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Dr. Digjay V Kabariya

Department of Veterinary
Pathology, College of Veterinary
Science and Animal Husbandry,
Kamdhenu University, Anand,
Gujarat, India

Dr. Manisha Parihar

Assistant Professor, Department
of Veterinary Pathology, RPS
College of Veterinary Science,
Mahendergarh, Haryana, India

Dr. DJ Ghodasara

Professor and Head, Department
of Veterinary Pathology, College
of Veterinary Science and
Animal Husbandry, Kamdhenu
University, Anand, Gujarat,
India

Corresponding Author:

Dr. Manisha Parihar

Assistant Professor, Department
of Veterinary Pathology, RPS
College of Veterinary Science,
Mahendergarh, Haryana, India

A comprehensive review on cardiovascular biomarkers in animals: Bridging conventional diagnostics and precision medicine

Digjay V Kabariya, Manisha Parihar, DJ Ghodasara

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Abstract

Heart diseases are a major cause of reduced performance, illness, and death in domestic and companion animals. The early recognition of cardiac disorders is often difficult because clinical signs may be subtle and advanced diagnostic imaging is not always available. Biomarkers have emerged as practical tools for identifying myocardial injury, ventricular stress, inflammatory activity, and metabolic disturbances using minimally invasive blood sampling. This review integrates current knowledge on cardiovascular biomarkers used in veterinary medicine, focusing on cardiac troponins, natriuretic peptides, and novel molecular markers. Their diagnostic value in equine and small animal cardiology is discussed, along with challenges related to biological variation, assay limitations, and reference interval standardization. Future directions emphasize multi-marker strategies, omics-based discovery, and precision approaches for veterinary cardiac care.

Keywords: Cardiac biomarkers, veterinary cardiology, troponin, NT-probnp, equine heart disease, canine cardiomyopathy, precision veterinary diagnostics

1. Introduction

In veterinary medicine, cardiac problems are a significant clinical issue that impact horses, dogs, cats, and animals that produce food. Cardiomyopathies, myocarditis, degenerative valve disease, irregular heartbeats, and congenital abnormalities are common disorders. Traditionally, a physical examination and imaging methods like radiography, electrocardiography, and echocardiography are used to make the diagnosis. While successful, these procedures need specialist equipment and may fail to identify early myocardial injury (Pierce, 2025)^[21].

Biomarkers are measurable biological substances that show whether a bodily process is normal or abnormal. They offer information on neurohormonal activation, inflammatory reactions, mechanical stress, and cardiac cell damage in cardiovascular medicine. Biomarkers like natriuretic peptides and cardiac troponins are well-established in human medicine. As research has demonstrated their applicability across animal species, their use in veterinary practice has grown (Prošek *et al.*, 2007, Scansen & Drees, 2020, De lima & Ferreira, 2017)^[23, 27, 6].

The need for quick, inexpensive, and minimally intrusive methods is reflected in the growing interest in biomarker-based diagnostics. Prior research in veterinary medicine has shown that biomarkers can identify cardiac involvement even when there are no obvious clinical symptoms. Biomarkers have been utilized to identify myocarditis and performance-limiting cardiac injury in horses, while they help differentiate heart illness from respiratory conditions in dogs and cats (Smith *et al.*, 2015)^[32].

Biomarker research has expanded to encompass genetic, metabolic, and RNA-based indicators in addition to protein markers thanks to recent technology advancements. These advancements point to a move toward more predictive and customized veterinary diagnostics. This review's goals are to provide an overview of the state of the art regarding cardiovascular biomarkers in animals, explain their molecular underpinnings and practical applications, and consider potential future directions (Gavazza *et al.*, 2018, Perera *et al.*, 2021&Pereraet *al.*, 2022)^[10, 19, 20].

2. Materials and Methods

2.1 Data Synthesis

The implementation of cardiovascular biomarkers in veterinary medicine requires on a structured understanding of their kinds, release mechanisms, diagnostic and prognostic importance, species-specific utility, methodological limits, and potential advances. A thorough synthesis of these elements is made possible by a systematic examination of the literature, which supports evidence-based interpretation in clinical practice.

2.1a Categories of Cardiac Biomarkers

Veterinary cardiovascular biomarkers are broadly classified into four major categories:

2.1a.1 Indicators of Myocardial Injury: The extremely specific indicators of cardiomyocyte injury are cardiac troponins (cTnI and cTnT). Their release is directly indicative of myocardial involvement and is brought on by necrosis, apoptosis, ischemia, or inflammatory damage (Langhorn & Willesen, 2016) [12].

