

Quantitative marker of myocardial injury, Troponin I

# Vcheck Canine Tnl

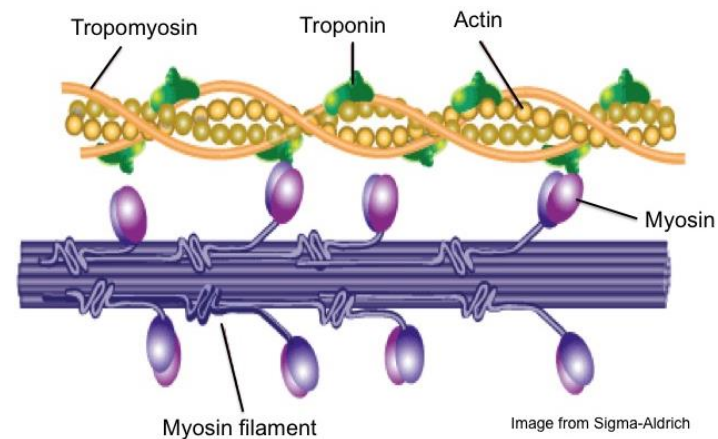
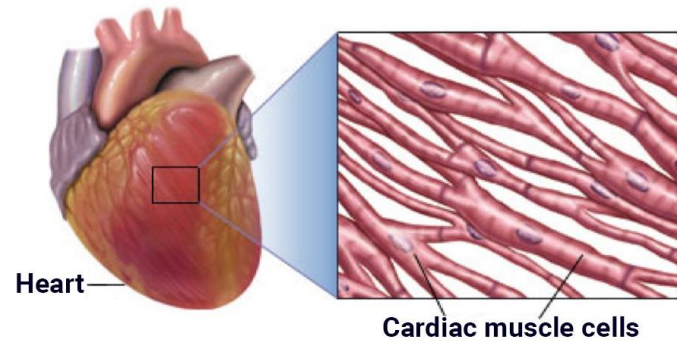
BIONOTE Marketing team

April 2021



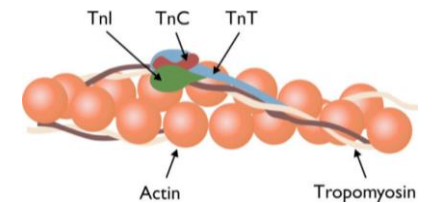
# New Cardiac Biomarker, TnI

## What is TnI?



In the Heart Muscle,  
The contractile apparatus is composed of ...

- **Actin**
- **Myosin**
- **Tropomyosin**
- **Troponin complex** (Regulatory proteins)
  - 1) Troponin T: binds to Tropomyosin
  - 2) Troponin C: binds to  $\text{Ca}^{2+}$
  - 3) **Troponin I**: inhibits the interaction



✓ Troponin I (TnI): cardiac, skeletal isoforms  
→ Only measures cardiac TnI

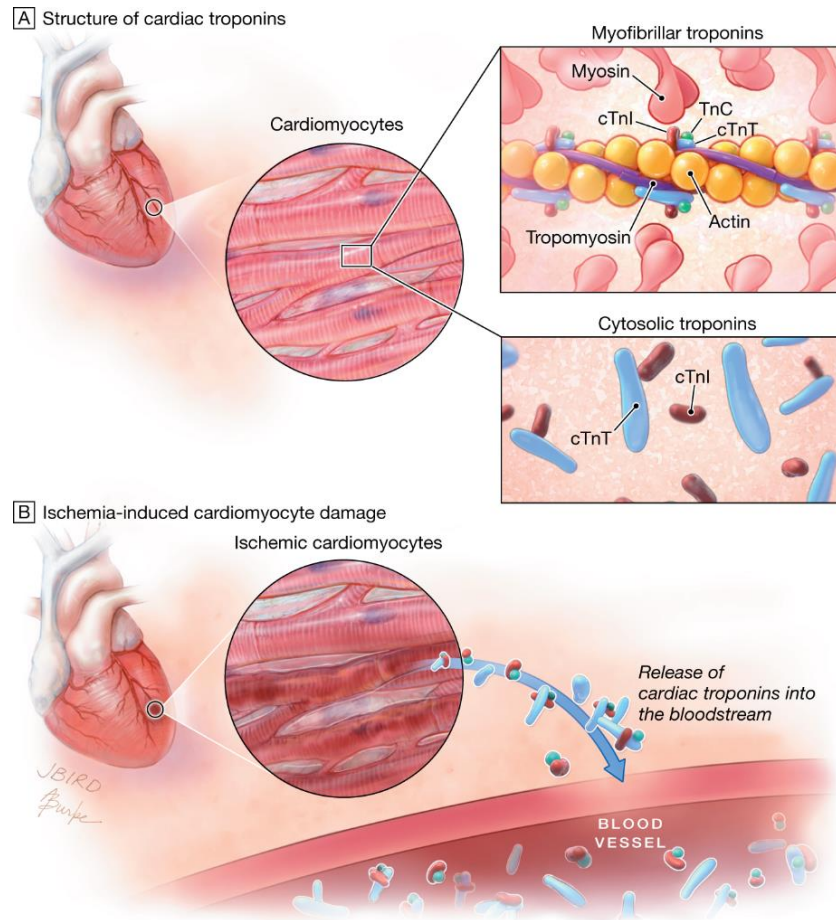
✓ **Cardiac TnI is a more sensitive marker of myocardial injury**  
when compared to cardiac TnT.

