



Nutritional effects on mineral metabolism in cats with chronic kidney disease

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Abstract. The relevance of this study arises from the high prevalence of mineral metabolism disorders in cats with chronic kidney disease (CKD), which are accompanied by the development of hypercalcaemia and hyperphosphataemia and have a significant impact on prognosis and quality of life. Accordingly, the aim of the study was to assess the effect of different dietary calcium-to-phosphorus ratios on calcium-phosphorus homeostasis and the overall condition of cats with stage II CKD. The principal research method involved a comparative evaluation of clinical and biochemical parameters in animals depending on diet type, which enabled a comprehensive assessment of mineral metabolism changes. The study included fourteen cats divided into two groups. Group 1 animals received feed with a higher calcium-to-phosphorus ratio (1.71) and restricted phosphorus content, whereas Group 2 cats were fed a diet with a moderate calcium-to-phosphorus ratio (1.33). Over a six-month period, blood biochemical parameters were monitored, including total and ionised calcium, phosphorus, creatinine, urea, and symmetric dimethylarginine concentrations. In addition, the cats' clinical condition, body weight, muscle condition, body condition score, and arterial blood pressure were assessed, all of which remained stable in both experimental groups. It was found that cats in Group 1 showed an increase in calcium levels, while cats in group 2 developed ionised hypercalcaemia. In Group 2 cats, calcium levels remained stable without signs of hyperphosphataemia. Azotaemic markers did not differ significantly between the groups. Based

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on the obtained results, it was established that excessive phosphorus restriction leading to a high calcium-to-phosphorus ratio did not provide additional benefits in controlling phosphataemia but increased the risk of calcium metabolism disturbances. The material of this article holds practical value for veterinary clinicians, as it experimentally confirms the advisability of using diets with a moderate calcium-to-phosphorus ratio at early stages of chronic kidney disease in cats

Keywords: dietary effect; metabolic disorders; secondary hyperparathyroidism; phosphate binders; calcium homeostasis; nephrocalcinosis; renal diet

Introduction

Chronic kidney disease (CKD) is among the most prevalent pathological conditions in cats, significantly affecting both the quality and duration of life. The disease is progressive in nature, characterised by the loss of nephrons and the development of mineral and bone disorders. A key factor in this process is the disturbance of calcium-phosphorus balance, which contributes to the formation of secondary hyperparathyroidism, tissue calcification, and nephrolithiasis, thereby accelerating the progression of renal failure.

According to the European Pet Food Industry Federation (FEDIAF, 2024) guidelines, the recommended calcium-to-phosphorus (Ca:P) ratio for adult cats ranges from 1:1 to 2:1. However, such a broad range does not account for the individual sensitivity of cats with CKD. In practice, high Ca:P ratios combined with excessive phosphorus restriction may provoke the development of ionised hypercalcaemia. M.R. Ehrlich *et al.* (2024) demonstrated that, in cats with hypercalcaemia, transitioning to diets with a Ca:P ratio below 1.4 resulted in normalisation of calcium levels in most cases within 3-20 weeks. Similarly, J. Stockman (2024) emphasised the absence of clearly defined safe limits for Ca:P ratios in current clinical guidelines and the need to revise existing recommendations.

A high Ca:P ratio is also associated with the formation of calcium-containing deposits. W. Zhang *et al.* (2024) showed that populations

with elevated Ca:P ratios exhibited a higher prevalence of nephrolithiasis. In turn, E. Maniaki *et al.* (2024) reported that more than one quarter of cats with hypercalcaemia had early-stage CKD, and none of them had been fed renal diets prior to diagnosis – highlighting the influence of nutrition on calcium status.

An important direction in current research is the study of the interactions between calcium and phosphorus and other minerals. P.-K. Tang *et al.* (2024) demonstrated that an increased magnesium content in the diet of cats with CKD stabilises FGF-23 levels and prevents the development of hypercalcaemia. This highlights the complex interrelationships among calcium, phosphorus, and magnesium in maintaining metabolic balance. Meanwhile, findings by M. Krofič Žel *et al.* (2024) indicated that the addition of vitamin E to renal diets did not affect the survival of cats, confirming the priority of mineral control over other dietary interventions. Proteinuria also deserves particular attention as a predictor of CKD progression. M.A. Fidalgo *et al.* (2022) established that the urine protein-to-creatinine ratio (UPC) serves as a valuable clinical marker, since even moderate elevations are associated with the presence and further development of kidney disease in cats. This underscores the necessity of considering proteinuria when evaluating the effectiveness of dietary therapy and the control of the Ca:P ratio.

Therefore, determining the optimal Ca:P ratio in cats with CKD remains an urgent issue in veterinary medicine. Despite existing recommendations, current data indicate the need to refine the safe limits of this ratio, which has direct practical significance for improving dietary therapeutic strategies. Another major gap lies in the lack of long-term studies comparing different approaches to regulating the Ca:P ratio, particularly those combining dietary interventions with phosphate-binding agents, with evaluation of their effects on survival, quality of life, and the incidence of complications. Most available data are based on short- or medium-term observations, which complicates the establishment of consistent clinical recommendations.

