



IDEXX SDMA – Effect on Clinical Decision Making

Graham Swinney, Medical Affairs Veterinarian



Overview

- Who am I?
- Renal Disease Diagnostics – Brief Review
- What is GFR?
- What is SDMA?
- SDMA Benefits?
- IRIS Kidney Disease Staging

SDMA – Australian Experience

- 2015
 - SDMA in Reference Laboratory
 - Which profiles?
 - Uptake
- Emphasis
 - Marker of GFR!
 - Reasons it can increase
- How is SDMA used?

SDMA – Australian Experience

IDEXX Recommended Profiles - Selection Guide

Let Medicine Specialist Dr Graham Swinney guide you



It's as easy as:

- 1 Select the species
- 2 Decide if you need interpretation (recommended for sick patient testing)
- 3 Select the profile with the disease specific tests required
- 4 Generate an online lab request via VetConnect® PLUS

| Test Description | Test Code | Price ex GST | Pathologist Interpretation | Internal Medicine Consult Available | Haematology | Core Chemistries | | | | | | | | | | | | | | | | | | | | | Disease Specific Tests | | | | Urine | | | | | | | | | |
|------------------|-----------|--------------|----------------------------|-------------------------------------|--|--------------------|------------------------------|---------|-----|-----|---------|-----------|-----|-------------|-----------|---------|----------|-------------|--------------------|------------|-----------------|-----|----------|---------|----------------|-------|------------------------|--------|-----------|-----------|---------------|------|----------------------|---------------|---------------|-------------------------|----------|------------------|------------|---------------------------|
| | | | | | IDEXX CBC™ (Comprehensive or Standard) | Reticulocyte Count | Reticulocyte Haemoglobin *** | Albumin | ALP | ALT | Amylase | Anion Gap | AST | Bicarbonate | Bilirubin | Calcium | Chloride | Cholesterol | C-Reactive Protein | Creatinine | Creatine Kinase | GGT | Globulin | Glucose | IDEXX SDMA**** | L-ALP | Lipase | Sodium | Phosphate | Potassium | Total Protein | Urea | Cardiopet® ProBNP*** | Spec cPL®**** | Spec iPL®**** | Faecal Antigen Panel*** | Total T4 | Specific Gravity | Urinalysis | Culture and Sensitivities |

Canine Reference Laboratory Profiles**

| Profile | Test Code | Price ex GST | Pathologist Interpretation | Internal Medicine Consult Available | IDEXX CBC™ (Comprehensive or Standard) | Reticulocyte Count | Reticulocyte Haemoglobin *** | Albumin | ALP | ALT | Amylase | Anion Gap | AST | Bicarbonate | Bilirubin | Calcium | Chloride | Cholesterol | C-Reactive Protein | Creatinine | Creatine Kinase | GGT | Globulin | Glucose | IDEXX SDMA**** | L-ALP | Lipase | Sodium | Phosphate | Potassium | Total Protein | Urea | Cardiopet® ProBNP*** | Spec cPL®**** | Spec iPL®**** | Faecal Antigen Panel*** | Total T4 | Specific Gravity | Urinalysis | Culture and Sensitivities | | | | | |
|----------------------------------|-----------|--------------|----------------------------|-------------------------------------|--|--------------------|------------------------------|---------|-----|-----|---------|-----------|-----|-------------|-----------|---------|----------|-------------|--------------------|------------|-----------------|-----|----------|---------|----------------|-------|--------|--------|-----------|-----------|---------------|------|----------------------|---------------|---------------|-------------------------|----------|------------------|------------|---------------------------|---|---|---|---|---|
| Complete Body Function with C&S | CBFC+ | \$225.30 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | | | |
| Off-Colour™ Profile | OCCP | \$197.00 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | | |
| Complete Body Function | CBFC | \$172.60 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | |
| Canine Diagnostic Profile | CTHP+ | \$170.10 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | |
| Canine Screening Profile with T4 | GER2 | \$125.70 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | |
| Canine Comprehensive Profile | CHBU | \$161.50 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | |
| Canine Total Health Profile | CTHP | \$128.20 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | |
| Canine Pancreatic Profile | CPP | \$110.90 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | |
| Canine Preventive Care Profile | CPCP | \$115.00 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |
| Total Annual Health Profile | TAHPC | \$86.70 | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • | • |

SDMA – Australian Experience

- 2017
 - Catalyst SDMA
 - Unwell patients
 - PU/PD
 - PreGA screening?
 - Wellness?



SDMA – Australian Experience

- Medical Consulting
 - Common Questions
 - Mild Increase in SDMA, all else within reference interval
 - Mild increase in creatinine, normal SDMA
 - Disproportionate increase in SDMA
 - No SDMA result on reference laboratory result
 - Explanation



SDMA – Australian Experience

| Testing Profiles Conducted | Total | Run with SDMA | % Elevated Creatinine | % Elevated SDMA |
|--|-------|------------------|-----------------------|-----------------|
| <i>Chemistry 10</i> | 36 | 3 | 3% | 0% |
| <i>Chemistry 15</i> | 0 | 0 | 0% | 0% |
| <i>Chemistry 17</i> | 261 | 176 | 7% | 30% |
| Breakdown by Species and Age | Total | % of Total Tests | Canine | Feline |
| <i>Juvenile</i> | 11 | 4% | 8 | 3 |
| <i>Adult</i> | 131 | 44% | 103 | 28 |
| <i>Geriatric</i> | 155 | 52% | 128 | 27 |
| Summary of Results | Total | % of Total Tests | Canine | Feline |
| <i>SDMA</i> | 179 | 60% | 138 | 41 |
| <i>Normal Creatinine Elevated SDMA</i> | 55 | 31% | 43 | 12 |

Kidney Disease

- Frequency
 - Dogs 1.5%
 - Cats
 - Young 1%
 - Adult/Senior 30-40%
 - Geriatric 60%



Kidney Disease Diagnosis

- Clinical Signs, Physical Examination
 - Important
 - Effect of stage on clinical signs
 - Diagnostics must be interpreted in light of the signs



Kidney Disease Diagnosis

Table 3

Common clinical signs and physical examination findings in cats and dogs with CKD

Clinical Signs

Physical Examination Findings

Polyuria and polydipsia

Palpable kidney abnormalities

Decreased appetite

Evidence of weight loss

Weight loss

Evidence of muscle loss

Lethargy

Dehydration

Bad breath

Pallor

Oral ulcers

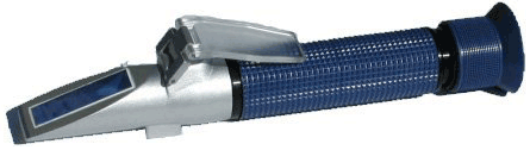
Hypertensive retinopathy

Glomerular Filtration Rate

- What is GFR?
 - How to measure it?
- GFR Influenced by
 - Renal Blood Flow
 - Intracapsular hydrostatic pressure in Bowman's space
 - Plasma colloid oncotic pressure
- Ideal Substance
 - Not protein bound
 - Freely passes glomerulus
 - No renal tubular resorption or secretion



