# Guidelines

# For The Management of

# Acute Kidney Injury

**By**

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Acute kidney injury (AKI) is a rapid deterioration of renal function, resulting in inability to maintain fluid, electrolyte and acid-base balance.
It is detected and monitored by serial serum creatinine readings (which rise acutely), urine output and eGFR fall.

AKI is defined as any of the following:
*Increase in S.Creatinine by ≥ 0.3 mg/dl (≥26.5 µmol/l) within 48 hours; or
* Increase in S.Creatinine to ≥ 1.5 times baseline within the prior 7 days; or
* Urine volume < 0.5 ml/kg/h for 6 hours or 8 hours in children and young people.
* In children or young people a fall in eGFR of 25% or more in the past 7 days.

The rise of serum creatinine may not be evident before 50% of the GFR is lost.
The stage of AKI affects both management recommendations and prognosis, hence the importance of defining consistent stages.
Initially the RIFLE (Risk, Injury, Failure, Loss, End stage kidney disease) system was set up in 2004. This was modified by the AKIN (Acute Kidney Injury Network) and further developed in 2012 by KDIGO (Kidney Disease: Improving Global Outcomes).

***The RIFLE criteria*** ***Table 1***
**Risk**: GFR decrease >25%, serum creatinine increased 1.5 times or urine production of < 0.5 ml/kg/h for 6 hours
**Injury**: GFR decrease > 50%, doubling of creatinine or urine production < 0.5 ml/kg/h for 12 hours
**Failure:** GFR decrease > 75%, tripling of creatinine or creatinine > 4 mg/dl (>355 µmol/l) with acute rise ≥0.5 mg/dL OR urine output below 0.3 ml/kg/h for 24 hours
**Loss**: persistent AKI or complete loss of kidney function for more than 4 weeks
**End-stage renal disease**: need renal replacement therapy (RRT) for more than 3 months.
For children the pRIFLE, stages 1 (risk), 2 (injury), and 3 (failure) are defined at specific falling levels of eGFR and falling urinary output.
***AKIN***
Introduced by the Acute Kidney Injury Network, specific criteria exist for the diagnosis of AKI:
Rapid time course (less than 48 hours)
Reduction of kidney function
Rise in serum creatinine, defined by either:
Absolute increase in serum creatinine of ≥ 0.3 mg/dl (≥26.4 µmol/l)
Percentage increase in serum creatinine of ≥50%
Reduction in urine output, defined as < 0.5 ml/kg/h for more than 6 hours
***KDIGO*** ***Table 2***
Defines stage 1, 2 and 3 through increasing rises in creatinine levels and drop in urinary output.
For children; a paediatric version of RIFLE (pRIFLE) is also in use.

**Assessment and investigations**
Look for treatable cause (e.g. obstruction, hypovolaemia, nephrotoxic drugs or glomerulonephritis). Often, however, there are multiple causes, and finding the cause will not always dictate specific management. The cause can be established by:

*History*
Drugs - nephrotoxic drugs, recreational drugs, over-the-counter drugs and herbal remedies.
Occupational or recreational history - exposure to sewer systems, tropical diseases, rodents.
Urinary symptoms.
Past medical history.

*Examination*
Signs of infection or sepsis.
Signs of acute or chronic heart failure.
Fluid status (dehydration or fluid overload).
Palpable bladder or abdominal/pelvic mass.
Features of underlying systemic disease (rashes, arthralgia).

*Urinalysis*
Dipstick urine for blood, nitrates, leukocytes, glucose and protein
Urine osmolality.

**Classic laboratory findings in AKI**

| | UOsm | UNa | FeNa | BUN/Cr |
|---|---|---|---|---|
| **Prerenal** | >500 | <10 | <1% | >20 |
| **Intrinsic** | <350 | >20 | >2% | <15 |
| **Postrenal** | <350 | >40 | >4% | >15 |

