Update in
Anaesthesia

Acute kidney injury – diagnosis, management and prevention

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Summary

This article describes the causes, diagnosis and management of acute kidney injury (AKI). Many centres in the developing world do not have access to renal replacement therapy and the emphasis is on prompt recognition, treatment and prevention of worsening AKI.

INTRODUCTION

The term *kidney failure* implies that the damage the kidney has been done, and this has now largely been replaced the term acute kidney injury (AKI), describing a pathology for which timely intervention can prevent or minimize organ damage. The formalisation of a definition for AKI is a significant step forward in our understanding of prevention and management of this extremely common problem, which affects approximately 1 in 5 patients admitted to hospital and 35% of those admitted to the intensive care unit.[1,2] In a multicentre observational study (the BEST study) 6% of those admitted to critical care units required renal replacement therapy.[3]

AKI is part of a multisystem disorder, whether it is the primary insult or secondary to other organ dysfunction. It may be that some doctors feel that as long as we can offer dialysis to these patients, then although they may die *with* renal failure, they will not die *because of* renal failure. This assumption is incorrect, particularly since the vast majority of developing world ICUs do not have access to renal replacement therapy. A rise in creatinine as small as 26mcmol.L^{-1} (0.3mg.dl^{-1}) is associated with a mortality that is four times higher than those patients who did not show an elevation of creatinine.[4] A rise in creatinine by 180mcmol.L^{-1} increased the risk of death by sixteen times. When corrected for comorbidity, age and disease severity, renal failure is associated with double the mortality in the critically ill.[5]

AKI has long term implications; at 3-year follow up 41.7% of patients haemofiltered for AKI had chronic kidney disease, with 15% still requiring dialysis.[6] It is therefore imperative that we concentrate our efforts on diagnosing and treating AKI efficiently, in order to improve patients' short and long term prognosis. This article explains the pathophysiology of the different forms of AKI, going on to explain how to detect, categorise and treat the patient presenting with an acute kidney injury.

DEFINITION

Historically, studies have used a threshold serum creatinine level, or the need for renal replacement therapy (RRT), to diagnose acute renal failure. This approach has led to difficulty in understanding the epidemiology of AKI and comparing various therapeutic options. The diagnosis of AKI has now been standardised, enabling clinicians to identify patients with an AKI, as well as those at risk of the development of renal failure. The Acute Dialysis Quality Initiative, a collaboration between nephrologists and critical care physicians, developed the RIFLE criteria (Figure 1).[5] The acute phase of AKI has been further refined by the Acute Kidney Injury Network.[7] Both use two criteria, creatinine and urine output, to diagnose AKI. A patient has AKI if they fulfill either criterion.

PATHOPHYSIOLOGY

Acute kidney injury should be seen as the final common pathway of a variety of insults, in much the same way that left ventricular cardiac dysfunction can be due to a variety of causes, including ischaemic heart disease, myocarditis, cardiotoxic medication or valvular disorders.

The driving force for filtration at the glomerulus is the pressure gradient between the glomerulus and the Bowman space - the glomerular filtration pressure. Glomerular pressure is primarily dependent on renal blood flow (RBF) and is controlled by the relative resistances of afferent (flowing into the glomerulus) and efferent (flowing away from the glomerulus) arterioles. Regardless of the cause of AKI, reductions in RBF represent a common pathological pathway for decreasing glomerular filtration rate (GFR). The aetiology of AKI can be usefully classified into three main mechanisms; prerenal, intrarenal (or intrinsic) and postrenal. Although a disease process can cause an AKI through any one of these pathological mechanisms, many diseases cause a combination of factors. For example in malaria, AKI can be triggered by associated sepsis, gastrointenstinal bleeding (prerenal), ischaemic acute tubular necrosis, interstitial nephritis and glomerulonephritis (intrarenal), and mechanical obstruction by affected erythrocytes causing haemoglobinuria (postrenal).

