Indian J Anim Health (2024), 63(1): 22-28
DOI: https://doi.org/10.36062/ijah.2024.08023

Review Article

Biomarkers in the cardiovascular system of animals: A review

E. B. Rebez[1] and Ninan J.[1*]

[1]Department of Veterinary Physiology, Rajiv Gandhi Institute of Veterinary Education and Research, Kurumbapet, Pondicherry- 605 009, India

Abstract

Clinical examination and evaluation of biochemical parameters, haematological parameters and urinalysis for diagnosis of cardiac functions have not been efficient and specific to measure the severity of cardiac diseases in animals. In consideration of the disadvantages of these diagnostic tools, biomarker assays are capable of specific diagnosis and aid in the detection of diseases of cardiac origin. Several reliable cardiac biomarkers have been identified and tested in animals. Currently, cardiac biomarkers like myoglobin, troponin (I, T), creatine kinase (CK), aspartate aminotransferase (AST) or serum glutamic-oxaloacetic transaminase (SGOT), lactate dehydrogenase (LDH), NT- ProBNP (N-Terminal pro B-type Natriuretic Peptide), etc have been of clinical utility. But concretely, in veterinary practice, clinicians assess the levels of cardiac troponins I (cTnI) and NT-pro BNP, as they are highly specific and predictable for cardiac diseases. The review of literature has provided evidence that quantitative measurement of cTnI can be used to determine the extent of heart damage in companion animals, farm animals and lab animals. But, cTnI cannot be helpful in distinguishing primary cardiac and non-cardiac diseases in animals. Contrastingly, NT-pro BNP levels can be assessed to overcome this limitation of cTnI as it can accurately discriminate animals with non-cardiac disease from those with cardiac disease. Thus, a combination of cTnI and NT-proBNP biomarker assay can be adopted by veterinary clinicians for efficient diagnosis. Species-specific models and clinical utility of biomarker assay in cardiac pathology warrant further research. If the reviewed limitations could be addressed, cardiac biomarkers would form the basis of veterinary cardiac practice.

Keywords: Cardiac biomarkers, cTnI, Myocardial damage, NT-proBNP

Highlights

- The current review will be a credible reference of viable information of the current status of cardiac biomarkers in clinical practice.
- This review will provide insights on the significance of biomarkers in cardiovascular system of animals. For instance, in canines, elevated levels of the biomarker, NT-proBNP may indicate heart failure, whereas decreased levels are more indicative of non-cardiac conditions.
- The limitations on the understanding and practical utility of biomarkers in cardiovascular system will draw research interest.

INTRODUCTION

The evaluation of normal and abnormal cardiac functions in animals can be challenging. The non-specific patient history, clinical signs, physical examination and evaluation of traditional parameters like biochemical analysis, haematological analysis, coagulative profile, blood culture, effusion analysis, urine and faecal analysis are not always reliable measures of cardiac disease severity. The assessment of these parameters can be routinely used to confirm a cardiopathy and monitor cardiac disease and can also be of prognostic importance, but these parameters are not highly specific to assess the cardiovascular system of animals. The other diagnostics like echocardiography and radiography are relatively expensive and not readily accessible. In particular, pulmonary pathology might interfere with the interpretation of cardiovascular functions using thoracic radiographs. In this regard, it has been established that blood-based biomarker assays can be of use in differentiating respiratory signs associated with cardiac causes from non-cardiac causes and in the diagnosis of preclinical cardiomyopathy. Moreover, increasing number of studies have established that cardiac biomarker testing can be a reliable diagnostic tool to assess the risk of morbidity and mortality in animals with cardiac diseases (Oyama, 2013). Nowadays, research has significantly focused on developing a more robust and simple method than other diagnostic technologies. In consideration of the limitations of other diagnostic tools, blood-based biomarkers that are capable of assessing cardiac

*Corresponding Author, E-mail: ninanjacob123@gmail.com

functions and detection of cardiac pathology are of considerable interest. Thus, cardiac biomarkers are evidently reshaping the research and development pathways.

Many studies have highlighted the importance of using cardiac biomarkers, as a reliable method for the evaluation of cardiac function and early detection of cardiac diseases. Additionally, several potential cardiac biomarkers have been identified and tested in animals.

