Vcheck
Canine NT-proBNP

BIONOTE Marketing team

Aug. 2020

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Vcheck Canine NT-proBNP

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What is NT-proBNP?

- **B-type natriuretic peptide (proBNP)**

  - Produced in the muscle cells of the heart

  - Increases with excessive stretching of the cells

- proBNP is cleaved into BNP and NT-proBNP*

  (*NT-proBNP: N-terminal pro-B type natriuretic peptide)
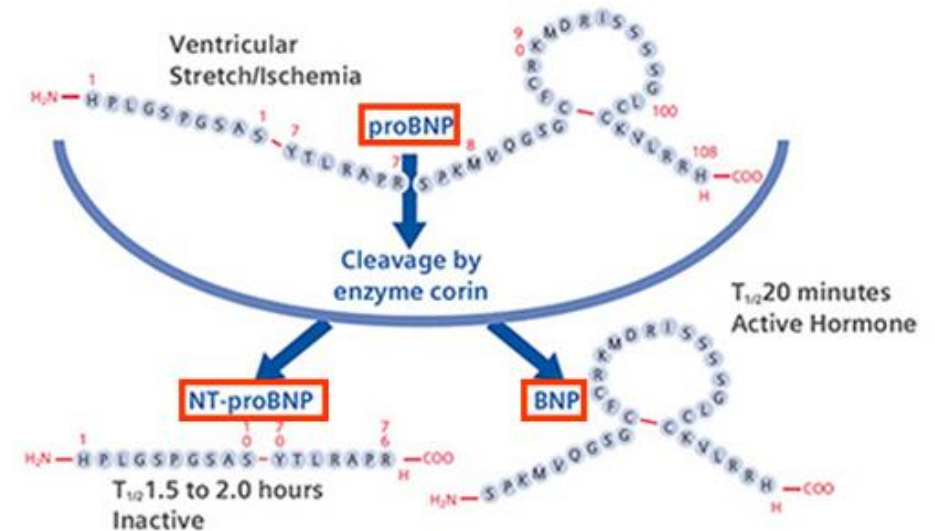
NT-proBNP is stable and has a long half-life, making it a more desirable biomarker.

⇒ **Thus, it is used to assess the magnitude of cardiac muscle stretching**

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NT-proBNP in Dogs
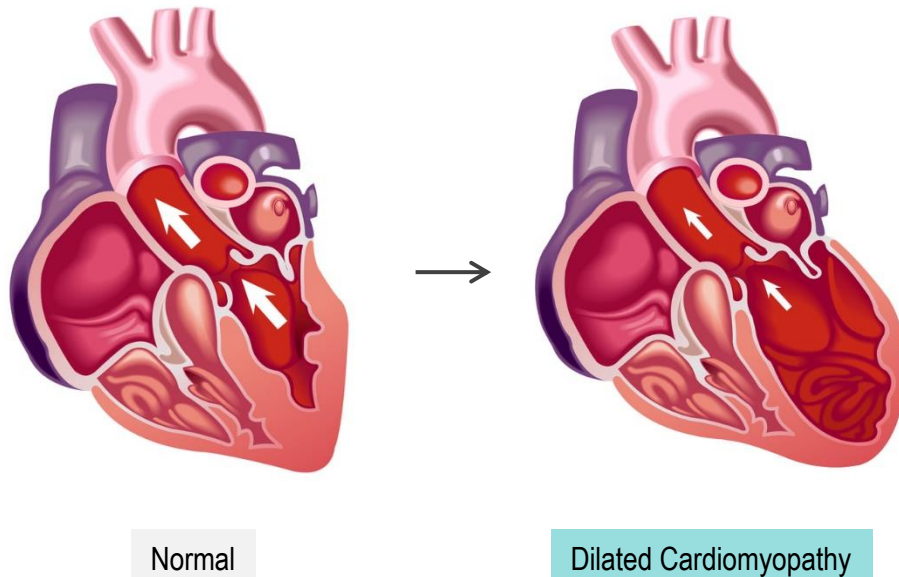
- What NT-proBNP levels tell us -

▲ A dog presenting difficulty breathing (dyspnea)

*DCM: Dilated Cardiomyopathy

- **Screens for asymptomatic DCM* in large breeds**
  - ✓ Highly sensitive and specific for detecting DCM

**MMVD: Myxomatous Mitral Valve Degeneration

- **Differentiates severe MMVD** patients from low-stage patients**
  - ✓ Differentiates dogs with and without heart failure among the MMVD patients