2.1a.2 Indicators of Cardiac Overload or Stretch: Ventricular wall stress causes the release of B-type natriuretic peptide (BNP) and NT-proBNP, which represent pressure or volume overload. These indicators correlate with ventricular remodeling and shed light on the degree of heart failure. (Takemura *et al.*, 2009, Wess *et al.*) [35].

2.1a.3 Inflammatory and Systemic Markers: The systemic inflammatory response associated with heart disease is represented by acute-phase proteins including serum amyloid A (SAA) and C-reactive protein (CRP), as well as cytokines like IL-6, TNF- α , and MCP-1. Despite their lack of specificity, these markers offer crucial prognostic data for progressive heart failure (Sasaki *et al.*, 2019) [42].

2.1b Novel Molecular Biomarkers: MicroRNAs, metabolomic profiles, and proteomic patterns are examples of emerging indicators that offer early and mechanistic insights into cardiac pathology. Before clinical or echocardiographic alterations become noticeable, circulating miRNAs have demonstrated potential in identifying early myocardial stress. (Michel *et al.*, 2022) [43].

2.1c Mechanisms of Biomarker Release

Cardiovascular biomarkers are released through distinct physiological and pathological pathways:

- **Troponins:** Released primarily due to cardiomyocyte necrosis or apoptosis. Subclinical elevations may occur following extreme exercise, sepsis, or systemic hypoxia (Van Der Vekens *et al.*, 2019) [36].
- **Natriuretic Peptides:** Synthesized and secreted by ventricular myocardium in response to stretch, volume overload, or pressure load, promoting natriuresis and vasodilation. They reflect hemodynamic stress rather than cellular injury (Wess *et al.*).
- **Acute Phase Proteins and Cytokines:** CRP, SAA, and pro-inflammatory cytokines are released by the liver and immune cells in response to systemic inflammation, infection, or tissue injury, including cardiac insult (Tidholm *et al.*, 2015) [13].
- **Molecular Biomarkers:** Circulating miRNAs, metabolomic fingerprints, and proteomic signatures arise from gene expression changes, cellular stress, and metabolic alterations during cardiac pathology, allowing

earlier detection of disease processes than traditional protein markers (Filipovic *et al.*).

2.1d Diagnostic and Prognostic Relevance

Cardiovascular biomarkers have significant diagnostic and prognostic utility:

- **Early detection:** cTnI and miRNAs can identify subclinical myocardial injury before overt echocardiographic changes (Shah *et al.*, 2025) [29].
- **Differential diagnosis:** NT-proBNP differentiates cardiac from pulmonary causes of dyspnea in dogs and cats (Sleeper *et al.*, 2001 & Noszczyk, 2011) [31, 15].
- **Disease severity and prognosis:** Elevated troponins and acute-phase proteins correlate with mortality and morbidity in chronic heart failure (Xiao *et al.*, 2021) [38].
- **Therapeutic monitoring:** Serial measurements of NT-proBNP and cTnI help monitor treatment efficacy and disease progression (Van Der Vekens *et al.*, 2019) [36].

2.1e Species-Specific Clinical Applications

- **Dogs and Cats:** NT-proBNP and cTnI are the most widely validated biomarkers. NT-proBNP is useful for differentiating cardiac vs respiratory dyspnea and monitoring CHF, while troponins detect myocardial injury (Sharkey & Rush, 2009, Langhorn & Willesen, 2016) [30, 12].
- **Horses:** cTnI and NT-proBNP detect subclinical myocarditis, valvular disease, and performance-limiting cardiac stress. Baseline reference ranges are influenced by training, exercise, and age (Van Der Vekens *et al.*, 2019) [36].
- **Food-producing animals (cattle, sheep, goats, pigs):** Troponins and CK-MB detect myocardial damage from infectious, traumatic, or nutritional etiologies. Reference intervals are limited, and validation studies remain sparse (Rebez & Ninan, 2024) [24].

