

IRIS Staging of CKD (modified in 2023)

1. Staging of CKD based on blood creatinine and SDMA concentrations

Staging is undertaken following diagnosis of chronic kidney disease (CKD) in order to facilitate appropriate treatment and monitoring of the canine or feline patient.

Staging is based initially on fasting blood creatinine or fasting blood SDMA concentration or (preferably) both assessed on at least two occasions in a hydrated, stable patient. The dog or cat is then substaged based on proteinuria and blood pressure.

Using these criteria, some empirical recommendations can be made about the type of treatment it would be logical to use for these cases. In addition, predictions based on clinical experience might be made about the likely response to treatment.

Stage	Blood creatinine*		Comments
	$\mu\text{mol/l}$ mg/dl		
	SDMA# $\mu\text{g/dl}$		
	Dogs	Cats	
1	<125 <1.4 <18	<140 <1.6 <18	Normal blood creatinine or normal or mild increase blood SDMA. Some other renal abnormality present (such as, inadequate urinary concentrating ability without identifiable non-renal cause (in cats not dogs), abnormal renal palpation or renal imaging findings, proteinuria of renal origin, abnormal renal biopsy results, increasing blood creatinine or SDMA concentrations in samples collected serially). Persistently elevated blood SDMA concentration (>14 $\mu\text{g/dl}$) may be used to diagnose early CKD
2	125 – 250 1.4 – 2.8 18 - 35	140 – 250 1.6 – 2.8 18 - 25	Normal or mildly increased creatinine, mild renal azotemia (lower end of the range lies within reference ranges for creatinine for many laboratories, but the insensitivity of creatinine concentration as a screening test means that patients with creatinine values close to the upper reference limit often have excretory failure). Mildly increased SDMA. Clinical signs usually mild or absent.
3	251 – 440 2.9 – 5.0 36 - 54	251 – 440 2.9 – 5.0 26 - 38	Moderate renal azotemia. Many extrarenal signs may be present, but their extent and severity may vary. If signs are absent, the case could be considered as early Stage 3, while presence of many or marked systemic signs might justify classification as late Stage 3.
4	>440 >5.0 >54	>440 >5.0 >38	Increasing risk of systemic clinical signs and uremic crises

*The blood creatinine concentrations apply to average size dogs – those of extreme size may vary. #The recommendations for SDMA are based on published literature which utilizes proprietary IDEXX technology for measuring SDMA. At this time, it is not known if other assays will provide equivalent results.

Discrepancies between creatinine and SDMA

IRIS CKD staging is based on fasting blood creatinine concentration and blood SDMA concentration. SDMA may be a more sensitive marker that is less impacted by loss of lean body mass.

DOGS:

If serum or plasma SDMA is persistently >18 µg/dl in a dog whose creatinine is <1.4 mg/dl (IRIS CKD stage 1 based on creatinine), this canine patient should be staged and treated as an IRIS CKD Stage 2 patient.

If serum or plasma SDMA is persistently >35 µg/dl in a dog whose creatinine is between 1.4 and 2.8 mg/dl (IRIS CKD stage 2 based on creatinine), this canine patient should be staged and treated as an IRIS CKD Stage 3 patient.

If serum or plasma SDMA is persistently >54 µg/dl in a dog whose creatinine is between 2.9 and 5.0 mg/dl (IRIS CKD stage 3 based on creatinine), this canine patient should be staged and treated as an IRIS CKD Stage 4 patient.

CATS:

If serum or plasma SDMA is persistently >18 µg/dl in a cat whose creatinine is <1.6 mg/dl (IRIS CKD stage 1 based on creatinine), this feline patient should be staged and treated as an IRIS CKD Stage 2 patient.

If serum or plasma SDMA is persistently >25 µg/dl in a cat whose creatinine is between 1.6 and 2.8 mg/dl (IRIS CKD stage 2 based on creatinine), this feline patient should be staged and treated as an IRIS CKD Stage 3 patient.

If serum or plasma SDMA is persistently >38 µg/dl in a cat whose creatinine is between 2.9 and 5.0 mg/dl (IRIS CKD stage 3 based on creatinine), this feline patient should be staged and treated as an IRIS CKD Stage 4 patient.

SDMA assays are offered by a number of laboratories throughout the world. The methodology used has not yet been standardized and the recommendations made above are based on the proprietary methodology offered by IDEXX Laboratories.

These recommendations are based on current state of knowledge where SDMA appears to be a more sensitive indicator of early stage CKD in the dog and cat.

Data are starting to emerge on conditions where SDMA may be elevated without a reduction in GFR, where serum creatinine values are unaffected. Lymphoma in dogs and cats is one such example. This illustrates the value of having two biomarkers which are surrogate markers for GFR which can be interpreted together.

Breed and size associated effects on serum creatinine and SDMA

Healthy Birman cats and greyhound dogs have been found to have higher serum SDMA values than other breeds. Both these breeds also have higher serum creatinine values taking some healthy individuals (up to 20% of Birman cats) outside laboratory reference intervals.

For further details on SDMA and creatinine as surrogate markers of GFR please refer to the education article entitled 'Utility of Creatinine, UPC, and SDMA in the Early Diagnosis of CKD' which provides more detailed information.

2a. Substaging by Proteinuria

The goal is to identify renal proteinuria having ruled out post-renal and pre-renal causes.