- **Distinguishes cardiac from respiratory disease**
  - ✓ Useful in dogs with dyspnea requiring an emergency care

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DCM (Dilated Cardiomyopathy)

- **Dilated Cardiomyopathy (DCM)**

◄ Doberman Pinscher

60% chance of developing DCM

The most common cause of heart disease <u>in large breeds</u>

(10% of all heart disease)

- Breed
  - **Large breeds** (Boxer Dogs, Doberman Pinschers, Great Danes, Irish Wolfhounds, Saint Bernards);
 - Rarely develops in small breeds

- Doberman Pinscher
  - Very high risk of developing cardiomyopathy
  - **Recommendation**: Echocardiogram + ECG (Holter) (Annually from 3-4 years of age)

- Clinical signs
  - Lethargy, weakness, weight loss, collapse
  - [Heart failure] dyspnea, increased respiratory rate, ….

Normal

Dilated Cardiomyopathy

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DCM (Dilated Cardiomyopathy)

- **Dilated Cardiomyopathy (DCM)**

Normal

Dilated Cardiomyopathy

Lung
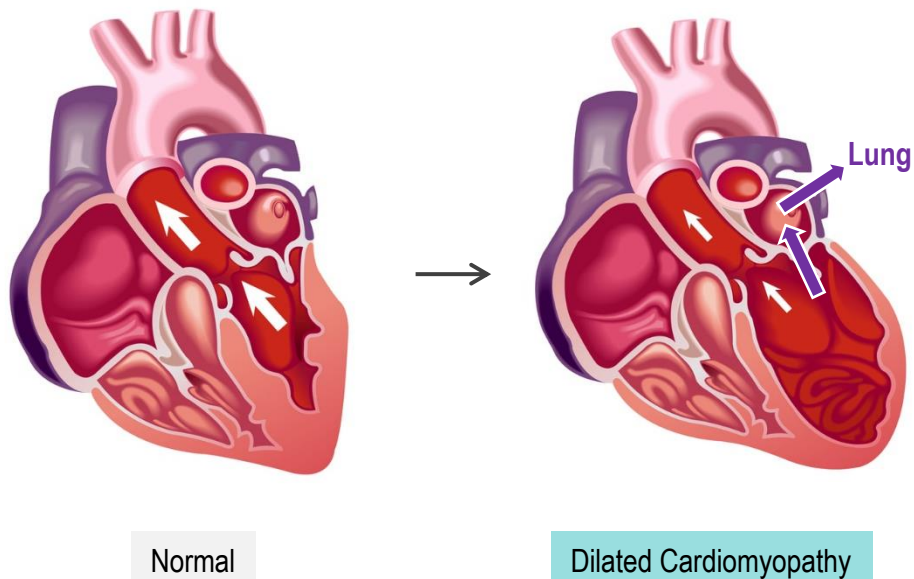
* Myocardial failure of the left side is most common.

Ventricular wall thinning; Heart muscle loses its contraction ability

↓

The pressure of the blood inside the heart causes the wall to stretch

☞ Increasing NT-proBNP levels

↓

Results in an enlarged heart

↓

Can cause heart failure (pulmonary edema)

DCM (Dilated Cardiomyopathy)

✓ **Diagnosis**

Clinical examination

- **Symptoms**: Exercise intolerance, lethargy, weakness…
- **Auscultation**: Systolic murmur(-/+), gallop rhythm (-/+)

Electrocardiography (ECG)

- <u>The best screening test</u> (**VPC***: a common finding in early DCM)
- **Holter monitor**: 24 hour electrocardiogram (> 50 (100) VPCs/24 hours)
- **5-minute ECG**: > 1 VPC/5 min.

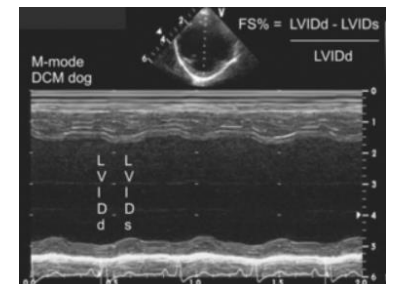 ***VPC**: Ventricular Premature Constration

Radiograph

- Not a good screening test in the early stages
- **Severe disease**: Enlarged left atrium, pulmonary edema…

▲ DCM patient with heart failure

Echocardiogram

- Systolic dysfunction (FS < 20%)
- Enlarged left atrium / Increased LVIDs, LVIDd

▲ DCM patient (Decreased FS)

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DCM (Dilated Cardiomyopathy)