*Blood tests*
This could involve:
-FBC, blood film. (Eosinophilia in acute interstitial nephritis, cholesterol embolisation, vasculitis. Thrombocytopenia and red cell fragments suggest thrombotic microangiopathy)
-Urea, electrolytes and creatinine.
-Coagulation studies: disseminated intravascular coagulation associated with sepsis.
-Creatine kinase, myoglobinuria: markedly elevated levels suggest rhabdomyolysis.
-C-reactive protein (CRP): nonspecific marker of infection or inflammation.
-Immunology:
Serum immunoglobulins, serum protein electrophoresis, Bence Jones' proteinuria:
Antinuclear antibody (ANA), anti-double-stranded DNA (anti-dsDNA) antibodies;
antineutrophil cytoplasmic antibody (ANCA) (associated with systemic vasculitis);
classical antineutrophil cytoplasmic antibodies (c-ANCA) and antiproteinase 3 (anti-PR3) antibodies associated with Wegener's granulomatosis;.

Complement concentrations: low in SLE, acute post-infectious glomerulonephritis, cryoglobulinaemia.
Antiglomerular basement membrane (anti-GBM) antibodies: present in Goodpasture's syndrome.
Antistreptolysin O and anti-DNase B titres: high after streptococcal infection.
-Virology: hepatitis B and C; HIV: (important for infection control within dialysis unit).

New biomarkers:**{**cystatin C, neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1) and interleukin-18 (IL-18)**}**.None been recommended for routine use.

*Ultrasound*
When obstruction is suspected or no cause has been identified.
*Other radiology*
CXR (pulmonary oedema).
Abdominal X-ray if renal calculi are suspected.
Contrast studies such as intravenous urogram (IVU) and renal angiography should be avoided because of the risk of contrast nephropathy.
Doppler ultrasound of the renal artery and veins (possible occlusion of the renal A.&V.).
Magnetic resonance angiography: for more accurate assessment of renal vascular occlusion.

**Differential diagnosis**
1. Chronic kidney disease: factors that suggest CKD include:
Long duration of symptoms. Nocturia. Absence of acute illness. Anaemia. Hyperphosphataemia, hypocalcaemia (but similar laboratory findings may complicate AKI).
Reduced renal size and cortical thickness on renal ultrasound (but renal size is typically preserved in patients with diabetes).
2. Acute on chronic renal failure.

**Management**
There is no specific treatment for AKI as the management is largely supportive.
The primary goals of treatment is treating the cause if possible, monitoring fluid and electrolyte balance; optimizing haemodynamic status with correction of hydration, biochemical, acid-base and hematological abnormalities.
*No therapeutic modalities to date have shown efficacy in treating the condition.*
*Therapeutic agents like dopamine, nesiritide, fenoldopam, mannitol are not indicated in the management of AKI and may be harmful*

*Dietary modification: restriction of salt and fluid as the kidneys do not adequately excrete toxins or fluids.
Restriction of potassium and phosphorus in the diet may be necessary, with guidance from frequent measurements.
In the polyuric phase of AKI, potassium and phosphorus may be depleted so that patients may require dietary supplementation and IV replacement.

Calculation of the nitrogen balance can be challenging, especially in the presence of volume contraction, hypercatabolic states, GI bleeding, and diarrheal disease. Critically ill patients should receive at least 1 g/kg/day protein but should avoid hyperalimentation, which can lead to an elevated blood urea nitrogen level and water loss resulting in hypernatremia.
*Nephrotoxic drugs (radiocontrast agents, antibiotics with nephrotoxic potential, heavy metal preparations, cancer chemotherapeutic agents, nonsteroidal anti-inflammatory drugs) should be avoided if possible or used with extreme caution with dose adjustment.
*Monitor creatinine, sodium, potassium, calcium, phosphate, glucose.
*Accurate measurement of urine output is essential to prevent volume overload or depletion.
*Correction of volume overload with furosemide
(Furosemide plays no role in converting an oliguric AKI to a nonoliguric AKI or in increasing urine output when a patient is not hypervolemic. However, response to furosemide can be taken as a good prognostic sign).
*Correction of severe acidosis with bicarbonate administration, which can be important as a bridge to dialysis
*Correction of hyperkalemia by:
•Decreasing the oral intake of potassium •Exchanging potassium across the gut lumen using potassium-binding resins•Promoting intracellular shifts in potassium with insulin, dextrose solutions, and beta agonists•Instituting dialysis
*Avoid hyperglycaemia. Insulin therapy may be required to maintain blood glucose levels; it has the effect of driving potassium into the cells, thus reducing blood levels.
Hypoglycaemia is also a potential risk in AKI, either with or without insulin therapy.
*Correction of hematologic abnormalities (e.g. anemia, uremic platelet dysfunction) with measures such as transfusions and administration of desmopressin or estrogens.
*Identify and treat infection
*Identify and treat acute complications: These include:
Hyperkalaemia. Acidosis. Pulmonary oedema. Bleeding.
*Acute renal artery thrombosis (of a single functioning kidney) may be treated surgically or by angioplasty and stenting.
*In rhabdomyolysis with myoglobulinuria, alkaline diuresis may prevent the development of severe renal failure, but must be undertaken with care in oliguric patients.
*Acute tubulo-interstitial nephritis may respond to a short course of high-dose corticosteroids,
*Haemolytic uraemic syndrome may respond to plasma exchange with fresh frozen plasma.
*Crescentic glomerulonephritis may respond to prednisolone, cyclophosphamide plasma exchange.

