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DIAGNOSTIC PROTOCOLS FOR CHRONIC KIDNEY DISEASE (CKD) IN DOGS: FROM CLINICAL SCREENING TO LABORATORY CONFIRMATION

PROTOCOLOS DE DIAGNÓSTICO DA DOENÇA RENAL CRÔNICA (DRC) EM CÃES: DO RASTREIO CLÍNICO À CONFIRMAÇÃO LABORATORIAL

PROTOCOLOS DIAGNÓSTICOS DE LA ENFERMEDAD RENAL CRÓNICA (ERC) EN PERROS: DEL CRIBADO CLÍNICO A LA CONFIRMACIÓN LABORATORIAL

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ABSTRACT

Chronic Kidney Disease (CKD) in dogs is a progressive clinical syndrome characterized by functional and structural renal loss, often diagnosed at advanced stages due to its initially asymptomatic nature. This study presents a narrative review of recent literature on diagnostic protocols for canine CKD, with emphasis on biomarkers, laboratory tests, and clinical parameters. The research was conducted using the PubMed database, including articles published in the last five years in Portuguese and English. Findings highlight the importance of symmetric dimethylarginine (SDMA) as a more sensitive biomarker than serum creatinine for early detection of reduced glomerular filtration rate, as well as the relevance of serial laboratory evaluations to confirm disease chronicity. Proteinuria was identified as a critical prognostic marker and therapeutic target, while the interaction between intestinal microbiota and renal function reinforces the systemic approach to the disease. Hormonal alterations, such as increased FGF-23 and parathyroid hormone (PTH) levels, as well as electrolyte disturbances, were also shown to be relevant for staging and clinical monitoring. It is concluded that the diagnosis of CKD in dogs should be based on integrative protocols combining functional biomarkers, proteinuria assessment, and monitoring of metabolic disorders, enabling early identification, severity stratification, and therapeutic decision-making aimed at slowing disease progression.

Keywords: Chronic Kidney Disease. Dogs. Diagnosis. Biomarkers. SDMA. Proteinuria.

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RESUMO

A Doença Renal Crônica (DRC) em cães é uma síndrome clínica progressiva, caracterizada pela perda funcional e estrutural dos rins, frequentemente diagnosticada em estágios avançados devido ao caráter inicialmente assintomático. Este estudo apresenta uma revisão narrativa da literatura recente sobre protocolos diagnósticos da DRC canina, com ênfase em biomarcadores, exames laboratoriais e parâmetros clínicos. A pesquisa foi conduzida na base PubMed, incluindo artigos publicados nos últimos cinco anos em português e inglês. Os achados destacam a importância da dimetilarginina simétrica (SDMA) como um biomarcador mais sensível que a creatinina sérica para detecção precoce da redução da taxa de filtração glomerular, além da relevância da avaliação seriada de parâmetros laboratoriais para confirmação da cronicidade da doença. A proteinúria foi identificada como marcador prognóstico crítico e alvo terapêutico, enquanto a interação entre microbiota intestinal e função renal reforça a abordagem sistêmica da doença. Alterações hormonais, como elevação de FGF-23 e PTH, bem como distúrbios eletrolíticos, também se mostraram relevantes para o estadiamento e monitoramento clínico. Conclui-se que o diagnóstico da DRC em cães deve ser baseado em protocolos integrativos, combinando biomarcadores funcionais, avaliação da proteinúria e monitoramento de distúrbios metabólicos, permitindo identificação precoce, estratificação da gravidade e definição de condutas terapêuticas que retardam a progressão da doença.

Palavras-chave: Doença Renal Crônica. Cães. Diagnóstico. Biomarcadores. SDMA. Proteinúria.