Click!



# New Cardiac Biomarker, TnI

## What is TnI?



- ✓ After cardiac insult, a rise of **Troponins** can be seen within 2-3 hours, and peak concentration is frequently reached in 18-24 hours.
  - A biomarker for the diagnosis of acute myocardial infarction (AMI) in humans, but AMI occurs very rarely in dogs and cats
- ✓ Still, dogs with cardiac diseases have chronically increased **Troponin** concentrations > signifying ongoing myocardial injury

# When TnI levels increase

In occasions which lead to cardiac injury,



## Cardiac Trauma

- hit-by-car trauma
- high-rise syndrome
- thoracic bite injuries

TnI for detecting or ruling out significant blunt cardiac injury



## Heart Disease

- mitral valve disease (MMVD)
- cardiomyopathy (DCM)
- congenital heart disease

TnI for signifying ongoing myocardial injury (worsening of cardiac function)



## Non-Cardiac Disease

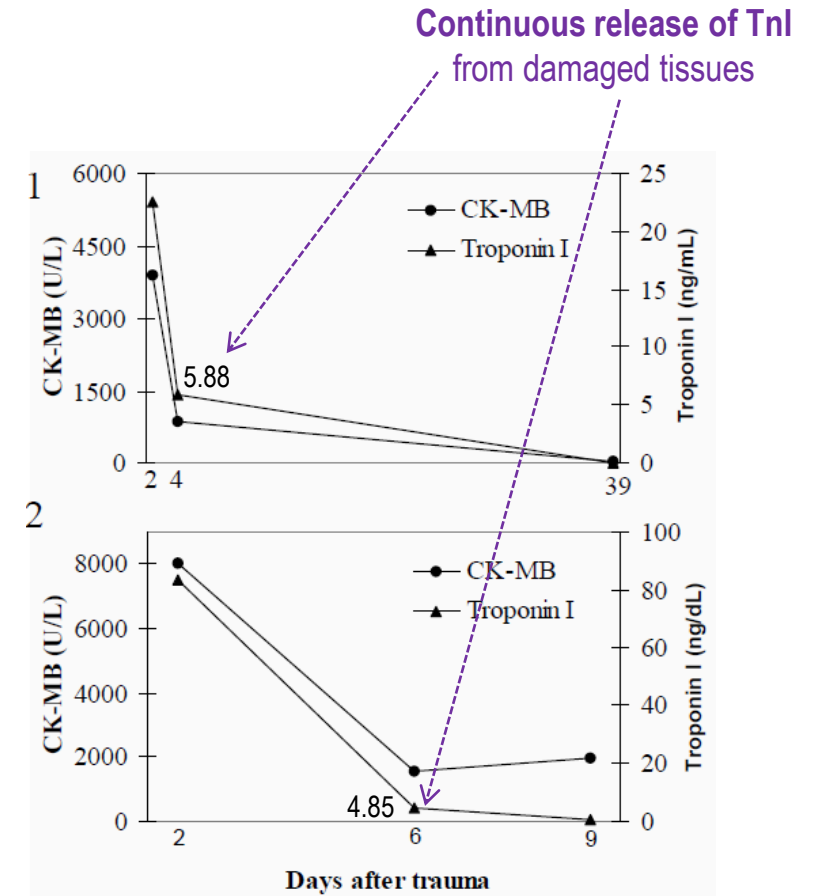
- inflammatory diseases
- neoplasia
- shock

TnI for discovering myocardial injury in critically ill individuals

# Clinical Utility of TnI in Dogs

## 1) After Cardiac Trauma

- **Direct cardiac trauma** occurs frequently in extreme conditions (hit-by-car trauma, high-rise syndrome, thoracic bite injuries)
  - The diagnosis of traumatic injury to the heart is important as it can lead to cardiogenic shock, acute heart failure, life-threatening arrhythmias, or structural damage.
- TnI levels accurately indicate **myocardial injury secondary to trauma.**



