The Role of Biomarkers in Diagnosis and Monitoring of Cats With CRI

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Q Why should early diagnosis of chronic renal insufficiency (CRI) in cats be a goal for veterinarians?

A The goal of early diagnosis and intervention is to improve patient outcomes, slow the progression of CRI, and help improve patient quality of life. By identifying CRI earlier through the use of biomarkers, we can hopefully better target potential treatment to slow or stop kidney injury and the progression of CRI.

Q What are the advantages and limitations of the CRI biomarkers being used today? Are additional options needed?

A **Serum creatinine** is probably the most familiar feline CRI biomarker to practising veterinarians, and it has played a significant role in International Renal Interest Society (IRIS) staging[1] for years. However, the use of serum creatinine as a biomarker of renal insufficiency has certain limitations:

- The greatest challenge in using serum creatine in early diagnosis of CRI is the steep curvilinear relationship with Glomerular Filtration Rate (GFR), marker of renal function. A significant reduction in GFR from normal is required before we see a corresponding increase in serum creatinine.[2]
- Serum creatinine is influenced by muscle mass; however, many CRI patients are geriatric with reduced muscle mass. Cachexia secondary to CRI may result in falsely low serum creatinine levels and the practitioner may overestimate the degree of kidney function left.

Symmetric dimethylarginine (SDMA) is a newer biomarker that is similar to serum creatinine and also believed to be an indicator of GFR. Studies have indicated SDMA may increase above the normal reference interval sooner in the medical process than serum creatinine[2] and is not affected by muscle mass.

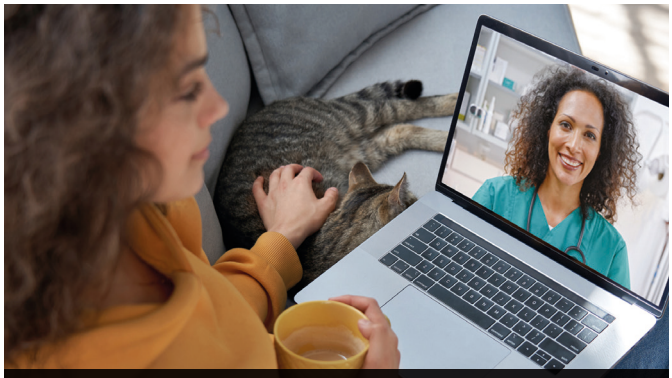
While SDMA might be an earlier marker of renal insufficiency in cats, I think it's too early to say it is better than serum creatinine. I recommend measuring and monitoring both SDMA and serum creatinine over time. Even small changes might indicate a decline in kidney function. Meanwhile, a new school of thought suggests we should perhaps be looking for additional biomarkers (such as FGF23) that let us know there is active kidney injury or inflammation. These may be helpful in determining if patients are either at risk of CRI or at risk of CRI progression if they already have it.

Q What is your recommended approach for diagnosis and management of cats with CRI?

A The prevalence of CRI is much higher in older cats, so I recommend blood work on cats starting at 8 to 10 years of age to identify a serum creatinine baseline and to monitor changes in SDMA levels. I also recommend routine urinalysis to look for evidence of proteinuria. Hypertension is another risk factor for CRI development, so monitoring blood pressure in cats as they age can be helpful.

Some of the best evidence for successful management of cats with CRI is to offer them a renal prescription diet beginning in IRIS Stage 2. Studies have shown cats with CRI (IRIS Stage 2 or higher) that were fed a renal prescription diet had improved survival times and fewer uraemic crises than cats not fed a renal prescription diet.[3,4,5] Managing hypertension, proteinuria and dehydration are also important.

In the future, my hope is that we will have more targeted treatments for feline CRI. New and better biomarkers that facilitate early diagnosis will be the key to achieving these goals.



Communicating with clients early and often about the CRI process and feeding patients a renal prescription diet can help improve the quality of life for cats.