Standard urine dipsticks can give rise to false positives therefore practitioners should consider using a more specific screening test such as the urine protein to creatinine ratio (UP/C) or a species-specific albuminuria assay.

The UP/C should be measured in all dogs and cats with CKD, provided there is no evidence of urinary tract inflammation or hemorrhage and the routine measurement of plasma proteins has ruled out dysproteinemias. Ideally substaging should be done on the basis of at least two urine samples collected over a period of at least 2 weeks.

UP/C value		Substage
Dogs	Cats	
<0.2	<0.2	Non-proteinuric
0.2 to 0.5	0.2 to 0.4	Borderline proteinuric
>0.5	>0.4	Proteinuric

Canine and feline patients that are persistently borderline proteinuric should be re-evaluated within 2 months and re-classified as appropriate.

UP/Cs in the non-proteinuric or borderline proteinuric range may be categorized as 'microalbuminuric'. The significance of microalbuminuria in predicting future renal health is not completely understood at present. IRIS' recommendation is to continue to monitor this level of proteinuria (dogs). Veterinarians might offer treatment for cats persistently in the borderline proteinuric or microalbuminuric range considering the association with proteinuria of this level and progressive kidney disease in the cat (see treatment guidelines).

Proteinuria may decline as renal dysfunction worsens and so may be less frequent in dogs and cats in Stages 3 and 4.

Response to any treatment given to reduce glomerular hypertension, filtration pressure, and proteinuria, should be monitored at intervals using UP/C.

2b. Substaging by Blood pressure

Canine and feline patients should be acclimatized to the measurement conditions and multiple measurements taken. The final classification should rely upon multiple systolic blood pressure determinations, preferably done during repeated patient visits to the clinic on separate days, but acceptable if during the same visit with at least 2 hours separating determinations. Patients are substaged by systolic blood pressure according to the degree of risk of target organ damage, and whether there is evidence of target organ damage or complications.

For most dogs and all cats, the IRIS blood pressure substages are as follows:

Systolic Blood Pressure mmHg	Blood Pressure Substage	Risk of Future Target Organ Damage
<140	Normotensive	Minimal
140 – 159	Prehypertensive	Low
160 – 179	Hypertensive	Moderate
≥ 180	Severely hypertensive	High

However, some breeds of dog, particularly sight hounds, tend to have higher blood pressure than other breeds. It is preferable to use breed-specific reference ranges if available. The classification of risk of future target organ damage in “high-pressure breeds” might be adjusted as follows:

Minimal risk – systolic pressure <10 mm Hg above the breed-specific reference range

Low risk – systolic pressure 10-20 mm Hg above the breed-specific reference range

Moderate risk – systolic pressure 20-40 mm Hg above the breed-specific reference range

High risk – systolic pressure >40 mm Hg above the breed-specific reference range.

As with proteinuria, in the absence of evidence of existing target organ damage, demonstration of persistence of blood pressure readings within a particular category is important. ‘Persistence’ of increase here should be judged on multiple measurements made over the following timescales in these blood pressure substages:

Hypertensive – systolic blood pressure 160 to 179 mm Hg measured over 1 to 2 weeks

Severely hypertensive – systolic blood pressure ≥180 mm Hg measured over 1 to 2 weeks.

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3. Revision of staging and substaging after treatment

The stage and substages assigned to the patient should be revised appropriately as changes occur. For example, a substantial increase in blood creatinine or SDMA concentration might warrant reassignment to a higher stage to reflect the new situation.

Similarly, if antihypertensive (or antiproteinuric) treatment has been instituted, the patient's classification on re-evaluation should be adjusted if necessary to reflect the new blood pressure (or UP/C) rather than the original status, with the addition of an indication that the current classification is affected by treatment.

The following two examples illustrate the process of revision, where 'treating' is used as an indicator of ongoing treatment.

Example 1

Euvolemic cat with stable renal function

Creatinine 200 µmol/l (2.3 mg/dl)

SDMA 22 µg/dl

UP/C 0.32

Systolic blood pressure 200 mm Hg

Classification – *IRIS CKD Stage 2, borderline proteinuric, severely hypertensive.*

Same cat after antihypertensive treatment

Creatinine 220 µmol/l (2.5 mg/dl)

SDMA 24 µg/dl

UP/C 0.12

Systolic blood pressure 155 mm Hg

New classification – *IRIS CKD Stage 2, non-proteinuric, prehypertensive (treating).*

Example 2

Euvolemic dog with stable renal function

Creatinine 230 µmol/l (2.6 mg/dl)

SDMA 39 µg/dl

UP/C 0.8

Systolic blood pressure 155 mm Hg

Classification – *IRIS CKD Stage 3,, proteinuric, prehypertensive*

*Note: As described above in the **Discrepancies between creatinine and SDMA** section, if blood SDMA is persistently >35 µg/dl in a canine patient whose blood creatinine is between 1.4 and 2.8 mg/dl (IRIS CKD stage 2 based on creatinine), this dog should be staged and treated as an IRIS CKD Stage 3 patient*

Same dog after antiproteinuric treatment

Creatinine 240 µmol/l (2.7 mg/dl)

SDMA 42 µg/dl

UP/C 0.4

Systolic blood pressure 155 mm Hg

New classification – *IRIS CKD Stage 3, borderline proteinuric (treating), prehypertensive.*