

Clinical approach for diagnosing chronic kidney disease based on a series of cases in dogs

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[Uma abordagem clínica para o diagnóstico de doença renal crônica baseada em uma série de casos em cães]

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ABSTRACT

Chronic kidney disease (CDK) is the condition most frequently diagnosed in nephrology in dogs. CDK is progressive and irreversible, but the patient can be treated to decrease the rate of progression and improve the quality of life. All CKD cases originate from some type of kidney injury (underlying disease), which can be eventually diagnosed and subject to therapeutic intervention. The present prospective study aimed to evaluate dogs referred to check-up or for showing any signs suggestive of kidney disease. The study included 129 dogs, of which 34 had no kidney disease (control group) and 95 had CDK. Among the patients with CDK, 17 CDK 1, 36 CDK 2, 23 CDK 3, and 19 CDK 4 were found, according to staging criteria of the *IRIS staging of CDK-2023*. The test carried out made possible the clinical diagnosis of four categories of underlying kidney disease (congenital nephropathy, glomerular or tubule-interstitial disease, glomerulopathy and pyelonephritis). The present study may contribute as an illustration of the diversity of CDK manifestations in dogs, and their implications for the selection of priority laboratory tests for clinical practice.

Keywords: chronic nephropathy, clinical diagnosis, dog

RESUMO

A doença renal crônica (DRC) é a condição mais frequentemente diagnosticada na nefrologia e na urologia em cães. A DRC é progressiva e irreversível, mas o paciente pode ser tratado tendo como objetivo reduzir a taxa de progressão e melhorar a qualidade de vida. Todos os casos de DRC se originam de algum tipo de lesão renal (doença de base), que pode ser eventualmente diagnosticada e passível de intervenção terapêutica. O estudo teve como objetivo avaliar cães encaminhados para check-up ou com algum sinal sugestivo de doença renal. Foram incluídos 129 cães, dos quais 34 não tinham doença renal e 95 apresentavam DRC. Entre os pacientes com DRC, encontram-se 17 DRC 1, 36 DRC 2, 26 DRC 3 e 19 DRC 4, de acordo com os critérios de estadiamento da Sociedade Internacional de Interesse Renal (IRIS)- 2023. Os exames realizados possibilitaram o diagnóstico clínico de quatro categorias de doença renal de base (nefropatias congênitas, doença glomerular ou túbulo intersticial, glomerulopatia e pielonefrite). Este estudo pode contribuir como ilustração sobre a diversidade de manifestações da DRC em cães e suas implicações para seleção dos exames laboratoriais prioritários para a prática clínica.

Palavras-chave: cão, diagnóstico clínico, nefropatia crônica

INTRODUCTION

Chronic Kidney Disease (CKD) is the most diagnosed renal condition in dogs and cats, especially in elderly individuals. The term CKD

implies the presence of structural and functional changes in the kidneys (Bartges, 2012; Polzin *et al.*, 2011, Polzin, 2011). The expression of the disease is variable and depends on the type and severity of the underlying condition that initiated the process, as well as its rate of progression.

Initially, at least, the reduction in renal function is a consequence of the patient's primary disease (Levey *et al.*, 2005). However, if a significant number of lesions have already occurred, CKD can become self-perpetuating, meaning that progression will no longer depend on the presence of the initial cause (Lees, 2005; Polzin *et al.*, 2011). The progressive decline of renal function among patients with CKD can result from a linear decrease or alternating periods of stability and steep declines until the disease progresses to the terminal stage (Polzin *et al.*, 2011, Kogika *et al.*, 2015).

Many factors may be involved in the progression of CKD and should be identified to enable diagnosis, treatment, and prognosis (Grauer, 2005). Patients with any underlying renal disease that directly affects nephron components, such as the tubules or glomerulus, or indirectly affects areas like the interstitium or blood flow, can be monitored long before clinical signs or functional deficits become apparent, allowing for early diagnosis of CKD (Grauer, 2007). It is equally important to consider the potential underlying causes of structural changes, such as infectious, inflammatory, immune-mediated, neoplastic, endocrine, congenital, hemodynamic, genetic, or nephrotoxic conditions (Cowgill *et al.*, 2016). Structural involvement refers to alterations within the nephron segments themselves (Pérez-Sánchez *et al.*, 2023) and while changes in blood flow can lead to structural modifications in the nephrons and interstitium, assessing structural involvement of blood vessels (vasculopathy) that may affect blood flow is more challenging in a clinical setting, even though techniques are being tested for such purposes (Kathir, *et al.*, 2015; Hanazono, *et al.*, 2022). In many cases of CKD, the primary etiology may remain undetermined, and multiple nephron segments may concurrently exhibit structural alterations. However, if examinations are not thorough, the diagnosis may remain inconclusive, leading to delayed detection of disease progression (Grauer, 2007).

