

IRIS Staging of CKD (modified 2017)

1. Staging of CKD based on blood creatinine concentration

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

Staging is based initially on fasting blood creatinine concentration, assessed on at least two occasions in the stable patient. The patient 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
	Dogs	Cats	
At risk	<125 <1.4	<140 <1.6	History suggests the animal is at increased risk of developing CKD in the future because of a number of factors (such as, exposure to nephrotoxic drugs, breed, high prevalence of infectious disease in the area, or old age).
1	<125 <1.4	<140 <1.6	Nonazotemic. Some other renal abnormality present (such as, inadequate urinary concentrating ability without identifiable nonrenal cause, abnormal renal palpation or renal imaging findings, proteinuria of renal origin, abnormal renal biopsy results, increasing blood creatinine concentrations in samples collected serially).
2	125 – 180 1.4 – 2.0	140 – 250 1.6 – 2.8	Mild renal azotemia (lower end of the range lies within reference ranges for many laboratories, but the insensitivity of creatinine concentration as a screening test means that animals with creatinine values close to the upper reference limit often have excretory failure). Clinical signs usually mild or absent.
3	181 – 440 2.1 – 5.0	251 – 440 2.9 – 5.0	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	>440 >5.0	Increasing risk of systemic clinical signs and uraemic crises

Note these blood creatinine concentrations apply to average size dogs – those of extreme size may vary

Symmetric dimethylarginine (SDMA) and IRIS CKD guidelines

IRIS CKD staging is based currently on fasting blood creatinine concentrations, but there are indications that SDMA concentrations in blood plasma or serum may be a more sensitive biomarker of renal function. Accordingly, if blood SDMA concentrations are known, some modification to the guidelines might be considered, as follows:

A persistent increase in SDMA above 14 µg/dl suggests reduced renal function and may be a reason to consider an adult dog or cat with creatinine values <1.4 or <1.6 mg/dl, respectively, as IRIS CKD Stage 1. The corresponding reference point suggested for dogs <1 year old is >16 µg/dl.

In IRIS CKD Stage 2 patients with low body condition scores, SDMA ≥25 µg/dl may indicate the degree of renal dysfunction has been underestimated. Consider treatment recommendations listed under IRIS CKD Stage 3 for this patient.

In IRIS CKD Stage 3 patients with low body condition scores, SDMA ≥45 µg/dl may indicate the degree of renal dysfunction has been underestimated. Consider treatment recommendations listed under IRIS CKD Stage 4 for this 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 comments are preliminary and based on early data from the use of SDMA in veterinary patients. We expect them to be updated as the veterinary profession gains further experience using SDMA alongside creatinine, the long-established marker in diagnosis and monitoring of canine and feline CKD.

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 sulfosalicylic acid turbidometric test.

The urine protein to creatinine ratio (UP/C) should be measured in all cases, provided there is no evidence of urinary tract inflammation or hemorrhage and the routine measurement of plasma proteins has ruled out dysproteinemias. Ideally staging 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

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 understood at present. IRIS' recommendation is to continue to monitor this level of proteinuria.

Proteinuria may decline as renal dysfunction worsens and so may be less frequent in animals 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

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, the IRIS blood pressure substages are as follows:

Systolic Blood Pressure mm Hg	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, 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 months

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

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 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

Cat before treatment

Creatinine 200 µmol/l (2.3 mg/dl)

UP/C 0.3

Systolic blood pressure 200 mm Hg

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

Same cat after antihypertensive treatment

Creatinine 300 µmol/l (3.4 mg/dl)

UP/C 0.3

Systolic blood pressure 155 mm Hg

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

Example 2

Dog before treatment

Creatinine 160 µmol/l (1.8 mg/dl)

UP/C 0.8

Systolic blood pressure 155 mm Hg

Classification – *IRIS CKD Stage 2, proteinuric, prehypertensive.*

Same dog after antiproteinuric treatment

Creatinine 170 µmol/l (1.9 mg/dl)

UP/C 0.4

Systolic blood pressure 155 mm Hg

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