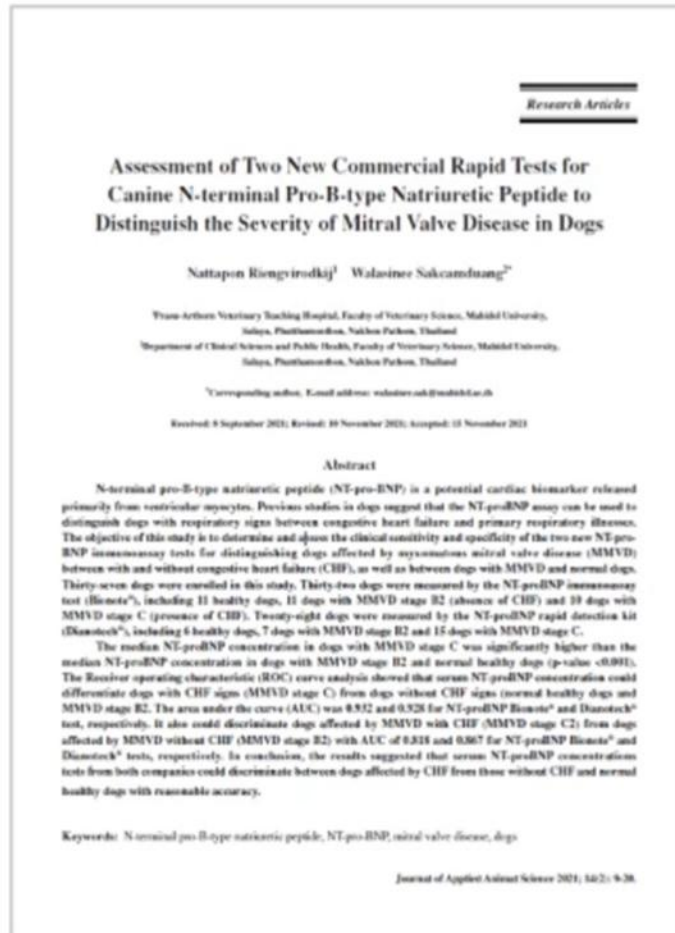
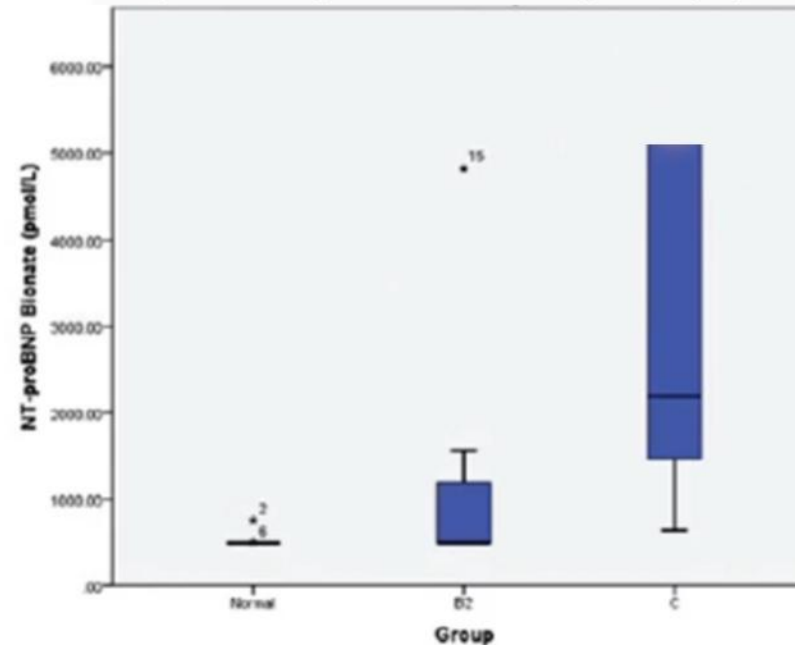
b. Canine Heart Disease Markers

Published in 2022

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[®] Canine-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 Canine-IA cNT-proBNP/ccTnI Rapid Quantitative Test is a fluorescence immunoassay used with the InSight Canine-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.





Thank You