2.1f Methodological and Biological Constraints

Despite their potential, cardiovascular biomarkers face several limitations:

- **Assay variability:** Human-based assays are often adapted for veterinary use, resulting in differences in sensitivity and specificity (Filipovic *et al.*).
- **Biological variability:** Age, sex, breed, stress, renal function, and exercise influence biomarker levels, complicating interpretation (Wess *et al.*).
- **Non-specificity:** Inflammatory markers and systemic proteins may rise in non-cardiac conditions, such as infection or trauma (Sasaki *et al.*, 2019) [42].
- **Reference intervals:** Many biomarkers lack species-specific reference ranges, limiting their clinical utility, especially in large animals and exotic species (Sasaki *et al.*, 2019) [42].

2.1g Prospective Innovations

Emerging approaches are focusing on:

- **Multi-marker panels:** Combining troponins, natriuretic peptides, miRNAs, and metabolomic signatures enhances sensitivity and specificity. (Michel *et al.*, 2022) [43].
- **Omics-based strategies:** Proteomics, transcriptomics, and metabolomics offer mechanistic insights and early detection of cardiac injury. (Dunn *et al.*, 2011, Zhao *et al.*, 2015, Michel *et al.*, 2022) [7, 39, 43].

- **Point-of-care assays and artificial intelligence:** Portable testing devices and AI-based integration of biomarker and imaging data are poised to improve real-time diagnosis and personalized veterinary cardiac care (Filipovic *et al.*; Van Der Vekens *et al.*, 2019)^[36].

3. Results

3.1 Categories of Cardiovascular Biomarkers

Veterinary cardiovascular biomarkers may be grouped into four main classes:

3.1.1 Markers of Myocardial Injury

Cardiac troponins, specifically cTnI and cTnT, are highly specific markers for cardiomyocyte injury. Troponins are released into circulation following necrosis, ischemia, or inflammatory damage of cardiac tissue. Studies in dogs and cats indicate elevated troponin concentrations in conditions such as myocarditis, dilated cardiomyopathy (DCM), hypertrophic cardiomyopathy (HCM), and congestive heart failure (CHF) (Langhorn & Willemsen, 2016; Van Der Vekens *et al.*, 2019)^[12, 36]. In horses, troponins are used to detect myocardial stress, subclinical myocarditis, and performance-limiting injury, while in livestock, elevated troponins correlate with traumatic or infectious cardiac lesions (Rebez & Ninan, 2024)^[24].

3.1.2 Markers of Cardiac Stretch

B-type natriuretic peptide (BNP) and its precursor, N-terminal pro-BNP (NT-proBNP), are secreted by ventricular myocardium in response to volume or pressure overload. These peptides regulate natriuresis, vascular tone, and neurohormonal activity, reflecting cardiac stress. NT-proBNP has been validated in dogs and cats for differentiating cardiac from pulmonary causes of dyspnea, assessing severity of valvular disease, and monitoring therapeutic response (Sleeper *et al.*, 2001; Wess *et al.*)^[35]. In equine medicine, natriuretic peptide concentrations correlate with valvular disease and myocardial remodeling, although age, exercise, and training status can influence baseline values (Van Der Vekens *et al.*, 2019)^[36].

3.1.3 Inflammatory and Systemic Biomarkers

Inflammation plays a significant role in the pathophysiology of cardiac diseases in small animals, particularly in dogs with congestive heart failure (CHF) resulting from conditions such as myxomatous mitral valve disease (MMVD) and dilated cardiomyopathy (DCM). Cardiovascular dysfunction is not solely hemodynamic; it also involves complex inflammatory and systemic responses that can be detected through specific biomarkers in serum or plasma (Ljungvall, *et al.*, 2010)^[13].

3.1.4 C-Reactive Protein (CRP)

C-reactive protein (CRP) is a major acute-phase protein synthesized by the liver in response to pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α). CRP rapidly increases during systemic inflammation and is widely used as a marker of inflammatory activity in dogs. In canine cardiovascular patients, higher CRP concentrations are observed in advanced stages of CHF compared with both asymptomatic patients and healthy controls, indicating its utility as a marker of disease severity and systemic inflammation.

CRP correlates positively with echocardiographic indicators of cardiac dysfunction, such as left ventricular ejection fraction and mitral valve inflow velocities, and with

neutrophil counts and total white blood cell counts, which typically rise alongside CRP in systemic inflammatory states (Cerón, *et al.*, 2005)^[3].