\*Normal range of TnI: < 0.03 ng/ml

\*Half-life of TnI: 1.85 h



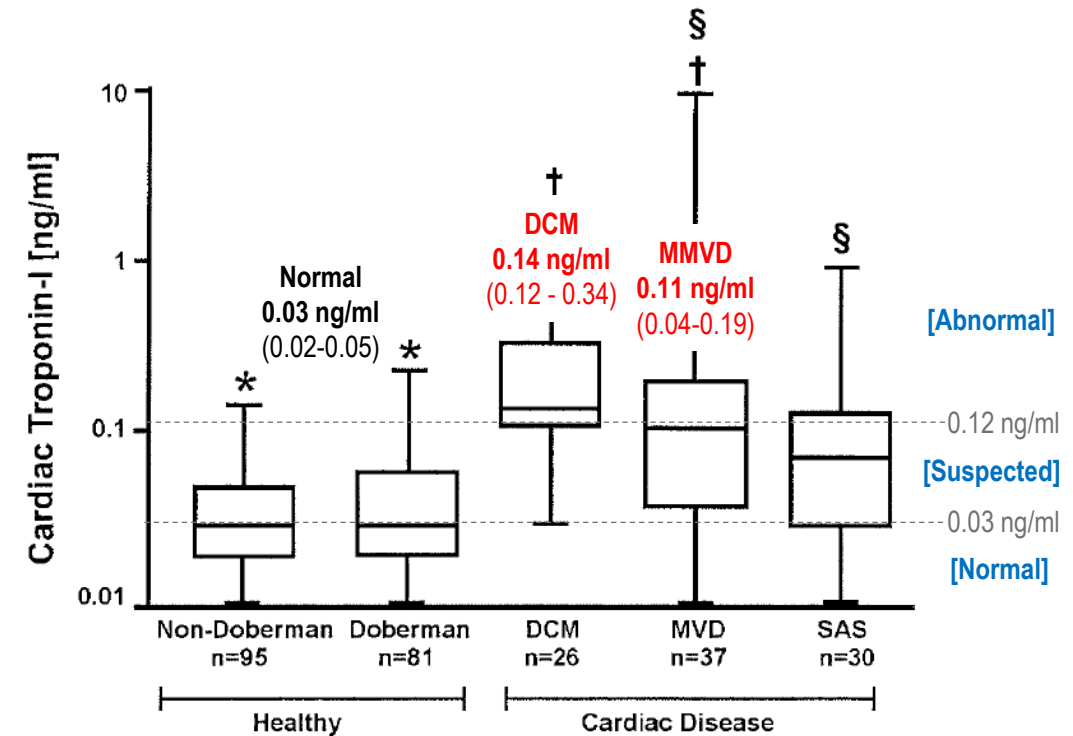
# Clinical Utility of TnI in Dogs

## 2) For Dogs with Primary Heart Diseases

- Increased TnI level means ongoing myocardial injury (damage).
  - 1) TnI levels are increased in dogs with heart disease.
    - **DCM**: median 0.14 ng/ml (0.12-0.34)
    - **MMVD**: median 0.11 ng/ml (0.04-0.19)
  - 2) TnI levels are significantly correlated with the left heart size. (correlation with La:Ao, LVDD, LVDs)



**TnI** for quantifying the extent of myocardial injury  
+ **Conventional examination** (X-ray, echocardiography)  
→ **Comprehensive evaluation for cardiac function**





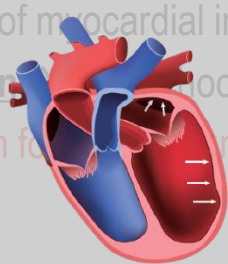
# Clinical Utility of Tnl in Dogs

## 2) For Dogs with Primary Heart Diseases

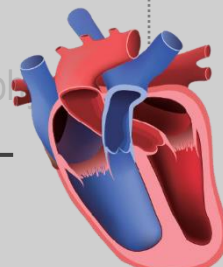
### DCM (Dilated Cardiomyopathy)

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

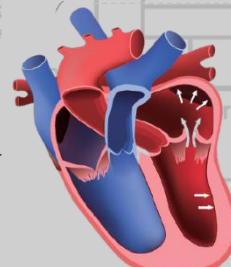
- **Age:** 3–7 years old
- **Breeds at elevated risk:** Large breeds (Boxer Dogs, Doberman Pinschers, Great Danes, Irish Wolfhounds, Saint Bernards)
- **Conditions:** Ventricular wall thinning  
→ Poor pumping ability