Considering the hypothesis that this type of failure may be very common, the aim of this study is to highlight the importance of various variables that stand out as effective biomarkers to support the diagnosis of chronic kidney disease through a series of clinical cases.

MATERIALS AND METHODS

Adult dogs, regardless of breed or gender, underwent evaluation for urinary tract assessment. The study included patients referred due to suggestive signs of renal disease or for routine check-ups. The most indicative clinical signs of chronic renal failure in dogs were dullness, depression, lethargy, paleness of the mucous membranes, weight loss, dehydration, inappetence, intermittent vomiting, and poor coat condition. Prior to initiation, the project obtained approval from the CEUA - Ethics Committee on Animal Use under protocol number 008835/18. The patients included in the study were those without any renal disease diagnosable through clinical means and patients with chronic kidney disease (CKD), as determined by conducted examinations and the inclusion in the study was subject to the free and informed consent of the respective guardians.

Exclusion criteria for patients encompassed incidents of acute kidney injury, renal neoplasia, traumatic renal injury, clinical complications, and inconclusive clinical diagnoses.

The specific clinical and laboratory evaluations for the study encompassed a review of medical history, physical examination, general clinical and laboratory assessment of the urinary tract, ultrasonographic examination, and others indicated as complementary or for differential diagnosis purposes. Documented results from examinations conducted by other specialized areas, as part of routine check-ups, were utilized for the diagnostic conclusion of comorbidities. The diagnosis of chronic kidney disease, staging, and sub-staging were conducted in accordance with the criteria established by the International Renal Interest Society (IRIS), as outlined in the Staging Chronic Kidney Disease (CKD) 2023 guidelines. Patients eligible for the study underwent routine examinations. Once the possibility of inclusion in the study was confirmed, the assessment was expanded to obtain the same set of clinical and laboratory parameters for all participants. The list of parameters included data obtained through a review of medical history, anamnesis, physical examination, measurement of systolic blood pressure (SBP), ultrasonography of the urinary tract, complete blood count, urinalysis, serum concentrations of urea (sUr), creatinine (sCr),

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phosphate (sP), total protein (sPt), and albumin (sAlb), as well as the urine protein/creatinine ratio (UP/C).

Systolic blood pressure (SBP) was measured using a Doppler device, following the guidelines of Brown (2016), as recommended by IRIS for the diagnosis, staging, and treatment of hypertension. Measurements were consistently taken on the thoracic limbs, in a controlled environment, after a 10-15 minute acclimation period. At least five measurements were taken per session, with the highest and lowest values discarded, and the average of the three remaining values was calculated. The measurements were repeated at intervals of at least 7 days until SBP values were confirmed as stable for each patient. Only the confirmed SBP values were used in the statistical analysis.

Once a patient was considered eligible for inclusion in the study, the diagnosis of chronic kidney disease (CKD) was confirmed through serial evaluations over approximately three months, ensuring that the alterations were stable and not the result of acute conditions. The diagnostic criteria included persistent alterations in urine density, renal-origin proteinuria, and renal azotemia, confirmed over these serial examinations. Thus, only patients with persistent and stable renal changes were included in the study. Those with acute alterations were initially excluded and were only considered for inclusion after medical treatment and follow-up confirmed their condition was stable and could be classified as CKD. The parameters evaluated in the statistical analysis were based on the assessments made once the patient was definitively classified as having CKD.

For patients with regular food intake, blood and urine samples for laboratory analyses were collected following a 12-hour overnight fast (with unrestricted water intake). For anorectic patients, sample collections were performed on the day of the initial consultation. Mild dehydration ($\leq 5\%$), common in chronic kidney disease patients, did not pose a restriction to sample collection. Whenever indicated, additional examinations necessary to complement, refine, or confirm the diagnosis, both renal condition and possible comorbidities, were conducted in the days following this sample collection. All patients with chronic kidney

disease (CKD) began receiving care and treatments according to their individual medical conditions, adjusted as needed.