Prerenal AKI

This is defined as AKI that is caused by a haemodynamic disturbance, resulting in a reduced pressure gradient

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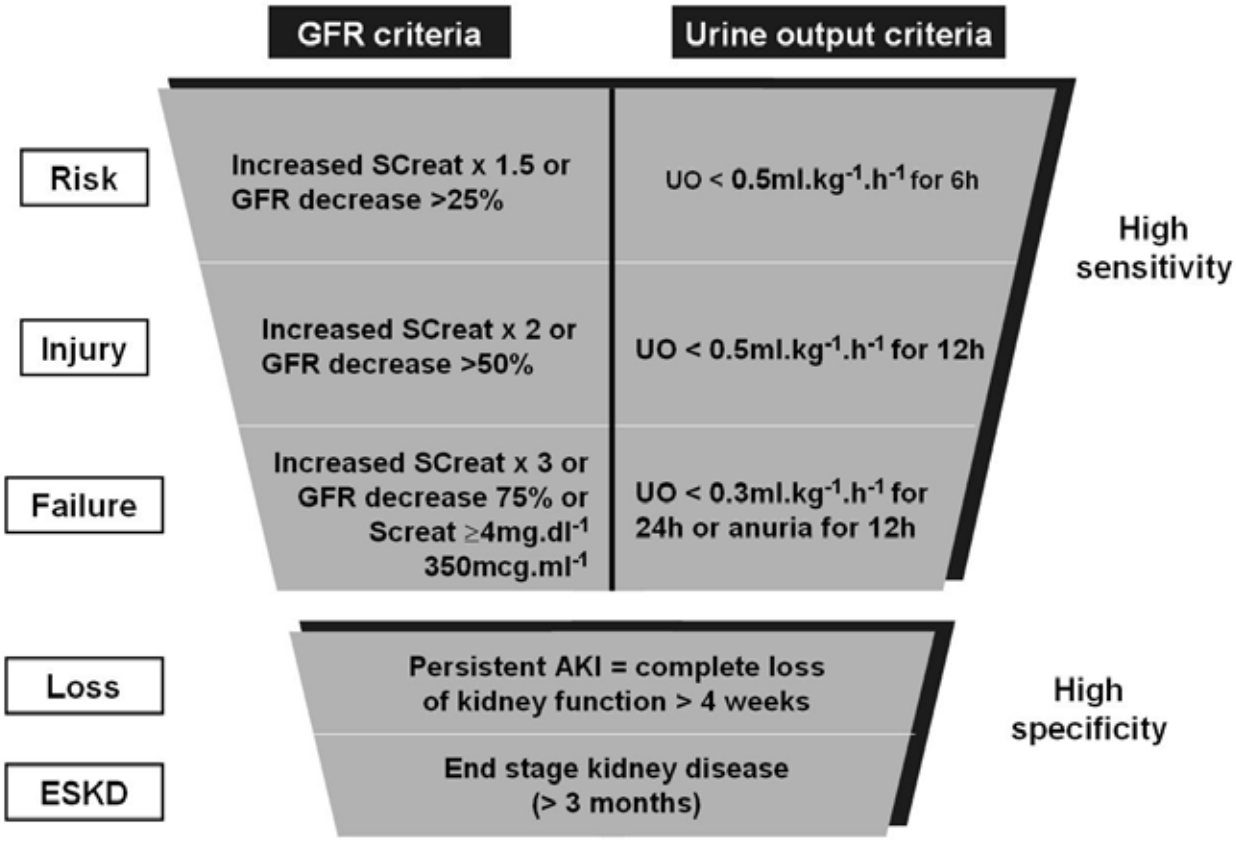

Figure 1. *The RIFLE criteria (Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-stage kidney disease). Note that the 'F' component is present even if the increase in serum creatinine (SCreat) is less than three-fold, as long as the new SCreat is greater than 4.0mg.dl^{-1} (350mcmol.L^{-1}) in the setting of an acute increase of at least 0.5mg.dl^{-1} (44mcmol.L^{-1}). The designation RIFLE-FC should then be used to denote 'acute-on-chronic' disease. Similarly, when the RIFLE-F classification is achieved by urine output (UO) criteria, a designation of RIFLE-FO should be used to denote oliguria. The shape of the figure denotes the fact that more patients will be included in the mild category (high sensitivity), including some without actually having renal failure (less specificity). In contrast, at the bottom of the figure the criteria are strict and therefore specific, but some patients will be missed (low sensitivity).*

between the glomerulus and Bowman's capsule. As there is no actual damage to the renal parenchyma, if the cause is corrected there is usually rapid recovery of function. However, it can lead to intrarenal AKI if it is not promptly corrected. Volume loss due to gastrointestinal, renal, or cutaneous (e.g. burns) disease, and internal or external haemorrhage can result in this syndrome.