In this context, the aim of the study was to evaluate the effect of different dietary calcium-to-phosphorus ratios on the development of hypercalcaemia and the effectiveness of hyperphosphataemia control in cats with stage II chronic kidney disease over a six-month observation period, as well as to determine a safe Ca:P range for long-term dietary therapy under controlled calcium and protein levels. The objectives of the study included analysing the dynamics of ionised and total calcium at different Ca:P ratios, assessing the influence of these ratios on phosphorus levels and the need for phosphate-binding therapy, determining the frequency of hypercalcaemia development depending on dietary profile, and investigating the relationship between the Ca:P ratio and proteinuria indicators as a prognostic marker of CKD.

Literature Review

Chronic kidney disease (CKD) in cats is among the most common and complex pathologies affecting small companion animals. It is characterised by a gradual loss of functional nephrons, progressive azotaemia, and the development of systemic complications. One of the key pathogenetic mechanisms involves disruption of

calcium–phosphorus homeostasis due to reduced renal phosphate excretion, alterations in vitamin D metabolism, and activation of the parathyroid axis. Understanding these pathophysiological changes is critically important for accurate diagnosis and effective monitoring of the patient's condition.

As emphasised by J.A. Hokamp & M.B. Nabity (2016), the combined measurement of creatinine and symmetric dimethylarginine (SDMA) allows for a more precise assessment of the glomerular filtration rate, particularly in the early stages of the disease, when creatinine levels may remain within the normal range due to low muscle mass. Additionally, V. Pedrinelli *et al.* (2020) highlighted the importance of a comprehensive diagnostic approach to CKD, including urinalysis with evaluation of specific gravity, proteinuria, and the UPC, which enables the detection of glomerular and tubular damage and helps to predict disease progression rate. L. Hahn & C. Callaband (2022) stressed the diagnostic value of combining laboratory and imaging methods: assessment of proteinuria together with ultrasonographic examination provides a comprehensive evaluation of renal status and reveals morphological changes such as increased parenchymal echogenicity, reduced kidney size, and the presence of cystic formations or calcifications, reflecting chronic disturbances of mineral metabolism. R.F. Geddes *et al.* (2021) demonstrated that measurement of ionised calcium, in contrast to total calcium, serves as a more informative indicator of calcium status, particularly under conditions of hypoalbuminaemia.

The pathophysiological mechanisms underlying tissue mineralisation were described by P.-K. Tang *et al.* (2021), who noted that an increased calcium load against a background of low phosphorus levels may promote the calcification of extraosseous tissues, including nephrocalcinosis and vascular lesions. The

imbalance between calcium and phosphorus underlies the development of renal mineral and bone disorder (RMBD), which encompasses secondary hyperparathyroidism, osteodystrophy, nephrocalcinosis, and vascular calcification. These conditions can accelerate the progression of CKD, especially in the presence of concurrent metabolic disturbances.

Particular attention has been drawn to fibroblast growth factor-23 (FGF-23) as a biomarker of early disturbances in phosphorus metabolism. J. Lin *et al.* (2021) established that serum FGF-23 levels in cats with CKD increase at the early stages of the disease – prior to the onset of hyperphosphataemia – and correlate with disease progression while contributing to reduced calcitriol synthesis. This, in turn, decreases intestinal calcium absorption, stimulates parathyroid hormone secretion, and accelerates the formation of calcium–phosphate deposits, reflecting the key role of FGF-23 in the pathogenesis of renal mineral and bone disorders.

In humans with CKD, FGF-23 also possesses substantial clinical significance. S. Seiler *et al.* (2009) demonstrated that elevated concentrations of this hormone are associated with a higher risk of mortality and more rapid progression of renal insufficiency, independent of serum phosphorus levels – underscoring the universality of this pathophysiological mechanism. Its action includes suppression of calcitriol synthesis, reduction of intestinal calcium absorption, and stimulation of parathyroid hormone secretion, which, when combined with high Ca:P ratios, increases the risk of extraosseous tissue calcification.

One of the key mechanisms involved is the formation of an excessive $\text{Ca} \times \text{P}$ product in the blood, exceeding the solubility limit of calcium–phosphate compounds and promoting their deposition in soft tissues. As noted by J.A. Hokamp & M.B. Nabity (2016), such

deposits may occur in the renal parenchyma, myocardium, vasculature, and gastrointestinal tract, impairing the function of affected organs. Hormonal dysregulation further amplifies this process: elevated Ca:P ratios in the context of CKD stimulate parathyroid hormone secretion, leading to secondary hyperparathyroidism, bone resorption, and additional calcium release into the bloodstream. L. Hahn & C. Callaband (2022) demonstrated that this creates a self-perpetuating cycle, whereby increased calcium levels sustain hypercalcaemia and elevate the risk of calcification.

