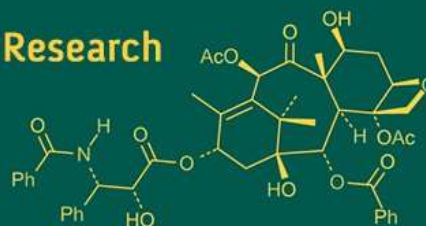
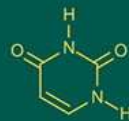
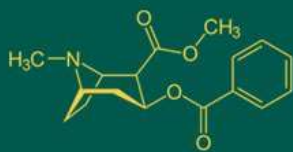


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Canine cardiorenal syndrome: Advances in pathophysiology, diagnostic biomarkers, and clinical management

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Abstract

Cardiorenal Syndrome (CRS) is a complex clinical disorder characterized by the bidirectional interaction between the cardiovascular and renal systems, whereby dysfunction of one organ initiates or aggravates dysfunction of the other. In dogs, CRS is increasingly recognized as a significant complication of chronic cardiac and renal diseases, particularly Degenerative Mitral Valve Disease (DMVD) and chronic kidney disease (CKD). The syndrome develops through a combination of haemodynamic disturbances, neurohormonal activation, inflammation, oxidative stress, and metabolic alterations, ultimately leading to progressive deterioration of both organ systems. CRS is classified into five subtypes based on the primary organ involved and the sequence of disease progression, each exhibiting distinct pathophysiological mechanisms and clinical manifestations. Affected dogs commonly present with nonspecific signs during the early stages, while advanced disease is characterized by clinical features associated with both cardiac and renal dysfunction. Recent advances in veterinary medicine have enhanced the diagnosis of CRS through the use of cardiac biomarkers, including cardiac troponins and N-terminal pro-B-type natriuretic peptide (NT-proBNP), renal biomarkers such as symmetric Dimethylarginine (SDMA) and cystatin C, together with echocardiography, electrocardiography, and routine laboratory investigations. Therapeutic management remains challenging because treatment must preserve cardiac function while minimizing further renal injury. Current strategies include renin-angiotensin-aldosterone system inhibitors, mineralocorticoid receptor antagonists, loop diuretics, pimobendan, digoxin, omega-3 fatty acid supplementation, and supportive therapy tailored to the individual patient. Early diagnosis, regular monitoring, and a multidisciplinary treatment approach are essential to improve clinical outcomes and delay disease progression. This review summarizes the current understanding of the epidemiology, classification, pathophysiology, clinical presentation, diagnostic biomarkers, imaging modalities, and therapeutic management of canine cardiorenal syndrome, highlighting recent advances and future directions for improving disease recognition and patient care.

Keywords: Cardiorenal syndrome, dog, chronic kidney disease, cardiac biomarkers, renal biomarkers, cardiac troponin, SDMA, renin-angiotensin-aldosterone system

Introduction

Cardiorenal Syndrome (CRS) is a multifactorial clinical disorder characterized by the intricate interplay between the cardiovascular and renal systems, in which dysfunction of one organ adversely influences the structure and function of the other. The syndrome involves complex haemodynamic alterations, neurohormonal activation, inflammatory responses, and adaptive physiological mechanisms that ultimately result in progressive impairment of both cardiac and renal function. Renal diseases may directly or indirectly contribute to cardiovascular complications, including left ventricular hypertrophy, systemic hypertension, electrolyte imbalances, fluid overload, and iatrogenic complications, thereby increasing the risk of cardiac dysfunction (Pouchelon *et al.*, 2015) ^[30].

The heart and kidneys maintain a close physiological relationship through the regulation of blood pressure, fluid balance, electrolyte homeostasis, and tissue perfusion. Consequently, pathological or functional impairment of either organ can initiate a cascade of events leading to dysfunction of the other. In dogs, both chronic kidney disease and cardiovascular disorders

can independently precipitate secondary injury to the counterpart organ, resulting in the development of cardiorenal syndrome. Despite increasing recognition of this interrelationship, comprehensive studies investigating the pathophysiology, diagnosis, and clinical management of canine CRS remain limited when compared with research focusing on isolated cardiac or renal diseases (Orvalho & Cowgill, 2017) ^[26].