3.1.5 Serum Amyloid A (SAA)

Serum amyloid A (SAA) is another acute phase protein that is widely recognised as a highly sensitive marker of systemic inflammation in dogs. SAA concentrations increase dramatically within 24 hours of inflammatory stimulation and decrease rapidly upon resolution, making it valuable for detecting ongoing systemic inflammatory responses. SAA has been shown to outperform CRP in diagnostic performance for systemic inflammation because of its wider concentration range in affected patients.

Although much research on SAA has focused on systemic inflammatory diseases such as sepsis, noninfectious inflammatory conditions, and trauma, its sensitivity makes it a promising tool for identifying inflammatory components in cardiac disease when interpreted alongside cardiac-specific biomarkers (Christensen, *et al.*, 2014)^[4].

3.1.6 White Blood Cell Count and Differentialfree

Systemic inflammation in CHF is often accompanied by elevations in white blood cell (WBC) counts and specifically neutrophil counts (NEUT). Studies have shown that dogs with decompensated heart failure exhibit significantly higher total WBC and neutrophil counts than healthy dogs or those with milder disease stages. These hematologic changes reflect systemic inflammatory activation and correlate with other markers such as CRP (Cunningham, *et al.*, 2012)^[5].

3.1.7 Cytokines and Chemokines

Inflammatory cytokines, such as monocyte chemoattractant protein-1 (MCP-1) and chemokines like keratinocyte-derived chemokine (KC-like), are elevated in dogs with advanced heart failure. These molecules contribute to inflammatory signaling and attract immune cells to sites of tissue injury. Their serum levels correlate with traditional cardiac measurements such as left atrial size and left ventricular dimensions, suggesting a mechanistic link between inflammation and cardiac remodeling. (Aronson, 2008)^[1].

3.1.8 Inflammation-Oxidative Stress Interplay

Inflammatory markers often co-exist with oxidative stress indicators in heart failure patients, reflecting a bidirectional relationship between these biological processes. Increased CRP, WBC, and cytokines accompany reduced antioxidant capacity and elevated oxidative stress in dogs with CHF, suggesting that inflammatory and oxidative pathways act in concert to exacerbate cardiac dysfunction (Pereira, *et al.*, 2016).

3.1.9 Clinical Relevance and Limitations

Inflammatory biomarkers such as CRP, SAA, WBC counts, and specific cytokines provide valuable supplementary information for assessing systemic involvement in cardiac disease. They help distinguish advanced CHF from compensated disease and may offer prognostic insight. However, they are nonspecific, as elevations can also result from infection, trauma, neoplasia, or other non-cardiac inflammatory conditions. Thus, interpreting these markers requires a holistic clinical context and correlation with cardiac imaging and functional tests (Ljungvall, *et al.*, 2010)^[13].

3.2 Emerging Molecular Biomarkers

Molecular biomarkers represent the next frontier in small animal cardiology, offering sensitive and specific indicators of cardiac disease beyond traditional protein markers such as

troponins and natriuretic peptides. These cutting-edge biomarkers include circulating microRNAs (miRNAs), proteomic signatures, and metabolomic profiles, which have demonstrated significant potential for early detection, disease staging, and therapeutic monitoring in dogs and cats (Perera *et al.*, 2022)^[19].

3.2.1 MicroRNAs: A New Class of Circulating Biomarkers

MicroRNAs (miRNAs) are short, non-coding RNA molecules that regulate gene expression post-transcriptionally and are increasingly recognized for their roles in cardiovascular diseases. Recent veterinary research emphasizes the diagnostic and prognostic value of miRNAs in small animal heart disease. Circulating miRNAs exhibit disease-specific expression patterns in conditions such as myxomatous mitral valve disease (MMVD), pulmonary stenosis, and cardiac hypertrophy, distinguishing affected animals from healthy controls with high sensitivity and specificity (Gidlöf *et al.*, 2013)^[11].

For example, in a pilot study of dogs with cardiac hypertrophy, differential expression of miRNAs such as cfa-miR-130b, cfa-miR-375, and cfa-let-7b was observed in animals with myxomatous mitral valve degeneration and pulmonic stenosis, suggesting potential utility as novel biomarkers and therapeutic targets.

Comprehensive reviews of veterinary miRNA research highlight their contribution to multiple cardiovascular pathways including myocardial growth, fibrosis, and remodelling, further supporting their candidacy as molecular biomarkers (Reis-Ferreira, *et al.*, 2022)^[6].