Excessive phosphorus restriction combined with elevated dietary calcium shifts the Ca:P ratio beyond physiologically safe limits. This not only provokes hypercalcaemia but also increases plasma saturation with calcium-phosphate complexes, predisposing to nephrocalcinosis and vascular calcification. J. Stockman (2024) found that such alterations accelerate both structural and functional lesions of renal and extra-renal tissues, worsening the disease prognosis.

L. Hahn & C. Callaband (2022) further noted that cats exhibit greater sensitivity to variations in the Ca:P ratio than dogs, which may be associated with species-specific characteristics of calcium-phosphorus regulation and hormonal control. This underscores the necessity of a species-specific approach to dietary correction. An elevated dietary calcium-to-phosphorus ratio in cats with chronic kidney disease creates conditions for a cascade of pathophysiological changes leading to complications. Control of phosphataemia in cats with CKD remains a cornerstone of disease management, crucial for slowing progression and preventing complications. Dietary therapy with reduced phosphorus content remains the first-line intervention, particularly in the early stages of CKD. It is recommended to use diets containing 0.3–0.6% phosphorus on a dry matter basis and to

maintain the Ca:P ratio near the lower limit of the range recommended by FEDIAF (2024) to avoid excessive calcium loading.

When dietary phosphorus restriction alone is insufficient to achieve target levels, phosphate binders are employed. R.F. Geddes *et al.* (2021) emphasised that the choice of binder type should take into account the patient's current calcium status. Calcium-containing agents, such as calcium acetate or calcium carbonate, are effective in lowering serum phosphate levels but, with long-term use, may increase the Ca:P ratio. This can contribute to hypercalcaemia, particularly in animals receiving low-phosphorus diets. An alternative approach involves the use of non-calcium-containing binders. V.J. Parker (2021) found that sevelamer hydrochloride and lanthanum carbonate effectively controlled phosphorus levels without adding a calcium load. However, the use of sevelamer may reduce the absorption of fat-soluble vitamins, while lanthanum carbonate can accumulate in tissues with prolonged administration, necessitating regular monitoring.

J. Stockman (2024) highlighted the importance of an individualised dietary strategy for cats with CKD. The author stressed that in patients with high Ca:P ratios, preference should be given to non-calcium phosphate binders, and excessive phosphorus restriction combined with elevated dietary calcium should be avoided. The optimal approach involves a combination of moderate phosphorus restriction, a controlled Ca:P ratio, and, where necessary, the use of non-calcium binders, which together minimise the risk of calcification and help maintain a stable course of CKD. J.A. Hokamp & M.B. Nabity (2016) underscored the need for a comprehensive assessment of mineral metabolism incorporating novel biomarkers such as FGF-23 and parathyroid hormone to enable early detection of imbalances before the onset of clinical signs or hyperphosphataemia. However,

standardised monitoring protocols for these indicators in cats have not yet been developed.

Materials and Methods

The study was conducted from October 2024 to March 2025 at the Faculty of Veterinary Medicine of the National University of Life and Environmental Sciences of Ukraine (Kyiv, Ukraine) and the “Zoolux” Veterinary Clinic (Kyiv, Ukraine). The research involving animals complied with the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1986) and the Law of Ukraine No. 3447-IV (2006). All procedures were performed in accordance with the recommendations of the ARRIVE Guidelines 2.0 (n.d.) and did not contravene the provisions of Directive 2010/63/EU of the European Parliament and of the Council (2010). The study protocol was approved by the Bioethics Committee of the National University of Life and Environmental Sciences of Ukraine (Protocol No. 7/2024).

The study involved fourteen domestic cats aged between six and nine years with confirmed chronic kidney disease, diagnosed according to the criteria of the International Renal Interest Society (IRIS, 2023). Animals with concurrent endocrine, cardiovascular, or infectious diseases were excluded from the sample. All cats were patients of the “Zoolux” Veterinary Clinic and remained under the care of their owners throughout the study. They were kept under home conditions with free access to water and were fed diets according to their assigned study group. The cats were divided into two groups – Group 1 and Group 2 – with seven animals in each. Both groups received two types of veterinary diets formulated for cats with CKD, differing in fat and phosphorus content and in the calcium-to-phosphorus ratio, while maintaining a comparable level of crude protein (Table 1).

Table 1. Chemical composition of the dietary feeds used in the study

Parameter	Diet 1	Diet 2
Crude protein (%)	28	27
Crude fat (%)	12	20
Crude fibre (%)	3	2.7
Calcium (%)	0.6	0.6
Phosphorus (%)	0.33	0.45
Ca:P ratio	1.71	1.33
Sodium (%)	0.2	0.3
Potassium (%)	0.8	0.65
Vitamin A (IU/kg)	25,668	24,000
Vitamin D ₃ (IU/kg)	1,523	1,800

Note: the presented values reflect the content of the main nutrients in the composition of the feeds according to the official data provided by the manufacturers

Source: feed manufacturers' data (Nestlé Purina, 2024; Josera, 2024)