DCM



Normal

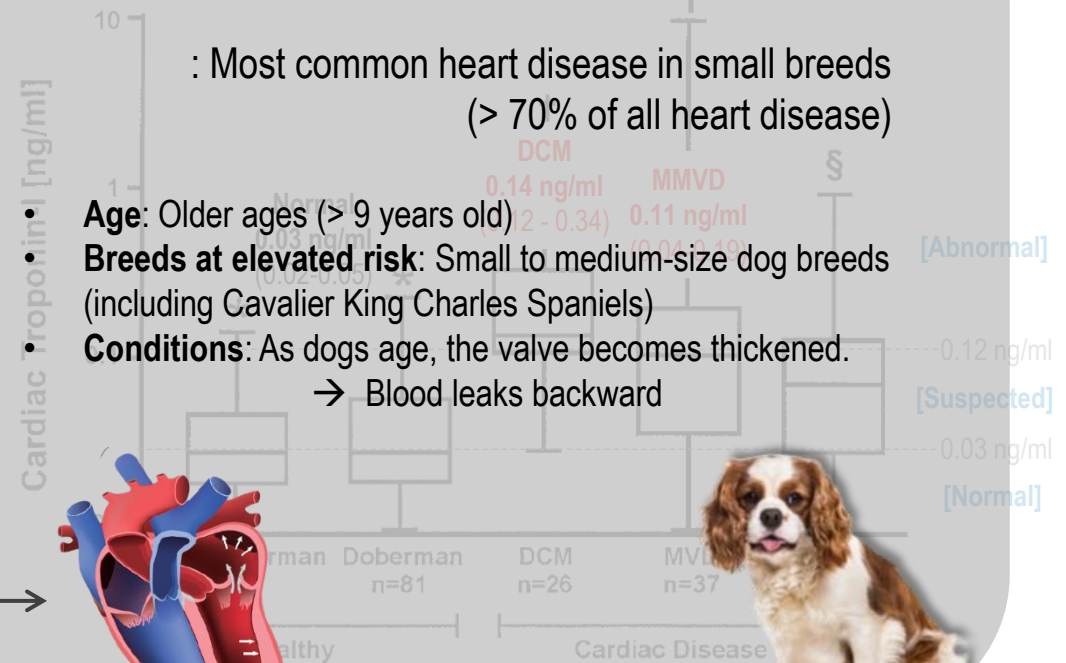


MMVD

### MMVD (Mitral valve disease)

: Most common heart disease in small breeds  
(> 70% of all heart disease)

- **Age:** Older ages (> 9 years old)
- **Breeds at elevated risk:** Small to medium-size dog breeds (including Cavalier King Charles Spaniels)
- **Conditions:** As dogs age, the valve becomes thickened.  
→ Blood leaks backward

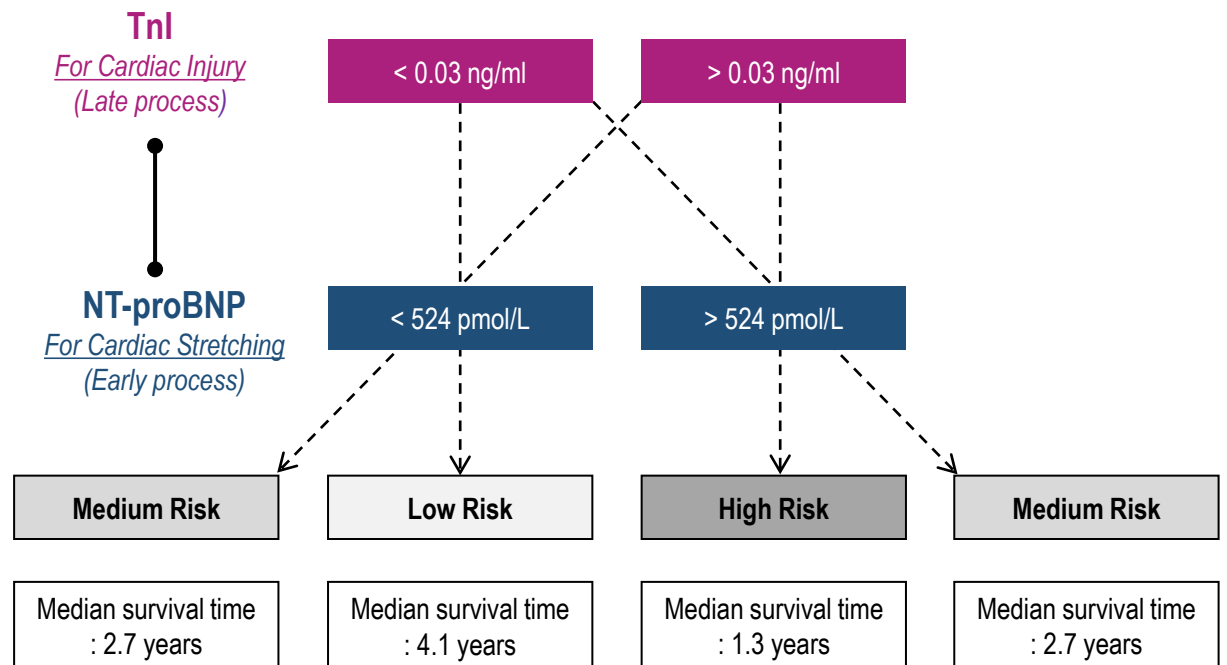


# Clinical Utility of Tnl in Dogs

## 2) For Dogs with Primary Heart Diseases

- Tnl and NT-proBNP should be measured in combination as a comprehensive evaluation.
  - **Tnl** for cardiac muscle injury
  - **NT-proBNP** for cardiac muscle stretching
- Combined measurement of Tnl and NT-proBNP is prognostically superior to measuring each alone.
- Monitor the rates of the changes of these markers **every 6 months** for further information