Prevalence

Recent epidemiological investigations have highlighted the increasing clinical significance of cardiorenal syndrome in dogs, particularly in association with Degenerative Mitral Valve Disease (DMVD). A recent study conducted in Hyderabad reported that cardiac disorders were diagnosed in 91 dogs, representing approximately 1.01% of the total canine population examined. Among these cardiac cases, DMVD was the most frequently diagnosed condition, accounting for 71%, followed by Dilated Cardiomyopathy (DCM) at 25.3%. Renal dysfunction was identified in 27 dogs with DMVD, resulting in a reported CRS incidence of 44.3% within the affected population (Sangeetha *et al.*, 2025).

Age-related analysis revealed that dogs between 8 and 10 years were most commonly affected (40.74%), followed by those aged 6-8 years (22.22%), 10-12 years (18.52%), over 12 years (11.11%), and less than 6 years (7.41%). The greater susceptibility of geriatric dogs is likely attributable to age-associated physiological changes, including reduced renal perfusion, progressive nephron loss, diminished renal functional reserve, and impaired tubular reabsorptive capacity, which collectively predispose older animals to concurrent cardiac and renal dysfunction (Grauer, 2005; Kralova *et al.*, 2010) ^[11, 16].

Breed-wise analysis demonstrated that Pomeranians exhibited the highest prevalence of CRS (40.74%), followed by Shih Tzus (22.22%), Pugs (11.11%), Lhasa Apsos (10%), Labrador Retrievers (10%), mongrel dogs (7.41%), and Chihuahuas (3.7%), suggesting that breed predisposition may influence the occurrence of cardiorenal syndrome in canine populations.

Definition

Cardiorenal syndrome (CRS) is defined as a disorder in which acute or chronic dysfunction of either the heart or the kidneys induces acute or chronic dysfunction of the other organ, resulting in a bidirectional cycle of progressive organ injury (Goh & Ronco, 2010) ^[9].

The pathophysiology of CRS reflects the close physiological interdependence between the cardiovascular and renal systems. The kidneys play a pivotal role in maintaining blood pressure, electrolyte balance, and extracellular fluid volume through filtration and excretion of metabolic waste products. Conversely, the heart ensures adequate renal perfusion by maintaining sufficient cardiac output. Therefore, normal homeostasis depends on the coordinated function of both organs, and impairment of either system can adversely affect the other, ultimately leading to cardiorenal dysfunction.

Classification of Cardiorenal Syndrome

Based on the primary organ affected and the temporal pattern of disease progression, cardiorenal syndrome is

classified into five distinct subtypes in both human and veterinary medicine:

Type 1: Acute Cardiorenal Syndrome

Type 2: Chronic Cardiorenal Syndrome

Type 3: Acute Renocardiac Syndrome

Type 4: Chronic Renocardiac Syndrome

Type 5: Secondary Cardiorenal Syndrome

This classification facilitates a better understanding of the underlying pathophysiological mechanisms and assists clinicians in selecting appropriate diagnostic and therapeutic approaches.

Clinical Conditions Associated with Cardiorenal Syndrome

The clinical manifestations of CRS vary according to the subtype and the primary organ involved. Type 1 CRS is commonly associated with acute heart failure and cardiogenic shock leading to acute kidney injury. Type 2 CRS is characterized by chronic heart failure with progressive chronic kidney disease, often referred to as congestive kidney failure. Type 3 CRS involves acute kidney injury resulting in cardiac complications such as arrhythmias, hyperkalaemia, uraemia, and acute heart failure. Type 4 CRS is associated with chronic kidney disease, chronic glomerular disorders, systemic hypertension, anaemia, and left ventricular hypertrophy. Type 5 CRS develops secondary to systemic disorders, with sepsis and diabetes mellitus being the most common underlying conditions affecting both the heart and kidneys simultaneously.

Pathophysiology

Type 1 Cardiorenal Syndrome (Acute Cardiorenal Syndrome)

Type 1 CRS is characterized by the rapid deterioration of cardiac function that subsequently results in acute kidney injury (AKI). Acute heart failure, acute exacerbation of chronic heart failure, myocardial infarction, severe infections, or postoperative cardiac complications may produce a sudden decline in cardiac output, thereby reducing renal perfusion (Orvalho, 2017) ^[26].