Kidney Disease Diagnosis

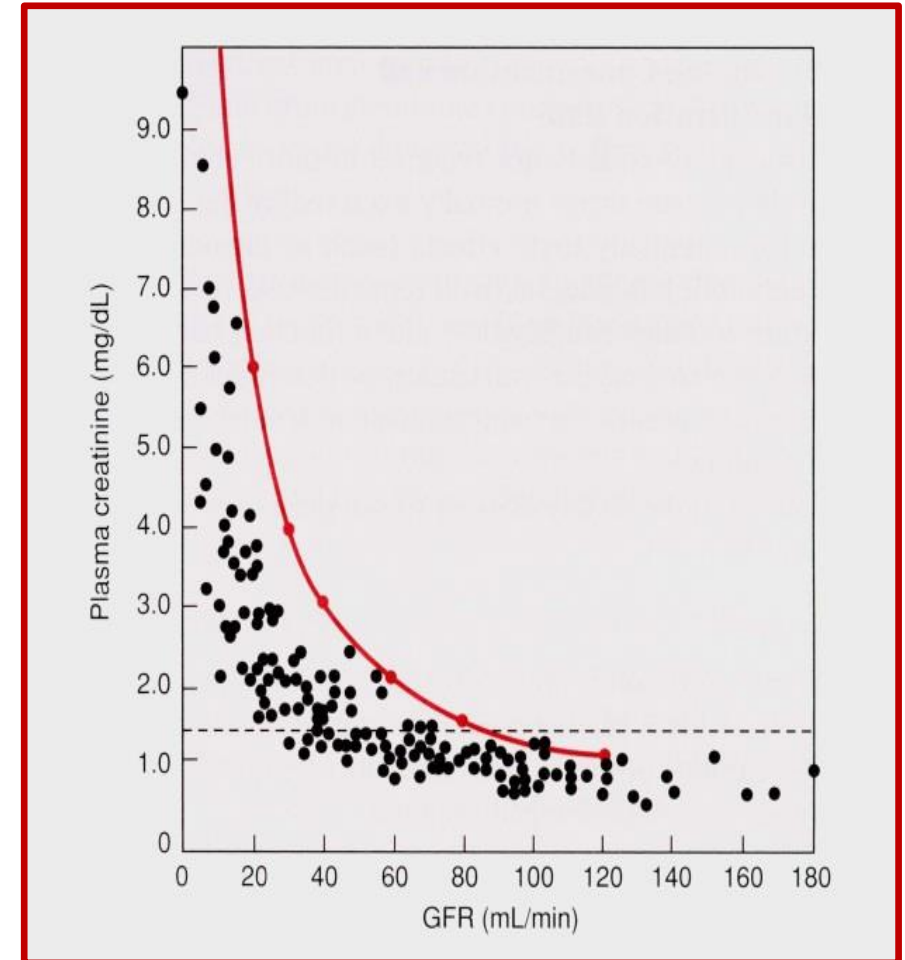


Kidney Disease Diagnosis

| Table 4 Interpretation of urine specific gravity (USG) in evaluating urine concentrating ability adapted from Watson et al,¹²² 2015 | | |
|---|-------------------------|---|
| USG | Classification | Interpretation |
| >1.030 (dog) >1.035 (cat) | Concentrated | Indicates adequate functioning nephrons (>33% functional nephrons) Suggests potential dehydration in azotemic animals |
| 1.013–1.029 (dog) 1.013–1.034 (cat) | Moderately concentrated | May be appropriate in well-hydrated animals Inappropriate in dehydrated animals Suggests kidney disease in azotemic animals |
| 1.008–1.013 | Isosthenuric | Inappropriate in dehydrated animals Substantial kidney disease in azotemic animals |
| < 1.008 | Dilute | May be appropriate in overhydrated animals Suggests retention of urine diluting ability (>33% functional nephrons) |

Creatinine and GFR

- Creatinine and GFR relationship
 - Not linear
- Increasing value of creatinine
 - Trending
- Influences on creatinine



SDMA is an essential element of the chemistry panel



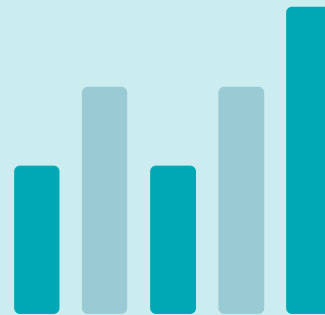
SDMA is a **sensitive indicator** of kidney function that detects as little as 25% loss of function.^{1,2}



SDMA is more **reliable** than creatinine as an indicator of kidney function because it is not influenced by common confounding conditions.^{4,5}



SDMA is an **earlier indicator** of progressive kidney function loss, often increasing before other parameters.¹⁻³



An increased SDMA may also serve as an indicator of **concurrent diseases** that may have a secondary impact on kidney function.⁶⁻⁸

Sources:

1. Nabity MB, Lees GE, Boggess M, et al. Symmetric dimethylarginine assay validation, stability, and evaluation as a marker for early detection of chronic kidney disease in dogs. *J Vet Intern Med.* 2015;29(4):1036–1044.
2. Hall JA, Yerramilli M, Obare E, Yerramilli M, Jewell DE. 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(6):1676–1683.
3. Hall JA, Yerramilli M, Obare E, Yerramilli M, Almes K, Jewell DE. Serum concentrations of symmetric dimethylarginine and creatinine in dogs with naturally occurring chronic kidney disease. *J Vet Intern Med.* 2016;30(3):794–802.
4. Hall JA, Yerramilli M, Obare E, Yerramilli M, Yu S, Jewell DE. Comparison of serum concentrations of symmetric dimethylarginine and creatinine as kidney function biomarkers in healthy geriatric cats fed reduced protein foods enriched with fish oil, L-carnitine, and medium-chain triglycerides. *Vet J.* 2014;202(3):588–596.
5. Hall JA, Yerramilli M, Obare E, Yerramilli M, Melendez LD, Jewell DE. Relationship between lean body mass and serum renal biomarkers in healthy dogs. *J Vet Intern Med.* 2015;29(3):808–814.
6. Drake C, Ogeer J, Beall MJ, Buch JS, Clements C, McCrann DJ, Relford RL. Investigation of the association between Lyme seroreactivity and chronic kidney disease in dogs [ACVIM Abstract ID08]. *J Vet Intern Med.* 2018;32(6):2264.
7. Ogeer JS, Drake C, McCrann DJ, Clements C, Beall M, Burton W. Investigating association between exposure to Ehrlichia and risk of developing chronic kidney disease in dogs [ACVIM Abstract ID07]. *J Vet Intern Med.* 2019;33(5):2490.
8. Coyne M, Drake C, McCrann DJ. The association between symmetric dimethylarginine concentrations and neoplasia in dogs and cats [ACVIM Abstract O05]. *J Vet Intern Med.* 2018;32(6):2216–2217.

Is an increased SDMA always kidney disease?

- No!
- Increased SDMA
 - Pre-renal
 - Renal
 - Post-renal
- Breeds
 - Greyhounds
 - Boxers
 - Birmans



Kidney Disease – Result Interpretation

- Variability of Kidney Biomarkers
 - Pre-analytical
 - Sample quality and storage
 - Analytical
 - Within or between instruments, methods
 - Biological
 - Interindividual
 - Intraindividual
 - Index of Individuality
 - Variability of individual result vs variability expected in population



Kidney Disease – Result Interpretation

- Creatinine
 - Low IOI
- SDMA
 - Moderate IOI
- This means a repeat SDMA more important to confirm values



Kidney Disease

Symmetrical Dimethylarginine: Evaluating Chronic Kidney Disease in the Era of Multiple Kidney Biomarkers

Helen Michael, DVM, PhD, DACVP^a, Donald Szlosek, MPH^a,
Celeste Clements, DVM, DACVIM^a, Rebekah Mack, DVM, DACVIM^{a,*}

KEYWORDS

• Nephrology • Veterinary • Creatinine • SDMA • Glomerular filtration rate

KEY POINTS

- Symmetric dimethylarginine (SDMA) is incorporated into the International Renal Interest Society guidelines for diagnosing, staging, and treating chronic kidney disease (CKD).
- Persistent mild increases in SDMA can be used to diagnose CKD.
- SDMA and creatinine correlate well with each other and with GFR.
- SDMA is affected by fewer nonrenal influences than creatinine.