[Prognostic Algorithm] For dogs with MMVD of varying severity

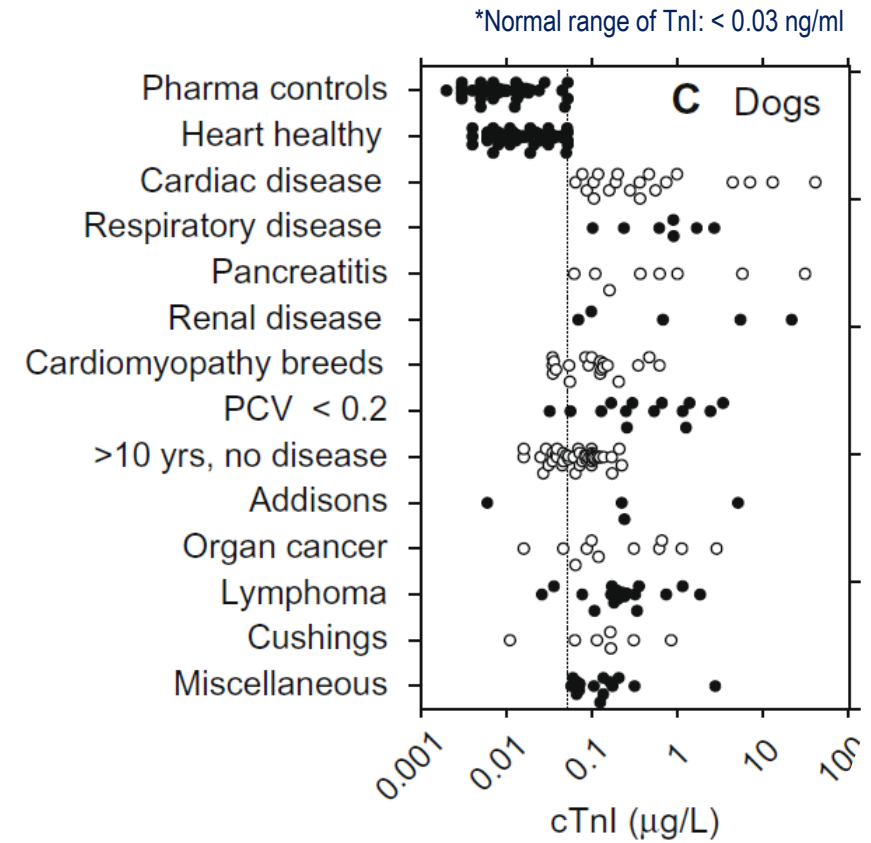




# Clinical Utility of Tnl in Dogs

## 3) In Dogs with Non-Cardiac Diseases

- Noncardiac critical disease can affect the heart, **causing myocardial injury**.
  - > **Need for close follow-up after hospital discharge**
- Interestingly, critically ill patients with noncardiac disease often have higher Tnl concentrations than the patients with severe primary cardiac disease.
- **Various diseases increasing Tnl levels**
  - Systemic inflammation
  - Parvoviral enteritis (parvovirus infection)
  - Pancreatitis
  - Cancer, lymphoma
  - Uncontrolled hyper(hypo)adrenocorticism
  - Respiratory disease
  - Anemia (moderate-marked)
  - Gastric dilatation-volvulus (GDV)
  - Infectious diseases (leptospirosis, leishmaniasis, babesiosis, ehrlichiosis)



