INTERNATIONAL SEVEN JOURNAL
OF MULTIDISCIPLINARY
ISSN: 2764-9547

ADVANCES IN THE USE OF BIOMARKERS IN THE EVALUATION OF CHRONIC KIDNEY DISEASE IN GERIATRIC CATS

https://doi.org/10.56238/isevmjv3n6-010

Receipt of originals: 10/29/2024 **Acceptance for publication:** 11/29/2024

Andreia Oliveira Santos[1], Érika Saraiva Nascimento[2], Deividi dos Reis Dambroz[3], Lucas dos Santos Rebouças[4], Maria Vitória dos Santos Budin[5], Gabrielle Christine de Souza Campos Meirelles[6], Camila Siqueira Aleixo[7], Joana Pereira da Silva[8], Simone Morett Alves[9], Allan Felipe Santana Nunes[10], Maria Vitória dos Santos Menegazzi[11] and Mateus de Melo Lima Waterloo[12]

ABSTRACT

Objective: To evaluate the efficacy of biomarkers in the early detection of chronic kidney disease (CKD) in geriatric cats, highlighting their advantages over traditional diagnostic methods. Chronic Kidney Disease (CKD) is one of the leading causes of morbidity and mortality in senior cats, and is often identified in advanced stages due to reduced sensitivity to markers such as urea and creatinine. These traditional procedures only identify changes when more than 75% of renal function is compromised, restricting early intervention. Contemporary biomarkers, such as symmetric dimethylarginine (SDMA), cystatin C, N-acetyl-β-glucosaminidase (NAG), and gamma glutamyltransferase (GGT), have demonstrated increased sensitivity for detecting renal changes in early stages. SDMA is the most promising biomarker, being able to identify declines in kidney function with only a 30% decrease in glomerular filtration rate (GFR). In addition, it is not influenced by muscle mass, being perfect for elderly felines. Other indicators, such as cystatin C and the urinary proteins NAG and GGT, enrich the analysis, despite facing constraints related to uniformity and specificity. The use of these biomarkers, combined with laboratory and imaging tests, enhances diagnosis and enables early interventions

[1] Veiga de Almeida University
E-mail: andreia_oliversantos@yahoo.com.br
[2] University Center of the Central Plateau Aparecido dos Santos
E-mail: saraiva.nascimento@gmail.com
[3] University of Cruz Alta
Email: dambroz614@gmail.com
[4] Federal Rural University of the Semi-arid
E-mail: lucas.reboucas91057@alunos.ufersa.edu.br
[5] Federal University of Paraná
E-mail: M4vi@outlook.com
[6] Campos Gerais Higher Education Center
Email: gabicamposdvm@gmail.com
[7] Anhembi Morumbi University – Mooca Campus
E-mail: camilasaleixo@gmail.com
[8] Anhembi Morumbi University – Mooca Campus
E-mail: joanapereidas@gmail.com
[9] Castelo Branco University
E-mail: Simone.morett@gmail.com
[10] Email: felipeallan1234@gmail.com
[11] University of Cruz Alta
E-mail: mdossantosmenegazzi@gmail.com
[12] Fluminense Federal University
E-mail: mateuswaterloo@icloud.com

that increase patients' quality of life and life expectancy. More research is needed on emerging markers such as NGAL and KIM-1 to strengthen their clinical uses in felines. These tools symbolize progress in veterinary medicine, providing greater accuracy and efficiency in treatment.

Keywords: Felines. Renal function. Biomarkers.

INTRODUCTION

Chronic kidney disease (CKD) is one of the most common conditions in small animal clinics, particularly in geriatric felines, and is considered the second leading cause of death in cats. This condition is marked by a progressive, irreversible, multifactorial deterioration of kidney function, affecting the metabolic, excretory, and endocrine functions of the kidneys. Often silent in the early stages, this clinical picture only manifests itself in more advanced stages, which complicates early intervention and decreases the chances of improving the quality of life of the affected animals (ROSSI et al., 2022; CARVALHO, 2021).