For the assessment, 6 mL of blood was collected through jugular or cephalic vein puncture. An additional 3-5 mL was collected for post-12-hour fasting analyses when necessary. For the complete blood count, 2 mL of blood was placed in a tube containing anticoagulant (10% ethylenediaminetetraacetic acid - EDTA). The remaining 4mL were stored in a tube without anticoagulant for serum collection. Serum was obtained by centrifuging the sample at 1800g for 5 minutes, intended for biochemical analyses (serum urea - sUr, serum creatinine - sCr, serum phosphate - sP, total serum protein - sPt, and serum albumin - sAlb).

Urine samples (10 mL), obtained through cystocentesis or clean catheterization, were promptly forwarded for urinalysis. The excess material (supernatant obtained by centrifugation at 1800g for 5 min.) was allocated for biochemical assays of urinary creatinine (uCr) and urinary protein (uPt).

Automated methods (ABXVetpack- ESV-60 - Horiba) were employed for complete blood counts. Blood smears stained with a mixture of Methanol, May-Gruwald, and Giemsa were examined under common light microscopy. Samples were processed within a maximum of one hour after collection.

For the serum samples, urea (Urease method), creatinine (Modified Jaffé method), albumin (Bromocresol Green method), total protein (Biuret method), and phosphorus (Phosphomolybdate method) were evaluated. For urine samples, creatinine (Modified Jaffé method) and protein (Pyrogallol Red method) were assayed. Proteinuria was estimated by the urinary protein/creatinine ratio (UP/C), derived from the concentration values of creatinine and protein obtained in the same urine sample. For the analyses, the Labmax Plenno automatic equipment and Labtest Diagnóstica® commercial kits were used.

The list of parameters included in the analyses comprised patient characterization (gender and age), serum concentrations of creatinine (sCr), phosphate (sP), and albumin (sAlb). Urinary

density (DU), urinary protein/creatinine ratio (UP/C), systolic blood pressure (SBP), number of red blood cells, number of white blood cells, and the clinical diagnosis of the most probable underlying renal diseases, determined based on a thorough clinical evaluation, were also included. Urine sediment analyses were performed, with active sediment defined as more than five red blood cells per high-power field, more than five white blood cells per high-power field, and any level of bacteriuria.

The study followed a randomized block design. The results were assessed through descriptive statistics and analysis of variance (One-way ANOVA) for non-parametric data (Kruskal-Wallis for ANOVA and Dunn for multiple comparisons). Statistical analyses and graphs were performed using GraphPad Prism version 8.3.1 (549), San Diego, California, USA.

RESULTS

Among the patients referred for urinary tract evaluation due to presenting any clinical or laboratory signs suggestive of disease or for check-ups, 129 dogs meeting the inclusion criteria were included in the study. According to the clinical diagnosis, 34 dogs did not have renal disease (control group), and 95 had chronic kidney disease, divided into 4 groups (17 CKD 1, 36 CKD 2, 23 CKD 3, and 19 CKD 4). Ages ranged from four months to 16 years, and there were intact or neutered males and females, distributed according to the stages of CKD (Table 1). In the analysis of variance, there was a significant age difference between the groups ($P < 0.0001$), and in multiple comparisons, the age of dogs in the control group was significantly lower than that of the four groups of dogs with CKD.

Table 1. Characteristics of dogs without kidney disease and those stratified in the four stages of CKD

Groups		Control	CDK 1	CDK 2	CDK 3	CDK 4	Total
Adults	n	31	15	34	21	18	119
Age (years)							
	Minimum	1	2	1	6	2	
	Median	4	9	10	10	8,5	
	Maximum	14	16	15	16	15	
Median CI							
	Inferior limit	3	7	9	8	6	
	Upper limit	5	10	13	14	12	
	CV	56.4%	44.27%	46.84%	27.65%	47.48%	
Puppies / young	n	3	2	2	2	1	10
Age (months)		4/8/9	5/5	4/4	4/7	7	
Sex							
	M intact (31.0%)	14	4	10	4	8	40
	M neutered (17.8%)	6	2	8	4	3	23
	F intact (18.6%)	7	4	5	6	2	24
	F neutered (32.6%)	7	7	13	9	6	42
Total		34	17	36	23	19	129

CI, confidence interval; CV, coefficient of variation. Control, no kidney disease; CKD, chronic kidney disease staged by the IRIS criteria staging of CKD, 2019; M, male; F, female.