Prerenal AKI can also result from decreased renal perfusion in patients with heart failure or shock (e.g. sepsis, anaphylaxis). The damage may occur on a macrovascular level, but is more commonly a microvascular problem at the level of the afferent and efferent arterioles or the capillary beds. Sepsis is responsible for 50% of AKI, causing a reduction in the mean arterial blood pressure and renal blood flow, as well as reduced vasomotor tone of the efferent arteriole, preventing the maintenance of intraglomerular pressure and resulting in a fall in perfusion pressure.

Intrarenal (intrinsic) AKI

Sources of damage to the kidney itself are termed intrinsic and can be due to damage to the glomeruli, renal tubules or the interstitium. Common causes of each are glomerulonephritis (GN), acute tubular necrosis (ATN) and acute interstitial nephritis (AIN) respectively.

Glomerulonephritis

GN is a renal disease (usually of both kidneys), characterised by inflammation of the glomeruli, or the small blood vessels in the kidneys. They are categorised into several different pathological patterns, which are broadly grouped into non-proliferative or proliferative types. Diagnosing the pattern of GN is important because the treatment and outcome differs in different types. Primary causes are intrinsic to the kidney; secondary causes are associated with certain infections (bacterial, viral or parasitic pathogens), drugs, systemic disorders (systemic lupus erythematosis, vasculitis), or diabetes.

Acute tubular necrosis

ATN may be classified as either toxic or ischemic. Toxic ATN occurs when the tubular cells are exposed to a toxic substance (also termed nephrotoxic ATN). Toxic ATN can be also caused by free pigments, such as haemoglobin or myoglobin, by medications, including antibiotics such as aminoglycosides and by cytoxic drugs such as cisplatin. Toxic ATN is characterised by proximal tubular epithelium necrosis, due to the toxic substance. Necrotic cells fall into the tubule lumen, obliterating it, and exacerbating the problem.

Table 1. *Causes of prerenal AKI.*

Fluid loss	Decreased cardiac output	Systemic vasodilation	Afferent arteriolar vasoconstriction	Renal arterial disease
Renal losses *diuretics, polyuria* GI losses *vomiting, diarrhoea* Cutaneous losses *burns, Stevens-Johnson syndrome* Haemorrhage	Heart failure Pulmonary embolus Acute myocardial infarction Severe cardiac valvular disease Abdominal compartment syndrome	Sepsis Anaphylaxis Anaesthetic agents Drug overdose	Hypercalcemia Drugs *NSAIDs, amphotericin B, ephedrine, metaraminol, radiocontrast agents* Hepatorenal syndrome	Renal arterial stenosis *atherosclerotic, fibromuscular dysplasia* Embolic disease *thrombus* *septic* *cholesterol*

Ischaemic ATN occurs when the tubular cells suffer from inadequate oxygen delivery, often resulting from prerenal causes. Tubular cells are highly sensitive and susceptible to hypoxia, due to their very high metabolic rate. ATN specifically causes skip lesions throughout the tubules, where certain portions of tubules remain unaffected. Often the tubule basement membrane remains intact, so regeneration of the tubular epithelium and reversal of AKI is possible.

Acute interstitial nephritis

AIN is a form of nephritis affecting the interstitial tissue that surrounds the tubules. The majority of cases of AIN are caused by drugs, such as penicillins, quinolones, sulphonamides and nonsteroidal anti-inflammatory drugs (NSAIDs). The time between exposure to the drug and the development of acute tubulointerstitial nephritis can be anywhere from five days to five months. The kidney is remarkably resistant to structural damage in bacterial infections and, in the absence of obstruction, damage from bacterial infection in the kidney parenchyma is unlikely to occur.