**Referral for renal replacement therapy (RRT)**
This should be considered if any of the following are not responding to medical management:
Fluid overload & pulmonary oedema.
Hyperkalaemia. Metabolic acidosis.
Symptoms or complications of uraemia such as pericarditis or encephalopathy.
Severe azotemia (BUN >80-100 mg/dl).

-This decision should be made on the basis of the overall condition of the patient, and should be discussed with the patient and/or relatives in accordance with shared decision-making guidelines.
- All patients receiving RRT should have an assessment by a dietician and advice about nutritional support.
- Urologist's advice may be required where there is an obstructive cause. Situations include renal calculi, papillary necrosis, tumours, strictures or prostatic enlargement

**Dialysis**

*Consider the broader clinical context, the presence of conditions that can be modified with RRT, and trends of laboratory tests rather than single BUN and creatinine thresholds alone when making the decision to start RRT.
*Patients with dialysis-dependent AKI should receive at least 3 hemodialysis treatments per week with a delivered Kt/V value of 1.2, or continuous hemodialysis (continuous venovenous hemodialysis or hemofiltration) of 20 mg/kg/h.
*No difference in outcome between the use of intermittent hemodialysis and continuous renal replacement therapy (CRRT). CRRT may have a role in patients who are hemodynamically unstable and who have had prolonged renal failure after a stroke or liver failure as may not tolerate the rapid shift of fluid and electrolytes caused during conventional hemodialysis.
*Peritoneal dialysis is not frequently used in patients with AKI. Nevertheless, it can technically be used in acute cases and probably is better tolerated hemodynamically than is conventional hemodialysis.
*Do not use diuretics to enhance kidney function recovery, or to reduce the duration or frequency of RRT.
*Use anticoagulation during RRT in AKI if a patient does not have an increased bleeding risk or impaired coagulation and is not already receiving systemic anticoagulation.
Base the decision to use anticoagulation on assessment of the patient’s potential risks and benefits.
*Patients without an increased bleeding risk or impaired coagulation and not already receiving effective systemic anticoagulation, it is suggested that:
.a) for anticoagulation in intermittent RRT, use either unfractionated or low-molecular weight heparin, rather than other anticoagulants.
.b) for anticoagulation in CRRT, use regional citrate anticoagulation rather than heparin in patients who do not have contraindications for citrate.
.c) for anticoagulation during CRRT in patients, who have contraindications for citrate, use either unfractionated or low-molecular-weight heparin, rather than other anticoagulants.
*Patients with increased bleeding risk who are not receiving anticoagulation, it is suggested to:
.a) use regional citrate anticoagulation, rather than no anticoagulation, during CRRT in a patient without contraindications for citrate.
.b) avoiding regional heparinization during CRRT in a patient with increased risk of bleeding.
*Patient with heparin-induced thrombocytopenia (HIT), all heparin must be stopped and use direct thrombin inhibitors (such as argatroban) or Factor Xa inhibitors (such as danaparoid or

fondaparinux) rather than other or no anticoagulation during RRT.
Patient with HIT who does not have severe liver failure; use argatroban rather than other thrombin or Factor Xa inhibitors during RRT.
*Initiate RRT in patients with AKI via an uncuffed nontunneled dialysis catheter, rather than a tunneled catheter.
*When choosing a vein for insertion of a dialysis catheter in patients with AKI, consider these preferences:
- First choice: right jugular vein;
- Second choice: femoral vein;
- Third choice: left jugular vein;
- Last choice: subclavian vein with preference for the dominant side.