Considering the classification of patients into five groups according to renal condition (control and the four stages of CKD), the analysis of variance, significant differences were identified between the groups for the variables sCr ($P < 0.0001$), DU ($P < 0.0001$), UP/C ($P < 0.0001$), sP ($P < 0.0001$), sAlb ($P < 0.0001$), and He

($P < 0.0001$). However, variations were not significant for the variables SBP ($P = 0.225$) and WBC ($P = 0.875$).

The results of multiple comparison tests between the groups are illustrated in Fig. 1 and 2.

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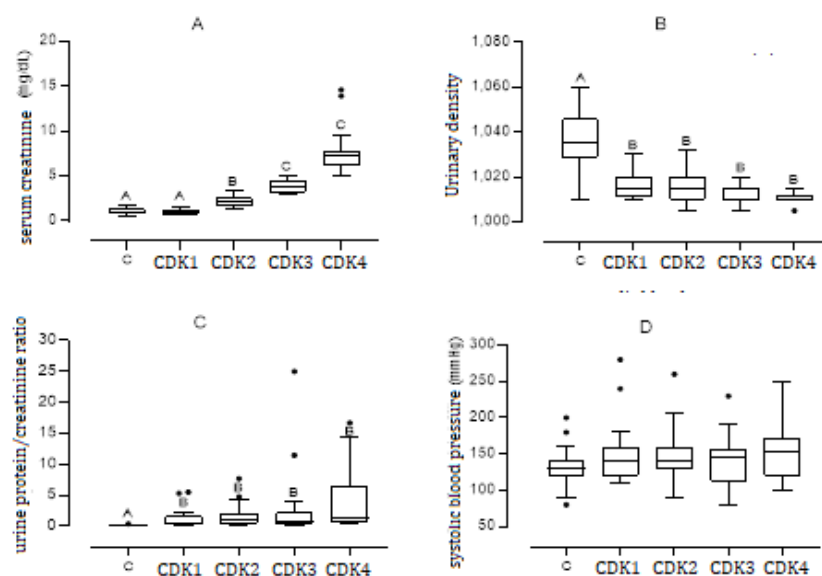


Figure 1. Graphic representations (Tukey boxplots) of medians, percentiles (75% and 25%), and extreme values distributed among control dogs (C, n=34) and patients (CKD1, n=17), (CKD2, n=36), (CKD3, n=23), (CKD4, n=19). Graph A shows serum creatinine, graph B shows urinary density, graph C shows urine protein/creatinine ratio, and graph D shows systolic blood pressure. Significant differences are indicated by uppercase letters above each box in graphs A, B, and C. The absence of markings in graph D indicates no significant difference between groups.