# Clinical Utility of Tnl in Dogs

\*Normal range of Tnl: < 0.03 ng/ml

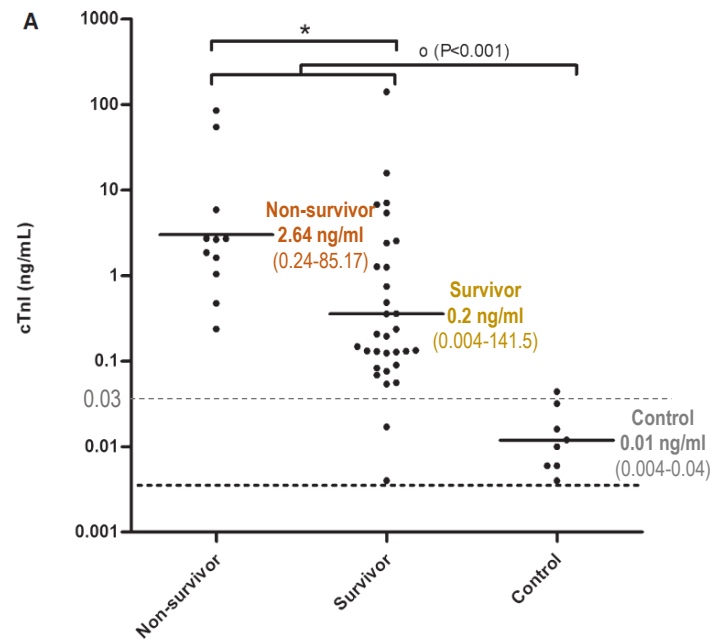
## 3) In Dogs with Non-cardiac Diseases

*For dogs with systemic inflammation*

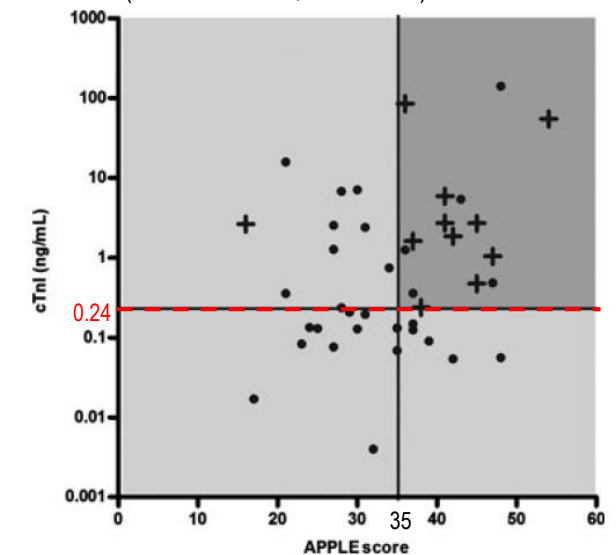
- Measurement of Tnl is necessary to discover the involvement of **myocardial injury in a patient's clinical status**.
- Presence of myocardial injury (high Tnl) is predictive of short-term survival (28-day case fatality).
- Cardiac Tnl is a marker of myocardial injury contributed independently to the APPLE score.
  - 1) APPLE score > 35
  - 2) Tnl > 0.24 ng/ml

→ Provides additional prognostic information

**Graph 1.** Tnl concentrations in dogs with systemic inflammation



**Graph 2.** The prognostic contribution of Tnl to APPLE score (+: non-survivors, •: survivors)



※APPLE: Acute Patient Physiologic and Laboratory Evaluation (Diagnosis-independent severity scores)



Product Introduction

# Vcheck Canine Tnl

# Product Introduction

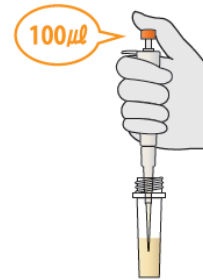
## Vcheck Canine Tnl

Quantitative marker of myocardial injury



- **Species:** Dog
- **Sample:** Serum 100  $\mu$ l
- **Testing Time:** 10 minutes
- **Measurement :** Quantitative
- **Measurement Range:** 0.01 – 20 ng/ml
- **Storage Condition:** 1 - 30 °C

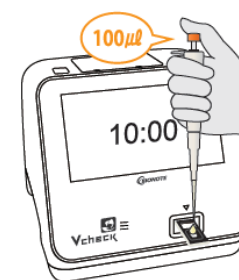
1 Add 100  $\mu$ l of the sample to the assay diluent tube



2 Mix well 5-6 times by using a 100  $\mu$ l pipette



3 Add 100  $\mu$ l of the mixed sample into the test device



※Samples should be tested immediately after collection.

(If not, freeze the samples at -20 °C or below for storage. Do not freeze and thaw repeatedly.)

< 0.03 ng/ml	0.03 – 0.12 ng/ml	> 0.12 ng/ml
Normal	Suspected Possibility of myocardial injury	Abnormal High possibility of myocardial injury

※Tnl concentrations should not be used to either confirm or exclude primary cardiac disease without the simultaneous use of echocardiography.

