Nutritional Management of Chronic Kidney Disease in Cats: Beyond Dietary Therapy

Susan Little, DVM, DABVP (Feline)

Content presented at the 2017 Hill's Global Symposium in Washington D.C., May 5 - 6, 2017.

Chronic kidney disease (CKD) is the most common renal disease in the cat. The prevalence of CKD seems to be increasing over time; estimates are that it affects about one third of cats over 15 years of age.[1] It is an important cause of mortality, especially in older cats. CKD is typically a progressive disease and can be accompanied by a wide range of clinical and pathological changes. The clinical presentation is variable from patient to patient.

The International Renal Interest Society (IRIS) has published guidelines for clinical staging and treatment targets for both canine and feline kidney disease (http://www.iris-kidney.com). Also, the International Society of Feline Medicine (ISFM) published Consensus Guidelines on the Diagnosis and Management of Feline Chronic Kidney Disease in 2016 (http://jfm.sagepub.com/site/Guidelines/Guidelines.xhtml).

The goals of CKD therapy are to:

- Minimize clinical signs of uremia
- Minimize disturbances of electrolytes, vitamins and minerals
- Provide adequate nutrition and hydration
- Improve quality of life (QOL), especially in IRIS stages 3 and 4
- Modify disease progression

The reader is referred to these documents for a complete discussion of CKD diagnosis and management.

Whenever possible, potential therapies should be evaluated, considering a specific treatment goal and based on available evidence. In some patients, multiple treatments may be indicated, but administration of multiple therapies must be balanced with QOL; prioritizing therapies most likely to benefit each patient is important. The clinician should always consider the possibility that a cat with CKD has another disease, as concurrent diseases are common in older patients (e.g., arthritis, hyperthyroidism, gastrointestinal disease). Diseases causing pain (e.g., musculoskeletal disease, oral disease) can contribute to poor appetite and body condition in cats with CKD.

Nutrient Restriction

Renal therapeutic diets are restricted in protein, phosphorus and sodium compared to maintenance diets. They may be increased in caloric density, are alkalinizing and have added potassium, B vitamins, antioxidants, and omega-3 fatty acids. In short, they bring many potential benefits to CKD patients. Studies have evaluated the effect of renal therapeutic diets on improving longevity and reducing clinical signs of uremia with good quality of evidence for a beneficial effect (see *Best Bets for Vets* evidence-based medicine review: https://bestbetsforvets.org/bet/146).[2-6]

In addition to dietary therapy, key management strategies

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to improve food intake and body condition include:

1 **Managing hydration:** Cats with CKD are predisposed to dehydration, especially in IRIS stages 3 and 4. Studies confirming the clinical impact of maintaining hydration are lacking, but it is considered a critical part of management. Maintaining hydration may help maintain QOL, address electrolyte and acid-base disturbances, and preserve renal blood flow by preventing dehydration (and potentially affecting disease progression). Unstable or decompensated cats with CKD may require hospitalization and intravenous (IV) fluid therapy, along with management of electrolyte and acid-base disturbances. Owners should also be educated about long-term management of hydration, including increasing voluntary water intake and home subcutaneous (SC) fluid therapy (up to 150 mL every 1-3 days). Fluid choices include balanced electrolyte solutions or 0.45% saline. Potassium chloride can be added if needed to treat hypokalemia.

2 **Managing serum phosphorus and calcium:** IRIS has established target serum phosphorus concentrations that should be reviewed. Maintaining serum phosphorus within the suggested targets may be accomplished in many cats with the use of a renal therapeutic diet. However, as disease progresses, some cats will require both a renal therapeutic diet and an oral phosphate binder. Also, some patients may be unable to eat a renal therapeutic diet for various reasons and may need earlier use of oral phosphate binders. Commonly used oral phosphate binders include aluminum hydroxide and calcium carbonate (initial daily dose for both is 90 mg/kg). The daily dose is always split into multiple administrations given in food or at the time of eating. Hyperphosphatemia can be associated with active vitamin D deficiency but supplementation with calcitriol is not well studied in cats. A single published study has failed to show a benefit.[7] Cats receiving calcium-containing phosphate binders should have serum ionized calcium monitored, as moderate to severe hypercalcemia is a potential cause of renal injury.

3 **Managing serum potassium:** Cats with CKD can become hypokalemic through various mechanisms. Hypokalemia is associated with lethargy, poor appetite, constipation, and muscle weakness but has not specifically been associated with effects on longevity or disease progression in CKD patients. Serum potassium should be routinely monitored and supplementation implemented when the concentration is less than 3.5 mmol/L. Renal therapeutic diets are supplemented with potassium but some cats may need additional oral supplementation with potassium gluconate or citrate (starting dose 1-4 mmol [mEq]/cat, every 12 hours). Some clinicians prefer to start supplementation earlier, when serum potassium is less than 4.0 mmol/L.