Postrenal AKI

Postrenal AKI occurs when there is bilateral (or unilateral in the case of a single kidney) obstruction of urine flow. Intratubular pressure increases and in turn decreases the glomerular filtration pressure. Obstruction of urine flow is a relatively uncommon cause of AKI and is more common in the community than in the intensive care unit (ICU). Postrenal AKI can be divided into renal and extrarenal causes. Extrarenal causes include prostatic disease, pelvic malignancy, and retroperitoneal disorders. Intrarenal causes include crystal deposition, as occurs in ethylene glycol ingestion, or uric acid nephropathy in tumor lysis syndrome. Cast formation and tubular obstruction also occur in light-chain diseases such as multiple myeloma. If the site of obstruction is unilateral, then there may be no rise in serum creatinine level due to contralateral renal function. However there may be a significant fall in GFR, with the risk of progression if the obstruction is not relieved.

Whatever the cause of the AKI, it results in the failure of the kidneys

Table 2. *Examples of pathological processes causing intrinsic (intrarenal) AKI.*

Glomerular	Toxic ATN	Ischaemic ATN	Interstitial
Anti-glomerular basement membrane (GBM) disease *Goodpasture's* Anti-neutrophil cytoplasmic antibody-associated glomerulonephritis (ANCA-associated GN) *Wegener's granulomatosis, Churg-Strauss syndrome, microscopic polyangiitis* Immune complex GN *Lupus, postinfectious, cryoglobulinaemia, primary membranoproliferative glomerulonephritis*	Haem pigment *rhabdomyolysis, intravascular haemolysis* Crystals *tumor lysis syndrome, seizures, ethylene glycol poisoning, acyclovir, methotrexate* Drugs *aminoglycosides, lithium, amphotericin B, cisplatin, radiocontrast agents*	Renal artery obstruction *thrombosis, emboli, dissection, vasculitis* Renal vein obstruction *thrombosis* Microangiopathy *disseminated intravascular coagulation, pre-eclampsia, sickle-cell crisis, malaria, haemolytic uraemic sundrome* Malignant hypertension Scleroderma renal crisis Transplant rejection Atheroembolic disease	Drugs *penicillins, cephalosporins, NSAIDs, proton-pump inhibitors, allopurinol, rifampicin, sulfonamides* Infection *pyelonephritis, viral nephritides* Systemic disease *Sjögren syndrome, sarcoid, lupus, lymphoma, leukaemia, tubulonephritis, uveitis*

to perform their three main functions:

1. Impairment of nitrogenous waste product (urea) excretion,
2. Loss of water and electrolyte regulation,
3. Loss of acid-base regulation.

CLINICAL PRESENTATION

History

Patients with AKI often do not have any specific symptoms and it is only detected through abnormal biochemistry results or a reduced urine output. However, an accurate and detailed history is essential to determine the cause of AKI and its investigation and treatment. It is important to distinguish between acute and chronic renal disease. Patients with chronic kidney disease often have symptoms such as fatigue, weight loss, nausea and pruritis. Asking about the patient's urine output can be helpful, as oliguria (a urine output of less than $0.5ml.kg.^{-1}h^{-1}$) generally favors AKI. Abrupt anuria (total lack of urine output) suggests acute urinary obstruction, acute and severe glomerulonephritis, or embolic renal artery occlusion. A gradually diminishing urine output may indicate a urethral stricture or bladder outlet obstruction due to prostate enlargement. In patients with chronic renal insufficiency, the decrease in functioning nephrons means that even a trivial nephrotoxic insult may cause AKI.

When working in the tropics, it is important to consider and screen for diseases that are specific to these areas, including malaria, typhoid, leptospirosis and viral haemorrhagic fevers. Exposure to plant toxins causing AKI is also more common in tropical countries, as patients are more likely to have sought the help of traditional healers prior to their admission to hospital.

In areas with a high prevalence of HIV/AIDS and tuberculosis, screen for these diseases by asking about symptoms such as recurrent infections (i.e. possible immunosuppression), weight loss and night sweats. Ask about the patient's family history to identify disorders such as sickle cell disease and glucose-6-phosphate dehydrogenase deficiency, in which an acute crisis can cause AKI.