3.2.2 Proteomic Biomarkers: Revealing Complex Pathophysiology

Proteomic analysis enables the identification of proteins whose expression changes with disease state. In chronic heart failure due to degenerative mitral valve disease, proteomic studies have revealed numerous up- and down-regulated proteins involved in immune response, hemostasis, oxidative stress, and energy metabolism.

These proteomic shifts reflect underlying pathophysiological processes and may serve as biomarkers for staging disease, identifying therapeutic targets, and monitoring treatment response. The complexity of these protein networks underscores the need for multi-marker panels rather than reliance on single molecular indicators (Zhang, *et al.*, 2017)^[40].

3.2.3 Metabolomic Approaches: Small Molecules as Sensitive Indicators

Metabolomic profiling examines low-molecular-weight metabolites that change with disease states. Emerging projects like MetaDog are applying metabolomics to identify novel cardiac biomarkers in dogs with dilated cardiomyopathy and other heart diseases, aiming to enhance early diagnosis and precision therapy through metabolic fingerprints.

Metabolites may reflect altered energy utilization, oxidative stress, or signaling pathway disruptions critical in cardiac pathology, offering a promise for next-generation diagnostics (Schober *et al.*, 2011 & Truppel, *et al.*, 2019)^[28, 34].

3.2.4 Beyond miRNAs and Proteins: Expanding the Molecular Biomarker Landscape

In addition to miRNAs and proteomics, recent feline studies have identified RNA markers such as WNT5A, IL-18, and IGFBP-2 that differ by disease stage in hypertrophic

cardiomyopathy, suggesting that RNA-based biomarker panels may outperform traditional proteins for specific cardiomyopathies.

Collectively, these molecular signatures offer a more nuanced understanding of disease processes at the transcriptional, translational, and metabolic levels, paving the way for precision veterinary cardiology (Li *et al.*, 2024)^[14].

3.3 Clinical and Translational Implications

While established biomarkers like troponins and natriuretic peptides remain valuable, molecular biomarkers promise:

- Earlier detection of cardiac disease before clinical signs emerge
- Disease subtype differentiation (e.g., concentric vs eccentric hypertrophy)
- Dynamic monitoring of therapy responses
- Identification of novel therapeutic targets

However, large-scale validation and standardization are still needed before widespread clinical implementation. The integration of molecular biomarkers with traditional diagnostics and imaging will likely provide the strongest predictive models for patient care.

3.4 Biomarkers in Equine Cardiology

Cardiovascular biomarkers are increasingly recognized as valuable tools in the diagnosis, monitoring, and prognostication of heart disease in horses. Unlike traditional diagnostic methods that rely largely on imaging and physical examination, biochemical markers can provide early, objective evidence of myocardial injury or physiological stress (Schwarzwalld, *et al.*, 2013)^[33].

3.4.1 Troponins as Primary Cardiac Injury Markers

Cardiac troponin I (cTnI) is the most studied and clinically useful biomarker in equine cardiology. Troponins are regulatory proteins in cardiomyocytes that are released into circulation when the heart muscle sustains injury. Elevated cTnI concentrations have been consistently observed in horses with confirmed myocardial disease, distinguishing them from healthy controls and those with structural abnormalities without direct myocardial damage.

Several studies have established reference ranges for cTnI in healthy horses (generally ≤ 0.03 ng/mL) and shown that values above these ranges are associated with pathologic conditions such as myocarditis and ventricular arrhythmias. Horses with ventricular arrhythmias and documented myocardial toxicity can exhibit markedly elevated troponin levels, while some horses with non-severe arrhythmias show modest elevations (Rishniw, *et al.*, 2019 & Oyama, & Sisson, 2004)^[26, 17].

3.4.2 Exercise-Related and Non-Cardiac Influences

Acute exercise triggers a transient increase in cardiac biomarkers, including cTnI, as part of normal physiological adaptation. For example, show jumping and other intense exercise sessions induce significant, but typically temporary, elevations in troponin and other markers (e.g., creatine kinase), which return to baseline within hours post-exercise. This highlights the importance of timing when collecting blood samples for accurate clinical interpretation.

Additionally, horses experiencing severe systemic illnesses such as colic with endotoxemia also show elevated cTnI levels indicative of myocardial injury secondary to systemic inflammation and stress. Horses with severe colic had

significantly higher troponin concentrations than healthy controls, and higher levels were associated with poorer clinical outcomes (Fox *et al.*, 2008 & Fox *et al.*, 2011)^[8, 9].

