Evidence-Based Management of Chronic Kidney Disease in Cats

AAFP 2016

Susan Little, DVM, DABVP (Feline)

Introduction

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 all 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. However, 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 (www.iris-kidney.com (http://www.iris-kidney.com)). As well, the International Society of Feline Medicine published *Consensus Guidelines on the Diagnosis and Management of Feline Chronic Kidney Disease* in 2016 (http://jfm.sagepub.com/site/Guidelines/Guidelines.xhtml (http://jfm.sagepub.com/site/Guidelines/Guidelines.xhtml)). The reader is referred to these documents for a complete discussion of CKD diagnosis and management.

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 (IRIS stages 2 and 3)

Wherever possible, potential therapies should be evaluated in light of 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.

Key management strategies for cats with CKD 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 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 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 as needed.
2. **Managing diet**: 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 reduction of 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 (https://bestbetsforvets.org/bet/146)).[2-5] Moderate protein restriction is recommended to avoid loss of lean body mass. Evidence that protein restriction alone slows progression of CKD is lacking; however, phosphorus restriction is thought to be the most important factor. Renal therapeutic diets should be considered for cats in IRIS stages 2–4, but the overall nutritional needs of the cat must also be considered as other disease processes may be present. A wide range of renal therapeutic diets is now available, each with different levels of protein restriction, so that diet recommendations can be tailored to the patient's needs. Even some 'senior' cat diets may be appropriate for cats with early CKD, although the nutrient profile must be evaluated before making a recommendation.

3. **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. As well, some patients may be unable to eat a renal therapeutic diet and may need earlier use of oral phosphate binders. Commonly used oral phosphate binders include aluminum hydroxide and calcium carbonate. The daily dose is always split into multiple administrations given with 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.[6] Cats receiving calcium-containing phosphate binders should have serum ionized calcium monitored as moderate to severe hypercalcemia is a potential cause of renal injury.
4. **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 [mEq]/L.
5. **Managing blood pressure**: Systemic hypertension can be seen in 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 (http://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2007.tb03005.x/pdf)). Drug therapy is indicated in patients with hypertension with the goal of maintaining SBP below 150–160 mm Hg. Amlodipine is currently the monotherapy drug of choice; monotherapy with ACE inhibitors or atenolol is not effective in most hypertensive cats. Telmisartan is a new drug in veterinary medicine that is showing promise as an antihypertensive.

< 4Kg 1/4 2.5mg SID
> 4Kg 1/2 2.5mg SID

6. **Managing proteinuria**: An increasing degree of proteinuria is associated with reduced longevity in cats, so CKD patients should be routinely assessed for proteinuria.[7] 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 (http://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2005.tb02713.x/pdf)) should be reviewed and suggest treatment when the UPC is >0.4. However, some clinicians recommend drug therapy when the UPC is >0.2, as cats with UPC <0.2 have better survival times than cats with higher values. Commonly used drugs include benazepril and telmisartan along with a renal therapeutic diet (see Best Bets for Vets review: https://bestbetsforvets.org/bet/389 (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.

0.5 mg/kg - 1.0 mg/kg SID TO BID

7. **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.[8-11] Treatment of anemia may therefore improve QOL and survival.[12] Darbepoetin (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.[13] Therapy is started when the PCV is persistently <20% and the target for treatment is maintaining the PCV at ≥25%. Concomitant iron therapy is recommended with injectable iron dextran (50 mg/cat monthly as needed). Frequent monitoring of PCV, reticulocyte count, and SBP is required, especially in the initial phase of treatment.
8. **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 (www.hindawi.com/journals/vmi/2011/263768/ (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.
9. **Managing clinical signs**: Cats with CKD may have nausea, vomiting, and inappetance as a result 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 (2 mg/kg PO every 24 hours) has been shown to reduce vomiting[14] and mirtazapine (1.88 mg/cat PO every 48 hours) has been shown to reduce vomiting and increase appetite and weight gain;[15] these drugs are preferred over H_2 blockers such as famotidine. Cats that are not responding to drug therapy may benefit from placement of an esophagostomy feeding tube to maintain hydration, administer drugs, and provide nutrition.

