

Gregory F. Grauer, DVM, MS, Diplomate ACVIM (Small Animal Internal Medicine), Kansas State University

Staging & Management of Feline Chronic Kidney Disease

P Profile

Definition

Loss of functional renal tissue (nephrons) due to a chronic (> 2 month) disease process

Systems. Renal

Genetic Implications. Medullary amyloidosis in Abyssinians and polycystic kidney disease in Persians are examples of heritable feline CKD.

Incidence/Prevalence. 1% to 3% of all cats; in geriatric populations at referral institutions, CKD may affect up to 35% of cats.

Geographic Distribution. Worldwide

Signalment

Species. Feline

Breed Predislection. See the heritable examples listed above.

Age and Range. All ages can be affected; however, most CKD is acquired and therefore more common in geriatric cats (> 8 years).

Gender. No difference has been reported.

Causes & Risk Factors

Causes are often difficult to determine since the structural and functional endpoint of irreversible nephron damage is the same. Renal diseases that have been associated



Typical gross appearance of chronic kidney disease. Note the irregular borders and "lumpy-bumpy" surface.

with the development of CKD in cats include amyloidosis, glomerulonephritis, primary tubulointerstitial disease, ascending urinary tract infections (bacterial pyelonephritis), nephrolithiasis, polycystic kidney disease, feline infectious peritonitis, and neoplasia.

Pathophysiology

Nephron damage associated with CKD is usually irreversible and can be progressive (stage I and early stage II CKD may not be progressive, but later stage II to IV is almost always progressive). Renal failure results when three quarters or more of the nephrons of both kidneys are not functioning. Whether the underlying CKD primarily

affects glomeruli, tubules, interstitial tissue, or renal vasculature, irreversible damage to any portion of the nephron renders the entire nephron nonfunctional. Healing of irreversibly damaged nephrons occurs by replacement fibrosis.

Progressive diseases that destroy nephrons at a slow rate allow intact nephrons to undergo compensatory hypertrophy which can delay the onset of renal failure. When renal failure finally occurs, the nephron hypertrophy can no longer maintain adequate renal function and < 25% of the original nephrons are functional.

The pathophysiology of CKD can be considered at both the organ and systemic level. At the level of the kidney, the fundamental pathology of CKD is loss of nephrons and decreased glomerular filtration. Reduced glomerular filtration results in increased plasma concentrations of substances that are normally eliminated from the body by renal excretion (eg, creatinine, urea nitrogen, and phosphorus). In addition to excretion of metabolic wastes and maintenance of fluid and electrolyte balance, the kidneys also function as endocrine organs and catabolize several peptide hormones. Thus, hormonal disturbances also play a role in the pathogenesis of CKD. Examples include decreased production of erythropoietin, which contributes to the nonregenerative anemia of CKD, decreased metabolism, and excretion of parathyroid hormone and gastrin, which contribute to osteodystrophy and gastritis, respectively.

CKD = chronic kidney disease

continues

Finally, part of the pathophysiology of CKD is brought about by compensatory mechanisms. For example, osteodystrophy occurs secondary to hyperparathyroidism, which develops in an attempt to maintain normal plasma calcium and phosphorous concentrations. Similarly, the individual glomerular filtration rate of intact nephrons increases in CKD in an attempt to maintain adequate renal function; however, proteinuria and glomerulosclerosis may be consequences or "trade-offs" of this hyperfiltration.

Signs

History. Dependent on the stage of CKD (see **Table 1**). History is often unremarkable in stage I and early stage II. In later stage II and beyond, history may include anorexia, weight loss, vomiting, polydipsia, and polyuria.

Physical examination. Dependent on the stage of CKD (see **Table 1**). Physical exam may be normal in stage I and early stage II. In later stage II and beyond, findings may include dehydration; poor body condition; uremic breath; oral ulcers; and small, firm, irregularly-shaped kidneys. Hypertensive retinopathy is possible.

Pain Index

In general, the kidneys of cats with CKD are not painful (exceptions may include lymphosarcoma causing renal swelling and the presence of nephroliths or ascending infections). Gastrointestinal irritation can result in mild to moderate pain; oral ulcers may be quite painful.