Depending on the underlying mechanism, acute heart failure may manifest as either high-output or low-output heart failure. High-output failure results primarily from decreased peripheral vascular resistance, whereas low-output failure is caused by a marked reduction in cardiac output. Reduced cardiac output activates the sympathetic nervous system, increasing heart rate and myocardial contractility as compensatory mechanisms. Simultaneously, renal hypoperfusion stimulates renin release, activating the renin-angiotensin-aldosterone system (RAAS).

Activation of RAAS promotes sodium and water retention through aldosterone and antidiuretic hormone (ADH), increasing circulating blood volume and atrial filling pressures. Although these responses initially maintain blood pressure, persistent activation leads to systemic vasoconstriction, elevated venous pressure, and further reduction in renal blood flow, thereby aggravating kidney injury. In right-sided heart failure, elevated central venous pressure increases renal venous congestion, further compromising renal perfusion and accelerating the development of AKI.

In response to myocardial stretch, brain natriuretic peptide (BNP) is released to counteract RAAS activation through vasodilation and natriuresis. Endogenous vasodilators, including nitric oxide, prostaglandins, and bradykinin, also help mitigate excessive neurohormonal activation. However, persistent inflammation associated with acute and chronic heart failure activates the innate immune system, promoting cytokine release and oxidative stress that further contribute to renal injury. Additionally, nephrotoxic drugs and contrast agents used during emergency angiographic procedures may exacerbate AKI in susceptible patients (Ronco *et al.*, 2018) [32].

Type 2 Cardiorenal Syndrome (Chronic Cardiorenal Syndrome)

Type 2 CRS is characterized by chronic cardiovascular disease that progressively impairs renal function, ultimately resulting in chronic kidney disease (CKD). Persistent heart failure reduces effective renal perfusion and promotes chronic renal venous congestion, commonly referred to as congestive kidney failure. These haemodynamic disturbances are accompanied by sustained activation of neurohormonal pathways, including increased production of epinephrine, angiotensin II, endothelin, natriuretic peptides, and nitric oxide, all of which contribute to progressive renal injury (Orvalho, 2017) [26].

Chronic cardiac disease also increases renal susceptibility to injury through multiple mechanisms, including genetic predisposition, persistently reduced cardiac output, endothelial dysfunction, chronic inflammation, and accelerated atherosclerosis. Progressive renal hypoperfusion, increased renal vascular resistance, venous congestion, thromboembolism, glomerulosclerosis, and renal fibrosis ultimately culminate in irreversible chronic kidney disease (Ronco *et al.*, 2018) [32].

Type 3 Cardiorenal Syndrome (Acute Renocardiac Syndrome)

Type 3 CRS occurs when acute kidney injury initiates acute cardiac dysfunction. Impaired renal function results in fluid overload, electrolyte abnormalities, neurohormonal activation, and accumulation of myocardial depressant substances, predisposing affected animals to arrhythmias, pericarditis, and acute heart failure (Orvalho, 2017) [26].

Reduced renal perfusion causes renal ischaemia, depriving renal tissues of oxygen and nutrients while impairing normal kidney function. Compensatory sympathetic activation initially attempts to restore tissue perfusion; however, prolonged vasoconstriction further aggravates renal ischaemia. Reduced responsiveness to vasoconstrictors such as catecholamines and angiotensin II further worsens renal hypoperfusion.

Persistent renal ischaemia induces tubular necrosis and apoptosis, accompanied by cytokine release, oxidative stress, and production of reactive oxygen species (ROS), including peroxynitrite. Inflammatory responses may lead to septic interstitial nephritis, glomerular microthrombi, renal hyperaemia, and disseminated intravascular coagulation (DIC). Collectively, these pathological mechanisms culminate in acute kidney injury and amplify the complex heart-kidney interaction, increasing the risk of systemic complications (Ronco *et al.*, 2018) [32].

Type 4 Cardiorenal Syndrome (Chronic Renocardiac Syndrome)

Type 4 CRS is characterized by primary chronic kidney disease leading to progressive cardiovascular dysfunction. Declining glomerular filtration rate activates the renin-angiotensin-aldosterone system, resulting in systemic vasoconstriction and persistent hypertension. Increased afterload promotes cardiac remodelling, including left ventricular hypertrophy, impaired systolic function, and structural alterations of the myocardium (Ronco *et al.*, 2018) [32].