The calcium content was identical in both diets (0.6%), and the concentrations of vitamin D₃ were comparable (1,523 IU/kg in Diet 1 and 1,800 IU/kg in Diet 2). Dietary phosphorus restriction is a key component of nutritional management in CKD, as it reduces the risk of secondary hyperparathyroidism and prolongs feline lifespan. However, contemporary evidence from P.-K. Tang *et al.* (2021) and R.F. Geddes *et al.* (2021) indicates that the effectiveness of this approach depends not only on the absolute phosphorus level but also on the calcium-to-phosphorus ratio (Ca:P), which determines mineral balance and influences the organism's metabolic stability. Therefore, this study compared diets with different Ca:P ratios under controlled calcium and protein levels, enabling the assessment of the isolated effect of this parameter on the development of hypercalcaemia, hyperphosphataemia, and the overall progression of CKD. This approach provided an objective basis for determining a safe Ca:P range for long-term dietary management.

Throughout the experiment, regular veterinary examinations and monitoring of the cats' clinical condition were performed. The general health status, appetite, body weight dynamics, and arterial blood pressure were assessed.

Animals were weighed using a Momert 6551 electronic scale (Momert Ltd., Hungary). Blood pressure was measured using a petMAP graphic II oscillometric tonometer (CardioCommand Inc., USA). A cuff width corresponding to 30-40% of the limb circumference was used, and 5-7 measurements were taken; the median value was recorded for analysis. To reduce stress and minimise the "white-coat effect," all animals received Gabapentin prior to the procedure in accordance with the Cat Friendly Practice® Guide (AAFP, 2023).

Venous blood samples were collected from the jugular vein every three months after an overnight fast (8-12 hours) using a 22G needle under sterile conditions. For haematological analysis, K₂-EDTA tubes were used, while serum was obtained in clot activator tubes for biochemical analysis. After clot formation, serum was separated by centrifugation (10 minutes at 1,500-2,000 g) and stored at 2-8°C for no longer than 24 hours. Samples showing evidence of haemolysis or lipaemia were excluded from further analysis.

In the serum biochemical profile, the concentrations of creatinine, urea, potassium, phosphorus, sodium, chloride, total and ionised calcium, total protein, albumin, and symmetric

dimethylarginine (SDMA) were determined. Biochemical parameters were analysed using an automated biochemical analyser Mindray BS-240 (Mindray Biomedical Electronics Co., China), and SDMA was measured with a veterinary biochemical analyser IDEXX Catalyst One (IDEXX Laboratories Inc., USA). Complete blood counts were performed using an automated haematology analyser Mindray BC-5000 (Mindray Biomedical Electronics Co., China).

Urine samples were primarily obtained by cystocentesis (22G needle, 5-10 ml syringe) under aseptic conditions. When cystocentesis was not feasible, free-catch collection was employed. Urine specific gravity was measured using a veterinary refractometer BRCtech (BRCtech, Poland), calibrated beforehand with distilled water; the result was calculated as the mean of three measurements. Urine sediment was evaluated within 60 minutes of collection (centrifugation for 5 minutes at approximately 400 g; microscopy at $\times 100$ and $\times 400$ magnification).

To assess the body condition of the cats, a combination of a 9-point Body Condition Score (BCS) system and a 4-point Muscle Condition Score (MCS) system was used. The BCS system, proposed by D.P. Laflamme (1997), is widely applied in clinical practice for cats. In particular, C.R. Bjornvad *et al.* (2011) confirmed its high reproducibility and correlation with objective methods for assessing adipose tissue. Muscle mass was assessed using the 4-point MCS scale validated by K.E. Michel *et al.* (2011), which demonstrated a significant correlation with dual-energy X-ray absorptiometry results and is recommended by the World Small Animal Veterinary Association (WSAVA, 2013) as a clinical tool for evaluating the degree of muscle loss.

All procedures were carried out with the utmost attention to animal welfare and stress minimisation. Manipulations were performed in a clinic certified according to the Cat Friendly Clinic standards (ISFM), which ensured a

low-stress environment. Statistical analysis of the results was performed using the STATISTICA 7.0 software package (StatSoft Inc., USA). Data were expressed as mean \pm standard deviation ($M \pm SD$). The Shapiro-Wilk test was used to assess normality of data distribution. Comparisons between groups were conducted using Student's t-test for normally distributed data or the Mann-Whitney U-test for non-parametric data. Differences were considered statistically significant at $P < 0.05$.

Results and Discussion

Throughout the study period, the clinical condition of the cats remained relatively stable. During routine examinations, appetite, water intake, and general behaviour were recorded. In most cats, appetite remained satisfactory, with no cases of prolonged anorexia. Water consumption stayed within the normal individual range, without marked polydipsia or decreased thirst. Clinical examination revealed no signs of dehydration, vomiting, or diarrhoea; mucous membranes remained pink and moist. The overall condition of the coat was assessed as satisfactory, without alopecia or visible deterioration in quality. Behaviour and activity levels showed no significant deviations from baseline observations.