✓ **Diagnosis**

Cardiac Biomarker: **NT-proBNP**

- A useful additional diagnostic test

- **Clinical utilities**

  ① Screens for DCM in Even Asymptomatic Dogs

  ② Evaluates the Survival Time

  ③ Increases the Diagnostic Accuracy When Used With a Holter Monitor
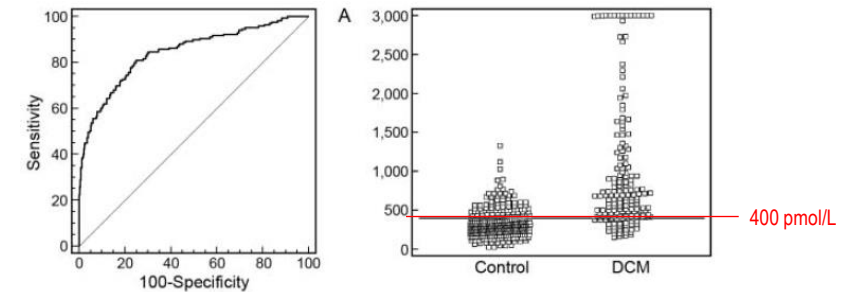
DCM (Dilated Cardiomyopathy)

✓ **Diagnosis**

Evaluation of N-terminal pro-B-type natriuretic peptide as a diagnostic marker of various stages of cardiomyopathy in Doberman Pinschers

Gerhard Wess, DVM, Dr med vet, Dr habil; Verena Butz, DVM, Dr med vet; Monia Mahling, Dip Stat; Katrin Hartmann, DVM, Dr med vet, Dr habil
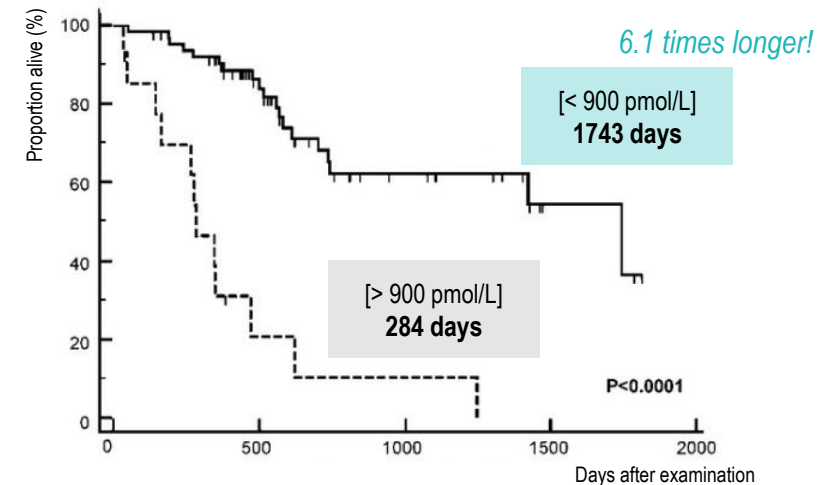
Cardiac Biomarker: **NT-proBNP**

- A useful additional diagnostic test

- **Clinical utilities**

  ① <u>Screens for DCM in Even Asymptomatic Dogs</u>

  ② Evaluates the Survival Time

  ③ Increases the Diagnostic Accuracy When Used With a Holter Monitor

400 pmol/L

NT-proBNP Conc. for detecting all stages of DCM

Cut-off (400 pmol/L) Sensitivity 81%, Specificity 75%

*Annual screening tests are recommended to determine if DCM is present **even if your dog appears to be healthy.***

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DCM (Dilated Cardiomyopathy)

✓ **Diagnosis**

Cardiac Biomarker: **NT-proBNP**

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6.1 times longer!

[< 900 pmol/L] **1743 days**

[> 900 pmol/L] **284 days**

P<0.0001

In asymptomatic Dobermans with DCM

DCM (Dilated Cardiomyopathy)

Prospective Evaluation of NT-proBNP Assay to Detect Occult Dilated Cardiomyopathy and Predict Survival in Doberman Pinschers