Water and sodium retention further elevate atrial pressure, contributing to ventricular hypertrophy and worsening cardiac function. Chronic kidney disease also disrupts mineral metabolism by reducing active vitamin D synthesis, leading to secondary hyperparathyroidism, hyperphosphataemia, and vascular calcification. These metabolic disturbances increase the risk of coronary artery disease and myocardial ischaemia. Furthermore, electrolyte abnormalities, particularly hyperkalaemia, predispose affected dogs to cardiac arrhythmias, chronic heart failure, and other cardiovascular complications (Ronco *et al.*, 2018) [32].

Type 5 Cardiorenal Syndrome (Secondary Cardiorenal Syndrome)

Type 5 CRS develops secondary to systemic disorders that simultaneously affect both the cardiovascular and renal systems. Common underlying conditions include sepsis, diabetes mellitus, hepatorenal syndrome, Fabry disease, and hyperadrenocorticism. In septic patients, systemic inflammation and microvascular dysfunction produce ultrastructural cellular damage in both organs, leading to simultaneous cardiac and renal impairment (Li *et al.*, 2009; Virzì *et al.*, 2016) [18, 42].

Diabetes mellitus and hyperadrenocorticism are important chronic diseases in dogs that adversely influence both urinary and cardiovascular function. Although several inflammatory mediators and signalling pathways have been implicated in sepsis-induced myocardial depression, the precise pathophysiological mechanisms remain incompletely understood. During septic acute kidney injury, inflammatory cytokines and tissue ischaemia stimulate the production of prostanoids, including thromboxane and prostacyclin, which impair coronary autoregulation and endothelial function. Elevated concentrations of tumour necrosis factor (TNF) and pro-inflammatory interleukins further contribute to myocardial dysfunction and multiorgan injury (Reines *et al.*, 1982) [31].

Clinical Signs

The clinical presentation of cardiorenal syndrome (CRS) is often subtle during the early stages, making diagnosis challenging before significant organ dysfunction develops. Initially, affected dogs may exhibit nonspecific signs such as reduced appetite, decreased feed intake, intermittent vomiting, and lethargy. As the disease progresses, clinical manifestations become more evident depending on the extent of cardiac and renal involvement.

Dogs with chronic kidney disease (CKD) commonly present with polyuria, polydipsia, anorexia, vomiting, progressive weight loss, poor body condition, pale mucous membranes, oral ulceration, halitosis, and acute blindness resulting from systemic hypertension. Animals with bacteraemia may

additionally exhibit lethargy, anorexia, gastrointestinal disturbances including vomiting and diarrhoea, fever, muscle tremors, lameness, and myalgia (Greene, 2012) ^[12].

Progressive renal dysfunction results in the accumulation of uraemic toxins, producing clinical signs such as a dull hair coat, anorexia, muscle weakness, persistent vomiting, lethargy, polyuria, polydipsia, visual impairment, and other ocular abnormalities. Advanced renal disease is frequently associated with hypertension, gastric ulceration, anaemia, electrolyte and acid-base disturbances, impaired fluid homeostasis, and abnormalities in calcium and phosphorus metabolism.

Cardiac involvement is characterized by clinical signs associated with impaired myocardial function and reduced tissue perfusion. Affected dogs commonly present with coughing, exercise intolerance, tachypnoea, dyspnoea, wheezing, and respiratory distress resulting from pulmonary congestion secondary to left-sided heart failure. Reduced cardiac output may also cause gastrointestinal hypoperfusion, leading to nausea, vomiting, diarrhoea, and reduced appetite. Chronic venous congestion may impair hepatic circulation, resulting in hepatic enlargement and inflammation. Additional manifestations include fever in infectious conditions, cardiac arrhythmias, thromboembolic events, generalized weakness, and progressive weight loss associated with chronic heart failure and dehydration (Chen *et al.*, 2020) ^[5].

Diagnosis

Historically, the diagnosis of cardiac and renal disorders relied primarily on clinical examination because advanced diagnostic facilities and cost-effective laboratory tests were limited. Recent advances in veterinary medicine have substantially improved the diagnosis of cardiorenal syndrome through the development of sensitive biomarkers, advanced imaging techniques, and functional cardiac assessments. Currently, a combination of cardiac biomarkers, renal biomarkers, echocardiography, electrocardiography, and routine laboratory investigations provides a comprehensive approach for the diagnosis and monitoring of CRS.