Dx Diagnosis

Definitive Diagnosis

Definitive diagnosis is traditionally based on loss of > 75% of the patient's nephrons, resulting in persistent azotemia superimposed on an inability to concentrate urine (USG < 1.035 to 1.040) along with chronic clinical signs of weight loss and polydipsia/polyuria. Preazotemic CKD may also be diagnosed in cats with persistent renal proteinuria, urine concentrating deficits, increases in serum creatinine over time even if the values remain in the normal range (eg, serum creatinine that increases from 0.6 to 1.2 mg/dl could indicate a 50% reduction in GFR), or renal abnormalities noted on palpation or ultrasound. The International Renal Interest Society (IRIS) has developed a staging system for feline CKD; it is based primarily on serum creatinine concentrations in stable, well-hydrated cats (**Table 1**).

Serum creatinine concentrations should always be interpreted in light of the patient's USG, muscle mass, and physical examination findings in order to rule out pre- and postrenal causes of azotemia. The stages are further classified by the presence or absence of proteinuria and systemic hypertension in **Table 2**.

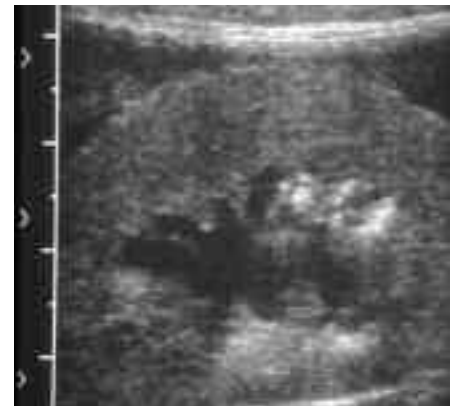
Differential Diagnoses

Hyperthyroidism, diabetes mellitus, FeLV-associated disease, primary gastrointestinal disease, neoplasia

Laboratory Findings/Imaging

In addition to the azotemia and inability to concentrate urine, nonregenerative anemia, hypokalemia, metabolic acidosis, and hyperphosphatemia are frequently observed. Small and irregularly shaped kidneys are often observed on radiographs and renal ultrasound findings may include increased cortical echogenicity with loss of the corticomedullary junction. Ascending infections may result in pyeloectasia on ultrasound and calcium oxalate nephroliths may be observed by radiographs and/or ultrasound.

Urinary tract infections are common in cats with CKD (especially female cats); therefore, urine cultures should be part of the initial and follow-up diagnostics. Fundic examination may reveal changes consistent with systemic hypertension (vessel tortuosity, hemorrhage, retinal detachment).



Ultrasound image of kidney demonstrating pyeloectasia, which may indicate an ascending urinary tract infection

Table 1. Feline CKD Staging

Serum Creatinine Concentration	Stage I Nonazotemic CKD	Stage II Mild renal azotemia	Stage III Moderate renal azotemia	Stage IV Severe renal azotemia
mg/dl	< 1.6	1.6–2.8	2.9–5.0	> 5.0
µmol/L	< 140	140–250	251–440	> 440

CKD = chronic kidney disease; FeLV = feline leukemia virus; GFR = glomerular filtration rate; USG = urine specific gravity

Postmortem Findings

Gastrointestinal tract irritation (mucosal ulceration); small, fibrotic kidneys; evidence of renal secondary hyperparathyroidism (soft tissue mineralization and osteodystrophy)

Renal histology: Morphologic heterogeneity between nephrons exists in CKD with changes ranging from severe atrophy to marked hypertrophy. Histologic changes are not process specific and, therefore, an etiologic diagnosis is frequently not possible.



Treatment

Inpatient or Outpatient

Depends on the severity of the patient's clinical signs. Many cats with CKD are better suited to outpatient treatment versus hospitalization.

Activity

Unrestricted

Client Education

CKD in cats is irreversible and often progressive. Frequent rechecks of the patient's body weight, hydration status, blood pressure, and laboratory parameters are often necessary. Medications and diet therapy require a high level of owner/patient compliance.