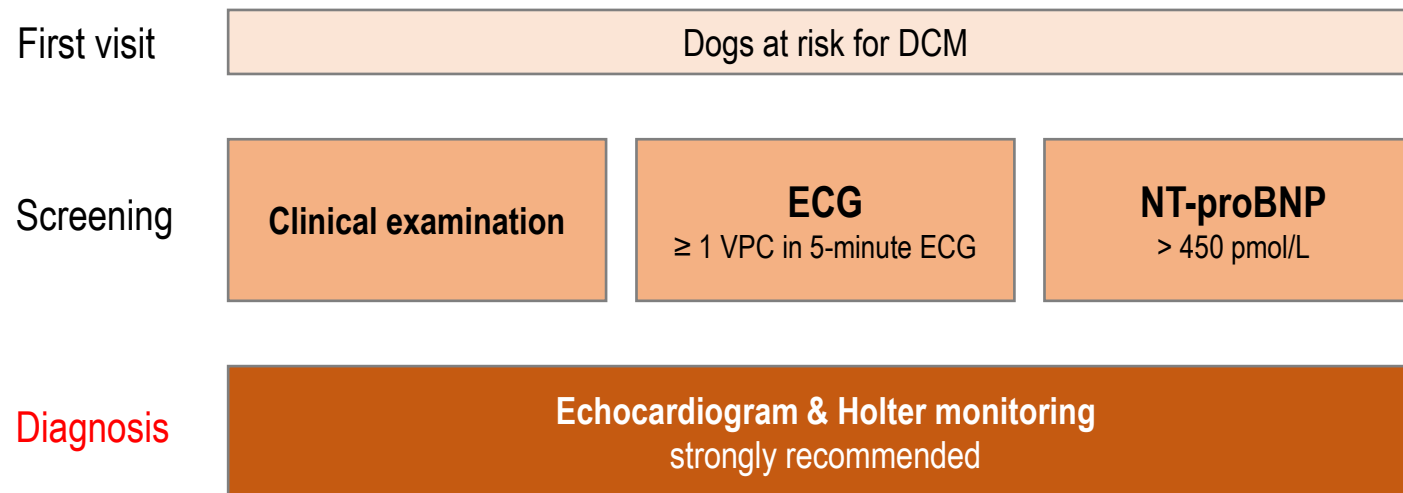G.E. Singletary, N.A. Morris, M. Lynne O'Sullivan, S.G. Gordon, and M.A. Oyama

✓ **Diagnosis**

Cardiac Biomarker: **NT-proBNP**

- A useful additional diagnostic test

- **Clinical utilities**

  ① Screens for DCM in Even Asymptomatic Dogs

  ② Evaluates the Survival Time

  ③ Increases the Diagnostic Accuracy When Used With a Holter Monitor

Criteria	Sens.	Spec.	Accuracy
NT-proBNP > 457	70 %	81 %	75.5 %
Holter monitoring	76.7 %	-	-
Holter or NT-proBNP > 457	94.5 %	87.8 %	91.0 %

▲ Diagnostic utility of NT-proBNP assay and Holter for the detection of occult DCM
(In 155 asymptomatic Dobermans)

The addition of NT-proBNP assay to Holter recording

as a diagnostic test improved sensitivity of detection!

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DCM (Dilated Cardiomyopathy)

✓ **Diagnosis** (Algorithm)

First visit	Dogs at risk for DCM

Screening	**Clinical examination**	**ECG** ≥ 1 VPC in 5-minute ECG	**NT-proBNP** > 450 pmol/L

Diagnosis	**Echocardiogram & Holter monitoring** strongly recommended

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MMVD (Myxomatous Mitral Valve Degeneration)
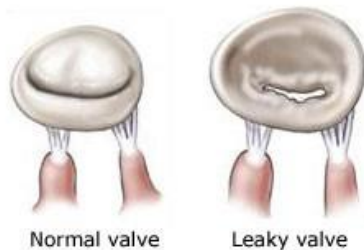
- **Myxomatous Mitral Valve Degeneration** (MMVD)

  ✓ **Most common heart disease**

  (> 70% of all cardiovascular disease in dogs)