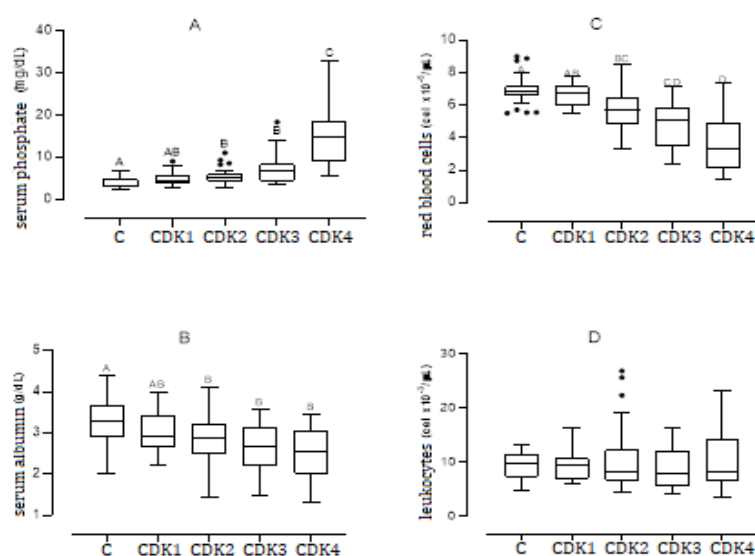


Figure 2. Graphic representations (Tukey boxplots) of medians, percentiles (75% and 25%), and extreme values distributed among control dogs (C, n=34) and patients (CKD1, n=17), (CKD2, n=36), (CKD3, n=23), (CKD4, n=19). Graph A shows serum phosphate, graph B shows red blood cells, graph C shows serum albumin, and graph D shows leukocytes. Significant differences are indicated by uppercase letters above each box in graphs A, B, and C. The absence of markings in graph D indicates no significant difference between groups.

Based on the clinical-laboratory data and the specialist's opinion, dogs with CKD were classified according to the most likely underlying disease through a 'clinical diagnosis.' Glomerular disease was identified in 26 dogs, characterized by persistent proteinuria (UP/C > 2.0) without evidence of lower urinary tract infection. Tubulointerstitial disease, observed in 52 dogs, was diagnosed in cases of proteinuria (UP/C typically between 0.5 and 2.0) along with a confirmed decrease in urine concentrating ability (isosthenuria). Congenital nephropathy, found in 10 dogs, was determined based on structural changes observed in imaging studies, supported by the animal's age, breed, and medical history. Pyelonephritis, diagnosed in 7 dogs, although considered a tubulointerstitial disease, was categorized separately due to its infectious nature, with diagnosis supported by positive urine cultures and imaging findings such as pyelectasia and/or varying degrees of ureteral dilation, with leukocytosis potentially present but not consistently required. The percentages of distribution frequencies within each stage of chronic kidney disease were calculated (Fig. 3).

The SBP data were categorized following the recommendations of IRIS (2023) into the following groups: normotensive (<140 mmHg), pre-hypertensive (140 to 159 mmHg), hypertensive (160 to 179 mmHg), and severely hypertensive (≥ 180 mmHg). When computing the distribution frequencies of SBP (Fig. 4), all three SBP categories were observed in every group, except in the CKD 1 group, where no patients fell into the hypertensive category. In the control group, 12.9% of patients exhibited hypertension, while among the animals with CKD, 34.5% had hypertension. Additionally, 25.82% of all animals enrolled in the study were classified as pre-hypertensive.

The distribution frequencies of proteinuria intensities (estimated by the UP/C value) were analyzed within each group (Fig. 5), and proteinuria was categorized as follows: non-proteinuric (UP/C < 0.2), borderline proteinuria (UP/C 0.2 to 0.5), mild proteinuria (UP/C 0.6 to 1.9), moderate proteinuria (UP/C 2.0 to 4.9), and severe proteinuria (UP/C ≥ 5.0).

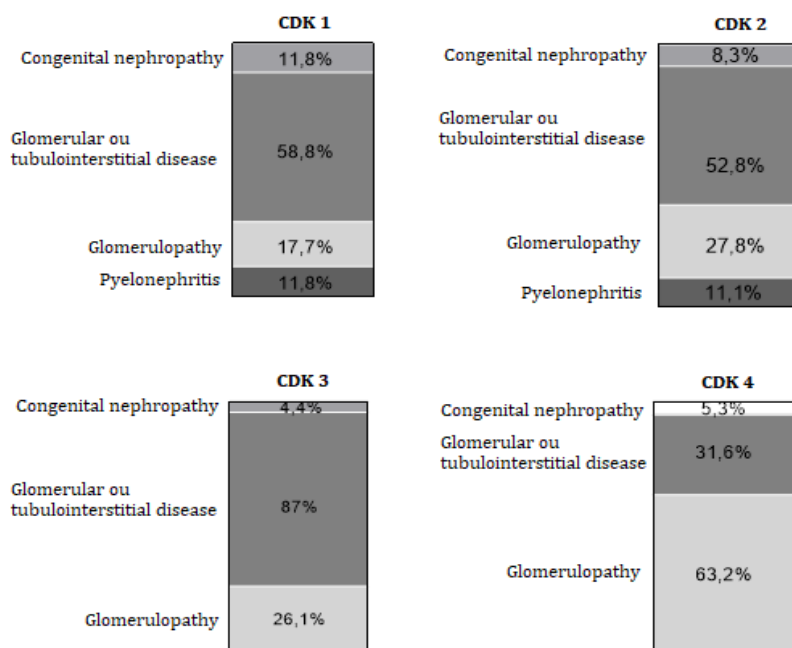


Figure 3. Graphic representation of the occurrence frequencies of underlying renal diseases for each group with chronic kidney disease staged according to the IRIS criteria, 2023, considering suggestive clinical diagnoses.