In the field of veterinary medicine, N-terminal pro-brain natriuretic peptide (NT-pro BNP) is the biomarker that is most predictive of cardiac disorders, followed by cardiac troponins I and T (cTnI and cTnT), and less frequently used, atrial natriuretic peptide, endothelin, tumour necrosis factor (TNF), and C-reactin protein (Baisan *et al*., 2016). In this article, the use of cardiac troponin, myoglobin (Carretón *et al*., 2011), NT-proBNP, creatine kinase (Baisan *et al*., 2016), AST/SGOT (Patibandla *et al*., 2022), LDH (Farhana and Lappin, 2023), miRNA (Ro *et al*., 2021) and interleukins (Kakkar and Lee, 2008) as cardiac biomarkers have been discussed. In particular, the use of cardiac troponins and NT-proBNP in veterinary practice has been highlighted. Further, biomarkers in cardiovascular system and their importance are detailed with specific stressor that can be of use to predict cardiac diseases in veterinary clinical practice. In addition, this article aims to review the current level of knowledge and highlight the significance of biomarkers in cardiovascular system of animals.

Significance of cardiac biomarkers

Recently, there has been rapid advancement in technologies and strategies to improve animal health by streamlining effective diagnostic tools. A wide range of analytical tools to study biological parameters has been adopted to improve animal health and production, which are referred to as biomarkers. The National Institute of Health Consortium in 2001 defined a biomarker as a "characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention". These biomarkers may be hormones, enzymes, or proteins that are released by the heart and can be used to evaluate the cardiac state.

Biomarker measurements have been helpful in relating the effects of interventions on cellular and molecular pathways to the response exhibited clinically and thus aid in describing the empirical results of clinical trials (Al-Mekhlafi *et al*., 2022). Hence, it provides an avenue for researchers to understand the clinical response that is being influenced by the unknown cause. There has been a considerable increase in research and adoption of cardiac biomarkers in the field of veterinary science as they are convenient, cost-effective, non-invasive, risk-free, efficient and highly predictive tests (Drobatz, 2009). A cardiac biomarker is a parameter that can predict or diagnose a cardiac disease, either if it is primary or secondary, with a high sensitivity and specificity (Baisan *et al*., 2016). In addition, the diagnosis of cardiac diseases in animals poses particular challenges to many practitioners, such as a high prevalence of sub-clinical cardiomyopathy, the inconclusive implications of heart murmurs in asymptomatic animals and most importantly the tendency of cardiac diseases to exhibit a sudden and severe clinical sign (Oyama, 2013; Borgeat *et al*., 2015). In this regard, these assays offer a straightforward and accessible test, which often features in the diagnostic investigation of cardiac diseases in animals (Borgeat *et al*., 2015). Thus, cardiac biomarkers play a significant role in clinical decision-making. The cardiac biomarkers have also been established to be of potential value in monitoring and providing prognostic information in cardiac disease conditions.

Cardiac biomarkers

The importance of cardiac biomarkers related to cardiac dysfunctions has increased drastically in veterinary medicine. An ideal cardiac biomarker is specific and sensitive to cardiovascular system, easy to measure, normally absent (trace) in blood, cost effectively detected and releases rapidly after myocardial injury.

Among the listed biomarkers in Table 1, myoglobin and AST/SGOT are non-specific, whereas troponin (I, T) is highly specific to cardiac muscle. The creatine kinase enzyme that provides energy during muscle contraction is found in the heart, skeletal muscle and brain. Its isoenzymes are CK-MM (Skeletal muscle), CK-MB (Heart muscle) and CK-BB (Brain, Gastro-intestinal tract). The CK-MB biomarker makes up 3-5% of the total creatine kinase enzyme levels and is good for early diagnosis.

AST/SGOT increases during damage to cardiac tissues, kidneys, skeletal muscles and RBC, and thus, they are not specific biomarkers to evaluate cardiac state. It was the first biomarker that was used in the diagnosis of Acute myocardial infarction (Patibandla *et al*., 2022).

Table 1. Cardiac biomarkers

SL. No.	Cardiac marker	Normal levels	Time sequence of appearance after cardiac injury			Reference
			Onset	Peak	Fall	
1	Myoglobin	70 µg/L	1 hr	4-12 hrs	12 hrs	Mair *et al*., 1992
2	Troponin a) Troponin I b) Troponin T	 0.04 ng/mL 0.01 ng/mL	2-4 hrs	12-24 hrs	10 days	Cleveland clinic.org
3	CK-MB	< 5 ng/mL (5-25 IU/L)	3-6 hrs	16-30 hrs	24-36 hrs	Cabaniss, 1990
4	AST/SGOT	8-10 IU/L	3-4 hrs	15- 28 hrs	5 days	Patibandla *et al.*, 2022
5	LDH	140-280 IU/L	12 hrs	24-48 hrs	10 days	Farhana and Lappin, 2023
6	NT- ProBNP	125-450 pg/mL	60-120 min	24 hrs	12 weeks	Corteville *et al*., 2007

