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IDENTIFYING DOGS TO BE SCREENED FOR CANINE CHRONIC KIDNEY DISEASE (cCKD)

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ABSTRACT

Canine chronic kidney disease (cCKD) is a condition that progresses over time and is frequently identified in its later stages. This study aimed to develop and validate a screening tool for cCKD, utilizing eight clinical and laboratory criteria to support early diagnosis.

INTRODUCTION

Canine Chronic Kidney Disease (cCKD) is a multifactorial disease characterized by persistent renal abnormalities, affecting up to 10% of geriatric dogs[1]. Diagnosis depends on evaluating simultaneously multiple biomarkers (serum creatinine, SDMA, and UP/C ratio), medical history, patient specific risk factors (e.g., age, breed, nutrition, genetics, comorbidities etc.)[2],combined with physical examination. Despite available tools, early detection remains limited due to the absence of a standardized screening method. This study aims to develop and validate a model combining clinical data and biomarkers to improve early diagnosis.

MATERIALS AND METHODS

Study Design
- Definition of eight cCKD screening criteria (Table 1)
- Multicenter prospective Real-World Data collection study in Greece (06/2023-03/2024)
- Development of data forms (demographics e.g., age, breed, weight, neuter status)

Participants' recruitment
- Enrollment of dogs ≥3 years old meeting ≥1 screening criterion
- Veterinarians from Greece
- Owner consent

Laboratory analysis
- Serum samples analysis for renal biomarkers
- IRIS staging at an ISO 9001-certified lab[3]

Statistical analysis
- Non-parametric Mann–Whitney U test for continuous variables
- Fisher's exact test for categorical diagnostic criteria
- Multivariable logistic regression model constructed with cCKD diagnosis as the dependent variable

Table 1: The eight screening criteria for cCKD

	Description
1	On a renal diet in the last 12 months
2	History of Acute Kidney Injury (AKI)
3	Loss of appetite, unexplained weight loss, or low Body Condition Score
4a	History of serum creatinine 1.2–2.8 mg/dL (in dogs >5 yo)
4b	History of serum phosphate ≥ 3.8 mg/dL (in dogs >5 yo)
4c	History of an increasing creatinine trend (in dogs >5 yo)
4d	History of increased SDMA with creatinine in reference values (in dogs >5 yo)
4e	History of an increasing phosphate trend (in dogs >5 yo)
5	Dental disease (in dogs >4 yo)
6	History of canine leishmaniosis and/or ehrlichiosis
7	Diagnosed osteoarthritis, with possible increasing creatinine trend
8	Breed-specific risk (e.g., Yorkie, Pomeranian >7 yo or Boxer <10 yo)

RESULTS

Demographics
- **46** veterinarians contributed data for **1.034** dogs
- **283 (27.4%)** dogs classified as **cCKD** cases
- Even population distribution by sex
- Mean age: **9.45 years (SD=3.4)**
- Mean body weight:**18.85 kg (SD=12.23)**

Univariate analysis:
- **Age** was significantly higher in dogs diagnosed with cCKD (p<0.001)
- **Renal diet** (p< 0.001) , **AKI** (p< 0.001), **loss of weight/appetite** (p=0.002), **elevated creatinine/phosphate** levels (p<0.001), **increasing creatinine trend** (p<0.001), **increased SDMA** (p=0.007), **dental disease** (p<0.001), and osteoarthritis (p<0.001) were **significantly associated** with cCKD cases (p<0.05).

Multivariate analysis (Logistic regression model):
Age and 6 screening criteria identified as significant predictors (Table 2).
- **Increasing creatinine trend** was the **strongest predictor**, followed by renal diet history and prior creatinine levels of 1.2–2.8 mg/dL.
- Effect of age was moderated by a significant interaction with dental disease: **for individuals without dental disease, each year of age increases the odds by approximately 9.4%**, whereas for those with dental disease, the age effect is reduced to approximately 4.4% per year.

Model's discriminative performance:
- **U**p to **80.9%** overall accuracy depending on the cut-off used (Table 3).

Table 2: Multivariable Logistic Regression Model for Predicting the Diagnosis of cCKD

Predictor Variable	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I. for EXP(B)
Main effects							
Age (Years)	.08	.03	10.24	1	.001	1.09	1.04 - 1.15
Renal Diet	1.54	.24	41.24	1	<.001	4.67	2.924 - 7.50
Acute Kidney Injury	.69	.31	5.07	1	.024	2.00	1.09 - 3.68
Appetite/Weight Loss	.68	.24	7.73	1	.005	1.97	1.22 - 3.20
Creatinine 1.2–2.8 mg/dL	1.34	.20	44.25	1	<.001	3.85	2.59 - 5.73
Increasing Creatinine	2.41	.33	54.52	1	<.001	11.18	5.89 - 21.22
Leishmaniosis /Ehrlichiosis	.56	.19	8.62	1	.003	1.75	1.20 - 2.54
Interaction Term							
Age by Dental Disease	-.04	.018	6.61	1	.010	.95	.92- .99
Constant	-2.78	.32	77.39	1	<.001	.06	

Table 3: Model Classification Performance and Key Metrics at Three Probability Cut-offs

	Cut-off = 0.500		Cutoff = 0.409		Cutoff = 0.241	
	cCKD Model prediction		cCKD Model prediction		cCKD Model prediction	
cCKD	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**
No	707	44	676	75	599	152
Yes	157	126	123	160	84	199
Performance Metrics						
Spec (%)	94.1		90.0		79.8	
Sens (%)	44.5		56.5		70.3	
PPV (%)	74.1		68.1		56.7	
NPV (%)	81.8		84.6		87.7	
Overall Accuracy (%)	80.6		80.9		77.2	

CONCLUSIONS

- The developed multivariable model could be used as a practical tool to support early identification of dogs at risk for cCKD → prompt intervention, improved prognosis, and enhanced quality of life for affected dogs
- The model uses readily available clinical data and flexible, threshold-based application for different practice needs
  - **For routine screening and early detection**: Youden threshold (0.241) is preferable with 70.3% sensitivity
  - **For confirmation:** default (0.500) threshold is the most suitable with 94.1% specificity
  - **For balanced routine practice**: intermediate threshold (0.409) offers the best compromise with 90% specificity 56.5% sensitivity and the highest overall accuracy (80.9%)
- Future work: validation and refinement of this screening model across diverse populations and integration into veterinary software and clinical guidelines.

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