Using Feline Patient Profiles to Select the Best Kidney Diagnostics
Rebekah Mack-Gertig DVM, DACVIM-SAIM
Learning Objectives

- Recall the importance of kidney health in cats
- Revisit currently available kidney biomarkers
- Understand how patient profiling can help guide decisions for lab work choices
- Recognize five clinical presentations where understanding kidney health is beneficial
- Use short case examples to reinforce importance of classifying a cat’s presenting needs
- Distinguish best practice for feline kidney health
The cat and the kidney

+ Kidney function is essential in maintaining systemic health

+ Kidneys play an integral role in other major body systems: blood pressure management, red blood cell production, hormonal balance and clearance of daily toxins

+ Both acute and chronic disease are common causes of morbidity and mortality in cats, rising sharply as they age

+ The prevalence of CKD in cats rises sharply with age, with an estimated prevalence of <1% in young cats, 30-40% in cats over 9, and 60% in geriatric cat

+ CKD monitoring and management goes beyond renal biomarkers alone to include serum calcium and phosphorus, electrolytes, urine and serum protein, and blood pressure
Currently Available Kidney Biomarkers

- Creatinine
- SDMA
- BUN
- Urine Specific Gravity
- Proteinuria

Muscle mass, age, breed, comorbidities, assay modality

Pathology, comorbidities, assay modality, water consumption, diet
Mechanisms for pathogenesis of CKD in cats

- **GFR impairment**
- **Maladaptation**
- **Uremic syndrome**

CKD

**Initiation**

- Aging
- Ischemia/AKI events
- Environmental factors

**Intrinsic Progression**

- Glomerulosclerosis
- Nephron Loss

**Progression**

- Interstitial inflammation
- Interstitial fibrosis
- Tubular Atrophy
Interstitial inflammation, tubular atrophy, and fibrosis with secondary glomerulosclerosis

Primary lesions are within the tubulointerstitial compartment with only mild, presumed secondary, sclerotic lesion (scarring) occurring within glomeruli.
Acute kidney event & chronic disease continuum

- **Prerenal**
  - CHF
  - Anesthesia
  - Addison’s, IBD, pancreatitis – intermittent bouts

- **Renal**
  - Recurrent infection, nephroliths
  - NSAID, lily/grapes, aminoglycosides, chemotherapy
  - Leptospirosis

- **Postrenal**
  - Urethral obstruction
  - Ureteral obstruction – prevalence increased
Traditional indirect functional markers are the current mainstay of kidney diagnostics

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<th>Analyte Concentration</th>
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*support citation listed in bibliography
Traditional indirect functional markers are the current mainstay of kidney diagnostics.
Consider your at-risk felines

A risk factor is defined as an attribute that is associated with increased risk of an outcome.

- Breed
- Age
- Sex
- Comorbidities
- Diet
- Drugs
- Acute Kidney Injury Event

All elements together – patient profile

Minimum Database

Signalmen

Breed

Well or Sick

Patient Needs Profile
Broad Categories of reasons for testing are helpful to decide on the diagnostics needed, establishing subject specific intervals.
Feline Patient Profiles for Kidney Function Assessment

01 Patients Presenting for a Wellness Exam
SDMA contributes to wellness screening by improving early detection of changes in kidney function.

02 Cats with Hyperthyroidism
A significant number of cats with hyperthyroidism have concurrent kidney disease.

03 Preanesthetic Patients
Many seemingly healthy surgical patients may have underlying conditions that could complicate anesthesia or the surgical procedure.

04 Patients Who Test Positive for Infectious and Vector-borne Disease Exposure
SDMA tests can increase awareness of concurrent disease and long-term health considerations.

05 Patients Presenting as Medical Cases
The importance of wellness screening centers on both identifying unknown health risks and confirming well status.

A normal result or patient baseline is of great value because it allows more individualized assessment in times of illness or provides early indications of change specific to that patient.