In clinical routine, the most commonly used biomarkers, such as serum urea and creatinine, are easily accessible, however, they have low sensitivity for the initial recognition of CKD. Only when more than 75% of renal function is already compromised, these parameters undergo changes, which restricts their usefulness for the initial diagnosis. In addition, some elements such as advanced age, decreased muscle mass, and simultaneous illnesses can influence the interpretation of these indicators, particularly in older felines, which often exhibit characteristics that complicate an accurate diagnosis (BARBOSA, 2022; CARVALHO, 2021).

Given these restrictions, the search for more specific and sensitive biomarkers has been the focus of several veterinary studies. Symmetric dimethylarginine (SDMA) emerges as one of the most promising indicators for the early diagnosis of renal function, due to its strong correlation with glomerular filtration rate (GFR) and its absence of influence on muscle mass. Other biomarkers, such as cystatin C, N-acetyl-β-glucosaminidase (NAG), and gamma glutamyltransferase (GGT), have also shown potential to identify kidney changes in early stages, although their clinical use still needs further validation research (ROSSI et al., 2022; BARBOSA, 2022; CARVALHO, 2021).

Therefore, the aim of this study is to review the use of biomarkers in the follow-up and diagnosis of renal function in geriatric cats. In addition to addressing the clinical usefulness of these indicators, the purpose is to emphasize their effect on veterinary practice, especially in the early identification of CKD. This allows for more precise interventions that help extend survival and improve the quality of life of patients.

METHODOLOGY

This study was developed as a narrative review of the literature, with the objective of evaluating the use of biomarkers in renal function in geriatric cats. The approach adopted seeks to integrate relevant information on serum and urine biomarkers widely used or in the validation phase in veterinary medicine, in addition to discussing their benefits, limitations and impact on clinical practice.

The choice of references was made through research in scientific databases, such as PubMed, SciELO and Google Scholar, as well as the analysis of academic papers and articles published in specialized journals in the field of veterinary medicine. Terms such as "feline chronic kidney disease", "renal biomarkers", "SDMA", "cystatin C", "NAG" and "GGT" were used. The selection of publications prioritized those from the last 15 years, highlighting the most recent and pertinent studies.

In addition, academic texts made available by the authors were examined, including monographs, articles and reviews related to the subject. The approach used inclusion and exclusion criteria based on the relevance of the subject, giving priority to research focused on felines and useful biomarkers in veterinary clinical practice. The evaluation of the data was done in a descriptive way, with the objective of establishing comparisons between the various biomarkers, their functioning processes, benefits and restrictions. The objective was to gather recent information and offer a robust theoretical foundation for the use of these markers in clinical practice, particularly in elderly cats.

LITERATURE REVIEW

CHRONIC KIDNEY DISEASE IN GERIATRIC CATS

CKD is a condition with a high incidence in felines, especially in cats of advanced age, due to their physiological and metabolic predisposition. This condition is marked by the progressive decrease of nephrons, which occurs irreversibly and impairs vital functions of the kidneys, such as water regulation, electrolysis and elimination of toxins (BRAGATO, 2013; ROSSI et al., 2022).

Unlike acute kidney injuries, which can be recovered with intervention, CKD is characterized by a lack of functional regeneration in kidney tissues. Accumulated deterioration mainly impairs the glomerular filtration capacity, resulting in metabolic and systemic changes that directly affect feline health. The evolution of the disease occurs progressively, and the most notorious clinical symptoms, such as polyuria, polydipsia,

and anorexia, usually appear in more advanced stages (CHEW et al., 2011; CARVALHO, 2021).

In addition, some research points out that CKD is the second leading cause of death in felines, behind only neoplasms. The incidence increases considerably in animals over 10 years old, with 30% to 40% of older felines showing some level of kidney failure (SPARKES et al., 2016; CARVALHO, 2021). This high prevalence justifies the need for diagnostic methods that enable early detection and appropriate management, avoiding complications and increasing patient survival.