3.4.3 Other Equine Biomarkers under Investigation

Beyond troponins, other biomarkers are being evaluated in equine medicine. Inflammatory markers such as serum amyloid A (SAA) and C-reactive protein (CRP) have been studied in response to vaccination and systemic challenges, sometimes showing correlations with myocardial stress indicators.

Although promising in humans and some animal species, microRNA panels developed for other species have demonstrated limited discriminatory power for equine cardiac disease, emphasizing the need for equine-specific molecular assays (Schwarzwald, *et al.*, 2013)^[33].

3.4.4 Challenges and Practical Considerations

Most commercially available cardiac assays were originally designed for humans and require careful validation before application in horses. Differences in protein structure and immunoassay reactivity have led to variability in reference intervals and the need for species-specific calibration and validation protocols.

Currently, cTnI remains the most sensitive and specific biomarker for detecting myocardial injury in horses, while additional markers (e.g., inflammatory proteins and advanced molecular profiles) are under investigation to enhance diagnostic precision (Rishniw, *et al.*, 2019)^[26].

Biomarkers in equine practice are particularly helpful for:

- Investigating unexplained poor performance
- Detecting subclinical myocardial disease
- Monitoring recovery after infectious illness
- Assessing cardiac risk in sport horses

3.5 Biomarkers in Small Animal Cardiology

3.5.1 Biomarkers in Small Animal Cardiology

Cardiovascular biomarkers have become integral tools in diagnosing, monitoring, and prognosticating heart disease in small animals, especially dogs and cats. These biomarkers are measurable substances released into circulation in response to cardiac injury or stress and provide valuable insights beyond traditional diagnostic methods such as auscultation and imaging (echocardiography, radiography) (Langhorn & Willesen, 2016, Rebez & Ninan, 2024)^[12, 24].

3.5.2 Primary Cardiac Biomarkers

3.5.2.1 Cardiac Troponin I (cTnI)

Cardiac troponin I is a highly specific marker of myocardial injury. Under normal conditions, little to no cTnI circulates in healthy dogs and cats, but concentrations rise significantly when cardiomyocytes are damaged (e.g., myocarditis, cardiomyopathy, ischemic injury). Troponin increases correlate with the extent of myocardial damage, making it a sensitive indicator of disease progression and severity. However, cTnI is not specific to disease etiology; elevations can occur with systemic illnesses (e.g., sepsis, renal disease) that secondarily impact the heart (Langhorn & Willesen, 2016)^[12].

3.5.2.2 N-Terminal pro-B-Type Natriuretic Peptide (NT-

proBNP): NT-proBNP is released by ventricular myocytes in response to increased wall stretch and pressure overload. It is widely used to differentiate cardiac from non-cardiac causes of respiratory distress in dogs and cats and to evaluate preclinical cardiomyopathy. Elevated NT-proBNP reflects volume overload states such as congestive heart failure and can be useful in monitoring treatment efficacy (Oyama, *et al.*, 2008 & O'Shaughnessy *et al.*, 2022)^[41, 16].

3.5.3 Clinical Utility in Small Animal Practice

3.5.3.1 Diagnosis and Differentiation

Cardiac biomarkers improve diagnostic confidence when combined with clinical signs and imaging. NT-proBNP concentrations assist in distinguishing cardiac from respiratory causes of dyspnea, a frequent challenge in small animal practice. Meanwhile, increased cTnI levels are strong evidence of myocardial injury, even in cases without clear imaging abnormalities (Oyama, *et al.*, 2008)^[41].

3.5.3.2 Prognosis and Monitoring

Studies support the prognostic value of these biomarkers. High NT-proBNP levels often correlate with more advanced disease and poorer outcomes, whereas dynamic changes in cTnI can reflect ongoing myocardial damage or therapeutic response. Both markers can be used serially to monitor disease progression and treatment effects (Oyama, *et al.*, 2008 & Boswood *et al.*, 2008)^[41, 2].

3.5.3.3 Biological and Analytical Considerations

Cardiac biomarkers are influenced by age, breed, renal function, exercise, and comorbid conditions. For example, biologic variation studies indicate that individual baseline values may differ significantly, suggesting that serial measurements in the same patient may be more informative than population reference intervals (Li *et al.*, 2024)^[14].