RESUMEN

La Enfermedad Renal Crónica (ERC) en perros es un síndrome clínico progresivo caracterizado por la pérdida funcional y estructural de los riñones, frecuentemente diagnosticado en estadios avanzados debido a su carácter inicialmente asintomático. Este estudio presenta una revisión narrativa de la literatura reciente sobre los protocolos diagnósticos de la ERC canina, con énfasis en biomarcadores, exámenes de laboratorio y parámetros clínicos. La investigación fue realizada en la base de datos PubMed, incluyendo artículos publicados en los últimos cinco años en portugués e inglés. Los hallazgos destacan la importancia de la dimetilarginina simétrica (SDMA) como un biomarcador más sensible que la creatinina sérica para la detección temprana de la reducción de la tasa de filtración glomerular, además de la relevancia de la evaluación seriada de parámetros laboratoriales para confirmar la cronicidad de la enfermedad. La proteinuria fue identificada como un marcador pronóstico crítico y objetivo terapéutico, mientras que la interacción entre la microbiota intestinal y la función renal refuerza el enfoque sistémico de la enfermedad. Alteraciones hormonales, como el aumento de FGF-23 y de la hormona paratiroidea (PTH), así como los trastornos electrolíticos, también demostraron ser relevantes para el estadiaje y el monitoreo clínico. Se concluye que el diagnóstico de la ERC en perros debe basarse en protocolos integrativos que combinen biomarcadores funcionales, evaluación de la proteinuria y monitoreo de alteraciones metabólicas, permitiendo la identificación temprana, la estratificación de la gravedad y la definición de conductas terapéuticas orientadas a retrasar la progresión de la enfermedad.

Palabras clave: Enfermedad Renal Crónica. Perros. Diagnóstico. Biomarcadores. SDMA. Proteinuria.

1 INTRODUCTION

The kidneys are extremely important organs for maintaining the circulatory volume and composition of plasma through the filtration and reabsorption of water, electrolytes and other compounds from the blood. In addition, it contributes to the body's acid-base balance, regulation of systemic blood pressure (SBP), and calcium and phosphorus hemostasis (Rabelo et al., 2022).

Chronic Kidney Disease (CKD) in dogs is a clinical syndrome characterized by the progressive and irreversible loss of kidney function and structure, persisting for a period equal to or greater than three months (Perondi et al., 2025). This pathology represents a significant challenge in veterinary medicine, as its clinical manifestations usually appear only when a considerable portion of the renal parenchyma is already compromised (Cavalera et al., 2022). The course of the disease often triggers serious systemic complications, including renal secondary hyperparathyroidism (RSHN), proteinuria, and kidney-gut axis disorders (Chen et al., 2025; Summers and Quimby, 2024).

Due to the progressive nature of CKD, understanding its pathophysiology is necessary to optimize the diagnosis, and thus initiate an effective treatment for each patient (Summers and Quimby, 2024). Laboratory tests include blood count, symmetrical perphyimethylarginine (SDMA), serum creatinine, urea, sodium and potassium, as well as clinical signs such as polyuria, polydipsia, weight loss, systemic arterial hypertension (SAH), urine density below the expected for the species (<1.025 in dogs and <1.035 in cats) or proteinuria, indicate the need for further diagnostic investigation. It is also important to analyze total proteins, total cholesterol, triglycerides, blood gas analysis, and imaging tests such as abdominal ultrasound to verify the structures of both kidneys (Rabelo et al., 2022).

Early diagnosis is the determining factor for the success of therapeutic interventions aimed at slowing the progression of the lesion (Cavalera et al., 2022). Historically, screening has been based on creatinine and urea dosage, however, the introduction of new biomarkers, such as symmetric dimethylarginine (SDMA), has brought greater sensitivity for the detection of early glomerular filtration dysfunctions (Hamlin et al., 2022). In addition, understanding the interaction between the gut microbiota and kidney function has opened up new avenues for clinical monitoring through uremic toxins (Summers and Quimby, 2024; Perondi et al., 2025).