*Use ultrasound guidance for dialysis catheter insertion.
*Obtain a chest radiograph promptly after placement and before first use of an internal jugular or subclavian dialysis catheter.
*Do not use topical antibiotics over the skin insertion site of a non-tunneled dialysis catheter in ICU patients with AKI requiring RRT.
*Do not use antibiotic locks for prevention of catheter-related infections of non-tunneled dialysis catheters in AKI requiring RRT.
*Use dialyzers with a biocompatible membrane for IHD and CRRT in patients with AKI.
*Use continuous and intermittent RRT as complementary therapies in AKI patients.
*Use CRRT rather than standard intermittent RRT for hemodynamically unstable patients & for patients with acute brain injury or other causes of increased intracranial pressure or generalized brain edema.
*Use bicarbonate, rather than lactate, as a buffer in dialysate and replacement fluid for RRT in patients with AKI with /out circulatory shock, liver failure and/or lactic acidemia.
*The dialysis fluids and replacement fluids in patients with AKI, at a minimum, should comply with American Association of Medical Instrumentation (AAMI) standards regarding contamination with bacteria and endotoxins.
*The dose of RRT to be delivered should be prescribed before starting each session of RRT with frequent assessment of the actual delivered dose in order to adjust the prescription.
*Deliver a Kt/V of 3.9 per week when using intermittent or extended RRT in AKI.
*Deliver an effluent volume of 20–25 ml/kg/h for CRRT in AKI which require a higher prescription of effluent volume.

**Further reading**

*In the absence of hemorrhagic shock; use isotonic crystalloids rather than colloids (albumin or starches) as initial management for expansion of intravascular volume in patients with or at risk for AKI.
*Use vasopressors in conjunction with fluids in patients with vasomotor shock with or at risk for AKI.
*Achieve a total energy intake of 20–30 kcal/kg/d in patients with any stage of AKI.
*Avoid restriction of protein intake with the aim of preventing or delaying initiation of RRT.

*Administering 0.8–1.0g/kg/d of protein in noncatabolic AKI patients without need for dialysis, 1.0–1.5 g/kg/d in patients with AKI on RRT, and up to a maximum of 1.7 g/kg/d in patients on continuous renal replacement therapy (CRRT) and in hypercatabolic patients.
*Providing nutrition preferentially via the enteral route in patients with AKI.
*Use insulin therapy targeting plasma glucose 110–149mg/dl (6.1–8.3mmol/l).
*Do not use diuretics to prevent or treat AKI except in the management of volume overload.
*Do not use low-dose dopamine, fenoldopam, atrial natriuretic peptide (ANP) nor recombinant human (rh) IGF-1 to prevent or treat AKI.
*A single dose of theophylline may be given in neonates with severe perinatal asphyxia, who are at high risk of AKI.
* Do not use aminoglycosides for the treatment of infections unless no suitable, less nephrotoxic, therapeutic alternatives are available.
*In patients with normal kidney function in steady state, aminoglycosides are administered as a single dose daily rather than multiple-dose daily treatment regimens.
*In the treatment of systemic mycoses or parasitic infections, use azole antifungal agents and/or the echinocandins rather than conventional amphotericin B, if equal therapeutic efficacy can be assumed.
*Apart from prevention of contrast-induced nephropathy; do not use N-acetylcysteine to prevent AKI in critically ill patients with hypotension nor be used for prevention of postsurgical AKI.

**Prognosis**
- Renal recovery is usually observed within the first 2 weeks, and many nephrologists tend to diagnose patients with end-stage (ie, irreversible) renal failure 6-8 weeks after the onset of AKI. It is always better to check these patients periodically, because some patients may regain renal function much later.
-Indicators of poor prognosis include older age, oliguria, hypotension, multiple organ failure, number of transfusions and acute on chronic renal failure.
-Prognosis is closely related to the underlying cause. Patients who need dialysis have a higher mortality but this is a reflection of the condition rather than a result of the treatment.
-The risk of mortality increases with the stage of AKI.
-Patients who have had AKI are at increased risk of developing chronic kidney disease..
-There may be an ongoing requirement for RRT.