LDH is an enzyme found in heart, skin, brain, liver and blood cells. It was the first cardiac biomarker used for identifying myocardial infarction. There are five isoenzymes: LDH 1 (heart), LDH 2 (RBC), LDH 3 (brain, pancreas, lung, spleen, kidney), LDH 4 (kidney, pancreas, placenta) and LDH 5 (liver, muscle). Normally LDH 2>LDH 1 in blood, but during a heart attack, LDH 1>LDH 2 (Flipped pattern). It has some limitations for utility as electrophoresis is required to determine the flipped pattern, and as a marker, it increases late after the cardiac insult.

NT- ProBNP (N-Terminal pro B-type Natriuretic Peptide) is synthesized in left ventricle by cardiomyocytes, endothelial cells, T-cells and macrophages. High level indicates heart failure and depicts the inability of the heart to pump the required amount of blood the body needs.

Hyun (2011) divided cardiac biomarkers into two broad divisions viz. leakage markers related to myocardial integrity (cardiac troponin-cTn, myoglobin and creatine kinase isoenzyme MB- CK-MB) and functional markers related to specific proteins of cardiac functions (brain natriuretic peptide – BNP, atrial natriuretic peptide – ANP and endothelin).

At present, in veterinary practice, cardiac troponins I (cTnI) and N-terminal pro-brain natriuretic peptide (NT-pro BNP) are the reliable markers with the highest predictability for cardiac diseases.

Cardiac troponin (cTn): Troponins are part of the contractile apparatus of muscle tissue and can be found both in skeletal and cardiac muscles. They are Ca^{++} regulating proteins. They form a complex consisting of three interacting proteins: troponin I, T and C (Sandersen *et al*., 2008). The troponin C binds to 3 Ca^{++} molecules in cardiac muscle and 4 Ca^{++} in skeletal muscle and is not a specific cardiac biomarker. On the other hand, cardiac troponin I (cTnI) and cardiac troponin T (cTnT) are isoforms that are expressed exclusively by cardiac myocytes and have been shown to be useful indicators of myocardial injury (Labonté *et al*., 2015). Cardiac troponin acts as a leakage marker as they are the contractile proteins in myocardium, which are released relatively in proportion to the level of tissue injury and disorganization of myocyte membranes. The troponin test is a diagnostic test that uses blood sample to measure the levels of troponin I and troponin T proteins to assess the level of myocardial damage. This test is most often used to diagnose heart attack and also to monitor angina, a condition that restricts blood flow to the heart and results in chest pain. Troponins are used as a marker to detect acute coronary syndrome (ACS), myocardial infarction, heart failure, dyspnoea, abnormal sweating, severe weakness, nausea, ischemia, pulmonary embolism and in chronic obstructive pulmonary disease (COPD) (Tanindi and Cemri, 2011; Garg *et al*., 2017). Troponin detection techniques such as gold-labelled immunoassay, chemiluminescence, fluorescence analysis, enzyme-linked immunosorbent assay (ELISA), and immunoturbidimetry have all been thoroughly studied by researchers and are useful in the detection process, and currently, biosensing strategies have been found to be significant (Chen *et al*., 2023). Troponins can also be detected by radioimmunoassay (RIA) (Cummins *et al*., 1987). Cardiac troponins have become well established as gold-standard blood biomarkers with high sensitivity (<0.005 ng/mL and specificity for myocardial degeneration in man (O'Brien *et al*., 2006). Similarly, in canines, evidence of the use of cardiac troponins as biomarkers with high sensitivity and specificity has been reported (Spratt *et al*., 2005). In comparison, even though there is significant variability in the application

of cardiac troponin, this assay has been growing in the field of veterinary cardiology and also in animal safety studies.