  - Age: Older dogs
  - Breeds at elevated risk: Small or toy breeds (< 9 kg)
    - Cavalier King Charles (Very high incidence)
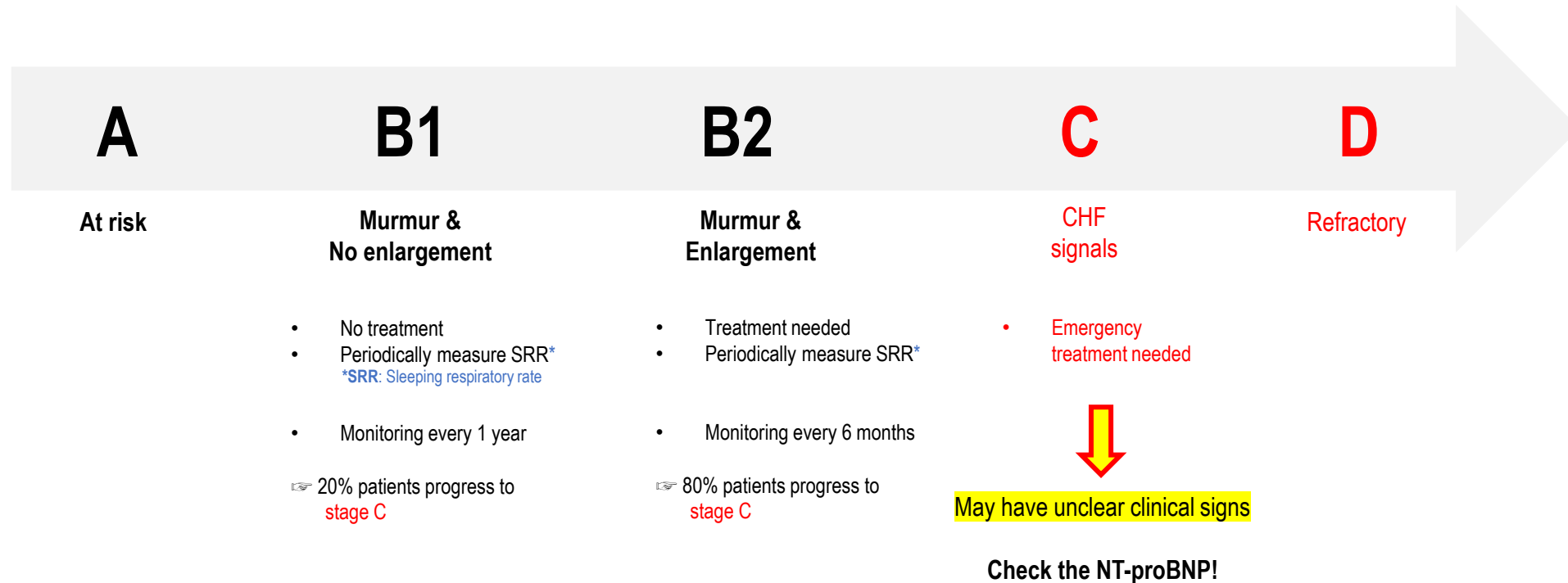
  ✓ **Pathophysiology** (left heart)

  ① As dogs age, the valve becomes thickened
  ② It starts to leak backwards ☞ MMVD
  ③ Abnormally high pressure
  ④ Could lead to pulmonary edema ☞ Heart failure

Normal valve   Leaky valve

Blood leaking back into left atrium

Left atrium

Lung

Mitral valve

Normal heart   MMVD

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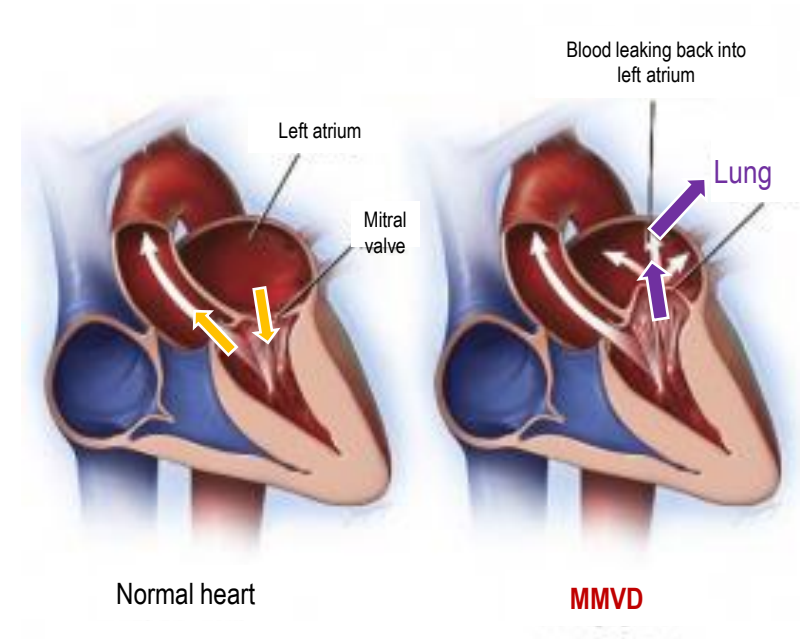
MMVD (Myxomatous Mitral Valve Degeneration)

- **ACVIM Consensus Classification**

ACVIM
American College of **Veterinary** Internal Medicine

A	B1	B2	C	D
At risk	Murmur & No enlargement	Murmur & Enlargement	CHF signals	Refractory