Remember that wellness testing provide both:
- Baseline results
- Trending (especially important to kidneys
- Individualized Care
Utilizing wellness lab work to assess kidney function is extremely important

N=65,779
Adult to Geriatric
IDEXX data on file
Broad Categories of reasons for testing are helpful to decided on the diagnostics needed, establishing subject specific intervals

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Consider the age, risks, and needs of your patient

### Kitten and Adult

*High or Low Risk Predispositions

Kidney + Liver Biomarkers, Electrolytes, CBC Standard (PCV/TS & Blood smear), Complete Urinalysis (USG). FELV/FIV

Full Chemistry, CBC Select, FIV/FELV + Heartworm, Urinalysis, T4

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In senior and geriatric cats more frequent and expansive testing is appropriate

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*High or Low Risk Predispositions

Kidney + Liver Biomarkers, Electrolytes, CBC (PCV/TS & Blood smear), Urinalysis (USG). FELV/FIV

Full Chemistry + Lytes, CBC, FIV/FELV + Heartworm, Urinalysis, T4

NTproBNP
In senior and geriatric cats kidney disease is more common, screening is important

### Kidney Profiling

*High or Low Risk Predispositions

Kidney + Liver Biomarkers, Electrolytes, CBC (PCV/TS & Blood smear), Urinalysis (USG), FELV/FIV

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Remember reference intervals are population based and we are treating individuals.

1) Ekelund, Suzanne. Reference Intervals and percentiles – implications for the healthy patient. Acutecaretesting.org
Elements influencing how serial samples are assessed

- **Reason for Testing**
  - Screening
  - Diagnosis
  - Monitoring

- **Chronicity of Testing**
  - Trending, serial sampling
  - Single time point

- **Assessment of value**
  - Reference Interval (population based)
  - Subject Specific

**Clinical Context**
- Signalment
- Healthy versus Disease GFR variability
- Stable versus progressive
- Comorbidities
Example how context can influence interpretation

- 24-hour glucose curve?
- 2-year serial measurement of SDMA?
- 4-year serial measurement of ALT?
- 72 hours measurement HCT?
Consider reasonable clinical points to build your individualized reference intervals
• Hyperthyroidism is the most common endocrinopathy affecting the geriatric feline population, with a prevalence of 6%–10% reported in cats greater than 10 years of age.

• Chronic kidney disease (CKD) is a common co-morbidity in this population, estimated to occur in 15%–50% percent of hyperthyroid cats.

• The hypermetabolic state caused by hyperthyroidism leads to increased glomerular filtration rate (GFR) and reduced muscle mass, often confounding the diagnosis of CKD.
Hyperthyroidism – Clinical presentation with common concurrent diseases (CKD & Heart Disease)

Clinical Presentation & Findings

- Tachycardia >240 bpm
- Murmur (New or Worse)
- Gallop sound/rhythm
- Tachypnea
- Reduced lung sounds
- Open mouth breathing
- Pulse deficits
- Small kidneys
- Irregular kidney margins

The importance of monitoring or evaluating kidney function in hyperthyroidism

Cats

Senior 9-12
Geriatric 13+
*occasionally younger, but rate

• Increased appetite
• Weight loss
• Poor haircoat
• Change in behavior

*Cats with kidney disease live approximately 1-2 years less than cats without.

A diagnostics that considers the kidneys

**Chemistry Profile**
- Key Analytes:
  - SDMA & Crea
  - ALT & ALP
  - K+
- Must know kidney function to start
- Baseline for therapy
- Liver can be driven by hypothyroidism of effected by therapy
- Hypokalemia

**Complete Blood Count**
- Key Elements:
  - HCT
- Many cats with sub clinical CKD have HCT trending down
- Baseline for therapy – CKD unmasked & bone marrow suppression

**Total T4**
- Primary Diagnosis:
  - T4
  - Otherwise Well Borderline Cat:
    - Free T4
- T4 is primary diagnostic for diagnosis and monitoring
- Free T4 can be falsely elevated in illness

**Urinalysis**
- Key Components:
  - USG
  - Protein
- Renal evaluation
- Proteinuria for renal evaluation, substaging and indication of hypertensive disease

**Diagnostic Extras:** UPC, Blood Pressure

In senior and geriatric cats with hyperthyroidism more frequent and expansive testing is appropriate

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*High Risk Predispositions

Full Chemistry +Lytes, CBC, Urinalysis, T4
NTproBNP
UPC, Blood Pressure
Treatment choices, and monitoring timelines for kidney function