It has been established that the most sensitive and used troponin in veterinary clinical practice is troponin I (Langhorn and Willesen, 2016). A study conducted in six different species (dog, cat, horse, cattle, rat and rabbit) revealed elevated cTnI in blood following cardiac injury as a common sequel to a wide array of both cardiac disease and diseases that do not primarily involve the cardiovascular system. In the study, increased cTnI was not found to correlate with the aetiology or pathogenesis of the disease, but was effective in detecting, monitoring and quantifying the ongoing cardiac injury (Serra *et al.*, 2010). An increase in cTnI has been reported in dogs with cardiomyopathy, sub-valvular aortic stenosis, mitral valve disease and cardiac causes of respiratory distress (Van DerVekens *et al*., 2012). Further, the clinical application of cTnI in bovine practice is multiple and has been evaluated in ruminant species with cardiac diseases such as pericarditis, endocarditis, as well as in neonates with congenital cardiac defects, myocarditis and other non-cardiac disorders (Smith *et al*., 2020). Studies have reported that the cTnI assay appears to be a sensitive and specific marker for myocardial injury in goat kids (Tharwat *et al*., 2013; Karapinar *et al*., 2016). Another study revealed that, in an ischemia-reperfusion model in pigs, cardiac troponin T (cTnT) and cardiac Troponin I (cTnI) could be useful in detecting myocardial cell damage (Bertsch *et al*., 2000). Currently, cardiac troponin I is the only cardiac biomarker which has been successfully used in equine veterinary practice for the evaluation of myocardial damage. In contrast to human medicine, the cardiac troponin T molecule has a lower diagnostic value in horses (Van Der Vekens *et al.*, 2012).

High troponin levels in cats have been linked to myocarditis when other potential causes of myocardial injury have been ruled out. This is because hypoxic stress and cardiomyocyte necrosis are linked to the production of cTnI (Bijsmans *et al*., 2017). Studies in cats have described the rise of cTnI in cats with cardiac dyspnea (Herndon *et al.*, 2008). Some studies in cats have described a transient thickening of the myocardium, which may be associated with high troponin values and can be suggestive of myocarditis. Troponins could be used to help in distinguishing hypertrophic cardiomyopathy and the transient thickening caused as a result of myocarditis, even if there is likely a clear overlay between the troponin values of the two categories. In addition, troponins have also been shown to be useful in evaluating the patient's prognosis in cats (Gavazza *et al.*, 2021).

In addition, a study using mouse and ferret models showed that in cardiotoxicosis due to doxorubicin, traumatic injury, ischemia, and cardiac puncture, cTnT could be an effective biomarker. The study concluded that cTnT is a powerful biomarker in laboratory animals in terms of the sensitivity and specificity detection of cardiac injury arising from various causes (O'Brien *et al*., 1997). A study in dogs concluded that high-sensitivity cTnI assays can be used to screen for dilated cardio myopathy in a cost-effective manner in general practice. In addition, it aids in identifying animals for further diagnostic assessment and thereby permits early therapeutic intervention in the preclinical phase (Dukes-McEwan, 2022). In animals, troponin concentration can be a good quantifiable measure of the extent of heart damage, but it does not provide information on the cause of injury, as it cannot distinguish between primary cardiac and non-cardiac diseases with secondary heart involvement (Gavazza *et al*., 2021). Future research must clearly define whether troponins can serve as specific markers in diagnosing and monitoring to guide efficient treatment.

N-terminal pro-B-type natriuretic peptide (NT-proBNP): The N-terminal pro-B-type natriuretic peptide (NT-proBNP) is formed when pro-B-type natriuretic peptide, its parent pro-hormone is cleaved into two molecules, NT-proBNP and C-BNP. The most studied natriuretic peptide in the field of veterinary cardiology is N-terminal fragment of BNP (NT-pro-BNP), also because this marker has a longer half-life (Gavazza *et al*., 2021). It has been studied that as a response to an increase in intra-cardiac hydrostatic pressure, increased cardiac wall stress, angiotensin II, myocardial hypoxia, and heightened sympathetic tone, the pro-B-type natriuretic peptide is produced (Oyama *et al*., 2009). Brain natriuretic peptide was first discovered in the porcine brain. It is currently often called the B-type natriuretic peptide (BNP) because its main production site is actually the heart. The BNP is much more related to ventricular pathological changes, in contrast to atrial natriuretic peptides (Van Der Vekens *et al*., 2012). The main impulse for the secretion of NT-proBNP is myocardial stretch due to volume overload (Klein *et al*., 2022).