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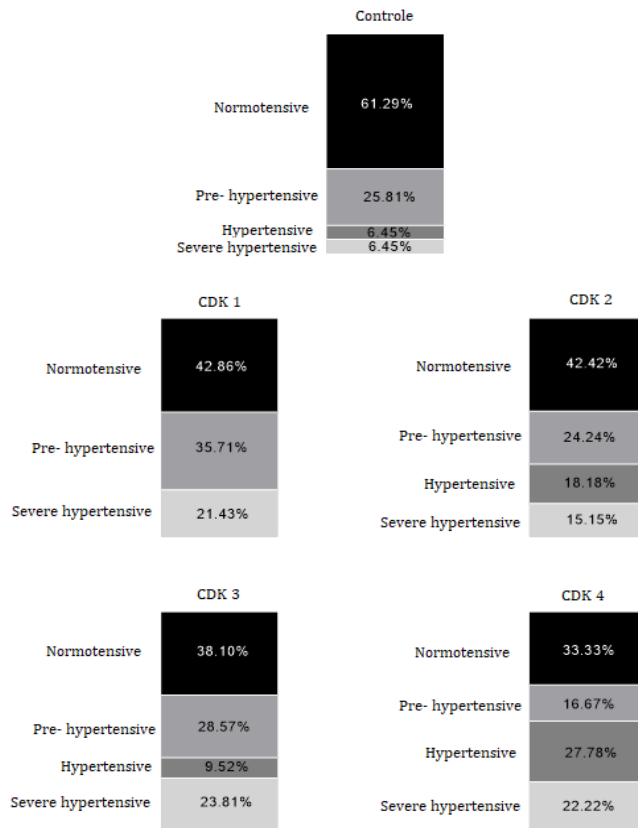


Figure 4. Graphic representation of the occurrence frequencies of systolic blood pressure categories: normotensive (<140 mmHg), pre-hypertensive (140 to 159 mmHg), hypertensive (160 to 179 mmHg), and severely hypertensive (≥ 180 mmHg), in the control group and at each stage of chronic kidney disease (IRIS staging of CKD, 2023).

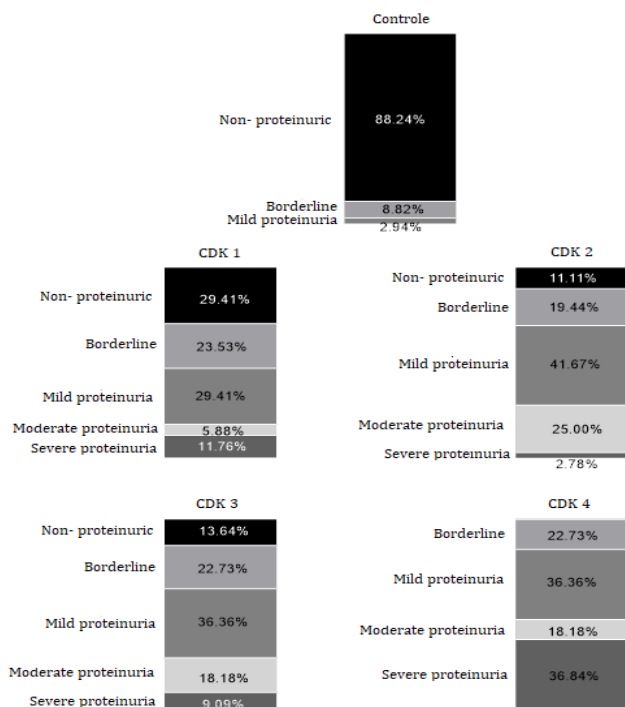


Figure 5. Graphic representation of the occurrence frequencies of proteinuria categories: non-proteinuric (UP/C<0.2), borderline (UP/C 0.2 to 0.5), mild proteinuria (UP/C 0.6 to 1.9), moderate proteinuria (UP/C 2.0 to 4.9), and severe proteinuria (UP/C ≥ 5.0), in the control group and at each stage of chronic kidney disease (IRIS staging of CKD, 2023).