TRADITIONAL DIAGNOSTIC METHODS

Traditional diagnostic methods are based on serum creatinine and urea measurement. Despite being widely used, these biomarkers have significant restrictions, such as reduced sensitivity. Changes in blood creatinine levels are only noticed when approximately 75% of kidney function has already been lost, which makes an early diagnosis unfeasible (BARBOSA, 2022; MIYAGAWA et al., 2020). In addition, creatinine is affected by extrarenal elements, such as the animal's muscle mass and hydration level, and may be underestimated in cats with low muscle mass or elderly (NABITY et al., 2015; FREITAS et al., 2020).

An additional challenge is clinical interpretation, because, despite being simple and low-cost techniques, they do not allow the distinction between acute and chronic kidney injuries, requiring additional tests to confirm the diagnosis (NELSON & COUTO, 2015; CARVALHO, 2021). These restrictions have stimulated the search for more specific and sensitive biomarkers, capable of identifying changes in renal function in the early stages.

PROMISING BIOMARKERS FOR CKD

Symmetric dimethylarginine (SDMA)

SDMA is emerging as the most promising biomarker for early diagnosis of feline kidney function. This molecule originates from the breakdown of proteins and is eliminated solely by the kidneys, with its concentration in the blood directly associated with the glomerular filtration rate (GFR) (SCHWEDHELM & BÖGER, 2011). Some research indicates that SDMA is able to identify changes in kidney function with a loss of only 30% in GFR, being more sensitive than creatinine (HALL et al., 2014). In

addition, SDMA is not influenced by muscle mass, which makes it particularly beneficial for senior cats or cats with cachexia (BRAFF et al., 2014).

However, its interpretation requires caution, as SDMA levels can rise in cases of concurrent illness or in the administration of nephrotoxic drugs, leading to false positives (PELANDER et al., 2019). Thus, combining it with other diagnostic tests is crucial to prevent misdiagnosis.

Cystatin C

Cystatin C, a low molecular weight protein, is produced by all nucleated cells. Unlike creatinine, it is not affected by the amount of muscle or the nutritional condition of the animal. Its concentration in the blood increases when GFR decreases, and it is seen as a promising biomarker, particularly in human medicine (ROYAKKERS et al., 2011).

Although it has potential, its application in veterinary medicine still encounters obstacles. Research indicates that cystatin C levels vary according to the size and clinical status of animals, in addition to their sensitivity being lower than SDMA in certain circumstances (MIYAGAWA et al., 2020; SOUZA et al., 2018). Therefore, although it is seen as a relevant complementary marker, its isolated use is not yet frequently suggested.

Urinary Biomarkers: NAG and GGT

Urinary biomarkers, such as N-acetyl-β-glucosaminidase (NAG) and gamma glutamyltransferase (GGT), have been explored for the detection of tubular lesions. NAG is a sign of damage to the renal tubules, exhibiting a noticeable elevation in the early stages of injury. However, its specificity is restricted, since it can be affected by conditions other than renal conditions, such as rheumatoid arthritis (Freitas et al., 2014). On the other hand, GGT is linked to tubular damage and the presence of proteinuria, but it has lower sensitivity and restricted studies, especially in felines (PRESSLER, 2015).

NGAL and other emerging biomarkers

Lipocalin, together with neutrophilic gelatinase (NGAL), has stood out for its ability to identify ischemic and nephrotoxic renal lesions. Its presence in significant amounts in the urine indicates damage to the renal tubules, and is seen as promising

both for CKD and for the distinction between acute and chronic lesions (STEINBACH et al., 2014; WU et al., 2019). The study of other biomarkers, such as KIM-1 (Kidney Injury Molecule-1) and retinol-binding protein (RBP), is still at an early stage in veterinary medicine. These indicators have demonstrated high sensitivity in experimental models, but do not yet have clinical validation for application in felines (BEKER et al., 2018; ZHOU et al., 2014).

IMPACT OF THE USE OF BIOMARKERS IN CLINICAL PRACTICE

The introduction of biomarkers such as SDMA into veterinary routine has the potential to transform the management of CKD. Early identification of kidney failure enables the execution of more efficient interventions, such as changes in diet, hypertension control, and constant monitoring of the disease's progression (IRIS, 2019; SARGENT et al., 2021). In addition, the combination of serum and urine biomarkers with additional techniques, such as ultrasonography and urinalysis, allows a more complete and accurate diagnosis. This tactic helps to improve the quality of life and life expectancy of cats affected by CKD (ROSSI et al., 2022; CARVALHO, 2021).