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IRIS and IDEXX SDMA

Step 1: Diagnose CKD

Clinical signs and physical examination findings worsen with increasing severity of kidney disease

Clinical presentation

Consider age, sex, breed predispositions, and relevant historical information, including medication history, toxin/toxicant exposure, and diet.

Can be subclinical in early stage CKD. Signs may include polyuria, polydipsia, weight loss, decreased appetite, lethargy, dehydration, vomiting, and bad breath.

Physical examination findings

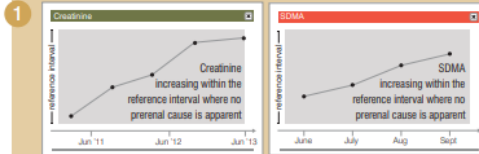
Can be normal in early stage CKD. Findings may include palpable kidney abnormalities, evidence of weight loss, dehydration, pale mucous membranes, uremic ulcers, evidence of hypertension, i.e., retinal hemorrhages/detachment.

To diagnose Stage 1 and early Stage 2 CKD

OR

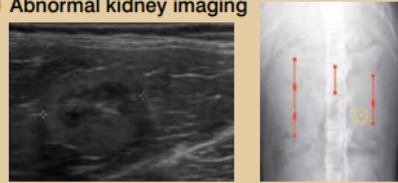
To diagnose more advanced CKD (late Stage 2–4)

One or more of these diagnostic findings:



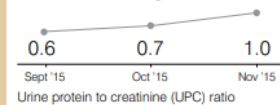
2 Persistent increased SDMA* > 14 µg/dL

3 Abnormal kidney imaging



4 Persistent renal proteinuria

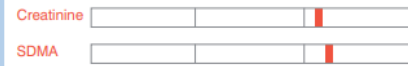
UPC > 0.5 in dogs; UPC > 0.4 in cats



See www.iris-kidney.com for more detailed staging, therapeutic, and management guidelines.

Both of these diagnostic findings:

Increased creatinine and SDMA concentrations



Results of both tests should be interpreted in light of patient's hydration status.

plus

Urine specific gravity < 1.030
Urine specific gravity < 1.035'



1.030 Canine 1.008
1.035 Feline 1.008

*Note that some cats can produce hypersthenuric urine in the face of renal azotemia.

Step 2: Stage CKD



Stage 1
No azotemia
(Normal creatinine)

Stage 2
Mild azotemia
(Normal or mildly elevated creatinine)

Stage 3
Moderate azotemia

Stage 4
Severe azotemia

| | | Stage 1 No azotemia (Normal creatinine) | Stage 2 Mild azotemia (Normal or mildly elevated creatinine) | Stage 3 Moderate azotemia | Stage 4 Severe azotemia |
|----------------------------------|---|---|--|------------------------------|----------------------------------|
| Creatinine in mg/dL | Canine | Less than 1.4 (125 µmol/L) | 1.4–2.8 (125–250 µmol/L) | 2.9–5.0 (251–440 µmol/L) | Greater than 5.0 (440 µmol/L) |
| | Feline | Less than 1.6 (140 µmol/L) | 1.6–2.8 (140–250 µmol/L) | 2.9–5.0 (251–440 µmol/L) | Greater than 5.0 (440 µmol/L) |
| SDMA* in µg/dL | Canine | Less than 18 | 18–35 | 36–54 | Greater than 54 |
| | Feline | Less than 18 | 18–25 | 26–38 | Greater than 38 |
| UPC ratio | Canine | Nonproteinuric <0.2 Borderline proteinuric 0.2–0.5 Proteinuric >0.5 | | | |
| | Feline | Nonproteinuric <0.2 Borderline proteinuric 0.2–0.4 Proteinuric >0.4 | | | |
| Systolic blood pressure in mm Hg | Normotensive <140 Prehypertensive 140–159 | | | | |
| | Hypertensive 160–179 Severely hypertensive ≥180 | | | | |

Note: In the case of staging discrepancy between creatinine and SDMA, consider patient muscle mass and retesting both in 2–4 weeks. If values are persistently discordant, consider assigning the patient to the higher stage.

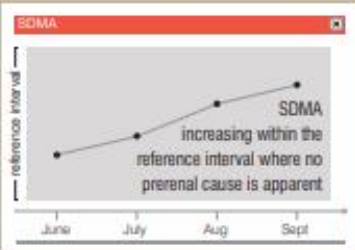
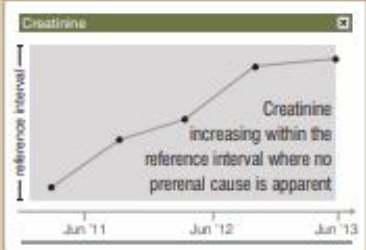

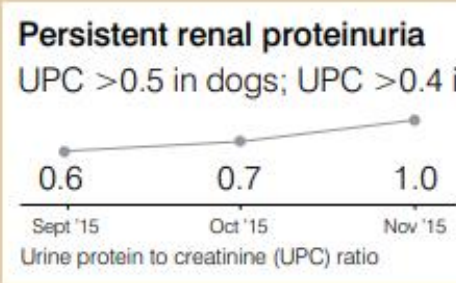
*SDMA = IDEXX SDMA® Test

See www.iris-kidney.com for more detailed staging, therapeutic, and management guidelines.

Diagnosing IRIS Stage 1 (Early) CKD

To diagnose Stage 1 and early Stage 2 CKD

One or more of these diagnostic findings:

- 
- Persistent increased SDMA* >14 µg/dL**
- Abnormal kidney imaging**

- Persistent renal proteinuria**
UPC >0.5 in dogs; UPC >0.4 in cats


| Date | UPC Ratio |
|----------|-----------|
| Sept '15 | 0.6 |
| Oct '15 | 0.7 |
| Nov '15 | 1.0 |

Urine protein to creatinine (UPC) ratio





Of

Clinical Symptoms?

www.iris-kidney.com

Staging CKD

Step 2: Stage CKD

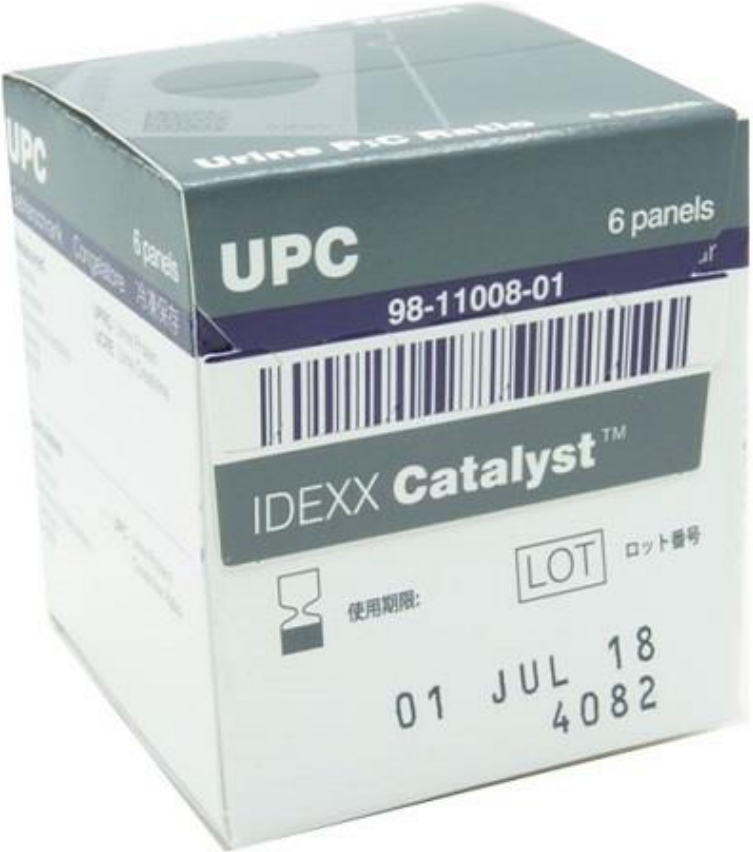
| | |  |  |  |  |
|---|--|---|---|---|---|
| | | Stage 1 No azotemia (Normal creatinine) | Stage 2 Mild azotemia (Normal or mildly elevated creatinine) | Stage 3 Moderate azotemia | Stage 4 Severe azotemia |
| Creatinine in mg/dL | Canine | Less than 1.4 (125 μmol/L) | 1.4–2.8 (125–250 μmol/L) | 2.9–5.0 (251–440 μmol/L) | Greater than 5.0 (440 μmol/L) |
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| | Feline | Nonproteinuric <0.2 Borderline proteinuric 0.2–0.4 Proteinuric >0.4 | | | |
| Systolic blood pressure in mm Hg | Normotensive <140 Prehypertensive 140–159 | | | | |
| | Hypertensive 160–179 Severely hypertensive ≥180 | | | | |