Biomarkers

Biomarkers are measurable biological molecules that indicate normal physiological processes, pathological changes, or responses to therapeutic interventions. Organ-specific biomarkers play a vital role in the early detection, diagnosis, prognosis, and monitoring of both cardiac and renal diseases (Atkinson *et al.*, 2001) ^[1].

A. Cardiac Biomarkers

Several cardiac biomarkers have been investigated for the diagnosis and monitoring of cardiovascular diseases in dogs, with cardiac troponins and N-terminal pro-B-type natriuretic peptide (NT-proBNP) being the most clinically valuable. These biomarkers are non-invasive, relatively inexpensive, rapidly measurable, and possess high diagnostic and prognostic accuracy, making them valuable tools in veterinary cardiology (Baisan *et al.*, 2016) ^[2].

Troponin

Troponins are regulatory proteins responsible for controlling calcium-mediated interactions between actin and myosin during striated muscle contraction. The troponin complex

consists of three subunits: Troponin I (TnI), Troponin T (TnT), and Troponin C (TnC). Among these, cardiac-specific TnI and TnT are highly sensitive indicators of myocardial injury because they are released into the bloodstream following cardiomyocyte membrane disruption and cellular necrosis (O'Brien, 2008; Liquori *et al.*, 2014) ^[20, 25].

In healthy dogs, serum cardiac troponin I (cTnI) concentrations are generally around 0.2 ng/mL, whereas the lower detection limits for most assays are approximately 0.02 ng/mL for cTnI and <0.05 ng/mL for cardiac troponin T (cTnT) (Sleeper *et al.*, 2001; Tarducci *et al.*, 2004) ^[37, 39]. Numerous studies have demonstrated that cTnI possesses greater sensitivity than cTnT for detecting myocardial injury (Linklater *et al.*, 2007). Increased serum cTnI concentrations have been reported in dogs with mitral valve disease (MVD) and are associated with myocardial fibrosis and intramyocardial arteriosclerosis (Falk *et al.*, 2013) ^[8]. Elevated cardiac troponin concentrations have also been documented in chronic inflammatory, metabolic, toxic, idiopathic, and parasitic cardiac diseases, reflecting ongoing myocardial damage.

Brain Natriuretic Peptide

Natriuretic peptides constitute a family of cardiac hormones that regulate sodium excretion, fluid balance, vascular tone, and neurohormonal activity, particularly through inhibition of the renin-angiotensin-aldosterone system (RAAS) (Liquori *et al.*, 2014) ^[20].

Table 1: Shows major natriuretic peptides include

Peptide	Primary Site of Expression
Atrial Natriuretic Peptide (ANP)	Atrial myocardium
B-type Natriuretic Peptide (BNP)	Ventricular myocardium
C-type Natriuretic Peptide (CNP)	Brain, vascular endothelium, kidneys, chondrocytes, and pituitary gland
D-type Natriuretic Peptide (DNP)	Venom gland of <i>Dendroaspis angusticeps</i> (Green Mamba)
Ventricular Natriuretic Peptide (VNP)	Primitive ray-finned bony fish heart

Source: Van Kimmenade & Januzzi (2009) ^[41]

Among these biomarkers, NT-proBNP, the inactive cleavage product of proBNP, has become one of the most valuable indicators of myocardial wall stress and heart failure. Both BNP and NT-proBNP are widely used in human medicine for diagnosing heart failure, acute coronary syndrome, and myocardial ischaemia and have subsequently been adopted for veterinary clinical practice (Braunwald, 2008; Januzzi *et al.*, 2005; Liquori *et al.*, 2014) ^[3, 14, 20].

In veterinary medicine, NT-proBNP concentrations are commonly measured using sandwich enzyme-linked immunosorbent assay (ELISA). Concentrations ≤1800 pmol/L are generally considered within the normal reference range. Values <900 pmol/L are usually not associated with significant myocardial stress, whereas concentrations >735 pmol/L in Doberman Pinschers indicate an increased risk of dilated cardiomyopathy (DCM) (Baisan *et al.*, 2016) ^[2]. A diagnostic cutoff value of 400 pmol/L has demonstrated a sensitivity of 81% and specificity of 75% for detecting DCM (Wess *et al.*, 2011) ^[43]. Furthermore, studies have shown that NT-proBNP concentrations >6.21 pg/mL identify occult DCM with a sensitivity of 95.2% and

specificity of 61.9%. When combined with 24-hour Holter monitoring, diagnostic sensitivity and specificity increase to 94.5% and 87.8%, respectively, while NT-proBNP concentrations remain independent of age (Oyama *et al.*, 2007; Singletary *et al.*, 2012) [27, 36].