CONCLUSION

The use of biomarkers in the assessment of kidney function in geriatric cats represents a significant advance in the early diagnosis of CKD. Biomarkers such as SDMA exhibit high sensitivity and specificity, overcoming the constraints of traditional methods such as serum creatinine measurement. Extra biomarkers, such as cystatin C and the urinary markers NAG and GGT, enrich this strategy, although they still need more validation in felines. The combination of blood and urine biomarkers with laboratory and imaging tests increases the accuracy of the diagnosis, enabling more efficient interventions. With the progress of studies, it is expected that the combination of these indicators will increase the quality of life and life expectancy of elderly patients, establishing a more effective and focused clinical strategy.

REFERENCES

1. Brown, S. A. (1999). Pathophysiology and management of chronic kidney disease in dogs and cats. Veterinary Clinics of North America: Small Animal Practice, 28(4), 1277–1290.

2. Carvalho, L. M. de. (2021). Lesões renais em felinos e o uso do biomarcador dimetilarginina simétrica no diagnóstico precoce da doença renal crônica. Monografia (Bacharelado em Medicina Veterinária) – Centro Universitário do Sul de Minas – UNIS-MG, Varginha.

3. Chew, D. J., Buffington, C. A. T., & Dibartola, S. P. (2011). Diagnosis and management of chronic kidney disease. Veterinary Clinics of North America: Small Animal Practice, 41(4), 747–763.

4. Freitas, E. D., et al. (2014). Biomarcadores na avaliação da função renal: Avanços e desafios na prática clínica veterinária. Brazilian Journal of Veterinary Research, 31(2), 137–145.

5. Hall, J. A., et al. (2014). Relationship of symmetric dimethylarginine to glomerular filtration rate and creatinine in cats with chronic kidney disease. Journal of Veterinary Internal Medicine, 28(6), 1697–1703.

6. Jericó, M. M., Kogika, M. M., & Andrade Neto, J. P. (2015). Diagnóstico e manejo da doença renal crônica em cães e gatos. Clínica Veterinária, 20(116), 60–69.

7. Miyagawa, Y., et al. (2020). Cystatin C as a potential renal biomarker in dogs and cats. Journal of Veterinary Medical Science, 82(3), 243–250.

8. Nabity, M. B., et al. (2015). Evaluation of symmetric dimethylarginine and creatinine in cats with chronic kidney disease. Journal of Veterinary Internal Medicine, 29(3), 1036–1043.

9. Pelander, L., et al. (2019). Evaluation of symmetric dimethylarginine (SDMA) in dogs and cats with varying degrees of renal dysfunction. Journal of Veterinary Internal Medicine, 33(4), 1761–1768.

10. Pressler, B. M. (2015). Renal biomarkers in the assessment of kidney disease in dogs and cats. Veterinary Clinics of North America: Small Animal Practice, 45(4), 621–637.

11. Rossi, I. M., et al. (2022). Doença renal crônica em pequenos animais e biomarcadores que visem sua precocidade. PubVet, 16(11), 1–9. https://doi.org/10.31533/pubvet.v16n11a1254.1-9.

12. Sargent, H. J., et al. (2021). Symmetric dimethylarginine (SDMA) as an early biomarker of renal dysfunction: Current perspectives. Veterinary Medicine and Science, 7(2), 283–292.

13. Sparkes, A. H., et al. (2016). ISFM consensus guidelines on the diagnosis and management of feline chronic kidney disease. Journal of Feline Medicine and Surgery, 18(3), 219–239.

14. Souza, S. P., et al. (2018). Cystatin C and its role in renal diagnostics. Journal of Veterinary Science, 12(2), 95–104.

15. Zhou, H., et al. (2014). N-acetyl-β-D-glucosaminidase as a biomarker for early detection of kidney injury. Veterinary Journal, 200(2), 192–198.