Note: In the case of staging discrepancy between creatinine and SDMA, consider patient muscle mass and retesting both in 2–4 weeks. If values are persistently discordant, consider assigning the patient to the higher stage.

*SDMA = IDEXX SDMA® Test

See www.iris-kidney.com for more detailed staging, therapeutic, and management guidelines.

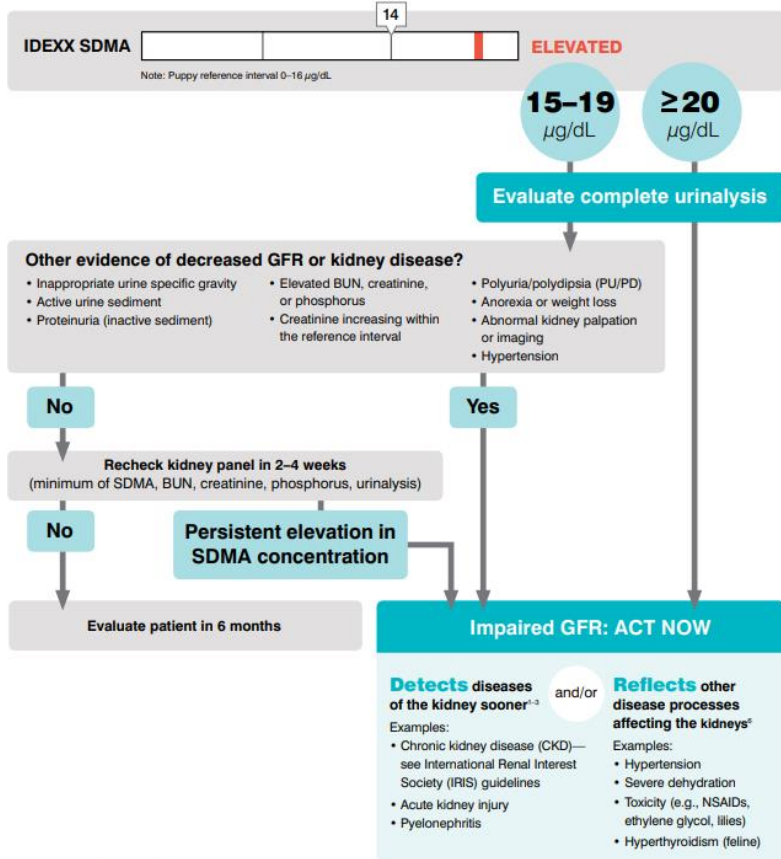
Staging CKD



What to do when SDMA is increased?

IDEXX SDMA algorithm

An elevated SDMA* concentration is a reflection of impaired glomerular filtration rate (GFR). Both primary kidney disease and secondary kidney insults, such as concurrent disease, can cause an elevation in SDMA concentration. Follow this algorithm to investigate elevated SDMA concentrations and determine whether acute, active, or chronic injury is occurring and how to begin to investigate, manage, and monitor disease.



See reverse for the initial steps in investigating, managing, and monitoring impaired GFR as identified by an elevated SDMA



Initial steps in investigating, managing, and monitoring impaired GFR as identified by an elevated SDMA

Investigate

Underlying cause, treatable condition, concurrent disease, chronic kidney disease (CKD)



Underlying cause

- Urinary tract infection (UTI)/pyelonephritis
- Toxicity (e.g., NSAIDs, ethylene glycol, lilies)
- Acute kidney injury
- Systemic hypertension
- Chronic kidney disease (CKD)



Consider performing

- Urine culture and minimum inhibitory concentration (MIC) susceptibility
- Infectious disease testing
- Abdominal imaging
- Urine protein:creatinine (UPC) ratio (proteinuria)
- Blood pressure



Concurrent condition to assess

- Hydration status
- Thyroid status (feline)

Manage

Treat underlying disease, manage assessed kidney injury, adjust care protocols



Treat appropriately

- Underlying disease (e.g., pyelonephritis, infectious disease)
- Dehydration
- Discontinue nephrotoxic medications (e.g., NSAIDs)
- Hypertension
- Proteinuria



Additional support

- Ample, clean water
- Kidney-supportive diet if warranted



Adjust anesthesia protocols

- Provide fluids (intravenous or subcutaneous)
- Oxygen support prior to, during, and after procedure
- Adjust pain management

Monitor

Manage and monitor outcomes



Monitor renal biomarkers

- Trended testing of the following: SDMA, BUN, creatinine, and phosphorus
- Urinalysis
- Blood pressure

Outcome

GFR impairment, stable



SDMA remains increased, but stable

- GFR remains impaired but stable
- Consider CKD diagnosis, refer to IRIS staging and treatment guidelines
- Institute appropriate supportive care and monitoring

GFR impairment, progressive



SDMA continues to increase

- Ongoing active kidney injury
- Revisit investigate: repeat or perform additional diagnostics
- Institute ongoing supportive care

GFR restoration



SDMA returns to normal

- Recovery from mild injury
- Response to appropriate therapy
- Compensatory mechanisms
- Recheck within 6 months–1 year

Remember that patients can move back to an investigation stage from management or monitoring depending on progression or change in renal status.

*Symmetric dimethylarginine.

For a complete list of references, visit idexx.com/sdma.

The information contained herein is intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical presentation, and complete laboratory data. With respect to any drug therapy or monitoring program, you should refer to product inserts for a complete description of dosages, indications, interactions, and cautions. Diagnosis and treatment decisions are the ultimate responsibility of the primary care veterinarian.

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SDMA Resource

Implications of a Mildly Increased SDMA in a Pre GA Screen

- Pre-renal vs Renal
- Is possible IRIS Stage 1 disease a preclusion to anaesthesia?
- Considerations
 - Fluids
 - BP
 - Analgesia
 - Follow Up

Kidney-supportive diet if warranted




Adjust anaesthesia protocols

Provide fluids (intravenous or subcutaneous)

Oxygen support prior to, during, and after procedure

Adjust pain management

GFR impairment progressive



GFR restoration





Jasper: Annual wellness visit

9-year-old, neutered male Siamese

Presenting reason

- Annual wellness visit

History

- Slight weight loss with possible decrease in appetite
- Increased vocalization
- Not sure about drinking or urinating
- Indoor/outdoor cat

Physical examination

- Bright, alert, responsive, and hydrated
- Abdominal palpation: normal
- Rest of examination: normal





Chemistry and urinalysis results

Chemistry

1/2/18

2:49 PM



| | | | |
|--|-----------|-----------------|--|
| >  IDEXX SDMA ▶ Learn More | 21 | 0 – 14 µg/dL | |
| >  Creatinine | 2.2 | 0.8 – 2.4 mg/dL | |
| >  BUN | 28 | 16 – 36 mg/dL | |
| >  Total T4 | 1.9 | 0.8 – 4.7 µg/dL | |

Urinalysis

1/2/18

2:49 PM



| | |
|--|-------------|
|  Specific Gravity | 1.022 |
|  Red Blood Cells | 6 - 20 /HPF |
|  Urine Protein | 30 |

Question?