B1 — Murmur & No enlargement
- No treatment
- Periodically measure SRR*
  *SRR: Sleeping respiratory rate
- Monitoring every 1 year

☞ 20% patients progress to stage C

B2 — Murmur & Enlargement
- Treatment needed
- Periodically measure SRR*
- Monitoring every 6 months

☞ 80% patients progress to stage C

C — CHF signals
- Emergency treatment needed

May have unclear clinical signs

**Check the NT-proBNP!**

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MMVD (Myxomatous Mitral Valve Degeneration)

1. Stacey Fox-Alvarez, DVM, MPH, University of Florida
2. Malcolm, E. L., et al. 2018
3. Borgeat K. *In Practice* 2020

- **Diagnosis**

Clinical examination

- **Symptoms**: Exercise tolerance, dyspnea, continuous panting, cyanosis …

- **Auscultation**: Murmur, crackle sound
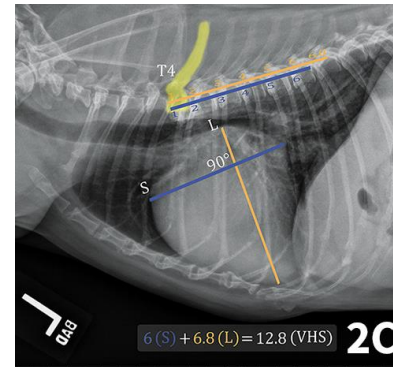
▲ Way to measure VHS in dogs
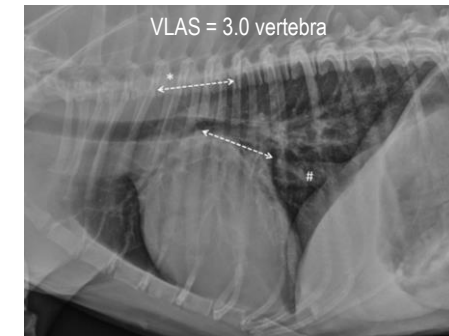
▲ Way to measure VLAS in dogs

Radiograph

- **Indicator of heart size**
  - VHS (Vertebral Heart Size) > 10.5 vertebrae
  - VLAS (Vertebral Left Atrial Size) > 3 vertebrae

- **Pulmonary patterns**
  - Assessment of pulmonary edema
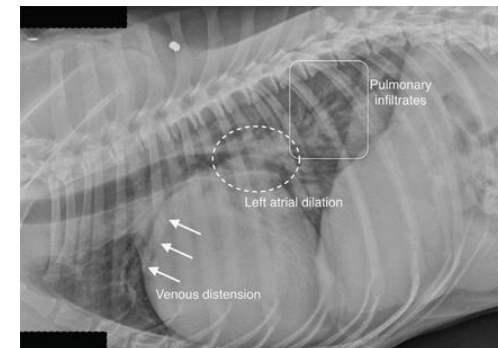
▲ Heart failure signs caused by mitral valve disease

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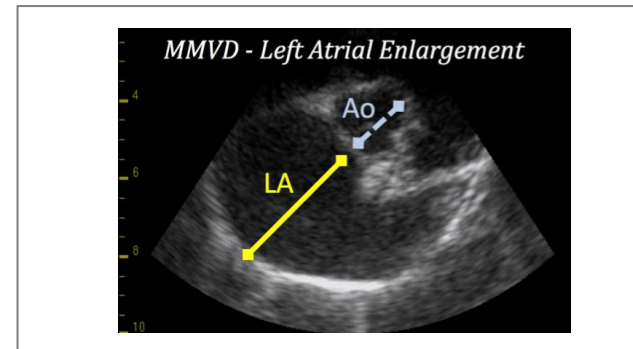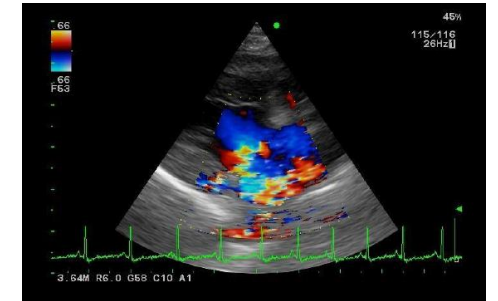# MMVD (Myxomatous Mitral Valve Degeneration)

- **Diagnosis**

  Echocardiogram

  - The best way to diagnose heart diseases

  - **2D mode**
    - Regurgitation to LA (at systole)
    - LA:Ao ≥ 1.6
    - Epeak ≥ 150 mm/s

  - **M mode**
    - LVIDd ≥ 25 mm (3kg)