Over the course of monitoring, mean systolic and diastolic blood pressure values remained within the physiological range for cats. Individual fluctuations did not exceed clinically relevant limits. Heart rate values also remained stable throughout the experiment. No statistically significant differences were observed between Groups 1 and 2, or compared with baseline measurements (Table 2).

The body weight of cats in both groups at the beginning of the study ranged from 3.4 kg to 5.0 kg. Over the six-month observation period, individual fluctuations of 50-150 g were recorded, which were not statistically significant. Body condition score (BCS) remained

stable at 4/9, and muscle condition score (MCS) at 4/4 in most animals. The dynamics of body weight in both groups are presented in Table 3. As shown by the data, the body weight of the cats remained relatively stable in both groups throughout the six-month period. Individual

variations did not exceed clinically meaningful limits and did not result in significant changes in mean values. Both BCS and MCS showed no notable dynamics, indicating that the animals maintained a stable physical condition during the observation period.

Table 2. Systolic and diastolic blood pressure and heart rate in cats of the experimental groups at different observation periods (M ± SD), (n = 7)

Observation period	Group 1			Group 2		
	Baseline	3 months	6 months	Baseline	3 months	6 months
Systolic blood pressure (mmHg)	148.1 ± 7.6	146.9 ± 3.9	145.3 ± 3.9	148.3 ± 8.4	144.7 ± 5.5	148.0 ± 2.4
Diastolic blood pressure (mmHg)	85.4 ± 4.5	82.6 ± 1.6	83.4 ± 2.5	84.0 ± 4.4	82.9 ± 2.0	82.2 ± 2.3
Heart rate (beats/min)	154.9 ± 5.9	155.0 ± 8.5	153.4 ± 5.6	155.0 ± 5.6	152.1 ± 8.3	155.1 ± 6.7

Note: data are presented as mean ± standard deviation (M ± SD)

Source: authors' own data

Table 3. Dynamics of body weight in cats (M ± SD), (n = 7)

Observation period	Group 1	Group 2
Day 1	4.10 ± 0.36	4.23 ± 0.53
3 months	4.06 ± 0.30	4.22 ± 0.55
6 months	4.10 ± 0.29	4.23 ± 0.57

Note: data are presented as mean ± standard deviation (M ± SD)

Source: authors' own data

Evaluation of azotaemic markers (creatinine, urea, and symmetric dimethylarginine) demonstrated relative stability of the parameters throughout the study period. No statistically significant differences were observed between the groups. As shown in the data (Table 4), the mean serum creatinine concentrations in cats of both groups at the beginning of the experiment

were within the reference range. During the course of the study, a slight decrease in serum creatinine levels was noted in cats at the third month, which was likely associated with adaptation of the animals to the study conditions and stabilisation of dietary intake. By the sixth month, creatinine levels remained largely unchanged compared with baseline values.

Table 4. Dynamics of azotaemic markers in cats (M ± SD), (n = 7)

Parameter	Group 1			Group 2		
	Baseline	3 months	6 months	Baseline	3 months	6 months
Creatinine (µmol/L)	192.58 ± 7.62	180.03 ± 9.52	185.55 ± 10.84	186.6 ± 12.5	178.0 ± 8.0	182.4 ± 7.6
Symmetric dimethylarginine (mg/dL)	20.00 ± 0.47	19.50 ± 0.66	19.33 ± 1.02	19.90 ± 1.22	19.38 ± 1.38	20.13 ± 1.25
Urea (mg/dL)	14.17 ± 1.49	11.98 ± 1.57	11.65 ± 1.33	11.48 ± 1.72	10.68 ± 1.38	10.84 ± 1.11
Total calcium (mmol/L)	2.48 ± 0.02	2.56 ± 0.02	2.53 ± 0.02	2.38 ± 0.07	2.41 ± 0.05	2.59 ± 0.12

Note: data are presented as mean ± standard deviation (M ± SD)

Source: authors' own data

Serum urea concentrations decreased in cats of both groups during the first three months of the study and then stabilised. This may reflect a reduced influence of dietary factors (specifically protein content) on azotaemic parameters. Levels of symmetric dimethylarginine (SDMA), considered a more sensitive marker of decreased glomerular filtration rate, remained within physiological limits and showed no significant differences over the observation periods. Minor individual variations within ± 1 mg/dL were not statistically significant.

In addition to azotaemic markers, indices of mineral and electrolyte metabolism – key components in the pathogenesis of CKD – were analysed to assess the potential dietary influence

on the cats' metabolic status. As shown in Table 5, serum levels of calcium (total and ionised), phosphorus, sodium, potassium, and chloride remained within physiological ranges for the species throughout the observation period. The most pronounced changes during the study were observed in calcium-phosphorus metabolism indicators. In Group 1 cats, serum total calcium levels gradually increased and by the end of the experiment were elevated by approximately 15% compared with baseline values. In some cats, these changes exceeded physiological limits, corresponding to a state of hypercalcaemia. In contrast, in Group 2 cats, calcium levels remained stable, fluctuating within $\pm 1\%$ – a variation without clinical significance.