**Oral or Transdermal medication**

Advantages:
- Good response rate
- No hospital stay
- Reversible

Disadvantages:
- Daily medication
- Initial follow up lab work
- Drug reactions

- Recheck T4 (2-4 weeks)
- Recheck Kidney (2-4 weeks) with every dose change
- Recheck CBC (1 month & 3 months post start date)
- Recommended lab work every 6 months
  * UPC & Blood Pressure

**Radioactive Iodine**

Advantages:
- Cure rate > 95%, carcinoma therapy
- One treatment
- Some risk of hypothyroidism

Disadvantages:
- Hospitalization
- Post-Care
- Not reversible
- Expensive

- Recheck 1-3 months after treatment
- Follow kidney function if compromised
  * UPC & Blood Pressure

**Surgical**

Advantages:
- Cure rate > 90%
- Only 30-60% one gland
- Rapid Cure

Disadvantages:
- Anesthesia in at risk patient
- Parathyroid Gland
- Hospitalization
- No reversal

- Recheck 1-3 months after treatment
- Follow kidney function if compromised
  * UPC & Blood Pressure

**Dietary**

Advantages:
- Diet change
- >82% cure rate on diet
- Reasonable for CKD patients

Disadvantages:
- Diet change
- Only food allowed
- Limited treats
- 100% relapse off diet

- Recheck 1-3 months after treatment
- Follow kidney function if compromised
  * UPC & Blood Pressure

Diagnostic Extras: UPC, Blood Pressure
It is NOT renoprotective to maintain T4 above the reference interval

**MYTH**

- Even mild FHT can cause or perpetuate CKD and glomerular damage
- Leaving catabolic state untreated masks kidney disease and provide false sense of well-being to owner
- Negative energy balance and lead to poor nutrient absorption and malabsorption contributing to negative energy balance
Iatrogenic Hypothyroidism is associated with azotemia

Cats with iatrogenic hypothyroidism have a greater incidence of increased Creatinine and SDMA.1

- Likely due to decreased GFR
- Worsening underlying kidney disease,2,3,4
- Development of azotemia negatively impacts survival time.1
- Restoring euthyroidism appears to reduce the occurrence of azotemia.1

4) Peterson ME, Nichols R, Rishniw M. Serum thyroxine and thyroid-stimulating hormone concentration in hyperthyroid cats that develop azotemia after radioiodine therapy. J Small Anim Pract. 2017;58(9):519-530
The kidneys are a key organ system to understand anesthetic needs in cats

- Kidneys are responsible for blood pressure regulation, and blood pressure can be impacted by anesthetic choices.

- Whether animals have normal or compromised kidney function, hypotensive events can be damaging—and therefore understanding a patient’s baseline function is a key component of good anesthetic choices.

- Early kidney disease is often not clinically evident, but can have a major impact on anesthetic health, screening diagnostics are low-cost, low-impact method to guide best practices.
There are two camps when it comes to preanaesthetic testing

- Limited benefit to preanaesthetic testing
- Especially in juvenile to adult animals
- Delays procedures
- Increases cost to owner

- Discoveries unknown systemic illness
- Improves anesthetic choices
- Important in Senior and Geriatric patients
- Improves care, regardless of cost

- Much of this is based on human literature and preanaesthetic data – but our patients cannot tell us if something is wrong:
  - Physical Exam and History
  - Relevance of the testing (age, previous illness, breed)
  - Owner comfort


The purpose of kidney biomarkers in preanaesthetic screening

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<th>Age at testing</th>
<th>Juvenile</th>
<th>Adult</th>
<th>Senior/Geriatric</th>
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<td>% Abnormalities</td>
<td>&lt;2%</td>
<td>2-6%</td>
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Blood pressure control
Excretion of waste
Drug metabolism and excretion
Control of vascular volume
Endocrine functions
Acid/base balance

Preanaesthetic bloodwork can be your chance to create a baseline for cats.
Examples of importance of preanesthetic testing

8-year-old FS Shorthair, presenting for mass removal over hip region, no previous major medical history

6-year-old MN Siamese, presenting for dental prophylaxis
Kidney health is important in feline infectious disease

- Most recently, there is strong support for understanding retrovirus status in cats, because it impacts overall systemic health and can also involve kidney health or be compounded by changes in kidney function.