DISCUSSION

The patient cohort included in this study encompasses all age groups, from puppies to seniors, and a relatively diverse representation of breeds, as expected in clinical practice. It is known that CKD is more prevalent in middle-aged or elderly dogs (Polzin *et al.*, 2011; Manaki and Finch, 2018; Bartges, 2012), which was confirmed in the present study.

When evaluating a patient with indicative signs of CKD and the confirmation of chronic kidney disease is established, the next step should be staging. According to the IRIS guidelines (2023), creatinine and SDMA are key biomarkers used for staging chronic kidney disease (CKD) in veterinary patients. In cases where azotemia or an increase in SDMA is not observed, staging may also rely on renal morphological changes, inadequate urinary concentration, and persistent renal proteinuria. Although the assessment of SDMA was not conducted in this study, CKD staging was determined using serum creatinine, along with ultrasonographic findings, persistent proteinuria, and the evaluation of inadequate urinary concentration. Staging aids in decisions related to prognosis, treatment, and monitoring (Polzin, 2013). However, various other tests are necessary to characterize each patient's specific condition, among which are assessments of blood pressure and proteinuria (iris, 2023).

The analysis of the results in this study revealed hypertension in 13 patients and severe hypertension in 17 CKD dogs, representing 32% of renal patients, which differs from the report by Bartges, *et al.* (1996), where an occurrence of 65 to 75% in dogs with CKD was reported. However, 12% of dogs in the control group (two cases of hypertension and two of severe hypertension) also experienced this condition. In all five groups, there were normotensive, pre-hypertensive, and severely hypertensive dogs, which may partially explain the lack of a significant difference in SBP between the groups. Hypertension has been proposed as an alteration associated with renal damage due to its role in causing glomerular hyperfiltration and intraglomerular hypertension, leading to glomerulosclerosis and proliferation of glomerular cells, representing a loss of renal function. There is potential for patients without

CKD to develop the disease, and those already affected may experience an increased rate of progression, contributing to the onset and development of proteinuria (Grauer, 2005; Acierno *et al.*, 2018; Bartges, 2012; Maniaki and Finch, 2018).

The study shows animals considered non-CKD (control group) with hypertension, which, as stated by Acierno *et al.* (2018) and Polzin (2011), if chronically maintained, can cause damage to various tissues, particularly the kidneys, eyes, brain, heart, and blood vessels. However, proteinuria may not only result from glomerular injury but also tubular, with its distinction depending on the magnitude. The severity of proteinuria can aid in the clinical differentiation between glomerular and tubulointerstitial disease. However, while the magnitude of proteinuria may suggest the likely origin, it does not provide a definitive distinction between these conditions. (Maniaki and Finch, 2018).

IRIS (2023) instructs the sub-staging of CKD patients based on proteinuria values estimated by UP/C into three categories: non-proteinuric (UP/C < 0.2), borderline proteinuria (UP/C 0.2 to 0.5), and proteinuric (UP/C > 2). The results obtained in this study showed a wide range of UP/C values, prompting the development of a new classification: non-proteinuric (UP/C < 0.2), borderline proteinuria (UP/C 0.2 to 0.5), mild proteinuria (UP/C 0.6 to 1.9), moderate proteinuria (UP/C 2.0 to 4.9), and severe proteinuria (UP/C ≥ 5.0). This classification was developed due to the clinical importance of evaluating this marker in the early diagnosis of CKD and its relationship with disease progression, as well as its relevance in animals with other conditions that lead to excessive protein loss in the urine (Grauer, 2005; Vaden and Elliott, 2016; Baumgartner, *et al.*, 2022). Similar to how the IRIS guidelines use the magnitude of blood pressure for hypertension staging to guide treatment and monitor outcomes, this proteinuria classification provides a more detailed framework that allows for an individualized approach to patient management.

By categorizing proteinuria into finer gradations, this classification aids in assessing the effectiveness of therapeutic interventions and in

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making informed decisions about treatment adjustments. However, it is important to recognize that all proteinuric animals, regardless of the magnitude of proteinuria, are at risk of the adverse effects associated with persistent renal proteinuria. Further research is needed to explore the impact of this stratification on broader clinical outcomes, such as the occurrence of nephrotic syndrome, survival rates, and specific assessments like protein electrophoresis and histopathological examination, to validate its clinical utility and long-term applicability.