Surgery

Usually indicated only for obstructive uropathy

Medications & Nutritional Aspects

In early to mid-stage CKD, specific treatment aimed at the primary underlying disease is important and may include antibiotics for ascending urinary tract infections, chemotherapy for lymphosarcoma, and surgery to relieve ureteral obstruction. Renoprotective treatments aimed at stabilizing any renal functional decline are also important in early to mid-stage CKD and may include renal

Table 2. Urine Protein/Creatinine Ratio & Blood Pressure

Urine Protein/Creatinine Ratio	Classification
< 0.2	Nonproteinuric
0.2–0.4	Borderline proteinuric
> 0.4	Proteinuric

Systolic Blood Pressure (mm Hg)	Diastolic Blood Pressure (mm Hg)	Risk Level
< 150	< 95	Minimal
150–159	95–99	Low
160–179	100–119	Moderate
> 180	> 120	High



Cat with gastrostomy feeding tube

diets (protein and phosphorous reduction, alkalization, omega-3 fatty acid supplementation), enteric phosphate binders, antihypertensive drugs (eg, calcium channel antagonists and ACE inhibitors), and antiproteinuric drugs (ACE inhibitors).

In the latter stages of CKD, treatments designed to relieve clinical signs become more important; examples include SC or IV fluids to correct dehydration, potassium supplementation, recombinant erythropoietin, antiemetics/antacids/gastrointestinal protectants, and feeding tube placement.

ACE = angiotensin-converting enzyme; CKD = chronic kidney disease; IV = intravenous; SC = subcutaneous

continues

Tx at a glance

Stages	Problems	Treatments
Early stages (I to early III)	Primary disease process	Specific treatment of primary disease: Examples include antibiotics for bacterial pyelonephritis, surgery for obstructive uropathy, and chemotherapy for renal lymphosarcoma
Mid stages (II to early IV)	Renal disease progression	Renoprotective therapy: Examples include renal diet therapy and enteric phosphate binders to control hyperphosphatemia, and ACE inhibitors to attenuate hypertension and proteinuria
Later stages (late II to IV)	Clinical signs	Treatment to relieve clinical signs: Examples include fluid therapy, correction of acid-base and electrolyte disorders, and antiemetics and antacids

Contraindications

Potentially nephrotoxic drugs, glucocorticoids

Precautions

Try to avoid sudden dietary change and stressful hospitalization.

Interactions

Diuretics, especially furosemide, may potentiate the effects of potential nephrotoxicants

Alternative Therapy

Renal replacement therapy (eg, dialysis and renal transplantation)

Follow-Up

Patient Monitoring

May range from 2 to 4 times/year in early stage CKD to several times per week in later stage CKD.

Prevention

Annual wellness exams are recommended to diagnose early stage CKD; this is the time when disease-specific and renoprotective treatments have the best opportunity for success.

Complications

Ascending infections, nephroliths, hypertension, proteinuria, gastrointestinal tract irritation, nonregenerative anemia, metabolic acidosis, potassium depletion

Course

Stage I and early Stage II CKD may be stable or progressive; later Stage II through Stage IV CKD is often progressive.

In General

Relative Cost

- Initial diagnosis and staging \$\$\$ (relatively speaking, the earlier the stage, the less expense for diagnosis and treatment)
- Disease specific treatment ranges from \$ for antibiotic treatment to \$\$\$\$\$ for surgery for relief of obstructive uropathy
- Renoprotective treatment and follow-up \$\$\$\$ (on an annual basis)
- Treatment for clinical signs and follow-up \$\$\$\$ to \$\$\$\$\$ (on an annual basis)

Cost Key

\$ = < \$100	\$\$\$\$ = \$500–1000
\$\$ = \$100–250	\$\$\$\$\$ = > \$1000
\$\$\$ = \$250–500	

Prognosis

Guarded, as CKD is irreversible and in many cases progressive.

Future Considerations

Enteric dialysis may play a role in relieving clinical signs in later stage CKD. ■

See Aids & Resources, back page, for references, contacts, and appendices. Article archived on www.cliniciansbrief.com

Editorial Preview

- Consultant on Call: Canine Congestive Heart Failure
- Diagnostic Tree: Canine Cough
- Procedures Pro: Thoracocentesis
- Applied Behavior: Escaping & Roaming Dogs

Plus, the ever-popular Capsules, Complications, The Next Level, Make Your Diagnosis, What's the Take-Home?, Devices, and much more