Summary

For each CKD patient, establish the IRIS stage and develop an individual treatment plan, taking into account what is most appropriate for each patient and owner. Prioritize the options based on the cat's medical needs and the owner's preferences and abilities. Review the plan with the

owner and confirm commitment. Establish a reassessment and monitoring schedule to assess the patient's response, make any necessary changes to the treatment plan, ensure the owner understands the treatments, and uncover compliance issues.

References

1. Reynolds BS, Lefebvre HP. Feline CKD: pathophysiology and risk factors - what do we know? *J Feline Med Surg*. 2013;15(1 Suppl):3–14.
2. Plantinga EA, Everts H, Kastelein AM, *et al*. Retrospective study of the survival of cats with acquired chronic renal insufficiency offered different commercial diets. *Vet Rec*. 2005;157:185–187.
3. Elliott J, Rawlings JM, Markwell PJ, *et al*. Survival of cats with naturally occurring chronic renal failure: effect of dietary management. *J Small Anim Pract*. 2000;41:235–242.
4. Ross SJ, Osborne CA, Kirk CA, *et al*. Clinical evaluation of dietary modification for treatment of spontaneous chronic kidney disease in cats. *J Am Vet Med Assoc*. 2006;229:949–957.
5. Harte JG, Markwell PJ, Moraillon RM, *et al*. Dietary management of naturally occurring chronic renal failure in cats. *J Nutr*. 1994;124:2660S–2662S.
6. Hostutler RA, DiBartola SP, Chew DJ, *et al*. Comparison of the effects of daily and intermittent dose calcitriol on serum parathyroid hormone and ionized calcium concentrations in normal cats and cats with chronic renal failure. *J Vet Intern* Med. 2006; 20:1307–1313.
7. Syme HM, Markwell PJ, Pfeiffer D, *et al*. Survival of cats with naturally occurring chronic renal failure is related to severity of proteinuria. *J Vet Intern Med*. 2006;20:528–535.
8. King JN, Tasker S, Gunn-Moore DA, *et al*. Prognostic factors in cats with chronic kidney disease. *J Vet Intern Med*. 2007;21:906–916.
9. Geddes RF, Elliott J, Syme HM. Relationship between plasma fibroblast growth factor-23 concentration and survival time in cats with chronic kidney disease. *J Vet Intern Med*. 2015;29:1494–1501.
10. Chakrabarti S, Syme HM, Elliott J. Clinicopathological variables predicting progression of azotemia in cats with chronic kidney disease. *J Vet Intern Med*. 2012; 26:275–281.
11. Kuwahara Y, Ohba Y, Kitoh K, *et al*. Association of laboratory data and death within one month in cats with chronic renal failure. *J Small Anim Pract*. 2006;47:446–450.
12. Chalhoub S, Langston C, Eatroff A. Anemia of renal disease: what it is, what to do and what's new. *J Feline Med Surg*. 2011;13:629–640.
13. Chalhoub S, Langston CE, Farrelly J. The use of darbepoetin to stimulate erythropoiesis in anemia of chronic kidney disease in cats: 25 cases. *J Vet Intern Med*. 2012;26:363–369.
14. Quimby JM, Brock WT, Moses K, *et al*. Chronic use of maropitant for the management of vomiting and inappetence in cats with chronic kidney disease: a blinded, placebo-controlled clinical trial. *J Feline Med Surg*. 2015;17:692–697.
15. Quimby JM, Lunn KF. Mirtazapine as an appetite stimulant and anti-emetic in cats with chronic kidney disease: a masked placebo-controlled crossover clinical trial. *Vet J*. 2013;197:651–655.

Speaker Information

(click the speaker's name to view other papers and abstracts submitted by this speaker)

Susan Little, DVM, DABVP (Feline) (/members/cms/project/defaultadv1.aspx?pId=20095&authorId=72294)

URL: https://www.vin.com/doc/?id=8292264 (https://www.vin.com/doc/?id=8292264)