The presence of pathologic protein in the urine can result from various conditions that can be divided into pre-renal, renal, and post-renal origins. Pathologic proteinuria of renal origin may suggest glomerular diseases when UP/C values are higher than 2.0 (Lees *et al.*, 2005). On the other hand, proteinuria resulting from tubular reabsorption changes, tubular injury, or tubulointerstitial inflammation and fibrosis usually shows lower UP/C values. This can serve as a clinical approach to determine a possible diagnosis (glomerulopathy, tubulopathy, etc.), as the definitive diagnosis includes specific tests such as electrophoresis for protein identification and renal biopsy (Vaden and Elliot, 2016; Maniaki and Finch, 2018).

In this study, 26 patients were clinically diagnosed with glomerular disease, and 52 with both glomerular and tubulointerstitial disease, as proposed by the IRIS consensus (2013b), which recommends the use of proteinuria as a marker to assist clinicians in disease characterization. While this classification was valuable for guiding clinical management, it is important to acknowledge that, without specific diagnostic tests such as renal biopsy or protein electrophoresis, the distinction between glomerular and tubulointerstitial involvement remains primarily clinical. Consequently, the percentages presented should be interpreted with the understanding that they reflect clinical estimates of the most likely affected region within the nephron, representing diagnostic possibilities, rather than definitive conclusions about the specific origin of the disease.

The clinical diagnosis of a possible primary disease is significantly important in planning and

establishing appropriate treatment, as well as determining prognosis (Polzin, 2011, Polzin, 2013). Therapies vary from patient to patient, and the occurrence of the diseases shown in the study illustrates the variety of possible diagnoses in the CKD population.

Other crucial aspects for the prognosis and treatment of dogs with chronic kidney disease include the presence or absence of anemia and serum concentrations of albumin and phosphate (Polzin *et al.*, 2011). The results from this study demonstrated a gradual decrease in the number of red blood cells starting from CKD 2, an expected event in CKD. The causes are mainly related to uremic state, implying a reduction in the survival time of red blood cells, a gradual decrease in erythropoiesis, and chronic blood loss through the gastrointestinal tract (Polzin, 2011; Torres *et al.*, 2017). Borin-Crivellenti *et al.* (2023) seem to relate the effects of tumor necrosis factor α (TNF α) on the hematopoiesis process, and Sannamwong *et al.* (2023) concluded that proteinuria may be associated with urinary loss of iron and transferrin, molecules important in red blood cell production.

Regarding sAlb, there was a significant decrease starting from stage 2. Although some patients showed albumin concentrations below 1.5g/dL, at the time of the evaluations, there were no clinical signs related to hypoalbuminemia or nephrotic syndrome. Hypoalbuminemia in CKD can result from decreased enteral absorption, deficient protein intake, and renal loss (Maniaki and Finch, 2018, IRIS, 2013a;), and it may decrease survival time, especially if nephrotic syndrome is present (Parker and Freeman, 2011).

The increase in serum phosphate concentration is one of the most dramatic effects in CKD due to its role in the development of secondary renal hyperparathyroidism. Among uremic toxins, excess parathyroid hormone stands out, which has deleterious effects on numerous physiological functions. Phosphate accumulates gradually as the glomerular filtration rate decreases (Cortadelas *et al.*, 2010; Polzin, 2011). The phosphate concentrations of the patients in this study increased significantly from stage 2, aligning with what the authors have stated.

CONCLUSION

While there is extensive information on the diagnosis and staging of chronic kidney disease (CKD) in dogs, the clinical approach must be comprehensive as there are correlated factors that affect the initiation of treatment, prognosis, and survival time. The presence of proteinuria can be considered both the origin and consequence of secondary alterations present in patients with renal disease and should be given the attention it requires. Further studies on patients with proteinuria are necessary to establish whether the proposed classification would help improve the clinical approach to proteinuric patients and convey a sense of urgency to veterinarians in clinical care. The refinement of the diagnosis, defining the possible underlying disease, its likely cause, and its consequences, is essential.

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