EXAMINATION

General examination

Certain rashes are suggestive of systemic vasculitis (livido reticularis, palpable purpura, digital ischaemia). Allergic interstitial nephritis

Table 3. *History in different types of AKI.*

Prerenal AKI

- Hypovolaemia causes thirst, decreased urine output, dizziness and orthostatic hypotension (i.e. hypotension on rising from lying to sitting or standing).
- Ask about fluid loss from vomiting, diarrhoea, sweating, polyuria, or haemorrhage.
- Consider sepsis as a contributing factor.
- Orthopnoea and paroxysmal nocturnal dyspnoea suggest significant cardiac failure leading to depressed renal perfusion.

Intrinsic (intrarenal) renal AKI

- A nephritic syndrome (haematuria, oedema and hypertension) indicates a glomerular aetiology of AKI.
- Ask about prior throat or skin infections (post-streptococcal GN).
- Suspect ischaemic ATN in any patient presenting after a period of hypotension secondary to cardiac arrest, haemorrhage, sepsis, drug overdose, or anaesthesia / surgery.
- Enquire about exposure to nephrotoxins, including a detailed list of all current medications and any recent radiological examinations (for exposure to radiological contrast agents).
- Toxic pigment-induced ATN should be suspected in patients with possible rhabdomyolysis (muscular pain, prolonged collapse, seizures, intoxication, excessive exercise or limb ischaemia) or haemolysis.
- Acute interstitial nephritis should be suspected with fevers, rash, arthralgia, and exposure to certain medications, including NSAIDs and antibiotics.

Postrenal AKI

- Usually occurs in older men with prostatic obstruction and symptoms of urgency, frequency, and hesitancy.
- Flank pain and haematuria may suggest renal calculi or papillary necrosis.
- Use of acyclovir, methotrexate, triamterene, indinavir, or sulfonamides implies the possibility of tubular obstruction by crystals of these medications.
- Retroperitoneal fibrosis is often associated with various immune-related conditions, malignancy and certain drugs (methysergide, hydralazine and beta blockers).

is associated with a maculopapular rash. Consider endocarditis and septic emboli in patients with a history or signs of intravenous drug abuse (track marks).

Eye examination may reveal keratitis, iritis, uveitis (autoimmune vasculitis), jaundice (liver disease) or signs of diabetes mellitus and hypertension. Hearing loss may be evident in aminoglycoside toxicity.

Cardiovascular examination

Assess the patient's volume status by examining skin turgor, mucous membranes and capillary refill time, as well as the pulse rate and lying and standing blood pressures, to assess for a postural drop. The jugular venous pressure (JVP) may be helpful and the lung bases and dependent areas should be assessed for the presence of oedema. Remember that oedema does not mean 'fluid overload', more that the fluid is in the wrong place and the patient may still be hypovolaemic in terms of their vascular space. In hospitalised patients, accurate daily records of fluid input and output and of the patient's weight should be recorded.

Other clinical findings that may point towards a diagnosis include:

- Irregular cardiac rhythms (e.g. atrial fibrillation) predispose to thromboembolic renal disease,
- Heart murmurs can be suggestive of underlying cardiac failure or endocarditis,
- A raised JVP, lung base crepitations and the presence of a third heard sound (gallop rhythm) suggests cardiac failure,
- Severe hypertension with renal failure suggests renovascular disease, glomerulonephritis, vasculitis, or atheroembolic disease.

Respiratory examination

- Kussmaul's (acidaemic) respiration suggests significant metabolic acidosis,
- Fine crackles and/or haemoptysis may indicate a pulmonary-renal syndrome such as Goodpasture's or Wegener's granulomatosis.

Abdominal examination

- Pulsatile abdominal masses and renal bruits suggest the presence of atheroembolic disease,
- Costovertebral (renal) angle tenderness is seen with renal stones, papillary necrosis, renal artery thrombosis and renal vein thrombosis,
- Abdominal, pelvic, rectal masses, prostatic hypertrophy can suggest a postrenal (obstructive) cause,
- A distended bladder is indicative of a postrenal AKI,
- A distended, tense abdomen suggests raised intra-abdominal pressure and possibly abdominal compartment syndrome (post laparotomy, trauma, abdominal aortic aneurysm repair).