- Prevalence of FIV and FELV reported at 2-6%

- Recrudescence of FELV virus at older ages

- Vector-borne disease such as bartonella, babesia, and cytozoon can illicit kidney damage or impact existing disease
Decline in kidney function is extremely common in sick cats

- SDMA_High: 22%
- CREA_High: 20%
- ALKP_High: 10%
- GLU_High: 9%
- ALT_High: 7%
- CREA_Low: 6%
- Reticulocytosis: 5%
- Leukocytosis: 4%
- CL_LOW: 4%
- ALKP_Low: 4%
- Anemia: 3%
- K_Low: 2%
- GLU_Low: 2%
- GLOB_High: 2%
- PHOS_Low: 2%
- LIPA_High: 2%
- CHOL_Low: 2%
- TP_High: 1%
- K_High: 1%
- GGT_High: 1%
- BUN_Low: 1%
- GLOB_Low: 1%

N=27663 Adult to Geriatric IDEXX data on file
Consider the age, risks, and needs of your patient

### Kitten and Adult

**High or Low Risk Predispositions**

Kidney + Liver Biomarkers, Electrolytes, CBC Standard (PCV/TS & Blood smear), Complete Urinalysis (USG). FELV/FIV

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Senior & Geriatric

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How do we classify CKD?

CKD traditional sense

- Biomarkers
- > 90 days persistent increases
- Irreversible, progressive

Continuum:
Acute on chronic

CKD Comorbidities
Kidney Disease & Heart disease (Cardio-renal or Renocardial Syndrome)
Kidney Disease

Cardiorenal Syndrome

- Recognize Primary Disease
  - Traditional Biomarkers
  - New Biomarkers

- Classify Disease
  - IRIS CKD Guidelines
  - Cardiac

- Recognition of Change in Disease State
  - Long-term monitoring
  - Acute on Chronic

- Multifactorial
  - Moving target
  - Progress unexpectedly

  Dependent on improvements in diagnosis and monitoring in veterinary medicine
Just consider, the possibility...

Baselines and trending really help identify early changes

Cardiac baselines in animals with abnormalities or senior patients can be helpful
Increased n-terminal pro-B-type natriuretic peptide is associated with increasing concentrations of renal biomarkers over time.
Kidney Disease and IBD correlated or coincidence?

CKD in cats rises sharply with age, with an estimated prevalence of <1% in young cats, 30-40% in cats over 9, and 60% in geriatric cats.

Acute kidney injury is often associated with inflammatory diseases.

Acute pancreatitis & Cholangiohepatitis are associated with nephritis.

Pancreatitis is an important and common disease of cats that may be associated with severe clinical disease and high mortality – reported in up to 67% of cats, including 45% of apparently healthy cats. In cats with IBD > 50% often also have pancreatitis.

IBD is described as common in cats but prevalence in unknown, perhaps 0.02-0.002% of cat population.

Of cats with IBD 10-25% of them have or transform into small cell lymphoma.


Significant connection between the gut and the kidney

IBD

SCL

Hepatitis

Pancreatitis

CKD

AKI

Microbiome

Vitamin D, PTH
Calcium, Phosphorus
Inflammatory mediators


Treatment used for GI disease cause impacts to kidneys

**Steroids**
- Expand vascular volume – increase blood pressure, affect cardiac function
- Cushing’s effect
- Increased Infection

**Diets**
- Lack protein restriction
- Metabolic balance
- Phosphorus sources and levels
- Fatty acids levels

**Immunosuppressives**
- Ciclosporine – renal toxicity
- Mycophenolate - diarrhea, pre-renal, Acute on Chronic
Feline Patient Profiles for Kidney Function Assessment

01 Patients Presenting for a Wellness Exam
SDMA contributes to wellness screening by improving early detection of changes in kidney function.

02 Cats with Hyperthyroidism
A significant number of cats with hyperthyroidism have concurrent kidney disease.

03 Preanesthetic Patients
Many seemingly healthy surgical patients may have underlying conditions that could complicate anesthesia or the surgical procedure.

04 Patients Who Test Positive for Infectious and Vector-borne Disease Exposure
SDMA tests can increase awareness of concurrent disease and long-term health considerations.

05 Patients Presenting as Medical Cases
Thank you for coming
Feel free to ask questions!
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