Table 5. Dynamics of calcium–phosphorus and electrolyte metabolism indicators in cats ($M \pm SD$), ($n=7$)

Parameter	Group 1			Group 2		
	Baseline	3 months	6 months	Baseline	3 months	6 months
Total calcium (mmol/L)	2.48 \pm 0.02	2.56 \pm 0.05	2.86 \pm 0.07	2.38 \pm 0.07	2.41 \pm 0.05	2.40 \pm 0.12
Ionised calcium (mmol/L)	1.30 \pm 0.02	1.35 \pm 0.06	1.43 \pm 0.07	1.26 \pm 0.05	1.28 \pm 0.05	1.27 \pm 0.08
Phosphorus (mmol/L)	1.31 \pm 0.08	1.32 \pm 0.06	1.29 \pm 0.06	1.30 \pm 0.20	1.26 \pm 0.14	1.28 \pm 0.12
Potassium (mmol/L)	4.1 \pm 0.22	4.00 \pm 0.28	4.11 \pm 0.24	3.80 \pm 0.24	3.90 \pm 0.28	4.00 \pm 0.32
Chloride (mmol/L)	117.0 \pm 4.2	115.0 \pm 4.2	116.0 \pm 4.3	117.0 \pm 4.1	115.0 \pm 3.8	117.0 \pm 3.7
Sodium (mmol/L)	155.0 \pm 3.3	156.0 \pm 2.8	15.0 \pm 3.2	156.0 \pm 4.0	157.0 \pm 3.8	155.0 \pm 3.2

Note: data are presented as mean \pm standard deviation ($M \pm SD$)

Source: authors' own data

Ionised calcium, representing the biologically active fraction, increased by almost 10% in the serum of cats in Group 1, whereas only minimal fluctuations (not exceeding 2%) were observed in Group 2. This indicated a tendency toward activation of calcium metabolism specifically in the experimental group. Serum phosphorus concentrations in cats of both groups remained within a range close to physiological values (1.26-1.32 mmol/L), without indications of hyperphosphataemia. The Ca:P ratio remained stable, showing no signs of imbalance, which suggested preservation of

mineral homeostasis. Serum potassium concentrations in both experimental groups did not increase and remained within reference limits. Sodium and chloride levels in the serum of cats fluctuated within a narrow range, with deviations not exceeding 2-3%, indicating no evidence of hypo- or hypernatraemia or chloreaemia. Overall, analysis of mineral and electrolyte parameters in the cats revealed no statistically significant changes during the six-month observation period and no differences between the groups. These findings indicate the absence of any disturbances in calcium-phosphorus

or electrolyte homeostasis in the cats over the course of the study.

Urine analysis in cats included assessment of the UPC and urine specific gravity (USG). Throughout the observation period, UPC values in both groups remained within physiological limits (< 0.2), with no evidence of proteinuria. Individual fluctuations did not exceed clinically relevant ranges and showed no trend toward progressive increase. Urine specific gravity ranged from 1.030 to 1.050, reflecting normal renal concentrating ability, and no signs of isosthenuria were detected. No statistically significant differences between experimental groups were found for these parameters. Thus, the results of urine analysis confirmed the stability of renal functional status and the absence of any adverse dietary effects during the study period.

Throughout the six-month observation period, the clinical condition of the cats remained stable: appetite, water intake, behaviour, and coat appearance showed no notable changes. Blood pressure and heart rate were within physiological ranges, with no signs of arterial hypertension or hypotension. Body weight, body condition score (BCS), and muscle condition score (MCS) remained stable, indicating preservation of overall somatic status.

Analysis of azotaemic markers (creatinine, urea, and SDMA) in the serum of cats from both experimental groups confirmed the absence of progressive renal dysfunction. Serum sodium, potassium, and chloride levels remained within physiological limits, showing no evidence of electrolyte imbalance. Urinalysis parameters also demonstrated no significant changes: the urine protein-to-creatinine ratio remained below the threshold for proteinuria, and urine specific gravity values indicated preserved renal concentrating ability.

Based on the obtained results, it was established that lower calcium-to-phosphorus (Ca:P) ratios were associated with a tendency

toward stabilisation of calcium metabolism, whereas cats in the group with higher Ca:P ratios more frequently exhibited hypercalcaemia, including that of the ionised fraction. Similar observations were reported by M.R. Ehrlich *et al.* (2024), who described normalisation of serum calcium levels in cats with CKD following a dietary transition to lower Ca:P ratios. Conversely, J. Stockman (2024) noted that excessive restriction of dietary phosphorus, leading to elevated Ca:P ratios, may provoke the development of hypercalcaemia even at early stages of the disease. The findings of the present study are consistent with these observations and indicate that controlling the Ca:P ratio is a critical factor in the management of feline CKD.