A study in dogs revealed that a combination of NT-proBNP biomarker assay and Holter monitoring test detected occult (asymptomatic) dilated cardiomyopathy (ODCM) with high accuracy. In the same study, it has been established that NT-proBNP

concentration predicts cardiovascular morbidity and all-cause mortality in dogs with degenerative mitral valve disease (Singletary *et al*., 2012). A study concluded that canine NT-proBNP in serum and plasma accurately distinguished dogs with cardiac disease from those with respiratory disease (Boswood *et al*., 2008). Similarly, another study reported that measuring serum NT-proBNP concentration in dogs with respiratory signs helps to differentiate between congestive heart failure and primary respiratory tract disease as an underlying cause (Oyama *et al*., 2009). Small animals seldom experience myocardial ischemia; however, in a canine model of the condition, a substantial rise in NT-proBNP concentration has been seen, much like in humans (Hori *et al*., 2012). Thus, the NT-proBNP assay appears to be a useful marker of the presence of cardiac disease. It has been documented that there is a considerable increase in NT-pro-BNP in cats with heart disease, and some have even determined an ideal NT-pro-BNP cut-off value with good sensitivity and specificity for the diagnosis of occult cardiomyopathy (Gavazza *et al*., 2021). In addition, NT-pro-BNP and NT-pro-ANP have been suggested as survival time predictors and, therefore, are of prognostic importance (Borgeat *et al*., 2014). In addition, no specific equine BNP or NT-proBNP test is yet available, and no equine-specific half-life has been determined (Van Der Vekens *et al*., 2012). But, Gehlen *et al*. (2007) and Trachsel *et al*. (2012) have found a positive correlation between ANP concentration and left atrial enlargement. Thus, more research efforts on finding the diagnostic importance of NT-proBNP in farm animals are needed.

Other markers: Recently, robust improvements in biomarker-associated studies have led to the identification of various novel biomarkers. To list a few, miRNA (Ro *et al*., 2021), interleukins (Soluble ST2) (Kakkar and Lee, 2008; Anderson *et al*., 2017), metabolomic profiling (Smith *et al*., 2022; Tahir *et al*., 2022) have been some of the highlighted novel cardiac biomarkers. Ro *et al*. (2021) found that cfa-miR-130b showed several characteristics as a novel biomarker for various heart diseases and can be considered a useful biomarker for early detection and monitoring of various heart diseases. Further, they concluded that it may be related to common physiological or pathological changes that can be induced by various heart diseases. Since cardiac disease involves a complex pathophysiology, a biomarker could be any molecule indicating cardiac stress, injury or dysfunction. Thus, an integrated approach in the use of biomarkers would validate efficient diagnosis.

Conclusion

The cTn and NT-proBNP have been of primary focus among the diagnostic markers in the cardiovascular system in veterinary practice. Even though these markers often feature in the diagnostic

Table 2. Biomarkers associated with cardiac diseases

SL. No.	Cardiac biomarker	Species	Condition	Concentration of the biomarker	References
1	cTnI	Canine	Cardiomyopathy Mitral valve disease Sub-valvular aortic stenosis	0.03-1.88 ng/mL 0.01-9.53 ng/mL 0.01-0.94 ng/mL	Oyama and Sisson, 2004
2	NT-proBNP	Canine and Feline	Cardiac disease	< 900 pmol/l (in dogs) or <100 pmol/l (in cats)	Polizopoulou, 2014
		Canine	Dilated cardiomyopathy	418.53 pg/mL	Sultana *et al*., 2019
3	miRNA	Canine	Myxomatous mitral valve degeneration (MMVD) stage B, patent ductus arteriosus, and pulmonic stenosis	Upregulation of cfa-miR-130b	Ro *et al*., 2021
			Concentric cardiac hypertrophy	Upregulation of cfa-miR-375 and cfa-let-7b	
4	Interleukins - Soluble ST2 (sST2)	Murine and Human	Heart failure or myocardial infarction	Increased levels	Kakkar and Lee, 2008
			Cardiomyopathy		Anderson *et al*., 2017

investigation, understanding the clinical utility in specific disease conditions needs to be emphasized. The existing literature with regard to species reveals that specific data relating to farm animal species is negligible, and future studies in this area should be given priority. Furthermore, there has been active adoption of cardiac biomarker tests by veterinarians, as these assays are straightforward and accessible. However, the understanding and interpretation of results need special knowledge as they are ever-evolving. Although many questions remain unresolved, the utility of biomarkers to diagnose cardiac diseases forms the basis of future veterinary cardiac practice.

Conflict of interest: Authors declare that they do not have any conflict of interest in the study.

Author's contributions: BRE: The acquisition of data and critically revising the manuscript; NJ: Substantial contribution to the conception and design, and critical revision of the manuscript.