- A. Jasper has chronic kidney disease (CKD).
- B. Jasper has active or acute kidney injury (AKI).
- C. I don't have enough information to make a diagnosis yet.



What should we do now?

- A. Recommend to recheck Jasper in 2–3 weeks.
- B. Put Jasper on a kidney therapeutic diet.
- C. Follow the IDEXX SDMA[®] Test algorithm.
- D. Put Jasper on a supportive kidney diet and an appetite stimulant.



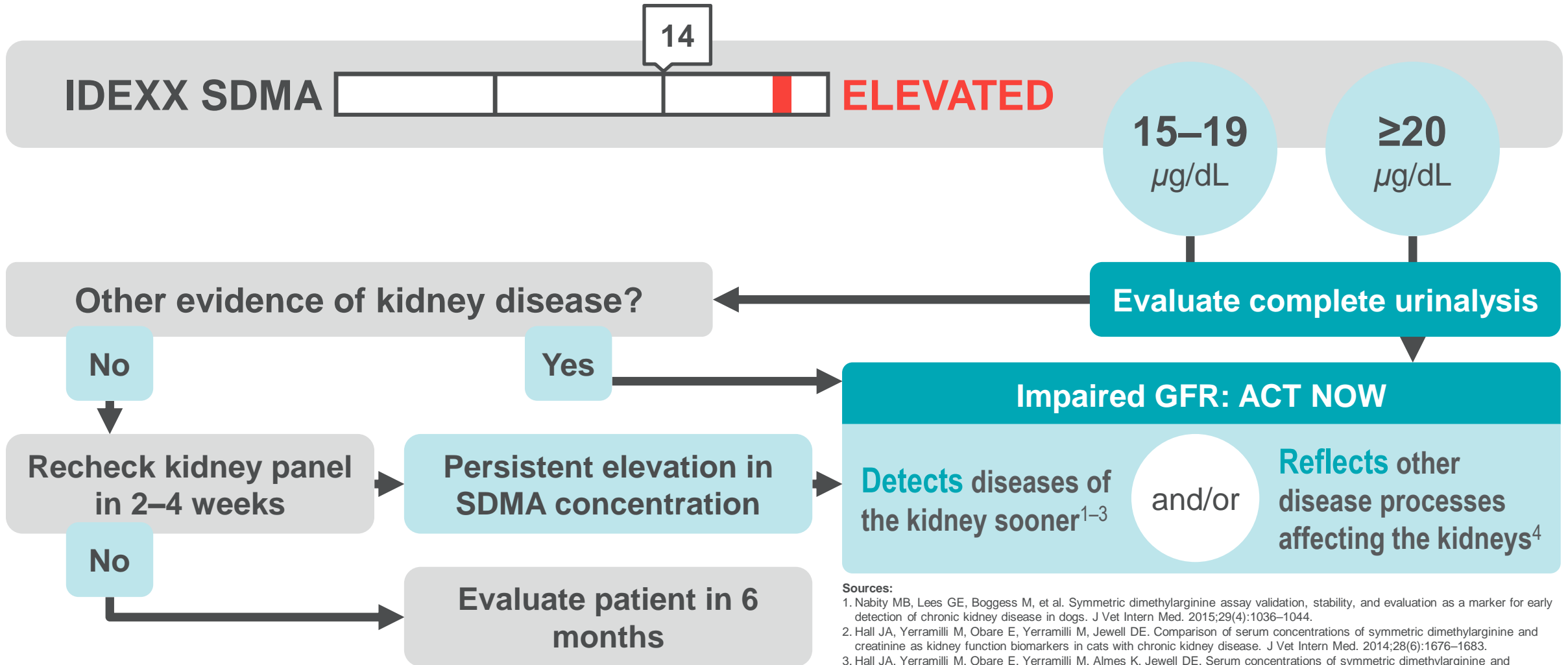
Differential diagnoses in VetConnect® PLUS



Increased IDEXX SDMA (>14 µg/dL)

- Kidney disease
 - Includes both acute and chronic kidney disease
 - Infection (e.g. upper UTI, leptospirosis, Lyme)
 - Inflammatory (e.g. glomerulonephritis, tubulointerstitial nephritis)
 - Toxic insult (e.g. NSAIDs, vitamin D toxicity, ethylene glycol)
 - Ischemia
 - Congenital kidney disease (e.g. polycystic kidney disease, renal dysplasia)
 - Renal amyloidosis
 - Renal neoplasia
- Secondary kidney injury associated with non-renal diseases:
 - Hyperthyroidism
 - Systemic hypertension
 - Vector-borne disease
 - Urinary obstruction - lower
 - Sepsis

The IDEXX SDMA[®] Algorithm



Sources:

1. Nabity MB, Lees GE, Boggess M, et al. Symmetric dimethylarginine assay validation, stability, and evaluation as a marker for early detection of chronic kidney disease in dogs. J Vet Intern Med. 2015;29(4):1036–1044.
2. Hall JA, Yerramilli M, Obare E, Yerramilli M, Jewell DE. 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(6):1676–1683.
3. Hall JA, Yerramilli M, Obare E, Yerramilli M, Almes K, Jewell DE. Serum concentrations of symmetric dimethylarginine and creatinine in dogs with naturally occurring chronic kidney disease. J Vet Intern Med. 2016;30(3):794–802.
4. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA.

What are their kidneys telling you?

Listen closer with IDEXX SDMA[®]

Detects

diseases of the
kidney sooner¹⁻³

Chronic kidney disease
Acute kidney injury
Pyelonephritis
Upper urinary obstruction
Kidney stones
Glomerulonephritis
Congenital disease



Reflects

other disease
processes affecting
the kidneys⁴

Hyperthyroidism
Vector-borne disease⁵
Systemic hypertension
Cardiorenal syndrome
Lower urinary obstruction
Sepsis
Cancer
Drug toxicity

Sources:

1. Nabyt MB, Lees GE, Boggess M, et al. Symmetric dimethylarginine assay validation, stability, and evaluation as a marker for early detection of chronic kidney disease in dogs. *J Vet Intern Med.* 2015;29(4):1036–1044.
2. Hall JA, Yerramilli M, Obare E, Yerramilli M, Jewell DE. 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(6):1676–1683.
3. Hall JA, Yerramilli M, Obare E, Yerramilli M, Almes K, Jewell DE. Serum concentrations of symmetric dimethylarginine and creatinine in dogs with naturally occurring chronic kidney disease. *J Vet Intern Med.* 2016;30(3):794–802.
4. Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA.
5. Drake C, Ogeer J, Beall MJ, Buch JS, Clements C, McCrann DJ, Relford RL. Investigation of the association between Lyme seroreactivity and chronic kidney disease in dogs [ACVIM Abstract ID08]. *J Vet Intern Med.* 2018;32(6):2264.