The development of structured diagnostic protocols for Chronic Kidney Disease (CKD) in dogs is essential to reduce underdiagnosis in the early stages and allow early therapeutic intervention. Currently, it is recommended that the diagnosis should not be based on a single single marker, but rather on a combination of detailed clinical evaluation, serial measurement of glomerular filtration biomarkers, investigation of proteinuria, and identification of persistent urinary alterations for a period equal to or greater than three months. In addition, the identification of hormonal disorders and associated systemic changes reinforces the concept of an integrative approach, consolidating a diagnostic protocol that contemplates both renal function and its metabolic and inflammatory repercussions (Cavalera et al., 2022; Hamlin et al., 2022; Park et al., 2022).

2 METHODOLOGY

The present study is characterized as a narrative literature review, developed with the objective of synthesizing and analyzing the most recent scientific evidence related to the diagnostic protocols of Chronic Kidney Disease in dogs. The search was carried out in the PubMed database, using the descriptors "Chronic Kidney Disease", "Dogs", "Diagnosis" and "Treatment", combined through the Boolean operators AND and OR, according to the terminology of Medical Subject Headings (MeSH). Articles published in the last five years, available in full and written in Portuguese or English, that directly addressed the topic, were included. Studies that did not have a direct relationship with the central theme, duplicate publications, narrative reviews with low methodological rigor, and articles not indexed in the database used were excluded. The selection of studies was conducted in two stages: screening of titles and abstracts, followed by the evaluation of full texts to confirm relevance. The information extracted was organized in a descriptive way.

3 RESULTS AND DISCUSSION

CKD is a multifaceted and highly prevalent condition in small animal clinics, whose diagnostic and therapeutic approach (EDUARDA TRENTIN) requires an integrated analysis of multiple pathophysiological mechanisms and laboratory parameters, such as glomerular filtration markers, evaluation of comorbidities, and monitoring of endocrine-metabolic disorders. The isolated interpretation of a single laboratory parameter can

result in underdiagnosis or inaccurate classification of disease severity, especially in the early stages.

Glomerular Filtration Monitoring: SDMA and Creatinine: Detection of decreased Glomerular Filtration Rate (GFR) is the cornerstone of diagnosis. Studies indicate that SDMA is a more sensitive biomarker than serum creatinine for early identification of kidney dysfunction, as it is not influenced by the animal's muscle mass (Cavalera et al., 2022; Hamlin et al., 2022). Dogs that have persistently elevated SDMA levels, even with creatinine within reference values, should be monitored for the development of azotemia in the following months (Cavalera et al., 2022).

In addition to the superior sensitivity of SDMA in the early detection of GFR reduction, it is critical that the interpretation of biomarkers be performed in a serial manner. The characterization of CKD requires persistence of laboratory abnormalities over time, since isolated elevations may be associated with transient causes or acute conditions (Perondi et al., 2025). The association between persistent increases in SDMA, borderline creatinine, and inadequate urine density reinforces the suspicion of chronic renal impairment (Cavalera et al., 2022; Hamlin et al., 2022).

Experimental evidence also indicates that renal biomarkers may reflect different compartments of the nephron, some of which are more related to tubular lesion and others to glomerular filtration, which reinforces the need for integrated interpretation. Thus, the combined use of SDMA and creatinine, associated with clinical and urinary assessment, expands screening capacity and reduces the risk of underdiagnosis in the early stages of Chronic Kidney Disease, consolidating a more sensitive and pathophysiologically based diagnostic protocol (Hamlin et al., 2022; Cavalera et al., 2022).

Staging of Chronic Kidney Disease (IRIS): After confirming the persistence of laboratory abnormalities for a period equal to or greater than three months, it is recommended to stage Chronic Kidney Disease based on the criteria established by the International Renal Interest Society (IRIS) in order to standardize the diagnosis and prognosis of CKD in Veterinary Medicine (IRIS, 2023).