REFERENCES

Al-Mekhlafi A, Becker T and Klawonn F, 2022. Sample size and performance estimation for biomarker combinations based on pilot studies with small sample sizes. Commun Stat Theory Methods, 51(16): 5534-5548, doi: 10.1080/03610926.2020.1843053

Anderson J, Seol H, Gordish-Dressman H, Hathout Y, Spurney CF *et al.*, 2017. Interleukin 1 Receptor-Like 1 Protein (ST2) is a potential biomarker for cardiomyopathy in Duchenne muscular dystrophy. Pediatr Cardiol, 38(8): 1606-1612, doi: 10.1007/s00246-017-1703-9

Baisan RA, De Rosa A, Di Loria A, Vulpe V and Piantedosi D, 2016. Cardiac biomarkers in clinical practice of dog and cat- A review. HVM Bioflux, 8(1): 50-58

Bertsch T, Janke C, Denz C, Weiss M, Luiz T *et al.*, 2000. Cardiac troponin I and cardiac troponin T increases in pigs during ischemia-reperfusion damage. Exp Toxicol Pathol, 52(2): 157-159, doi: 10.1016/S0940-2993(00)80111-6

Bijsmans ES, Jepson RE, Wheeler C, Syme HM and Elliott J, 2017. Plasma N terminal probrain natriuretic peptide, vascular endothelial growth factor, and cardiac troponin I as novel biomarkers of hypertensive disease and target organ damage in cats. J Vet Intern Med, 31(3): 650-660, doi: 10.1111/jvim.14655

Biomarkers Definitions Working Group, 2001. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. Clin Pharmacol Ther, 69(3): 89-95, doi: 10.1067/mcp.2001.113989

Borgeat K, Connolly DJ and Luis Fuentes V, 2015. Cardiac biomarkers in cats. J Vet Cardiol, 17(Suppl 1): S74-S86, doi: 10.1016/j.jvc.2015.08.001

Borgeat K, Sherwood K, Payne JR, Luis Fuentes V and Connolly DJ, 2014. Plasma cardiac troponin I concentration and cardiac death in cats with hypertrophic cardiomyopathy. J Vet Intern Med, 28(6): 1731-1737, doi: 10.1111/jvim.12459

Boswood A, Dukes-McEwan J, Loureiro J, James RA, Martin M *et al.*, 2008. The diagnostic accuracy of different natriuretic peptides in the investigation of canine cardiac disease. J Small Anim Pract, 49(1): 26-32, doi: 10.1111/j.1748-5827.2007.00510.x

Cabaniss CD, 1990. Creatine Kinase. In: Clinical Methods, The History, Physical, and Laboratory Examinations (Walker HK, Hall WD, Hurst JW, eds) Chapter 32, 3rd edn. Butterworths, Boston. Available in: https://www.ncbi.nlm.nih.gov/books/NBK352/

Carretón E, Corbera JA, Juste MC, Morchón R, Simón F *et al.*, 2011. *Dirofilaria immitis* infection in dogs: cardiopulmonary biomarker levels. Vet Parasitol, 176(4): 313-316, doi: 10.1016/j.vetpar.2011.01.015

Chen Q, Wu W, Wang K, Han Z and Yang C, 2023. Methods for detecting of cardiac troponin I biomarkers for myocardial infarction using biosensors: A narrative review of recent research. J Thorac Dis, 15(9): 5112-5121, doi: 10.21037/jtd-23-1263

Corteville DC, Bibbins-Domingo K, Wu AH, Ali S, Schiller NB *et al.*, 2007. N-terminal pro-B-type natriuretic peptide as a diagnostic test for ventricular dysfunction in patients with coronary disease: data from the heart and soul study. Arch Intern Med, 167(5): 483-489, doi: 10.1001/archinte.167.5.483

Cummins B, Auckland ML and Cummins P, 1987. Cardiac-specific troponin-I radioimmunoassay in the diagnosis of acute myocardial infarction. Am Heart J, 113(6): 1333-1344, doi: 10.1016/0002-8703(87)90645-4

Drobatz KJ, 2009. Measures of accuracy and performance of diagnostic tests. J Vet Cardiol, 11(Suppl 1): S33-S40, doi: 10.1016/j.jvc.2009.03.004

Dukes-McEwan J, Garven KE, Lopez Alvarez J, Oliveira P, Motskula PF *et al.*, 2022. Usefulness of cardiac biomarker screening to detect dilated cardiomyopathy in Dobermans. J Small Anim Pract, 63(4): 275-285, doi: 10.1111/jsap.13455