Impaired GFR: Investigate, manage, and monitor

Investigate

- Investigate an underlying cause
- Consider performing additional diagnostics
- Assess for a concurrent condition

Manage

- Treat appropriately
- Provide additional support
- Adjust anaesthesia protocols

Monitor

- Monitor renal biomarkers
- Take steps based on the outcome

Impaired GFR: Investigate

Investigate



Investigate an underlying cause

- Urinary tract infection (UTI/pyelonephritis)
- Toxicity (e.g., NSAIDs, ethylene glycol, lilies)
- Acute kidney injury
- Systemic hypertension
- Chronic kidney disease (CKD)



Consider performing additional diagnostics

- Urine culture and minimum inhibitory concentration (MIC) susceptibility
- Infectious disease testing
- Abdominal imaging
- Urine protein:creatinine (UPC) ratio (proteinuria)
- Blood pressure

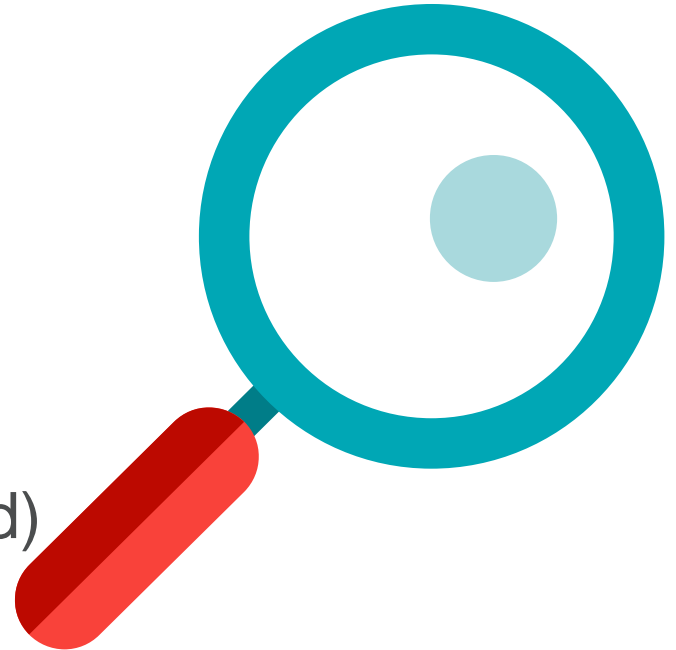


Assess for a concurrent condition

- Hydration status
- Thyroid status (feline)

What diagnostics should we recommend?

- A. Urine culture and MIC susceptibility testing
- B. Blood pressure measurement
- C. Urine protein:creatinine (UPC) ratio
- D. Abdominal imaging (radiographs and/or ultrasound)



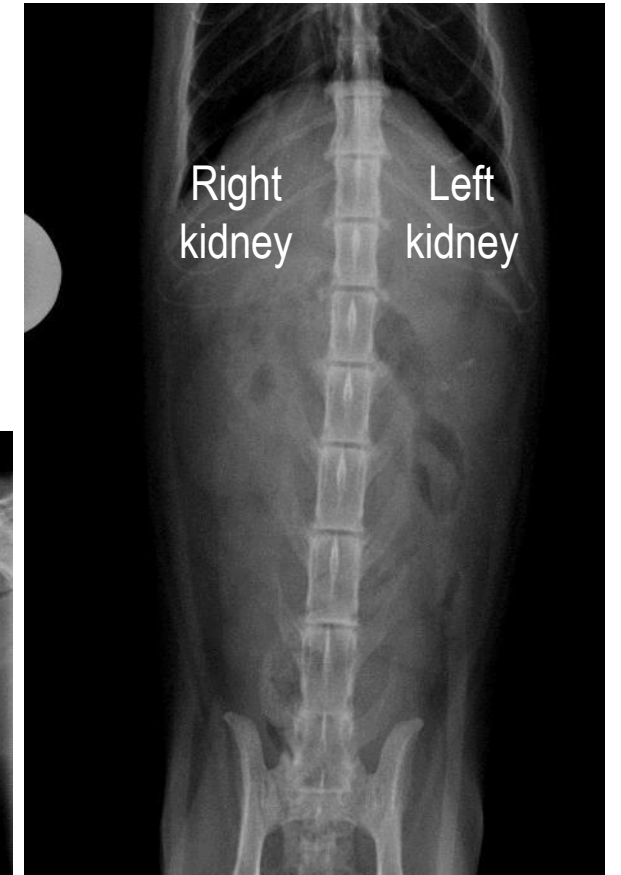
Investigation

Urine culture: Negative

Systolic blood pressure: 151 mm Hg (borderline hypertensive)

UPC: 0.18 (normal)

Radiographs: Slightly small, irregular kidneys, with small irregular areas of mineralization, likely representing kidney stones



Can Jasper be diagnosed with CKD now?

- A. Yes
- B. No
- C. I don't know



Impaired GFR: Investigate, manage, and monitor

Investigate

Refer to a specialist for abdominal ultrasound:

- Confirm kidney stones
- Rule out stones causing obstruction

Manage

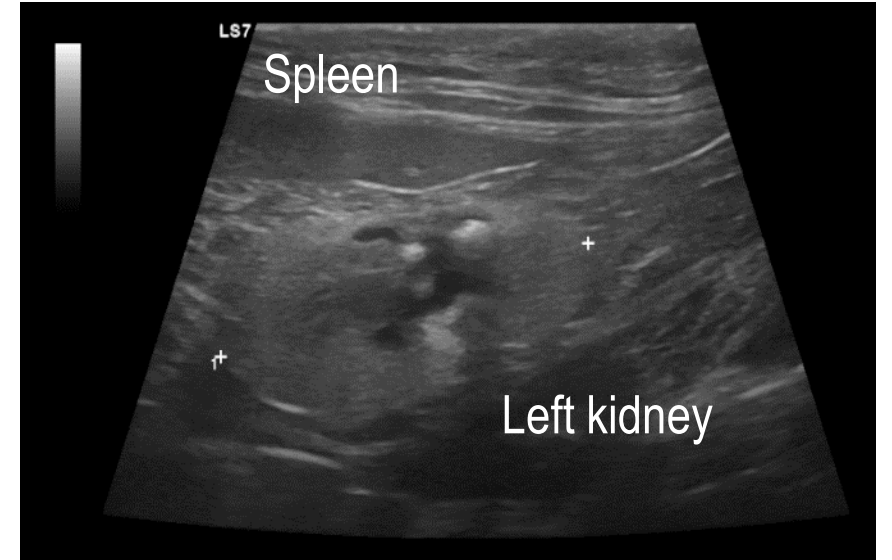
Plenty of fresh, clean water sources

Monitor

Recheck in 2 to 3 weeks

3-week recheck visit summary

- Jasper doing same at home
- Ultrasound at specialist confirmed kidney stones but no evidence stones causing obstruction



Chemistry

1/23/18
2:49 PM



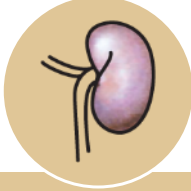



1/2/18
2:49 PM



| | | | | |
|---|-----------|-----------------|--|-----------|
| ▶ IDEXX SDMA ▶ Learn More | 17 | 0 – 14 µg/dL | | 21 |
| ▶ Creatinine | 2.1 | 0.8 – 2.4 mg/dL | | 2.2 |
| ▶ BUN | 29 | 16 – 36 mg/dL | | 28 |

What IRIS stage is Jasper's CKD?