▲ 2D mode

▲ 2D mode

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MMVD (Myxomatous Mitral Valve Degeneration)
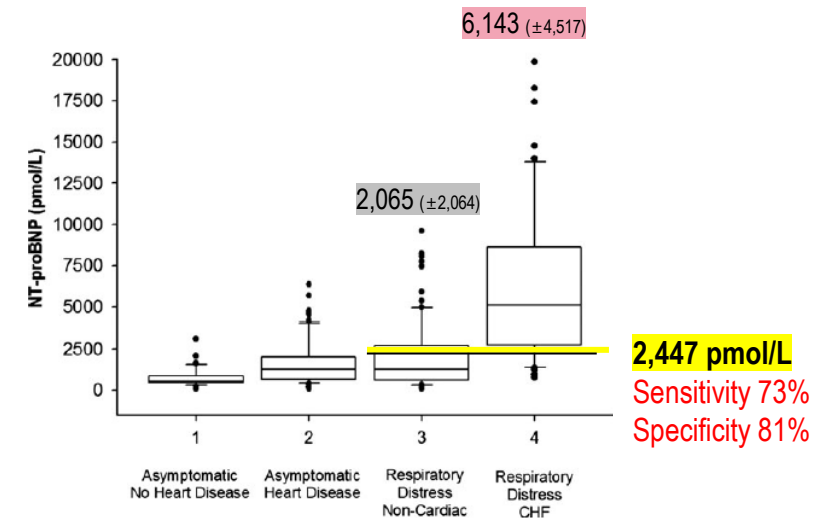
- **Diagnosis**

NT-proBNP (Biomarker)

- A useful clinical test for assessing the severity of heart disease

- **Clinical utilities**
  ① Helps Discriminate Cardiac from Noncardiac Causes of Dyspnea
  ② Discriminates Between Asymptomatic Dogs and Dogs With Heart Failure
  ③ Monitors the Effectiveness of Medical Treatment for Heart Failure
  ④ Predict Survival in Dogs With Heart Failure

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MMVD (Myxomatous Mitral Valve Degeneration)

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6,143 (±4,517)

2,065 (±2,064)

2,447 pmol/L
Sensitivity 73%
Specificity 81%

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MMVD (Myxomatous Mitral Valve Degeneration)

- ## Diagnosis

  NT-proBNP (Biomarker)

  - A useful clinical test for assessing the severity of heart disease

  - **Clinical utilities**
    1. Helps Discriminate Cardiac from Noncardiac Causes of Dyspnea
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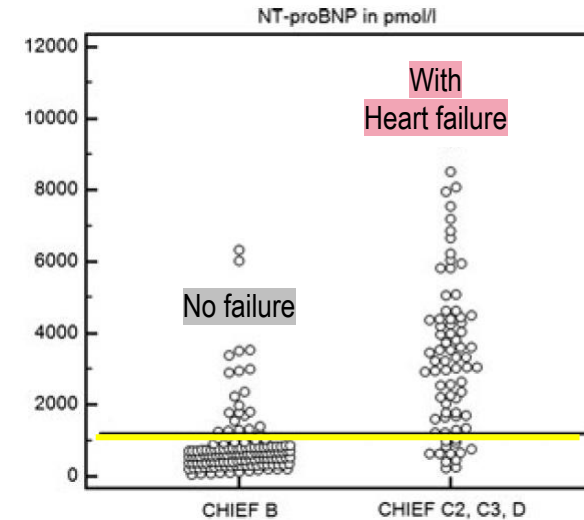   4. Predict Survival in Dogs With Heart Failure

ORIGINAL RESEARCH

The diagnostic relevance of NT-proBNP and proANP 31–67 measurements in staging of myxomatous mitral valve disease in dogs

Johanna Wolf[1], Nicola Gerlach[1], Karin Weber[1], André Klima[2], Gerhard Wess[1]

[1]Clinic of Small Animal Medicine and [2]Statistical Consulting Unit, LMU University, Munich, Germany

NT-proBNP in pmol/l

With Heart failure

No failure

1207 pmol/L
Sensitivity 83%
Specificity 85%

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MMVD (Myxomatous Mitral Valve Degeneration)