The primary staging is performed based on serum creatinine concentration, classifying patients into four progressive stages of renal impairment. In Stage 1, the absence of azotemia is observed, but with structural or functional evidence of renal injury; Stage 2 is characterized by mild azotemia; Stage 3 corresponds to moderate azotemia;

and Stage 4 represents severe azotemia, associated with a higher risk of systemic complications (IRIS, 2023).

In addition to creatinine-based staging, IRIS recommends substaging according to the presence of persistent proteinuria (urinary protein:creatinine ratio), and measurement of systemic blood pressure, considering the risk of end-organ damage secondary to hypertension (IRIS, 2023).

The inclusion of symmetric dimethylarginine (SDMA) as a complementary biomarker has been recognized in recent updates to the guidelines, especially for early identification of Stage 1 patients in whom creatinine is still within reference values (IRIS, 2023; Hamlin et al., 2022).

Evaluation of Proteinuria and the Kidney-Intestine Axis: Proteinuria is a critical prognostic marker and a direct therapeutic target, as it is one of the main indicators of glomerular injury. Persistent loss of protein in the urine not only signals the severity of the actual damage, but also contributes to a progression of tubulointerstitial fibrosis (Chen et al., 2025). The use of vitamin D analogues, such as paricalcitol, has shown potential in reducing urinary protein excretion and attenuating HPSR (Chen et al., 2025).

In addition, studies on the renin-angiotensin-aldosterone system (RAAS) indicate that dogs with glomerular diseases may present differentiated regulation of this hormonal axis, which reinforces the need for etiological characterization within the diagnostic protocol. Thus, the investigation of proteinuria should not be seen as an isolated complementary test, but as a structuring component of staging and clinical decision-making (Chen et al., 2025; Grandt et al., 2022).

At the same time, gastrointestinal health emerges as a relevant diagnostic component; Gut dysbiosis in kidney patients promotes the accumulation of uremic toxins, such as indoxyl sulfate and p-cresol sulfate, which contribute to systemic inflammation (Summers and Quimby, 2024). The use of probiotics has been tested to mitigate these effects and improve clinical parameters (Perondi et al., 2025).

Therefore, the evaluation of intestinal health becomes essential in the follow-up of a CKD patient. The use of supplements containing probiotics has been investigated as a tool to frame the intestinal microbiota, seeking to reduce the levels of circulating toxins and improve clinical parameters and fecal scores of renal patients. In this way, making the diagnosis more generalized, considering proteinuria and intestinal homeostasis as

fundamental pillars of staging and for the definition of therapeutic conducts (Perondi et al., 2025).

Measurement of Systemic Blood Pressure: The measurement of systemic blood pressure (SBP) is a fundamental step in the diagnostic protocol and in the understaging of Chronic Kidney Disease in dogs, since systemic arterial hypertension (SAH) is a frequent complication and factor in the progression of kidney injury (IRIS, 2023). Persistent elevation of blood pressure promotes increased intraglomerular pressure, contributing to glomerular sclerosis, worsening of proteinuria, and acceleration of functional loss of remaining nephrons (Grandt et al., 2022).

In addition to the direct impact on the renal parenchyma, hypertension secondary to CKD is associated with the occurrence of lesions in target organs, especially the retina, central nervous system, heart, and kidneys, constituting a condition of relevant systemic risk. SBP values equal to or greater than 160 mmHg are associated with a higher probability of damage to target organs, which may result in target organ damage (LOA) (IRIS, 2023).

From a pathophysiological point of view, dysregulated activation of the renin-angiotensin-aldosterone system (RAAS) plays a central role in the maintenance of hypertension and the perpetuation of kidney damage, especially in glomerular diseases, reinforcing the interdependence between hemodynamic changes and CKD progression (Grandt et al., 2022).

Hormonal Disorders and Electrolyte Imbalances: Disorders of mineral and bone metabolism are an integral part of the diagnostic process of CKD, since hormonal changes can occur early in the course of the disease.