- A. Stage 1
- B. Stage 2
- C. Stage 3
- D. Stage 4

| | |  |  |  |  |
|----------------------------|--------|---|---|---|---|
| | | Stage 1 No azotemia (Normal creatinine) | Stage 2 Mild azotemia (Normal or mildly elevated creatinine) | Stage 3 Moderate azotemia | Stage 4 Severe azotemia |
| Creatinine in mg/dL | Canine | Less than 1.4 (125 μmol/L) | 1.4–2.8 (125–250 μmol/L) | 2.9–5.0 (251–440 μmol/L) | Greater than 5.0 (440 μmol/L) |
| | Feline | Less than 1.6 (140 μmol/L) | 1.6–2.8 (140–250 μmol/L) | 2.9–5.0 (251–440 μmol/L) | Greater than 5.0 (440 μmol/L) |
| SDMA in μg/dL | Canine | Less than 18 | 18–35 | 36–54 | Greater than 54 |
| | Feline | Less than 18 | 18–25 | 26–38 | Greater than 38 |

Impaired GFR: Manage

Manage



Treat appropriately

- Underlying disease (e.g., pyelonephritis, infectious disease)
- Dehydration
- Care with nephrotoxic medications (e.g., NSAIDs)
- Hypertension
- Proteinuria



Provide additional support

- Ample, clean water
- Kidney-supportive diet if warranted



Adjust anesthesia protocols

- Fluids (intravenous or subcutaneous)
- Oxygen support prior to, during, and after procedure
- Adjust pain management

Impaired GFR: Monitor

Monitor



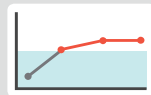
Monitor renal biomarkers

Trended testing of:

- SDMA, BUN, creatinine, and, phosphorus
- Urinalysis
- Blood pressure

Take steps based on outcomes:

SDMA remains increased, but stable



GFR impaired but stable

- Consider CKD diagnosis, refer to IRIS staging and treatment guidelines
- Institute appropriate supportive care and monitoring

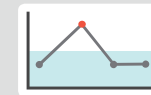
SDMA continues to increase



GFR impairment is progressive

- Ongoing active kidney injury
- Revisit investigate: repeat or perform additional diagnostics
- Institute ongoing supportive care

SDMA returns to normal



GFR restores

- Recovery from mild injury
- Response to appropriate therapy
- Compensatory mechanisms
- Recheck 6 months–1 year

Impaired GFR: Investigate, manage, and monitor

Manage

- Treat based on IRIS CKD Stage 2 guidelines:
- Plenty of fresh, clean water sources
 - Kidney therapeutic diet to prevent progression of CKD and new stone formation

Monitor

Owners instructed to monitor for any increase in drinking or urination, appetite change, vomiting, or lethargy

Recheck in 2 to 4 months:

- Feline senior bundle with Catalyst[®] SDMA
- Blood pressure
- Radiographs to monitor stones

Clinical impact of increased SDMA

- Including the Catalyst[®] SDMA Test in Jasper's chemistry panel with his routine preventive care lab testing lead to an early diagnosis of CKD with concurrent kidney stones.
- Earlier treatment of CKD will help delay progression and prevent additional kidney stones from forming.



Question

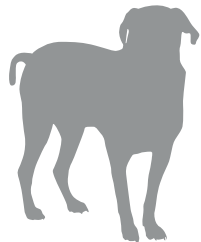
- What is the implication of a single, mild increase in SDMA?



Study design



Patient records screened



3.6 million
dogs



1.6 million
cats



Inclusion criteria

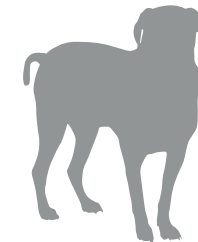
≥3 SDMA test results paired with creatinine

First SDMA result within the reference interval (0–14 µg/dL)

First creatinine result within the reference interval (dogs <132 µmol/L; cats <203 µmol/L)



Patients included in retrospective analysis



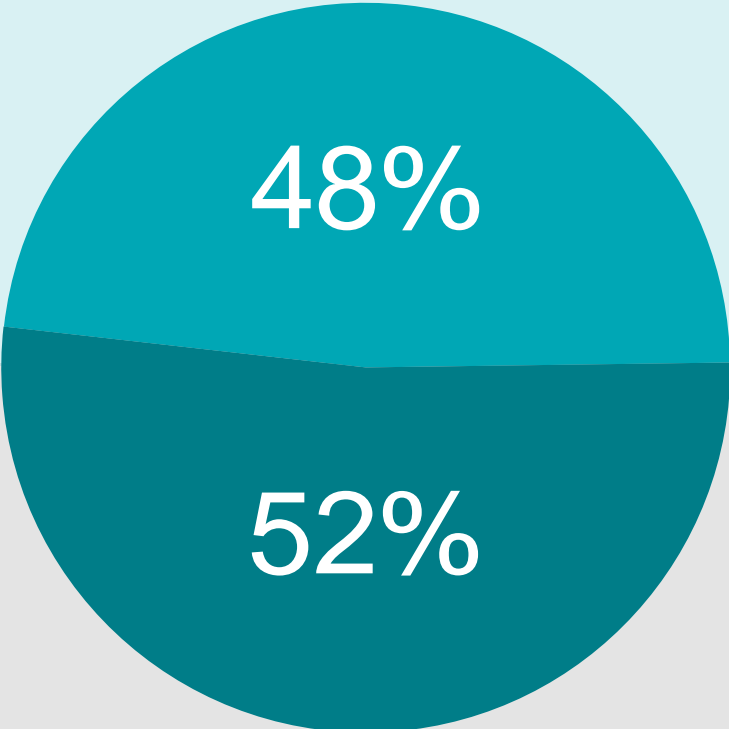
16,523 dogs



16,454 cats

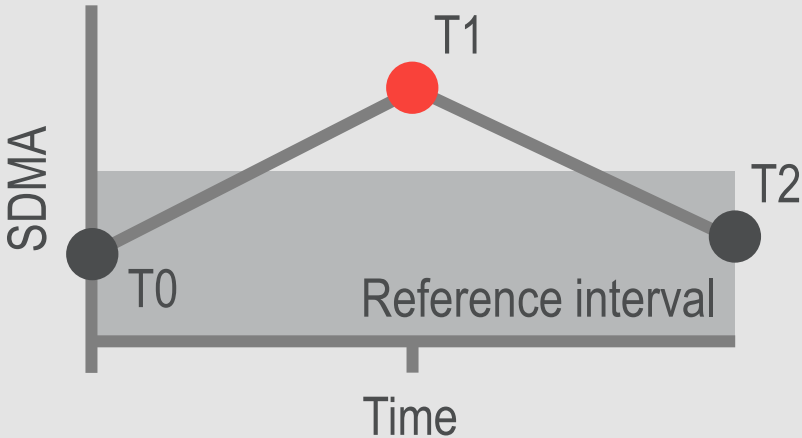
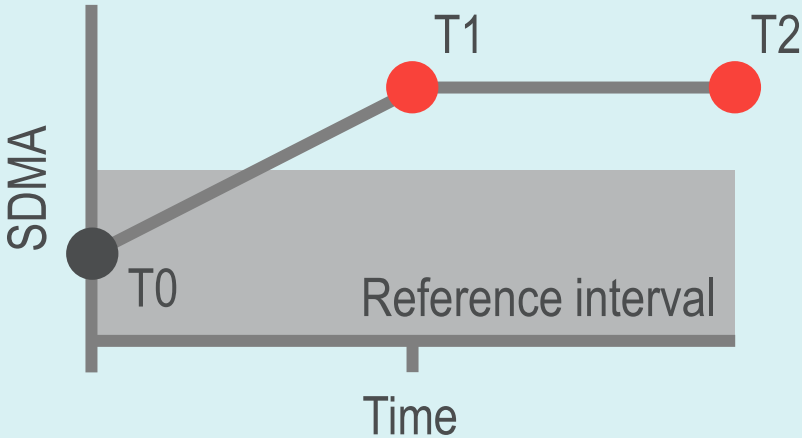
Source: Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA. 092_White-Paper_200121093103.