# Product Introduction

## Vcheck Canine Tnl

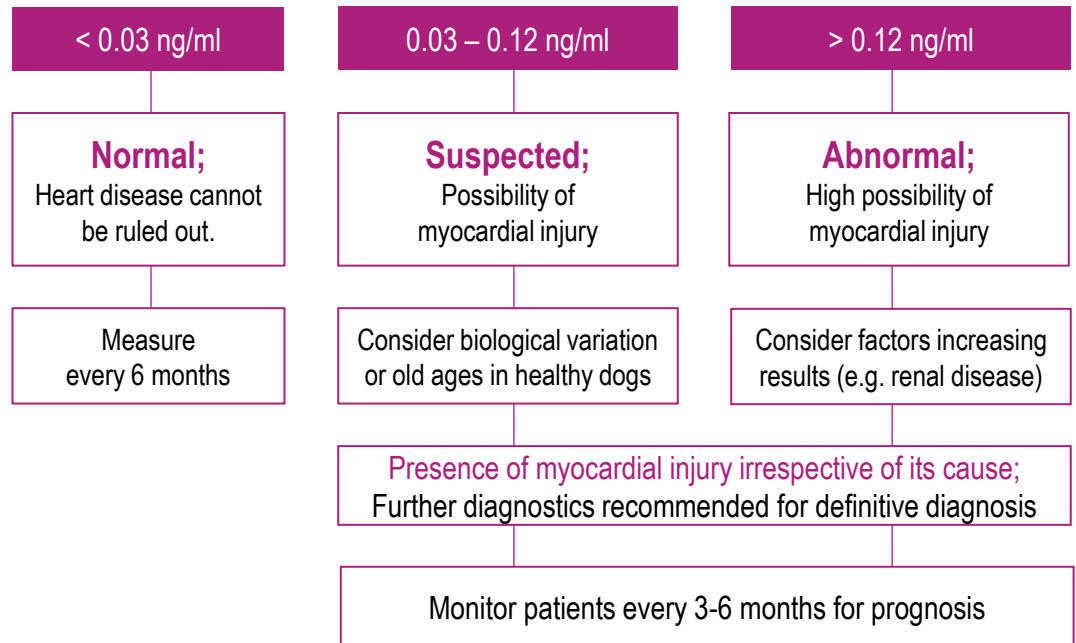
Quantitative marker of myocardial injury



- **Species:** Dog
- **Sample:** Serum 100 µl
- **Testing Time:** 10 minutes
- **Measurement :** Quantitative
- **Measurement Range:** 0.01 – 20 ng/ml
- **Storage Condition:** 1 - 30 °C

### • Diagnostic Algorithm

- Tnl levels reflect heart muscle injury from cardiac or non-cardiac diseases
- Include measurement of Tnl among routine biochemical testing (Renal, hepatic +Cardiac)



#### ※Caution

- Extreme exercise can cause transient myocardial injury in dogs, increasing Tnl levels.
- In older dogs, Tnl levels can be elevated because of myocardial changes leading to Tnl leakage.

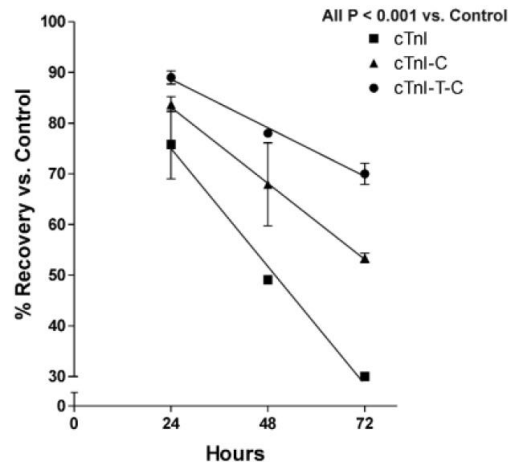
# Factors which may affect results

- Storage Conditions**

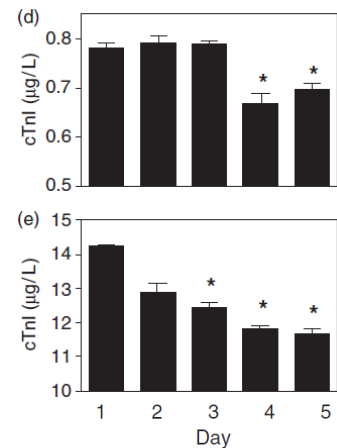
- Degradation by serum **proteases** reduces the stability of Tnl  
(**Not stable at room or refrigeration temperature**)
- The freeze-thaw cycles can affect Tnl concentrations.

→ **Samples should be tested immediately after collection.** (If not, freeze the samples at -20 °C or below for storage. Do not freeze and thaw repeatedly.)

**Graph 1.**  
At room temperature



**Graph 2.**  
At refrigerator temperature (2–8°C)  
→ 15-18% decrease



- Interference**

- **Vcheck Canine Tnl**

No interference was observed for each substance up to the concentration presented in the following table.

Interfering substances	Concentration
Hemoglobin	< 150 mg/dl
Intralipid	< 2,500 mg/dl
Cholesterol	< 250 mg/dl
Bilirubin (total)	< 20 mg/dl
Vitamin C	< 1 mg/ml

→ **Moderate or Severe hemolysis** can falsely increase Tnl levels.