**Prevention**
- Best treatment of acute kidney injury (AKI) is prevention and identification of patients at risk.
-All acutely ill patients in hospital should be closely monitored for signs of AKI with close monitoring of urinary output and creatinine levels to allow early detection.
-Avoidance of nephrotoxic drugs and iodinated contrast agents in these patients reduces the risk for AKI.
-At-risk patients who need iodinated contrast agents should be offered intravenous volume expansion with isotonic sodium bicarbonate or 0.9% sodium chloride to reduce the risks of developing AKI

**Prevention of Contrast-Induced Nephropathy**

1. Saline: prophylactic administration of IV fluid has been shown to decrease the incidence of contrast nephropathy. Although controversy exists regarding the ideal fluid, normal saline and isotonic NaHCO3 have proved to be effective. A normal saline solution of 1 mL/kg/h administered 12 hours before the procedure and then 12 hours after the procedure is recommended for most patients.
2.NaHCO3 :In patients who are at high risk for volume overload—in particular, those with chronic heart failure who have a left ventricular ejection fraction of less than 40%—isotonic NaHCO3 solution should be administered before and after the procedure. It can be prepared by mixing 3 ampules of NaHCO3 in a liter of 5% dextrose in water (D5W) and can be given at a rate of 3 mL/kg/h for 1 hour prior to the procedure, with the rate decreased to 1 mL/kg/h during the procedure and for 6 hours afterward.
3. N –acetylcysteine: orally at a dosage of 1200 mg every 12 hours. This is administered to high-risk patients the day before a contrast study is performed and is continued the day of the procedure.
4. Diuretics, nonsteroidal anti-inflammatory drugs (NSAIDs), and possibly angiotensin-converting enzyme (ACE) inhibitors should be withheld near the time of the procedure.

Other measures used to protect renal function perioperatively (eg, the administration of dopamine, diuretics, calcium-channel blockers, NSAIDs, ACE inhibitors, or hydration fluids) found no reliable evidence that these interventions are effective.

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**Table 1: RIFLE Classification System for Acute Kidney Injury**

| Stage | GFR** Criteria | Urine Output Criteria | Probability |
|---|---|---|---|
| Risk | SCr† increased × 1.5 *or*<br>GFR decreased >25% | UO‡ < 0.5 mL/kg/h × 6 h | High sensitivity<br><br>(Risk >Injury >Failure) |
| Injury | SCr increased × 2 *or*<br>GFR decreased >50% | UO < 0.5 mL/kg/h × 12h | |
| Failure | SCr increased × 3 *or*<br>GFR decreased 75% *or*<br>SCr ≥4 mg/dL; acute rise ≥0.5 mg/dL | UO < 0.3 mL/kg/h × 24 h (oliguria) *or*<br>anuria × 12 h | |
| Loss | Persistent acute renal failure: complete loss of kidney function >4wk | | High specificity |
| ESRD* | Complete loss of kidney function >3 mo | | |

*ESRD—end-stage renal disease **GFR—glomerular filtration rate
†SCr—serum creatinine ‡UO—urine output

**Table 2: KIDAGO**

| Stage | Serum creatinine | Urine output |
|---|---|---|
| **1** | 1.5–1.9 times baseline OR<br>≥ 0.3 mg/dl (≥26.5 mmol/l) | <0.5 ml/kg/h for 6–12 hrs |
| **2** | 2.0–2.9 times baseline | <0.5 ml/kg/h for ≥12 hrs |
| **3** | 3.0 times baseline OR<br>Increase in serum creatinine to ≥4.0 mg/dl (≥353.6 mmol/l) OR<br>Initiation of renal replacement therapy<br>OR, In patients <18 years, decrease in eGFR to <35 ml/min /1.73 m2 | <0.3 ml/kg/h for ≥24 hrs<br>OR<br>Anuria for ≥12 hrs |