B. Renal Biomarkers

Several biomarkers have been developed to assess renal function and detect kidney injury in dogs, including blood urea nitrogen (BUN), serum creatinine, symmetric dimethylarginine (SDMA), cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), and clusterin. Early recognition of renal involvement provides an opportunity for timely therapeutic intervention and may help preserve both renal and cardiac function in animals with cardiorenal syndrome (Orvalho & Cowgill, 2017) [26].

An ideal renal biomarker should detect kidney injury at an early stage, identify the site of injury (glomerular, tubular, or mixed), distinguish renal disease from pre-renal or post-renal causes, predict disease severity, and monitor therapeutic response.

Symmetric Dimethylarginine (SDMA) and Creatinine

SDMA has emerged as a highly sensitive biomarker for the early detection of renal dysfunction because it increases before measurable elevations in serum creatinine occur. Although SDMA and cystatin C provide superior early diagnostic value, their routine clinical use remains limited because of higher testing costs. Currently, increases in serum creatinine and SDMA remain the standard indicators for identifying renal involvement in dogs with cardiac disease, although these markers generally become abnormal only after substantial loss of renal function (Orvalho & Cowgill, 2017) [26].

Table 2: Shows reference ranges for dogs with chronic kidney disease are as follows:

CKD Stage	Creatinine (mg/dL)	SDMA (µg/dL)
Stage 1	<1.4	<18
Stage 2	1.4-2.8	18-35
Stage 3	2.9-5.0	36-54
Stage 4	>5.0	>54

Emerging biomarkers such as urinary clusterin, serum and urinary cystatin B, serum inosine, and urinary NGAL have also shown promise for the early detection of renal injury associated with cardiovascular disease (Orvalho & Cowgill, 2017) [26].

Cystatin C

Cystatin C is a low-molecular-weight cysteine protease inhibitor continuously produced by all nucleated cells. It is freely filtered through the glomerular membrane and is almost completely reabsorbed and metabolized by the proximal renal tubules under normal physiological conditions. Impaired glomerular filtration or tubular dysfunction results in increased circulating and urinary concentrations of cystatin C.

Urinary cystatin C is considered a sensitive indicator of tubular injury because its presence reflects impaired tubular reabsorption. In human medicine, urinary cystatin C has demonstrated high diagnostic accuracy for detecting both isolated tubular injury and combined tubulointerstitial-glomerular diseases, suggesting its potential application as

an early biomarker of renal dysfunction in veterinary patients (Conti *et al.*, 2016) [6].

Echocardiography and Electrocardiography

Echocardiography, commonly referred to as cardiac ultrasonography, is a non-invasive imaging technique routinely employed for the diagnosis, monitoring, and follow-up of canine cardiac diseases, particularly congenital and acquired heart disorders. The technique utilizes high-frequency ultrasound waves that are transmitted into the thoracic cavity and reflected from cardiac structures to generate real-time images of the heart. Echocardiography provides comprehensive information regarding cardiac anatomy, chamber dimensions, myocardial function, valvular morphology, blood flow patterns, and haemodynamic status while minimizing the need for invasive procedures such as cardiac catheterization.

The principal applications of echocardiography include evaluation of ventricular systolic and diastolic function, assessment of chamber size, detection of valvular lesions, congenital shunts, myocardial abnormalities, intracardiac masses, pericardial effusion, stenotic lesions, and Doppler assessment of blood flow. In degenerative mitral valve disease, early lesions are generally characterized by smooth, nodular thickening producing a club-shaped appearance of the valve leaflets. As the disease progresses, the lesions become larger, irregular, and are frequently associated with severe mitral regurgitation, left atrial and ventricular enlargement, and occasionally thrombus formation within the cardiac chambers. In infective endocarditis, vegetative lesions most commonly involve the mitral valve, followed by the aortic valve, whereas pulmonary and tricuspid valve involvement is relatively uncommon.