3.5.3.4 Emerging Biomarkers

Research in feline hypertrophic cardiomyopathy (HCM) has identified potential novel biomarkers such as WNT5A, IL-18, and IGFBP-2 RNA, suggesting a future where multi-parameter molecular profiles may refine diagnosis and risk stratification beyond traditional proteins (Li *et al.*, 2024)^[14].

3.6 Limitations and Interpretation

While valuable, cardiac biomarker testing should not replace imaging or clinical assessment. Interpretation of results requires context; for instance, elevated NT-proBNP may be seen in non-cardiac diseases affecting cardiac filling pressures, and cTnI can be influenced by systemic illnesses. Therefore, clinical decisions should integrate biomarker data with physical examination, echocardiography, and other laboratory tests (Oyama, *et al.*, 2008)^[41].

3.7 Conventional Tests versus Cardiac Biomarkers

Traditional laboratory enzymes such as creatine kinase, lactate dehydrogenase, and aspartate aminotransferase lack specificity for heart tissue and may increase due to skeletal muscle or liver damage. In contrast, modern cardiac biomarkers offer greater organ specificity and diagnostic relevance. Nevertheless, they should complement rather than replace imaging and clinical assessment.

Table 1: Conventional Cardiac Tests vs Cardiac Biomarkers in Veterinary Medicine (Langhorn & Willesen, 2016) ^[12]

Aspect	Conventional Tests (ECG, X-ray, Echo, Enzymes: CK, AST, LDH)	Cardiac Biomarkers (cTnI, cTnT, NT-proBNP, BNP)
Nature of test	Functional and anatomical assessment	Biochemical and molecular indicators
Sample required	Imaging or electrical signal; sometimes blood	Blood (serum or plasma)
Time to result	Minutes to hours (depending on imaging availability)	Minutes to few hours (POC or lab assay)
Detection of early disease	Limited (often detects advanced disease)	High sensitivity for subclinical myocardial injury
Specificity for heart	Moderate (CK, AST, LDH are non-specific)	High (troponins and BNP are cardiac-specific)
Detection of myocardial injury	Indirect (wall motion change, arrhythmia)	Direct biochemical evidence of cardiomyocyte injury
Heart failure detection	Requires echo/radiograph	NT-proBNP directly reflects cardiac stretch
Differentiation of cardiac vs respiratory disease	Requires imaging and expertise	NT-proBNP provides rapid discrimination
Portability	Limited (echo/X-ray machines required)	High (POC kits available)
Field applicability	Low to moderate	High
Cost per test	High (equipment & expertise)	Moderate
Monitoring therapy	Subjective and operator-dependent	Objective, quantitative
Exercise influence	ECG/echo affected by stress	Biomarkers affected but interpretable with timing
Breed/size influence	Equipment dependent	Requires reference intervals
Detection of myocarditis	Often missed	Troponin sensitive
Screening asymptomatic animals	Not practical	Highly practical
Utility in wildlife/zoo	Difficult	Highly useful
Reproducibility	Operator dependent	Highly reproducible
Skill required	Specialist training	Basic lab handling
Biological interpretation	Structural/functional	Cellular injury & stress
Integration with AI	Limited	Highly compatible
Future expansion	Hardware-based	Multi-omics expansion (Wilkins <i>et al.</i> , 2010) ^[37]

Table 2: Omics Approaches for Cardiovascular Biomarkers in Animals (Perera *et al.*, 2022) ^[19]

Omics Type	What It Studies	Biological Sample	Key Cardiovascular Biomarkers / Targets	Diagnostic / Clinical Use in Animals	Species Studied
Genomics	DNA sequence & genetic variants	Blood, tissue, saliva	Gene mutations (MYBPC3, TNNT2, dystrophin), SNPs	Identifies inherited cardiomyopathies, breed predisposition	Dog, cat, horse, cattle
Transcriptomics	mRNA expression (gene activity)	Heart tissue, blood	Cardiac stress genes (NPPA, NPPB, MYH7), inflammatory genes	Detects early myocardial stress and remodeling	Dog, horse, pig, rodents
Proteomics	Protein profiles	Serum, plasma, heart tissue	Troponin, BNP, cytokines, oxidative proteins	Detects myocardial injury & heart failure	Dog, cat, horse, cattle
Metabolomics	Small metabolites	Serum, urine, tissue	Lactate, acylcarnitines, TCA cycle metabolites	Reveals ischemia, energy metabolism failure	Dog, horse, pig, fish
Lipidomics	Lipid species & pathways	Plasma, tissue	Ceramides, phospholipids, triglycerides	Identifies cardiometabolic risk and myocardial membrane injury	Dog, cat, pig, cattle
Multi-omics	Integrated omics layers	Combined samples	Combined gene-protein-metabolite networks	Precision diagnosis and prognosis	All species (research)

