

Filtering the Facts of Chronic Kidney Disease

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Chronic kidney disease (CKD) is a common feline disease. Its prevalence will vary between populations, but a large UK study estimated that the prevalence of feline renal disease in first opinion practices was ~4% (CKD was the seventh most common specific diagnosis made). CKD is more common in older cats, and may affect ≥30–40% of cats over 10 years of age. Renal disease was the most common cause of mortality in cats ≥5 years of age in a UK study, being the cause of death of >13% of cats at a median age of 15 years.

The underlying etiology of CKD often remains obscure. Most cats investigated have chronic tubulointerstitial nephritis and renal fibrosis on histology and variety of potential underlying etiologies may include toxic insults, hypoxia, chronic glomerulonephritis, chronic pyelonephritis, upper urinary tract obstructions, and potentially viral infections involving retroviruses as well as a recently recognized morbillivirus. Other specific causes of CKD sometimes recognized include amyloidosis, polycystic kidney disease, renal lymphoma, hypercalcemic nephropathy and congenital disorders – some of these have breed associations.

Historical and clinical findings suggestive of CKD, such as weight loss, altered kidney size, unexplained dehydration, PU/PD, systemic hypertension or an unexplained low USG (<1.035–1.040), also justify further investigation. In clinical practice feline CKD is often diagnosed on the basis of:

- An increased serum creatinine concentration >140 µmol/l (>1.6 mg/dl); together with
- An inappropriately low USG (<1.035); and
- Evidence that these changes are sustained (over several weeks or months) or with a history suggesting sustained clinical signs consistent with CKD.

Where CKD is suspected, a minimum routine database should ideally include:

- Full history and physical examination;
- Routine urinalysis (to include USG, ‘dipstick’ analysis, urine sediment analysis, urine protein:creatinine ratio [UPCR], and culture where indicated);
- Routine serum biochemistry, to include a minimum of proteins, urea, creatinine, electrolytes (Na⁺, K⁺, Ca²⁺, Cl⁻, PO₄⁻), and other analytes (eg, thyroxine in an older cat) as relevant;
- Routine hematology;
- Systolic blood pressure (SBP);
- Diagnostic imaging (renal ultrasonography is generally more valuable than radiography);
- In some situations (eg, unexplained renomegaly) a kidney biopsy or fine-needle aspiration may be desirable.

IRIS staging in cats (International Renal Interest Society) classifies chronic kidney disease (CKD) into four stages (I–IV) based on blood creatinine/SDMA levels. Cats are further classified by Proteinuria (UPC ratio: <0.2 nonproteinuric; 0.2–0.4 borderline; >0.4 proteinuric) and Blood Pressure (Normotensive <140mmHg; Prehypertensive 140–159mmHg; Hypertensive 160–179mmHg; Severely Hypertensive ≥180mmHg).

IRIS Staging of Feline CKD:

Stage	Creatinine	SDMA
I	<140 µmol/l / <1.6 mg/dl	<18 µg/dl
II	140 – 250 µmol/l / 1.6 – 2.8 mg/dl	18 – 25 µg/dl
III	251 – 440 µmol/l / 2.9 – 5.0 mg/dl	26 – 38 µg/dl
IV	>440 µmol/l / >5.0 mg/dl	>38 µg/dl

Management of CKD is largely focused on supportive and symptomatic therapy with the aim of improving the quality of life (QoL) of affected cats (especially those in CKD stages 3 and 4) and, where possible, slowing the progression of disease (especially in CKD stages 2 and 3).

Long-term maintenance of hydration

- **Voluntary water intake:** Free access to good quality water should be provided at all times.
- **Use of feeding tubes** Water can also be administered via a feeding tube, and this may be preferable to subcutaneous fluids in many cases. A feeding tube is suitable for long-term maintenance of hydration and is a more physiological approach. It also allows for nutritional support when needed.
- **Subcutaneous fluid therapy** Repeated subcutaneous fluid therapy (75–150 ml every 1–3 days) can be used on an outpatient basis or by caregivers at home to maintain hydration. This is most commonly employed in cats with advanced (stages 3 and 4) CKD, but should be considered on a case-by-case basis. Cats should be carefully monitored to ensure there is clinical benefit and to avoid overhydration.

Dietary manipulation is a mainstay of CKD therapy in veterinary patients. Renal formulated diets are restricted in both protein and phosphorus, but other features include an increased calorie density, sodium restriction, potassium supplementation, alkalinization, and supplementation with B vitamins, antioxidants and omega-3 fatty acids. Low dietary phosphate or higher calcium to phosphorus ratio could possibly lead to development of hypercalcemia in cats and this should be monitored in cats on renal diets. As CKD progresses, serum phosphate tends to increase and may become more refractory to control with dietary phosphate restriction. Where diet alone is insufficient, the use of intestinal phosphate binders is important. Feline CKD can lead to excessive kaliuresis, which may be compounded by reduced potassium intake, vomiting and transcellular shifts. Hypokalemia may cause or contribute to clinical signs such as lethargy, inappetence, constipation and muscle weakness, and may contribute to development of acidosis, but has not been identified as a risk factor for disease progression or outcome. Although renal diets are typically supplemented with potassium, hypokalemia may still be seen in some cats requiring potassium supplementation. If progressive hypokalemia is noted despite supplementation, hyperaldosteronism is a possible differential and measuring serum aldosterone should be done.

Management of hypertension is aimed at preventing TOD and calcium channel blocker amlodipine is an effective monotherapy for most cats but other drugs such as angiotensin receptor blocker telmisartan can be used as well.

Anemia of varying severity is seen in 30–65% of cats with CKD. A relative lack of erythropoietin (EPO) in CKD produces a non- or poorly-regenerative anemia, which may be exacerbated by blood loss and/or shortened red blood cell (RBC) survival. Anemia has been identified as a dependent or independent risk factor for progression of CKD and there is evidence that treatment with erythrocyte-stimulating agents or Molidustat (brand name Varenzin-CA1), a HIF prolyl-hydroxylase inhibitor may improve QoL and potentially survival in some cats with CKD.

CKD is generally associated with increased intraglomerular capillary pressure and other changes that impair glomerular permselectivity, leading to increased loss of albumin (and other proteins) into tubular fluid; this appears to directly contribute to disease progression by promoting tubular inflammation and fibrosis.

Although there may be species differences in pathophysiology, increased proteinuria in cats with CKD (assessed with UPCr and not routine dipsticks, which are inappropriate for assessment of feline proteinuria) is also known to carry a poorer prognosis and the IRIS and ACVIM guidelines suggest antiproteinuric therapy (eg. telmisartan) should be instituted in CKD cats with a UPCr >0.4.

Cats with CKD can suffer from nausea, vomiting and inappetence as a result of uremic toxins affecting the central chemoreceptor trigger zone. Inappetence is a significant QoL concern for caregivers, and in the CKD

patient could result in protein and calorie malnutrition with its many adverse consequences. A reduced appetite should therefore be actively managed, along with complications of CKD that can contribute to inappetence, such as dehydration, hypokalemia, acidosis and anemia. Centrally acting antiemetics such as maropitant, mirtazapine and ondansetron and should be considered for management. In placebo-controlled trials of cats with stage 2 or 3 CKD, maropitant (given orally for 2 weeks) was shown to reduce vomiting and mirtazapine (given orally for 3 weeks) reduced vomiting and also increased appetite and weight. Mirtazapine may therefore be a useful adjunct to the nutritional management of cats with CKD.

References:

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