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ACUTE KIDNEY INJURY. A PRACTICAL APPROACH TO AKI IRIS GRADING SYSTEM

Acute kidney injury (AKI) refers to a wide spectrum of clinical conditions in which the kidneys are abruptly damaged, leading to parenchymal injury with or without loss of function. Only in recent years have we come a little closer to a uniform and widely accepted definition of the disease, in particular concerning the degree of function loss and its timing. Already minimal increases in serum creatinine (0.3 mg/dl, 26 µmol/l) have been shown in human and small animal medicine to be associated with a worse outcome, independently of the underlying disease. It has long been thought that this merely reflected a more severe underlying disease and that the kidneys just mirrored this fact. However, multiple lines of evidence from experimental medicine and observational studies suggest that the kidney injury itself, rather than the organ failure, has far-reaching multi-systemic consequences that can lead to myocardial injury and other organ damages. When more severe renal failure develops, the resulting uremic syndrome with its toxic, metabolic and inflammatory components markedly exacerbates the systemic manifestations and the multiple organ injuries.

With the change in nomenclature from "acute renal failure" to "acute kidney injury", the main aim was to sensitize the clinicians to the recognition of possible secondary AKI in the course of another significant disease. The term AKI refers thus to all forms of acute kidney disease, with or without obvious function loss or organ failure. To account for the severity of the function loss, a grading system has been proposed by the International Renal Interest Society (IRIS, AKI grading system), based on the fasting serum creatinine concentration and the urine production.

The classification scheme consists of five grades. **IRIS AKI Grade I** includes non-azotemic dogs and cats (<1.6 mg/dl, <140 µmol/l) with historical, clinical, laboratory and imaging evidence of AKI. The Grade I includes animals with progressive increases in blood creatinine of ≥ 0.3 mg/dl (≥ 26.4 µmol/l), within the non-azotemic range during a 48 h interval. It includes also animals whose oliguria is fluid responsive to a urine production >1 ml/kg/h within 6 h and/or decrease in blood creatinine to baseline in 48 h. IRIS AKI Grade II includes animals with documented AKI characterized by mild azotemia (1.7-2.5 mg/dl, 141-220 µmol/l) in addition to other historical, biochemical, anatomic, or urine production characteristics of AKI (as for Grade I), and similarly includes those whose oliguria and/or azotemia is readily fluid volume responsive. Fluid volume responsiveness represents an increase in urine production to >1 ml/kg/h within 6 h and/or decrease in serum creatinine to baseline over 48 h. **IRIS AKI Stage II** also includes animals that have an increase from their baseline creatinine concentration of ≥0.3 mg/dl (≥ 26.4 µmol/l) during a 48-hour interval associated with pre-existing chronic kidney disease (CKD). **IRIS AKI Grade III** (2.6-5.0 mg/dl, 221-439 µmol/l), **IV** (5.1-10.0 mg/dl, 440-880 µmol/l) and **V** (>10.0 mg/dl, >880 µmol/l) define dogs and cats with documented AKI and progressively increase of structural damage and functional failure, inducing uremia.

Unlike IRIS staging for CKD, grading of AKI does not imply that the kidney disease is stable or at steady-state. An animal's AKI grade will therefore vary over time, initially increasing as the disease worsens and hopefully stabilizing and improving later. Full recovery potential is present for a long time after initial injury, depending on the underlying cause of AKI. Improvement of renal function is commonly observed for weeks to months after discharge from hospital and it results from both true recovery and compensative adaptation with glomerular hyperfiltration.

Each grade of AKI is further subgraded in relation to **urine production** as oligoanuric (O: oliguria, < 1 ml/kg/h or anuria, no urine production, over 6 h), and depending on the requirement for **renal replacement therapy** (RRT).

Although the grading system is based on the serum creatinine concentration, it should not be forgotten, that this only suits the purpose of grading and not necessarily of diagnosis. Similarly to the staging of CKD, the grading of AKI is performed after establishing a diagnosis of AKI. Other evidence of AKI should be used for the diagnosis in conjunction with the presence of azotemia. The presence of systemic hypertension, electrolyte or acid-base disorders, abnormalities in the urine sediment examination or the urine concentration ability, the presence of renal glucosuria, proteinuria,

enzymuria, or abnormal findings on renal ultrasound examination may indicate an AKI. However, none of these parameters is specific and a global approach should always be considered. A typical workup for a dog or a cat with a clinical suspicion of AKI should therefore include a detailed history and physical examination (with fundic and rectal examination, blood pressure measurement), hematology, complete biochemical profile, venous blood gas analysis, urinalysis and urine culture, and diagnostic imaging (abdominal radiographs and ultrasound). In addition to these tests, as function of the clinical suspicion, infectious disease screening should be performed (e.g., leptospirosis in the dog), and possibly toxicology testing (e.g., ethylene glycol).

The fact that this grading system is based on the serum creatinine concentration reflects in its main strengths (ease of measurement) and weaknesses (variability of the assays between institutions, dependence on muscle mass). AKI being typically a non-steady state condition, the serum creatinine concentration reflects the glomerular filtration rate with a 1-2 d delay, both during the development and during the recovery from the disease. Therefore, a dog with an AKI Grade II may well have an actual GFR of 0 and be completely anuric and a dog with an AKI Grade V may in some situations have a better actual function. It should therefore always be kept in mind that this is a dynamic situation and that serial measurements are necessary, especially when major treatment decision must be taken.