Neurological and extremities

- Confusion is caused by many factors, including uraemia, vasculitic and embolic disease,
- Focal neurological findings may indicate embolic disease,
- Asterixis (a flapping tremor) is suggestive of uraemia or hepato-renal failure,
- Limb oedema can suggest underlying cardiac failure or hypoalbuminaemia secondary to albumin loss from an intrarenal pathology,
- Absent peripheral pulses suggest atheroembolic disease,
- Limb ischaemia can be indicative of rhabdomyolysis causing a toxic ATN.

INVESTIGATING THE CAUSE OF AKI

Several laboratory tests are useful for assessing the aetiology of AKI, and the results may determine the appropriate treatment. These tests include a full blood count (FBC), serum biochemistry, urine analysis with microscopy and urine electrolytes.

Plasma biochemistry	
Urea and creatinine	Raised levels confirm the presence of an AKI
Potassium	May be dangerously high in the presence of a severe AKI, prompting rapid treatment
pH	To assess the presence of a metabolic acidosis due to dysfunction of renal acid-base balance
Lactate dehydrogenase	Acute elevation occurs in renal infarction
Creatine kinase	Acute elevation occurs in rhabdomyolysis
Plasma electrophoresis	As part of a multiple myeloma screen

Haematology

- Eosinophilia may suggest a suggests vasculitis,
- Raised erythrocyte sedimentation rate suggests vasculitis,
- Fragmented red cells and/or thrombocytopenia suggests intravascular haemolysis due to accelerated hypertension or haemolytic uraemic syndrome.

Blood film

This may demonstrate schistocytes (haemolytic uraemic syndrome) or increased rouleaux formation multiple myeloma), or a heavy burden of malarial parasites.

Immunology

Where available, measurement of complement components, autoantibodies and cryoglobulins aid in the diagnosis.

Urine biochemistry

- 24-hour creatinine clearance is useful in measuring the severity of renal failure.

Table 4. *Interpretation of urine analysis and microscopy.*

Urinalysis	
Haematuria	Haematuria on a dipstick, with the absence of red cells on microscopy, suggests myoglobinaemia (rhabdomyolysis)
Proteinuria	Strongly suggestive of glomerular disease
Glycosuria	With a normal blood sugar indicates tubular disease
Microscopy	
White cells	Suggests an active bacterial urinary infection and possible pyelonephritis
Eosinophilia	Strongly suggestive of allergic tubulo-interstitial nephritis
Granular casts	Formed from abnormal cells within tubular lumen. Indicates ATN
Red cell casts	Highly suggestive of GN

- Urinary osmolarity can be used as a measure of the concentrating ability of the kidney, which is lost in intrarenal AKI.
- Urine electrophoresis is necessary for the detection of light chains when multiple myeloma is suspected.

Microbiology

Urine culture	To diagnose pyelonephritis
Antibodies to streptococcal antigens	If post-streptococcal GN is possible
Antibodies to HIV	
Early morning urine and sputum culture	Acid-fast bacilli to detect tuberculosis
Thick and thin blood films	Malaria
Widal test for typhoid, blood and urine test for Leptospirosis	

Electrocardiography (ECG)

The characteristic changes of hyperkalaemia are usually seen with a potassium level above 6.5mmol.L^{-1} - tall tented T waves, flat P waves and increased PR interval. QRS widening, a sinusoidal pattern and VF are seen with extreme hyperkalaemia.

Renal tract ultrasound

Renal ultrasonography is useful for evaluating existing renal disease and to identify or exclude obstruction of the urinary collecting system. The degree of hydronephrosis does not necessarily correlate with the degree of obstruction. Mild hydronephrosis may be observed with complete obstruction if found early. Small kidneys suggest chronic renal failure.

Doppler scans rarely differentiate between prerenal and intrarenal AKI, but can be useful if thromboembolic or renovascular disease is suspected.

Other investigations

Radionuclide imaging (e.g. with technetium^{99}) can be used to assess renal blood flow and tubular function but, because of a marked delay in tubular excretion of radionuclide in prerenal disease and intrarenal disease, the value of these scans is limited. Aortorenal angiography (using computed tomography and magnetic resonance imaging studies) can be helpful in establishing the diagnosis of renal vascular diseases, including renal artery stenosis, renal atheroembolic disease, and atherosclerosis with aortorenal occlusion. The radiocontrast used with CT is nephrotoxic and can exacerbate an AKI.