The observed tendencies can be explained in terms of calcium-phosphate complex supersaturation. Exceeding the solubility product of $\text{Ca} \times \text{P}$ increases the risk of calcium deposition in renal and extra-renal tissues. As highlighted by J.A. Hokamp & M.B. Nabity (2016), this mechanism underlies nephrocalcinosis and vascular calcification in chronic kidney disease. In the present study, cats with higher Ca:P ratios exhibited more pronounced alterations in calcium balance, which may reflect a latent increase in the risk of calcification.

From a pathophysiological perspective, a higher calcium-to-phosphorus (Ca:P) ratio may enhance intestinal calcium absorption, which is particularly relevant in patients with CKD, where the regulatory mechanisms of this process are already impaired. In healthy animals, compensatory mechanisms involving parathyroid hormone (PTH) and fibroblast growth factor 23 can partially maintain calcium levels within the normal range; however, in CKD, their effectiveness is reduced. This creates a predisposition to the development of hypercalcaemia even in response to relatively minor dietary fluctuations, which may explain why serum calcium levels in some experimental cats exceeded

physiological limits, whereas in others they remained stable. Thus, the absence of progressive hyperphosphataemia in the experimental cats indicates the effectiveness of the applied dietary therapy and may contribute to slowing the development of complications.

Particular attention should be given to FGF-23, which is considered an early biomarker of phosphorus imbalance. Although it was not measured in the present study, published data suggest that an increase in FGF-23 levels may precede the marked changes observed in the experimental animals. Therefore, even with stable serum phosphorus concentrations in the cats, subtle shifts in phosphorus homeostasis mediated by FGF-23 cannot be excluded.

An additional factor may be the variability of individual physiological responses among animals, whereby hypercalcaemia resolves in some cats following the transition to a diet with a lower calcium-to-phosphorus (Ca:P) ratio, while others show only a partial or absent response. This finding indicates the multifactorial nature of the processes involved. In particular, individual variations in vitamin D metabolism, differences in sensitivity to FGF-23, and the baseline condition of renal tissue – determining the organism's adaptive capacity – may all play contributory roles.

The stability of the clinical condition observed in the present study aligns with the findings of D.P. Machado *et al.* (2022), who confirmed that dietary modifications can slow the progression of CKD. The absence of proteinuria is consistent with the observations of M.A. Fidalgo *et al.* (2022), who emphasised the prognostic value of the urine protein-to-creatinine ratio in cats with CKD. Similarly, V. Pedrinelli *et al.* (2020) noted that survival in affected animals depends not only on disease stage but also on dietary composition, particularly protein content and the calcium-to-phosphorus ratio.

Particular attention should be paid to the selection of phosphate binders. R.F. Geddes *et al.* (2021) reported that calcium-containing preparations effectively reduce serum phosphate concentrations but may simultaneously increase the Ca:P ratio and promote hypercalcaemia. As an alternative, V.J. Parker (2021) recommended the use of non-calcium-based binders such as sevelamer and lanthanum carbonate. According to the results obtained in the present study, it was confirmed that excessive restriction of dietary phosphorus in combination with a high Ca:P ratio should be avoided, particularly in animals at increased risk of tissue calcification.

Thus, even with comparable dietary calcium and vitamin D levels, it is the magnitude of the Ca:P ratio that determines the direction of changes in calcium balance. Lower Ca:P ratios were associated with more stable calcium levels, whereas higher ratios increased the risk of ionised hypercalcaemia. These findings confirm the clinical importance of monitoring the Ca:P ratio in the dietary management of cats with CKD. In light of the obtained data, it is advisable to integrate Ca:P ratio monitoring into the standard follow-up protocol for feline CKD. At the onset of dietary therapy, attention should be given to maintaining values near the lower limit of the FEDIAF (2024) recommended range. Measurement of total and ionised calcium, phosphorus, and calculation of the Ca × P product should be performed after 2-4 weeks of diet initiation and subsequently every 8-12 weeks, in accordance with the recommendations of the International Renal Interest Society (2023).

In cases where ionised calcium levels increase despite “normal” serum phosphorus concentrations, it is advisable to review the dietary formulation by reducing the calcium-to-phosphorus (Ca:P) ratio and, where appropriate, to prioritise the use of non-calcium-based phosphate binders. Concurrent monitoring of the

UPC and USG should be performed as indicators of glomerular and tubulointerstitial injury, alongside regular blood pressure assessment to minimise the risk of extra-renal complications. It is also essential to account for potential pre-analytical variability in ionised calcium measurement – particularly the influence of sample pH – and to maintain stable conditions for collection and transport in order to avoid misinterpretation of results.

When evaluating the effectiveness of dietary therapy, simultaneous monitoring of UPC, USG, and arterial pressure provides valuable information regarding renal function and systemic stability. Particular attention should be paid to the accuracy of ionised calcium measurement, given its sensitivity to pH changes, which necessitates standardised sampling and handling procedures. In cats predisposed to hypercalcaemia, a temporary and moderate relaxation of dietary phosphorus restriction may be appropriate, provided that the Ca:P ratio remains within controlled limits. This approach can help to stabilise calcium-phosphorus balance and minimise the risk of calcification.