Table 3: Cardiovascular Biomarkers in Veterinary animals - Diagnostic Utility (Polizopoulou, 2017) ^[22]

Species	Major Cardiac Diseases	Primary Biomarkers	Diagnostic Significance	Remarks / Limitations
Dog	DCM, DMVD, myocarditis, CHF	NT-proBNP, cTnI, cTnT	NT-proBNP: differentiates cardiac vs respiratory dyspnea; Troponin: myocardial injury	Influenced by renal disease and age
Cat	HCM, RCM, myocarditis, CHF	NT-proBNP, cTnI	Detects occult cardiomyopathy; troponin indicates myocardial necrosis	Stress and restraint affect BNP
Horse	Myocarditis, valvular disease, arrhythmia	cTnI, cTnT, NT-proBNP	Identifies myocardial damage and valvular overload	Exercise alters values
Cattle	Traumatic reticulopericarditis, cardiomyopathy	cTnI, CK-MB, AST	Troponin detects myocardial damage	Non-specific markers influenced by muscle injury
Sheep	Cardiomyopathy, parasitic myocarditis	cTnI, CK-MB	Myocardial injury indicator	Reference ranges limited
Goat	Myocarditis, nutritional cardiomyopathy	cTnI, CK-MB	Reflects myocardial necrosis	Sparse validation studies
Pig	Stress cardiomyopathy, myocarditis	cTnI, BNP	Detects ischemic myocardial damage	Handling stress affects levels
Camel	Cardiomyopathy, infectious myocarditis	cTnI, CK-MB	Myocardial damage	Limited published data
Buffalo	Pericarditis, myocarditis	cTnI, CK-MB	Indicates myocardial injury	Similar to cattle
Poultry	Ascites syndrome, cardiomyopathy	cTnI, LDH	Detects myocardial stress	Small sample volume limits testing
Turkey	Dilated cardiomyopathy	cTnI	Myocardial damage marker	Experimental use mainly
Rabbit	Cardiomyopathy, myocarditis	cTnI, BNP	Myocardial injury	Limited clinical use
Guinea pig	Spontaneous cardiomyopathy	cTnI	Detects myocardial injury	Research-oriented
Dog (working/athlete)	Exercise-induced stress	cTnI, NT-proBNP	Differentiates physiological vs pathological stress	Post-exercise timing critical
Horse (race)	Poor performance, myocarditis	cTnI, NT-proBNP	Screening poor performers	Exercise confounder

Table 4: Clinical use category (Polizopoulou, 2017)^[22]

Purpose	Recommended Biomarkers
Early myocardial damage	cTnI
CHF detection	NT-proBNP
Myocarditis	cTnI + CRP/SAA
Exercise stress (horse/dog)	cTnI
Herd screening (cattle/sheep)	cTnI + CK-MB

4. Discussion

The incorporation of cardiovascular biomarkers into veterinary practice mirrors developments in human cardiology. Troponins and natriuretic peptides have enabled earlier detection of myocardial injury and cardiac dysfunction. However, interpretation remains challenging due to interspecies variation, age-related changes, renal clearance effects, and exercise-induced fluctuations.

Analytical differences between assays and limited standardization further complicate clinical use. These limitations highlight the importance of integrating biomarker data with physical examination and diagnostic imaging.

Future biomarker research is expected to focus on molecular technologies that reveal disease-specific signatures. Multi-marker panels combining protein and RNA-based indicators may enhance diagnostic accuracy. Portable testing devices will increase field applicability, particularly in equine and rural practice. Artificial intelligence tools may assist clinicians in interpreting complex biomarker datasets.

5. Conclusion

Cardiovascular biomarkers have become important tools in veterinary diagnostics. Cardiac troponins and natriuretic peptides are currently the most reliable and widely applied markers across animal species. Their combined use with imaging and clinical evaluation improves diagnostic confidence and disease monitoring. Advances in molecular biomarker discovery promise to further refine veterinary cardiology by supporting early detection and individualized therapeutic strategies.

Conflict of Interest

Not available

Financial Support

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