Renal biopsy

A renal biopsy can be useful in establishing the diagnosis of intrarenal causes of acute kidney injury (AKI) and can be justified if it will change management (e.g. initiation of immunosuppressive medications). Renal biopsy may also be indicated when renal function does not return for a prolonged period and a prognosis is required to develop long term management.

QUANTIFYING THE SEVERITY OF AKI

Oliguria is a marker of an AKI and is defined as a urine output of less than 0.5ml.kg^{-1}.h^{-1}. Creatinine is a breakdown product of creatine phosphate in muscle and is usually produced at a constant rate by the body. Serum levels correlate directly with the glomerular filtration rate (GFR) of the kidneys and can be used to quantify and monitor renal function. However, the level of serum creatinine is also affected by the muscle mass of the individual patient and therefore by their age, sex and ethnicity. The normal upper limit of serum creatinine in different patient groups is best estimated with reference to your local laboratory.

Glomerular filtration rate (GFR)

The serum creatinine level can also be used to estimate the glomerular filtration rate of the kidneys, using a formula (see box below). According to the National Kidney Foundation, normal results range from 90-120ml.min^{-1} per 1.73m^2 body surface area.

Box 1. *Estimated GFR (eGFR) using the Modification of Diet in Renal Disease (MDRD) formula*

For creatinine in mcmol.L^{-1}:

eGFR = **32788** x serum creatinine-1.154 x age-0.203 x [1.212 if black] x [0.742 if female]

For creatinine in mg.dl^{-1}:

eGFR = **186** x serum creatinine-1.154 x age-0.203 x [1.212 if black] x [0.742 if female]

Creatinine levels in mcmol.L^{-1} can be converted to mg.dL^{-1} by dividing them by 88.4.

The RIFLE model[5]

As shown in Figure 1, the RIFLE criteria quantify the severity of the AKI. 'Loss' and 'end-stage renal disease' (ESRD) are separated to acknowledge the important adaptations that occur in ESRD, that are not seen in a persistent acute kidney injury. Persistent AKI (loss) is defined as need for renal replacement therapy (RRT) for more than 4 weeks, whereas ESRD is defined by need for dialysis for longer than 3 months.

The classification system includes separate criteria for creatinine and urine output (UO). A patient can fulfil the criteria through changes in serum creatinine (SCreat) or changes in UO, or both. The criteria that lead to the worst possible classification for that patient should be used. As serum creatinine levels and eGFR are affected by additional factors not considered in their calculation or the normal values, it is most useful if a baseline level is known. However, if it is not known, using normal levels as an estimated baseline function is acceptable.

MANAGEMENT OF THE PATIENT WITH AKI

The sooner AKI is recognised and treated, whatever its severity, the higher the chances of recovery of renal function. As well as following the basic measures detailed below, it is often appropriate to seek specialist advice, especially if the measures below do not cause improvement within the first twenty-four hours.

Correction of the underlying cause

Measures to correct underlying causes of acute kidney injury should begin at the earliest indication of renal dysfunction. A large proportion of the renal mass is damaged before any biochemical evidence of renal dysfunction; the relationship between the GFR and the serum creatinine level is not linear, especially early in disease. A rise in serum creatinine may not be evident until 50% of the GFR is lost.

- In a prerenal AKI - improve renal perfusion e.g. treat sepsis, treat haemorrhage and rehydrate,
- In a intrarenal AKI - treat the cause e.g. remove nephrotoxic drugs, give steroids in GN,
- In a postrenal AKI - remove the cause of obstruction e.g. catheterise the bladder.

Optimization of conditions for recovery

Maintenance of volume homeostasis remains the primary goal of treatment. In patients with prerenal AKI, aggressive fluid resuscitation if often required to improve renal perfusion. It is appropriate to start with 0.9% saline or Ringer's lactate, aiming to restore circulating volume but avoid volume overload, as this may worsen renal function. Once the patient is fluid resuscitated it is important that further fluid input matches their output.

Clinically reassess the patient's response to fluid resuscitation frequently. If large fluid volumes or vasopressors are required, or if the patient has cardiac dysfunction, some form of cardiac output monitoring is useful (see page 51).