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1. IRIS Guidelines for Staging of CKD: http://www.iris-kidney.com/guidelines/staging.html

2. Hall JA, Yerramilli M, Obare E, et al. Comparison of Serum Concentrations of Symmetric dimethylarginine and Creatinine as Kidney Function Biomarkers in Cats with Chronic Kidney Disease. J Vet Intern Med 2014;28:1676-83.

3. Ross SJ, Osborne CA, Kirk CA, et al. Clinical evaluation of dietary modification for treatment of spontaneous chronic kidney disease in cats. JAVMA 2006 Sept 15;229(6):949-57.

4. Plantinga EA, Everts H, Kastelein AMC, et al. Retrospective study of the survival of cats with acquired chronic renal insufficiency offered different commercial diets. Vet Rec 2005 Aug 13; 157(7):185-7.

5. 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 June;41(6):235-42.

Tailor Renal Diet Recommendations to Patient Needs

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Feeding cats with chronic renal insufficiency (CRI) requires a holistic approach. I emphasise to clients that we are feeding their cat, not just their cat's kidneys, and that a cat's dietary needs may change over time. Following are five leading considerations.

1. Provide targeted nutrition with a renal prescription diet.

Nestlé Purina offers two options for dietary management of cats with CRI. The first is Purina® PRO PLAN® Feline NF Renal Function™ Early Care, which contain a moderate amounts of high-quality protein and restricted phosphorus to nutritionally support cats with CRI. The second is NF Renal Function™ Advanced Care, with a reduced amounts of high-quality protein and restricted phosphorus to nutritionally manage cats with CRI.

The primary difference between these diets is the level of protein. Cats with more advanced CRI may retain uremic toxins, which can cause nausea and inappetence. Some of these toxins are breakdown products of protein metabolites. While the protein level in Advanced Care is reduced, it still provides adequate protein for cats with CRI assuming appropriate intake.

2. Determine what the cat will eat.

While the diets are designed for staged feeding, there are no hard and fast rules dictating when to feed a particular formulation. In fact, cats at any stage of CRI may benefit from either formulation, and the decision of which is optimal might boil down to which one the cat will eat. If you believe the cat will benefit from a slightly higher or lower protein level, you might try Early or Advanced Care. If you're looking for a way to contribute to the cat's total water intake, a canned or pouch formulation—which contains significant moisture—may be your recommended choice. If you have a cat that needs a calorically-dense diet and doesn't eat a lot of volume, one of the dry formulations may be the best option.

3. Keep the cat adequately hydrated.

It is common for cats with CRI to have increased difficulty maintaining hydration, which can cause them to be nauseated and inappetent. Strategies to consider include feeding a wet food, adding a feline complementary pet food for hydration such as Purina® PRO PLAN® Hydra Care™ to support hydration, or administering fluids subcutaneously or through an enteral feeding tube.

4. Encourage consumption.

Many cats prefer to eat alone in a quiet environment. If cats prefer to graze all day, a dry diet may work best. With canned food, temperature can be important. If the cat prefers the food to be between room temperature and body temperature, clients will need to gently warm it prior to serving. Other cats like their canned food cold. I encourage clients to experiment with different food temperatures.

Ensuring that cats with CRI continue to eat often requires additional steps as the condition progresses. Purina® PRO PLAN® Feline FortiFlora® may enhance palatability without significantly impacting phosphorus intake, and can be sprinkled on the cat's food. Mirtazapine is a medication with an appetite stimulant and anti-nausea properties for cats with CRI that is available both in oral form and as a transdermal gel applied to the ear. An oesophagostomy tube is also a good option for many cats. It's easy for veterinarians to place, comfortable for the cat, and can be used long-term to provide nutrition, hydration, and, in some cases, medication.

5. Consider other factors that may affect consumption.

It's important to refer to the patient's history, clinical signs, and physical exam to ensure a concurrent issue isn't affecting the cat's willingness to eat. Does the cat have a dental or GI issue? Is the patient arthritic and needing their food positioned differently? Is there competition for food or bullying from a dog or another cat in the home? Are there cognitive issues? If the sole focus is on the cat's kidneys, something else may be missed.