Standard transthoracic echocardiography is generally performed using transducers with frequencies ranging from 5.0 to 7.5 MHz. Important echocardiographic measurements include aortic root diameter, left atrial size, right ventricular internal diameter at end-diastole (RVIDd), left ventricular internal diameter during diastole and systole (LVIDd and LVIDs), interventricular septal thickness during diastole and systole (IVSd and IVSs), and left ventricular free wall thickness during diastole and systole (LVFWd and LVFWs). These parameters provide valuable information regarding myocardial contractility, ventricular remodelling, and disease progression.

Electrocardiography (ECG) complements echocardiography by evaluating cardiac rhythm and electrical activity. In dogs with cardiorenal syndrome, ECG abnormalities commonly include nonspecific ST-segment and T-wave alterations, flattened or inverted T waves, prominent U waves, and prolongation of the QT interval. Dogs with renal disease may exhibit increased P-wave and QRS complex amplitudes together with mild T-wave changes resulting from electrolyte disturbances (Thakur & Thakur, 2018) [40]. In puppies affected with canine parvovirus infection, electrocardiographic findings such as reduced T-wave amplitude, decreased QRS voltage, shortened QT interval, and ST-segment elevation have been associated with poor prognosis.

The combined effects of impaired cardiac output and renal dysfunction frequently result in electrolyte imbalances that alter myocardial depolarization and repolarization. Severe disturbances may predispose affected animals to ventricular tachycardia and other life-threatening arrhythmias. Dogs

with ascites secondary to advanced cardiac disease may develop atrial fibrillation characterized by the absence of P waves and an irregularly irregular rhythm.

Electrolyte abnormalities, particularly alterations in serum potassium concentration, have characteristic electrocardiographic manifestations. Hypokalaemia, which may result from prolonged vomiting, diarrhoea, diuretic therapy, or corticosteroid administration, typically produces flattened or inverted T waves together with prominent U waves. Conversely, hyperkalaemia accelerates myocardial repolarization, resulting in tall, peaked T waves and progressive conduction abnormalities (Mohapatra *et al.*, 2022) ^[24]. Similarly, dogs with canine ehrlichiosis have been reported to exhibit prolonged QRS duration and reduced P-wave amplitude (Lima *et al.*, 2019) ^[19].

In addition to imaging modalities, enzyme-linked immunosorbent assay (ELISA) has become an important laboratory technique for measuring circulating cardiac biomarkers, thereby improving the diagnosis and monitoring of cardiovascular diseases (Szczepankiewicz *et al.*, 2019) ^[38].

Medical Management of Cardiorenal Syndrome

The management of cardiorenal syndrome (CRS) remains one of the greatest therapeutic challenges in veterinary medicine because treatment must simultaneously preserve cardiac function while minimizing further renal injury. At present, no universally accepted treatment protocol exists for canine CRS. Consequently, successful management requires an individualized approach based on the severity of both cardiac and renal dysfunction. Collaborative care involving veterinary cardiologists and nephrologists may improve therapeutic outcomes by optimizing treatment for both organ systems.

Angiotensin-Converting Enzyme (ACE) Inhibitors and Angiotensin Receptor Blockers (ARBs)

ACE inhibitors and ARBs constitute the cornerstone of therapy for many cardiovascular and renal disorders because they suppress activation of the renin-angiotensin-aldosterone system (RAAS). These drugs reduce systemic vasoconstriction, decrease arterial blood pressure, improve cardiac output, and slow the progression of renal injury. Nevertheless, renal function should be carefully monitored during therapy, as excessive RAAS inhibition may worsen azotaemia in susceptible patients. Measurement of systolic arterial blood pressure using Doppler ultrasonography is recommended before and during treatment.

Commonly used ACE inhibitors include Benazepril (0.25-1.0 mg/kg PO every 24 hours), Enalapril (0.25-0.5 mg/kg PO every 12 hours), Imidapril (0.25-0.5 mg/kg PO every 24 hours), and Ramipril (0.1-1.0 mg/kg PO every 24 hours). Among ARBs, Telmisartan (1-1.5 mg/kg PO every 12 hours) has demonstrated efficacy in reducing systemic hypertension and proteinuria (Hadjiphilippou & Kon, 2016) ^[13].