- **Diagnosis**

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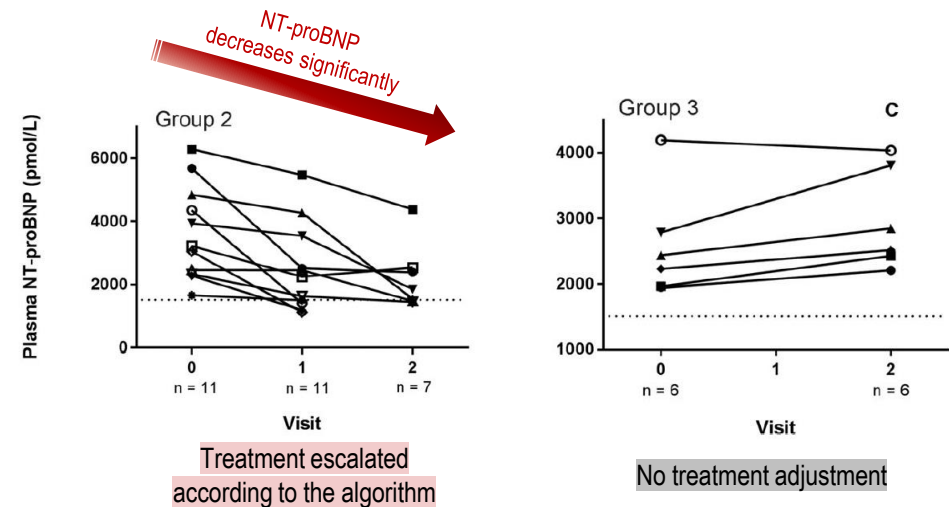 4. Predict Survival in Dogs With Heart Failure

Effect of prespecified therapy escalation on plasma NT-proBNP concentrations in dogs with stable congestive heart failure due to myxomatous mitral valve disease

Melanie J. Hezzell[1] | Chloë L. Block[1] | Danielle S. Laughlin[1] | Mark A. Oyama[1]

NT-proBNP decreases significantly

Group 2 — Treatment escalated according to the algorithm

Group 3 — No treatment adjustment

MMVD (Myxomatous Mitral Valve Degeneration)

Lowered N-terminal pro-B-type natriuretic peptide levels in response to treatment predict survival in dogs with symptomatic mitral valve disease

Johanna Wolf, MRCVS [a], Nicola Gerlach, DVM [a], Karin Weber, DVM [a], André Klima, Dip Stat [b], Gerhard Wess, DVM, Dr. habil [a,*]

- ## Diagnosis

NT-proBNP (Biomarker)

- A useful clinical test for assessing the severity of heart disease

- **Clinical utilities**
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NT-proBNP 7–30 days after initial diagnosis of CHF

- < 965 pmol/l: had significantly longer cardiac survival times

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02 Product Introduction

Vcheck Canine NT-proBNP

- Specifications

- Key Features

- Test Procedure & Reference Range

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Vcheck Canine NT-proBNP

Specifications

- ✓ **Species** : Dog
- ✓ **Sample** : Serum 100 μl
- ✓ **Testing Time** : 15 minutes
- ✓ **Measurement** : Quantitative
- ✓ **Measurement Range** : 500 – 10,000 pmol/L
- ✓ **Storage Condition** : 2 - 8 °C

Key Features

- Quantitative Analysis
  Numerical results, not qualitative

- Proven Accuracy and Reproducibility
  Correlated against a laboratory ELISA method

- Rapid and accurate results
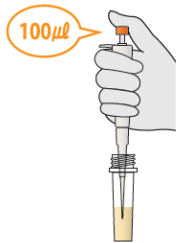 Simple procedure and quick results within 15 min.

Product No.	Product Name	Product Type	Packing Unit
VCF132DC	Vcheck Canine NT-proBNP	Device	5 Tests/Kit

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Test Procedure & Reference range

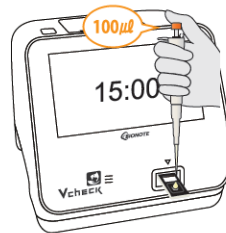==The samples should be tested immediately after collection.==

If serum samples are not tested immediately, freeze the serum for storage (-20 ℃ or colder).

Add 100 μl of the sample to the assay diluent tube

* Stored samples should be placed at room temperature 30 min. before use.

Mix well 5-6 times

Add the mixed sample (100 μl)

< 900 pmol/L	900 – 1,800 pmol/L	> 1,800 pmol/L
Normal	**Suspected*** Additional diagnostics are recommended	**Abnormal*** Additional diagnostics are recommended

* 'Abnormal' or 'Suspected' NT-proBNP test results should always be interpreted in combination and other diagnostic findings, such as an echocardiogram.

** Concentration over 735 pmol/L in Doberman Pinschers indicates an increased risk for occult DCM.

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Thank you
Any Questions?

BIONOTE Marketing team

Aug. 2020

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