Farhana A and Lappin SL, 2023. Biochemistry, Lactate Dehydrogenase. Stat Pearls, Treasure Island (FL). Available in: https://www.ncbi.nlm.nih.gov/books/NBK557536/

Garg P, Morris P, Fazlanie AL, Vijayan S, Dancso B *et al.*, 2017. Cardiac biomarkers of acute coronary syndrome: from history to high-sensitivity cardiac troponin. Intern Emerg Med, 12(2): 147-155, doi: 10.1007/s11739-017-1612-1

Gavazza A, Marchegiani A, Guerriero L, Turinelli V, Spaterna A *et al.*, 2021. Updates on laboratory evaluation of feline cardiac diseases. Vet Sci, 8(3): 41, doi: 10.3390/vetsci8030041

Gehlen H, Sundermann T, Rohn K and Stadler P, 2007. Plasma atrial natriuretic peptide concentration in warmblood horses with heart valve regurgitations. J Vet Cardiol, 9(2): 99-101, doi: 10.1016/j.jvc.2007.10.003

Herndon WE, Rishniw M, Schrope D, Sammarco CD, Boddy KN *et al.*, 2008. Assessment of plasma cardiac troponin I concentration as a means to differentiate cardiac and

noncardiac causes of dyspnea in cats. J Am Vet Med Assoc, 233(8): 1261-1264, doi: 10.2460/javma.233.8.1261

Hori Y, Ohshima N, Chikazawa S, Kanai K, Hoshi F *et al.*, 2012. Myocardial injury-related changes in plasma NT-proBNP and ANP concentrations in a canine model of ischemic myocardial injury. Vet J, 191(1): 46-51, doi: 10.1016/j.tvjl.2011.01.018

Hyun C, 2011. Cardiac biomarkers in small animal practice-can we detect heart disease with blood samples. World Small Animal Veterinary Association World Congress Proceedings

Kakkar R and Lee RT, 2008. The IL-33/ST2 pathway: therapeutic target and novel biomarker. Nat Rev Drug Discov, 7(10): 827-840, doi: 10.1038/nrd2660

Karapinar T, Eroksuz Y, Hayirli A, Beytut E, Kaynar O *et al.*, 2016. The diagnostic value of two commercially available human cTnI assays in goat kids with myocarditis. Vet Clin Pathol, 45(1): 164-171, doi: 10.1111/vcp.12328

Klein S, Nolte I, Granados-Soler JL, Lietz P, Sehn M *et al*, 2022. Evaluation of new and old biomarkers in dogs with degenerative mitral valve disease. BMC Vet Res, 18(1): 256, doi: 10.1186/s12917-022-03343-z

Labonté J, Roy JP, Dubuc J and Buczinski S, 2015. Measurement of cardiac troponin I in healthy lactating dairy cows using a point of care analyzer (i-STAT-1). J Vet Cardiol, 17(2): 129-133, doi: 10.1016/j.jvc.2015.02.003

Langhorn R and Willesen JL, 2016. Cardiac troponins in dogs and cats. J Vet Intern Med, 30(1): 36-50, doi: 10.1111/jvim.13801

Mair J, Artner-Dworzak E, Lechleitner P, Morass B, Smidt J *et al.*, 1992. Early diagnosis of acute myocardial infarction by a newly developed rapid immunoturbidimetric assay for myoglobin. Br Heart J, 68(5): 462-468, doi: 10.1136/hrt.68.11.462

O'Brien PJ, Dameron GW, Beck ML, Kang YJ, Erickson BK *et al.*, 1997. Cardiac troponin T is a sensitive, specific biomarker of cardiac injury in laboratory animals. Lab Anim Sci, 47(5): 486-495

O'Brien PJ, Smith DEC, Knechtel TJ, Marchak MA, Pruimboom-Brees I *et al.*, 2006. Cardiac troponin I is a sensitive, specific biomarker of cardiac injury in laboratory animals. Lab Anim, 40(2): 153-171, doi: 10.1258/002367706776319042

Oyama MA and Sisson DD, 2004. Cardiac troponin I concentration in dogs with cardiac disease. J Vet Intern Med, 18(6): 831-839, doi: 10.1892/0891-6640(2004)18<831:ctcidw>2.0.co;2

Oyama MA, 2013. Using cardiac biomarkers in veterinary practice. Vet Clin North Am Small Anim Pract, 43(6): 1261-1272, doi: 10.1016/j.cvsm.2013.07.010