Mineralocorticoid Receptor Antagonists

Mineralocorticoid receptor antagonists, such as Spironolactone (2-4 mg/kg/day PO divided twice daily), provide both cardiac and renal protective effects by inhibiting aldosterone-mediated sodium retention, myocardial fibrosis, and vascular remodelling. However,

careful monitoring is necessary because hyperkalaemia may develop during prolonged therapy.

Omega-3 Fatty Acid Supplementation

Dietary supplementation with omega-3 polyunsaturated fatty acids (PUFAs) has been shown to exert anti-inflammatory, antioxidant, and renoprotective effects. Fish oil rich in eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) reduces intraglomerular pressure, decreases renal inflammation, improves lipid metabolism, and may slow the progression of chronic kidney disease. Since dogs have limited ability to synthesize EPA and DHA from plant-derived fatty acids, supplementation with marine fish oil is recommended. A commonly recommended dosage is approximately 10 mg per 100 kcal of dietary energy.

Loop Diuretics

Loop diuretics remain the primary treatment for volume overload associated with congestive heart failure. By inhibiting sodium, potassium, and chloride reabsorption in the thick ascending limb of the loop of Henle, these agents promote diuresis, reduce venous congestion, improve glomerular filtration rate, and relieve pulmonary oedema. However, excessive diuresis may result in dehydration, electrolyte imbalance, and deterioration of renal function. Furosemide may be administered as a continuous rate infusion (CRI) at 1 mg/kg/hour following an initial bolus or orally at 1-4 mg/kg every 12 hours. Other loop diuretics include Bumetanide (1-3 mg/kg every 24 hours) and Torsemide (0.1-0.6 mg/kg every 24 hours). Combination therapy with loop and thiazide diuretics should be used cautiously because of the increased risk of severe volume depletion and electrolyte disturbances.

Nitroglycerin and Natriuretic Peptides

Nitroglycerin is a potent vasodilator that reduces preload and myocardial oxygen demand by relaxing vascular smooth muscle. Although its clinical use in dogs is relatively limited, it may be beneficial in selected cases of severe congestive heart failure. The recommended dosage is approximately 4-12 mg/kg every 12 hours.

Endogenous B-type natriuretic peptide (BNP) plays an important physiological role in regulating vascular tone, sodium excretion, and extracellular fluid balance. Increased circulating BNP concentrations also serve as valuable biomarkers of myocardial stress and heart failure.

Pimobendan

Pimobendan is an inodilator widely used in dogs with congestive heart failure. It enhances myocardial contractility through calcium sensitization of cardiac troponin C while simultaneously producing peripheral vasodilation via inhibition of phosphodiesterase III (PDE III). Improved cardiac output may also enhance renal perfusion and glomerular filtration rate. The recommended dosage in dogs is 0.25-0.6 mg/kg orally every 12 hours.

Digoxin

Digoxin, a cardiac glycoside derived from *Digitalis lanata*, exerts positive inotropic effects by increasing myocardial contractility while simultaneously reducing heart rate through enhanced parasympathetic stimulation of the atrioventricular node. Owing to its predominant renal

elimination, serum digoxin concentrations and renal function should be carefully monitored, and dose adjustments may be necessary in dogs with impaired kidney function (Orvalho, 2016).

Conclusion

Cardiorenal syndrome represents a complex clinical entity characterized by intricate interactions between the cardiovascular and renal systems. Multiple haemodynamic, neurohormonal, inflammatory, and metabolic mechanisms contribute to the initiation and progression of organ dysfunction. Activation of the renin-angiotensin-aldosterone system, impaired renal perfusion, venous congestion, and chronic inflammation play central roles in the development of the syndrome.

The diverse pathophysiological mechanisms underlying the five subtypes of CRS highlight the close interdependence of cardiac and renal function. Early recognition through clinical evaluation, advanced imaging techniques, and sensitive biomarkers is essential for timely diagnosis and therapeutic intervention. Although standardized treatment protocols for canine CRS remain limited, individualized multimodal management aimed at preserving both cardiac and renal function may improve clinical outcomes and quality of life. Continued research is warranted to enhance understanding of disease mechanisms and to develop evidence-based therapeutic strategies for affected dogs.

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