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4 **Managing blood pressure:** Systemic hypertension occurs in many cats with CKD so routine monitoring of systolic blood pressure (SBP) is indicated. The potential for target organ (eyes, heart, cerebrovascular tissue, kidney) damage from hypertension has been well established. In addition, hypertension has been associated with proteinuria in cats (see below). Doppler and high-definition oscillometric devices are the most commonly recommended for cats. Measuring SBP in cats can be challenging – Guidelines for the Identification, Evaluation, and Management of Systemic Hypertension in Dogs and Cats have been published and should be consulted (http://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2007.tb03005.x/pdf). Practical step by step instructions for measuring SBP in cats, along with a blood pressure assessment form, are available from ISFM (https://icatcare.org/vets/guidelines/hypertension-cats). Drug therapy is indicated in patients with hypertension with the goal of maintaining SBP below 150-160 mmHg. Amlodipine (0.625-1.25 mg/cat, PO, every 12-24 hours) is currently the monotherapy drug of choice; monotherapy with ACE inhibitors or atenolol is not effective in most hypertensive cats.

5 Managing proteinuria: An increasing degree of proteinuria is associated with reduced longevity in cats so CKD patients should be routinely assessed for proteinuria.[8] Urine protein:creatinine ratio (UPC) is the recommended test. Drug therapy is indicated for cats that are persistently proteinuric without evidence for another cause (such as infection). The American College of Veterinary Internal Medicine proteinuria guidelines (http://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2005.tb02713.x/pdf) should be reviewed and suggest treatment when the UPC is greater than 0.4. However, some clinicians recommend therapy when the UPC is greater than 0.2 as cats with UPC less than 0.2 have better survival times than cats with higher values. Commonly used drugs include telmisartan (1 mg/kg, PO, every 24 hours) and benazepril (0.25-0.5 mg/kg, PO, every 12 hours) along with a renal therapeutic diet (see Best Bets for Vets review: https://bestbetsforvets.org/bet/389). Patients on drug therapy should be monitored for adverse effects (e.g., worsening azotemia, hypotension) although they are uncommon in cats.

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6 Managing anemia: A non- or poorly regenerative anemia associated with a relative lack of erythropoietin may be seen in some cats with CKD. In addition to the impact on QOL, anemia is an independent risk factor for progression of CKD.[9-12] Treatment of anemia may therefore improve QOL and survival.[13] Darbopoietin (1 µg/kg, SC, weekly until PCV >25%, then 1 µg/kg, SC, every 2-3 weeks based on PCV) appears less likely to induce anti-red blood cell antibodies in cats than erythropoietin.[14] Therapy is started when the PCV is persistently less than 20% and the target for treatment is maintaining the PCV at 25% or higher. Concomitant iron therapy is recommended with injectable iron dextran (50 mg/cat, IM, monthly as needed). Frequent monitoring of PCV, reticulocyte count, and SBP is required, especially in the initial phase of treatment.

7 Managing urinary tract infections: CKD predisposes cats to urinary tract infection (UTI), especially older female cats. Many infections are subclinical although changes may be evident on urinalysis. The most common isolate is *Escherichia coli.* The significance of subclinical UTI is unknown, so routine monitoring of urine cultures is controversial. Cats with clinical signs of UTI and/or pyuria (>5 white blood cells/hpf) should have a urine culture performed to guide therapy. Treatment guidelines for UTI published by the International Society for Companion Animal Infectious Diseases (http://www.hindawi.com/journals/vmi/2011/263768/) should be consulted. Therapy can be started with amoxicillin (11-15 mg/kg, PO, every 8 hours) while results of urine culture and sensitivity are pending.

8 Managing other clinical signs: Cats with CKD may have nausea, vomiting, and inappetence because of uremic toxins affecting the central chemoreceptor trigger zone. Owners identify poor appetite as an important QOL concern; it could also result in protein and calorie malnutrition. A reduction in appetite should be actively investigated and treated; nausea should always be considered as a possible cause even if the cat is not vomiting. Maropitant (1 mg/kg, PO, every 24 hours) has been shown to reduce vomiting[15] and mirtazapine (1.88 mg/cat, PO, every 48 hours) has been shown to reduce vomiting, increase appetite and promote weight gain.[16] Other effective anti-emetic drugs include ondansetron (0.5-1 mg/kg, IV, SC or PO, every 8 hours) and dolasetron (0.6-1 mg/kg, IV, SC or PO, every 24 hours).[17] While hyperacidity may occur in some cats with CKD, gastric ulceration is typically not found. Instead, gastric mineralization and fibrosis are the most significant lesions.[18] If therapy for hyperacidity is considered, omeprazole (1 mg/kg, PO, every 12 hours) is superior to famotidine.[19,20] Cats that are not achieving adequate food intake with drug therapy may benefit from placement of an esophagostomy feeding tube to maintain hydration, administer drugs and provide nutrition.

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Summary

For each CKD patient, the IRIS stage should be established and an individual treatment plan should be developed, considering what is most appropriate for each patient and owner. The options should be prioritized based on the cat's medical needs and the owner's preferences and abilities. The plan should be reviewed with the owners and their commitment confirmed. A reassessment and monitoring schedule should be established to assess the patient's response, make any necessary changes to the treatment plan, ensure the owner understands the treatments and uncover compliance issues.

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