Oyama MA, Rush JE, Rozanski EA, Fox PR, Reynolds CA *et al.*, 2009. 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. J Am Vet Med Assoc, 235(11): 1319-1325, doi: 10.2460/javma.235.11.1319

Patibandla S, Gupta K and Alsayouri K, 2023. Cardiac Biomarkers. In: Stat Pearls, Treasure Island (FL); PMID: 31424800

Polizopoulou ZS, 2014. The diagnostic significance of cardiac biomarkers in veterinary medicine. J Hellenic Vet Med Soc, 65(3): 205-214, doi: 10.12681/jhvms.15536

Ro WB, Kang MH, Song DW, Kim HS, Lee GW *et al.*, 2021. Identification and characterization of circulating microRNAs as novel biomarkers in dogs with heart diseases. Front Vet Sci, 8: 729929, doi: 10.3389/fvets.2021.729929

Sandersen C, Remy B, Olejnik D and Amory H, 2008. Intérêt de la troponine sérique en tant que marquer d'une myocarde en médecine vétérinaire. Ann Med Vet, 152: 180-190

Serra M, Papakonstantinou S, Adamcova M and O'Brien PJ, 2010. Veterinary and toxicological applications for the detection of cardiac injury using cardiac troponin. Vet J, 185(1): 50-57, doi: 10.1016/j.tvjl.2010.04.013

Singletary GE, Morris NA, Lynne O'Sullivan M, Gordon SG and Oyama MA, 2012. Prospective evaluation of NT-proBNP assay to detect occult dilated cardiomyopathy and predict survival in Doberman Pinschers. J Vet Intern Med, 26(6): 1330-1336, doi: 10.1111/j.1939-1676.2012.1000.x

Smith CE, Parnell LD, Lai CQ, Rush JE, Adin DB *et al.*, 2022. Metabolomic profiling in dogs with dilated cardiomyopathy eating non-traditional or traditional diets and in healthy controls. Sci Rep, 12(1): 22585

Smith JS, Varga A and Schober KE, 2020. Comparison of two commercially available immunoassays for the measurement of bovine cardiac troponin I in cattle with induced myocardial injury. Front Vet Sci, 7: 531, doi: 10.3389/fvets.2020.00531

Spratt DP, Mellanby RJ, Drury N and Archer J, 2005. Cardiac troponin I: evaluation of a biomarker for the diagnosis of heart disease in the dog. J Small Anim Prac, 46(3): 139-145, doi: 10.1111/j.1748-5827.2005.tb00304.x

Sultana F, Changkija B, Kalita D, Deka P, Baishya BC *et al.*, 2019. Evaluation of NT-proBNP a cardiac biomarker for the early diagnosis of cardiac disease in dogs. Int J Livest Res, 9(10): 86-96, doi: 10.5455/ijlr.20190701045412

Tahir UA, Katz DH, Avila-Pachecho J, Bick AC, Pampana A *et al.*, 2022. Whole genome association study of the plasma metabolome identifies metabolites linked to cardiometabolic disease in black individuals. Nat Commun, 13(1): 4923, doi: 10.1038/s41467-022-32275-3

Tanindi A and Cemri M, 2011. Troponin elevation in conditions other than acute coronary syndromes. Vasc Health Risk Manag, 7: 597-603, doi: 10.2147/VHRM.S24509

Tharwat M, Al-Sobayil F and El-Sayed M, 2013. Cardiac troponin I in healthy newborn goat kids and in goat kids with cardiac nutritional muscular dystrophy. Acta Vet Hung, 61(4): 442-453, doi: 10.1556/AVet.2013.041

Trachsel DS, Grenacher B, Weishaupt MA and Schwarzwald CC, 2012. Plasma atrial natriuretic peptide concentrations in horses with heart disease: A pilot study. Vet J, 192(2): 166-170, doi: 10.1016/j.tvjl.2011.06.035

Van DerVekens N, Decloedt A, De Clercq D, Veheyen T and Van Loon G, 2012. The use of cardiac biomarkers in veterinary medicine: The equine perspective. Vlaams Diergeneeskd Tijdsch, 81(6): 319-327 doi: 10.21825/vdt.v81i6.18315

Received- 17.08.2023, Accepted- 26.01.2024, Published- 20.02.2024 (Online), 01.06.2024 (Print)
Section Editor: Dr. A. K. Patra, Associate Editor