Complete diagnosis should include the evaluation of hormones such as FGF-23 and PTH, which rise early in the course of the disease, mainly due to phosphate retention and reduced calcitriol production (Chen et al., 2025). In addition, the behavior of the circulating Renin-Angiotensin-Aldosterone System (RAAS) may vary according to the etiology of kidney disease, and is often underregulated in dogs with glomerular diseases (Grandt et al., 2022). The identification of these alterations contributes not only to the confirmation of chronicity, but also to the evaluation of the severity and systemic impact of the disease. In specific cases of advanced CKD associated with other comorbidities, atypical disorders such as isolated hypoaldosteronism, manifested by persistent

hyperkalemia and hyponatremia may occur (Park et al., 2022). These changes indicate the importance of metabolic monitoring of CKD.

Thus, the inclusion of hormonal and electrolyte evaluation in the diagnostic protocol expands the understanding of the disease as a systemic entity, allowing for more accurate and individualized metabolic monitoring (Chen et al., 2025; Park et al., 2022).

Integration of Laboratory Findings in Confirmation of CKD

Confirmation of CKD should not be based on an isolated marker, but on the integration of functional, structural, and systemic parameters. The combination of persistent reduction in GFR (assessed by creatinine and SDMA), the presence of proteinuria, changes in urine density, and mineral metabolism disorders allows us to characterize not only the presence of the disease, but also its severity and potential for progression (Cavalera et al., 2022; Chen et al., 2025; Hamlin et al., 2022). In addition, understanding the kidney-intestine axis broadens the clinical approach by recognizing CKD as a systemic condition, associated with chronic inflammation and accumulation of uremic toxins (Perondi et al., 2025; Summers and Quimby, 2024).

Therefore, the diagnosis of Chronic Kidney Disease should not be precipitated by accidental laboratory findings. Functional or structural changes need to persist for a minimum of three months, ensuring that glomerular filtration markers are not influenced by physiological variations or transient acute conditions (Perondi et al., 2025).

Thus, the diagnosis should be understood as an integrated clinical-laboratory process, in which biomarkers guide the investigation, but the clinical manifestation and the temporal evolution of the alterations are determinant for the characterization of chronicity and for individualized therapeutic planning. (Summers and Quimby, 2024).

4 CONCLUSION

Chronic Kidney Disease (CKD) in dogs is a systemic and multifactorial condition, characterized by progressive functional and structural loss of the kidneys, often diagnosed late due to its initially asymptomatic course. Faced with this challenge, success in management and clinical prognosis depends on the adoption of structured and, above all, **integrative diagnostic protocols**.

The cornerstone of this approach is the early detection of reduced Glomerular Filtration Rate (GFR). In this regard, **Symmetric Dimethylarginine (SDMA)** represents a crucial advance, standing out as a more sensitive biomarker than serum creatinine for

the identification of renal dysfunction in early stages. The combined and serial use of SDMA and creatinine, associated with detailed clinical evaluation, significantly strengthens the screening and follow-up of the disease.

Confirmation and staging of CKD, based on the International **Renal Interest Society (IRIS) criteria**, requires the integration of multiple parameters, not the evaluation of an isolated marker. It is essential to measure **Proteinuria** (as a prognostic marker and therapeutic target), **Systemic Blood Pressure (SBP)** measurement for substaging, and monitoring Hormonal **and Metabolic Disorders** (such as changes in FGF-23, PTH, and electrolyte imbalances).

The understanding of CKD as a systemic condition is reinforced by the recognition of the **kidney-gut axis interaction**, which broadens the diagnostic and therapeutic perspective to include gastrointestinal health and the management of uremic toxins.

In summary, the implementation of an integrative diagnostic protocol, based on the strategic combination of functional biomarkers, evaluation of proteinuria, and monitoring of metabolic and hemodynamic alterations, is an essential tool for the early identification of CKD in dogs, allowing the appropriate staging and definition of individualized therapeutic conducts, which aim to delay the progression of the disease and improve the long-term prognosis.

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