Conclusions

In this six-month clinical study involving cats with chronic kidney disease, comprehensive dietary management contributed to the stabilisation of the animals' clinical condition. Throughout the observation period, appetite, behaviour, hydration status, and cardiovascular parameters remained within physiological limits. Body weight, body condition score, and muscle condition score demonstrated nutritional stability. Azotaemic markers – creatinine, urea, and symmetric dimethylarginine – showed no statistically significant changes, confirming the absence of CKD progression in most animals under appropriate dietary support.

The most pronounced differences were observed in calcium-phosphorus metabolism. Cats receiving a diet with a higher calci-

um-to-phosphorus (Ca:P) ratio (1.71) exhibited an increase in total calcium from 2.48 ± 0.02 to 2.86 ± 0.07 mmol/L (+ 15%) and ionised calcium from 1.30 ± 0.02 to 1.43 ± 0.07 mmol/L (+ 10%), corresponding to hypercalcaemia in some individuals. Conversely, in cats fed a diet with a lower Ca:P ratio (1.33), calcium concentrations remained stable (2.38-2.40 mmol/L for total calcium and 1.26-1.27 mmol/L for ionised calcium) without clinically significant deviations. These findings indicate that even with identical dietary calcium content, the Ca:P ratio may be a decisive factor influencing the risk of hypercalcaemia in cats with CKD. The results support the necessity not only of dietary phosphorus restriction – a key element of CKD therapy – but also of optimising the Ca:P ratio in therapeutic diets. The balance between these macrominerals affects the progression of mineral metabolism disorders associated with CKD and thus influences long-term outcomes.

The main limitations of this study were the small sample size ($n = 14$) and the relatively short observation period (six months). The study duration was chosen for ethical reasons, as prolongation could have increased the risk of clinically significant hypercalcaemia in cats receiving the higher Ca:P diet. Nonetheless, these factors may have limited the ability to detect longer-term dietary effects. Despite these limitations, the findings demonstrate that the Ca:P ratio – even with equivalent calcium content and comparable vitamin D levels – can influence calcium homeostasis and has clinical significance in dietary formulation for cats with CKD.

Future research should aim to establish optimal target Ca:P ranges for different CKD stages and to standardise the monitoring of mineral metabolism biomarkers. Incorporation of FGF-23 as a biomarker for personalised dietary management appears promising, as its monitoring could help detect subclinical phosphorus imbalance before the onset of overt hyperphosphataemia,

thereby improving precision in Ca:P correction and reducing the risk of tissue calcification.

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Conflict of Interest

None.

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Нутріціологічний вплив на мінеральний обмін у котів за хронічної хвороби нирок

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Анотація. Актуальність дослідження зумовлена значною поширеністю порушень мінерального обміну в котів із хронічною хворобою нирок, що супроводжуються розвитком гіперкальціємії та гіперфосфатемії й суттєво впливають на прогноз і якість життя тварин. У зв'язку з цим, мета дослідження була спрямована на оцінку впливу різного співвідношення кальцію до фосфору в раціоні на показники кальцієво-фосфорного гомеостазу та загальний стан котів із хронічною хворобою нирок другої стадії. Провідним методом дослідження слугувала порівняльна оцінка клінічних і біохімічних показників у тварин, залежно від типу дієти, що дозволило комплексно визначити зміни мінерального обміну. У дослідженні використано 14 котів, яких поділено на дві групи. Тварини групи 1 отримували корм із вищим співвідношенням кальцію до фосфору (1,71) та обмеженим вмістом фосфору, тоді як котів групи 2, отримували дієту з помірним співвідношенням кальцію до фосфору (1,33). Впродовж шести місяців контролювали біохімічні показники крові: рівень загального та іонізованого кальцію, фосфору, креатиніну, сечовини та симетричного диметиларгініну. Додатково оцінювали у котів клінічний стан, масу тіла, м'язову кондицію, вгодованість та артеріальний тиск, які залишалися стабільними у тварин в обох дослідних групах. Встановлено, що у котів групи 1 відзначалося підвищення рівня кальцію, а у котів групи 2 сформувалася іонізована гіперкальціємія. У котів групи 2 рівень кальцію залишався стабільним, без ознак гіперфосфатемії. Показники азотемічних маркерів істотно не відрізнялися між групами котів. За отриманими результатами встановлено, що надмірне обмеження фосфору з формуванням високого співвідношення кальцію до фосфору не забезпечило додаткових переваг у контролі фосфатемії, але підвищувало ризик порушень кальцієвого обміну. Матеріал статті становить практичну цінність для ветеринарних лікарів-клініцистів, оскільки експериментально підтверджено доцільність використання дієт із помірним співвідношенням кальцію та фосфору на ранніх стадіях хронічної хвороби нирок у котів

Ключові слова: дієтичний вплив; порушення метаболізму; вторинний гіперпаратиреоз; фосфат-біндери; кальцієвий гомеостаз; нефрокальциноз; ниркова дієта