Employing a holistic approach while keeping individual patient nuances top of mind can go a long way toward achieving successful nutritional management of cats with CRI.

Dry vs. Wet for Cats with CRI

Weighing the renal prescription diet choices

WET DIET	DRY DIET
Optimal choice if cat accepts; supports hydration	Option for cats that won't eat canned diets or require a nutritionally dense food
Best for cats that are "meal" feeders	Best for "grazers"
May need to experiment with food temperature to appeal to the cat	Consider hydration to promote adequate fluid intake in cats

Proactive Approach Paves the way for Better CRI Patient Outcomes

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Feline chronic renal insufficiency (CRI) is typically an issue of older cats, but a key to a better outcome is to start screening when cats are younger.

Our practice is an urban veterinary hospital that caters to a clientele with a holistic pet-care mindset. Clients with this outlook believe in the importance of preventive care and regular screening. They are also committed to providing good nutrition for their pets, because they understand the connection to health. As a veterinarian, my job is to educate my clients and help guide them toward making educated decisions backed by research.

Starting young sets the stage for early intervention.

Diagnosing feline CRI early is dependent on detecting changes seen on bloodwork before the cat begins exhibiting clinical signs. I recommend annual bloodwork for cats starting at 1 year of age, and we price screenings affordably to help clients.
By obtaining annual bloodwork, I am able to monitor trends in the patient. Once the cat reaches senior status, when CRI is more likely to manifest, we closely monitor symmetric dimethylarginine (SDMA) values in addition to other blood and urine parameters.

If bloodwork and urinalysis indicate the onset of CRI, the first thing I do is thank clients for allowing us to catch the condition early. I also assure them that cats with CRI can live long lives and that we will have options along the way that will help them play active roles in providing care.

Nutrition is the cornerstone of patient management.

Diet and hydration form the foundation of managing cats with CRI, whether we catch the medical condition early or don't see a patient until they are at IRIS Stage 4. Every cat needs to eat and drink,so we can always do a great deal for our patients, even if feeding a renal prescription diet is the only change a client is willing to make.

It's important to manage cats as individuals when it comes to diet and fluids. A cat with severe periodontal affection may not be able to eat dry food, and a cat that grazes vs. eating meals may not be a candidate for a wet diet. While I prefer for CRI patients switch to wet food if possible, a newer option for cats on dry diets is to add Purina® PRO PLAN® Hydra Care™ to support hydration.

Stay a step ahead of patient interventions.

The education of clients is often an overlooked part of veterinary practice. I strive to prepare clients for what may come next. For example, I'll talk to them about the administration of subcutaneous fluids before they're needed, so they'll be ready when the time comes. I also explain that we have therapeutic options like anti-nausea medications to reduce vomiting and appetite stimulants if their cats become unwilling to eat.

With cats, gradual changes are almost always better than sudden ones. When cats transition to a diet or transition from Purina® PRO PLAN® Feline NF Renal Function™ Early Care formulas to NF Advanced Care formulas, I recommend they do so over a 7- to 10-day period or longer. I have had excellent dietary acceptance, even with cats that are known to be selective, provided we don't rush the dietary change.

The key to managing cats with CRI is educating clients and building trust. When clients understand that we are treating their cats as individuals and considering their needs and priorities, we can work together to do what's best for their pets.

Routine blood screening that includes a metabolic panel starting at a young age, along with SDMA testing when cats reach senior status, is key to early diagnosis of feline CRI.

Key Takeaways

- Obtaining bloodwork on cats starting at 8 to 10 years of age to identify a serum creatinine baseline and to monitor changes in SDMA levels—in addition to performing routine urinalysis and monitoring blood pressure—can help with early detection of impaired kidney function.
- Feeding cats with chronic renal insufficiency (CRI) requires a holistic approach. Emphasise to clients the importance of feeding their cat, not just their cat's kidneys, and that a cat's dietary needs may change over time.
- A proactive approach to diagnosis of feline CRI can facilitate early intervention and equip clients to partner with the veterinary team in managing the patient.

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