Patients with persistent increases in SDMA had two consecutive elevated results in a row



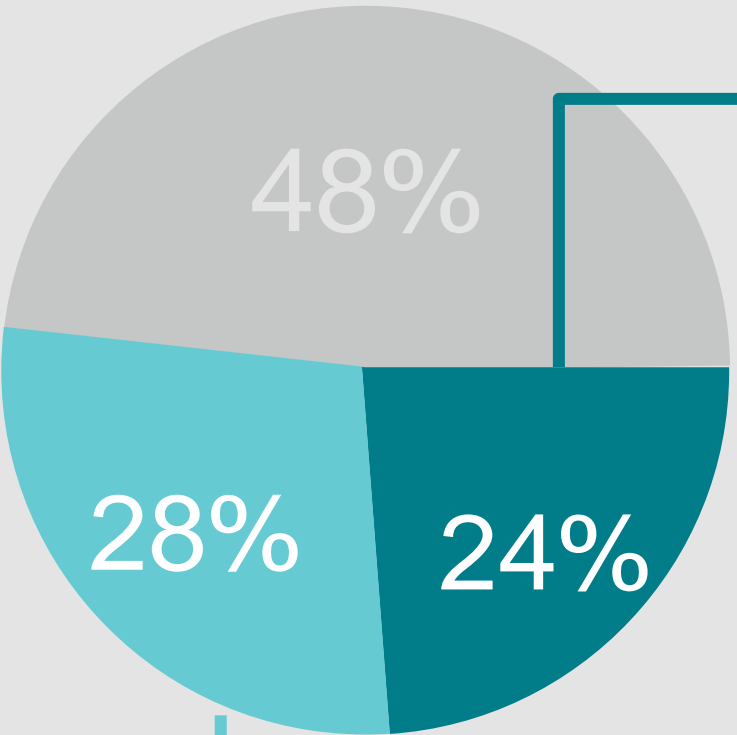
SDMA remains increased (T2)

GFR returns to within reference interval (T2)

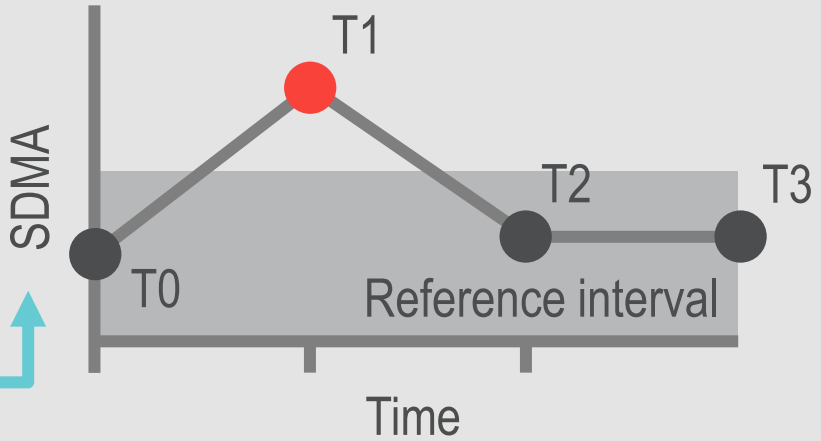
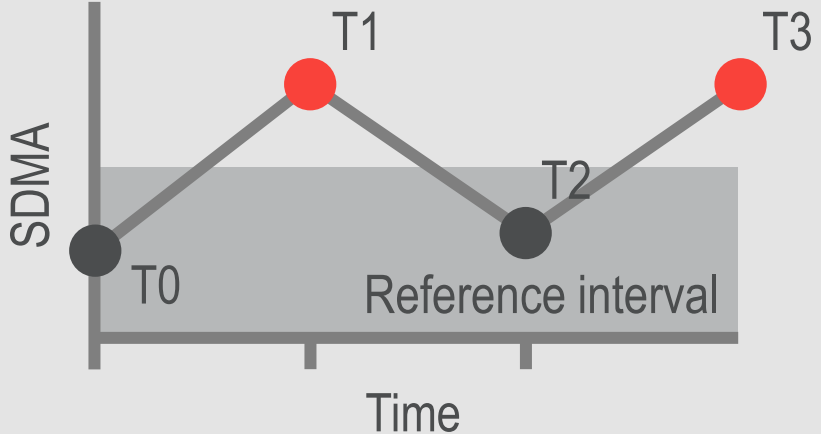


Source: Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA. 092_White-Paper_200121093103.

Of the 52% of patients with restored GFR, about half risked another increase in SDMA within 12 months



Within the next 12 months

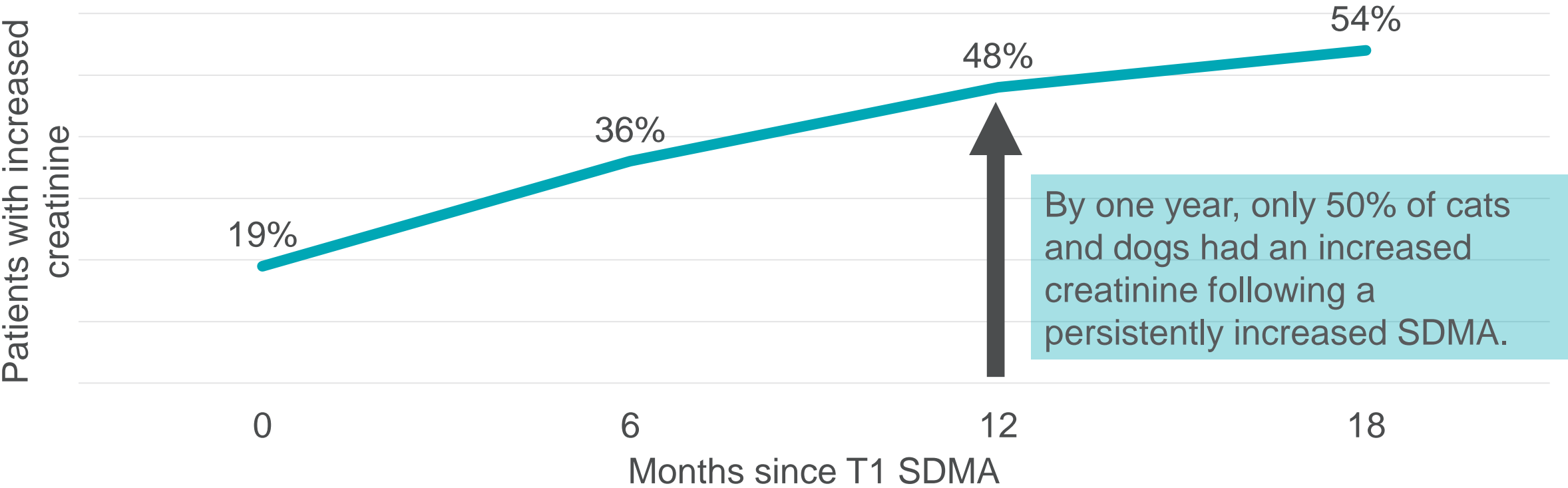


Source: Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA. 092_White-Paper_200121093103.



SDMA can be the earliest indicator of progressive decline in renal function

Percent of patients with increased creatinine by time interval since persistent mildly elevated T1 SDMA concentration



Source: Data on file at IDEXX Laboratories, Inc. Westbrook, Maine USA. 092_White-Paper_200121093103.

Summary



- SDMA is a valuable parameter
- Earlier detection of reduced GFR
 - IRIS Stage 1 disease
 - Opportunities
 - Look for a cause – drives further diagnostics
 - Manage to slow progression of disease
 - 72% chance mild elevation will persist
- SDMA has a place in a PreGA screen
 - Management

IDEXX

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IDEXX is green

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