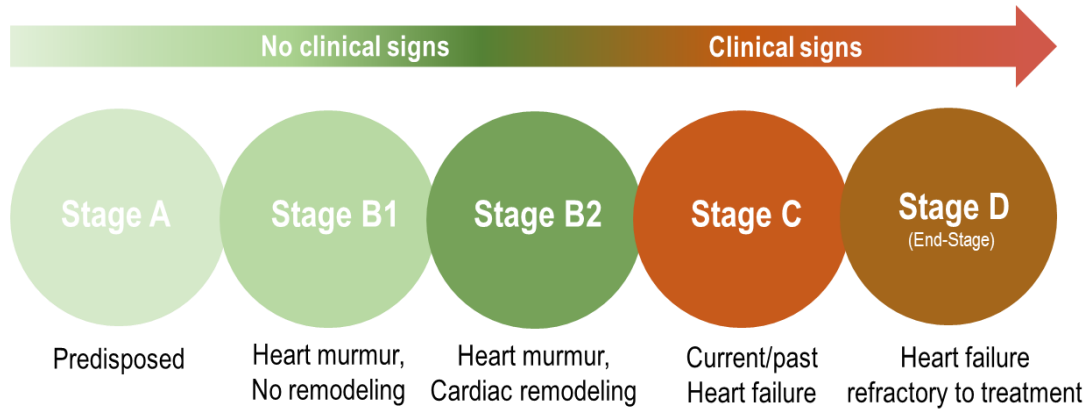
- Other Tnl Increasing Factors**

- Renal disease
- Old ages (> 10 years)
- Extreme exercise



# Clinical evaluation

- Tnl concentrations in MMVD dogs**



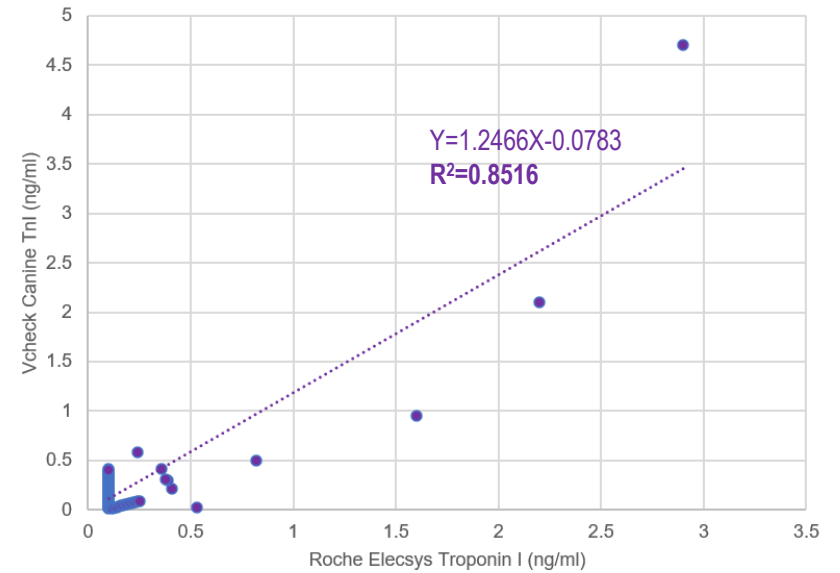
**Table1.** Concentrations of Tnl according to ACVIM stages in dogs

AVG±SD (ng/ml)	Normal (N=50)	Stage B1 (N=3)	Stage B2 (N=9)	Stage Cc (N=25)	Stage D (N=2)	P value
<b>Vcheck</b>	0.06±0.06 <sup>a</sup>	0.07±0.06 <sup>a</sup>	0.11±0.07 <sup>a</sup>	0.24±0.45 <sup>b</sup>	0.46±0.06 <sup>a</sup>	<0.001
<b>Roche</b>	0.10±0.13 <sup>a</sup>	0.20±0.18 <sup>b</sup>	0.18±0.15 <sup>b</sup>	0.28±0.50 <sup>b</sup>	0.46±0.51 <sup>b</sup>	<0.001
<b>ANI***</b>	0.01±0.01 <sup>a</sup>	0.04±0.03 <sup>b</sup>	0.038±0.04 <sup>a</sup>	0.25±0.71 <sup>b</sup>	1.48±2.06 <sup>b</sup>	<0.001

\*Different alphabets mean significant differences between groups (p < 0.05).

- High correlation with a Reference method**

Vcheck Canine Tnl has a high correlation (Y=1.2466X-0.0783, R<sup>2</sup>=0.8516) with Roche Elecsys Troponin I.



**Graph1.** Correlation of Vcheck and Roche Troponin I in 100 dogs

# Q&A Session

BIONOTE Marketing team

April 2021