There is no evidence that diuresis using furosemide is beneficial and the majority of patients with AKI will be unresponsive to diuretics. It is reasonable to attempt diuresis with furosemide where you are sure that they are hypervolaemic, particularly where RRT is not available. High doses may need to be administered and doses over 80-100mg should be given as an infusion due to the risk of ototoxicity. In some patients, where RRT is unavailable, symptomatic hypervolaemia, causing pulmonary oedema can be treated by venesection of blood (to a volume that improves symptoms).

There is no evidence for using low dose dopamine for renal protection. Lactic acidosis should be treated by optimising the circulation, not with sodium bicarbonate.

Maintain biochemical homeostasis

Dietary modification is an important consideration in the treatment of acute kidney injury. Salt and fluid restriction becomes crucial in the management of oliguric renal failure, because the kidneys do not excrete toxins and fluids adequately. Potassium and phosphate are excreted poorly in AKI; where available, blood levels should be measured at least daily, with prompt treatment of levels that are symptomatic or very elevated. Critically ill patients should receive at least $1 g.kg^{-1}$ of protein in their diet per day, but should avoid over-feeding (hyperalimentation), which can increase blood urea nitrogen levels, exacerbate metabolic acidosis and cause water loss resulting in hypernatremia.

Protection from further damage

Whatever the initial cause of the AKI, the kidneys remain vulnerable to the toxic effects of various chemicals. All nephrotoxic agents (e.g. radiocontrast agents, antibiotics with nephrotoxic potential, heavy metal preparations, cancer chemotherapeutic agents and NSAIDs) should either be avoided or used with extreme caution. A common dilemma is whether to give contrast for a CT abdomen in a patient with an AKI, who needs to be investigated for abdominal sepsis - the need to reach a diagnosis and therefore initiate appropriate treatment usually supersedes the risks of radiocontrast to the kidneys, but it is reasonable to perform a non-contrast scan first, as this may show an obvious diagnosis and negate the need for contrast.

The doses of all medications cleared by renal excretion (most commonly antibiotics in the ICU setting) should be adjusted appropriately. (See 'The Renal Drug Handbook' in Further Reading).

Management of life-threatening complications

Severe metabolic acidosis

Correcting severe acidosis (pH < 7.2) with intravenous bicarbonate administration can be an important 'holding measure', either whilst initiating emergency RRT or waiting for treatment, such as fluid resuscitation, antibiotics and vasopressors, to take effect. There are no specific therapeutic agents for AKI and dopamine, nesiritide, fenoldopam and mannitol may cause harm.

Hyperkalaemia

Serum potassium levels of greater than $6.5 mmol.L^{-1}$ require urgent treatment. Protection from its effects on cardiac conduction can be achieved with intravenous calcium administration (10ml 10% calcium gluconate or chloride IV over 10 minutes), repeated whenever the ECG changes worsen.

Reduction of potassium levels can be achieved through the careful administration of intravenous insulin, which drives potassium into the cells from the serum. Add 15 units of fast-acting insulin, such as Actrapid, to 50mls 50% glucose and administer over 30 minutes. Nebulised salbutamol (5mg) also drives the passage of potassium into cells. These are again holding measures, while the underlying cause is treated or dialysis is started. Potassium will leak back into the serum and these treatments may need to be repeated. Calcium resonium (15g every eight hours orally or via an NGT) can be used to help to remove potassium via the gastrointestinal tract.

Uraemic pericarditis, cardiac tamponade and pulmonary oedema

These serious complications are best treated by dialysis, although symptomatic management with oxygen, peripheral vasodilators, pericardiocentesis (drainage of pericardial fluid) and occasionally venesection can be helpful whilst waiting for dialysis to be started.

Managing Resolving AKI

During tubular dysfunction the patient is oliguric or anuric. Glomerular filtration tends to return before regeneration of the tubules, particularly their ability to concentrate the urine by retention of water. This, together with a high osmotic load from renal toxin accumulation, can drive profound polyuria or poorly concentrated urine. Urine volumes may be as high as 10 litres per day. Few patients can comfortably maintain an intake of more than 4 litres per day orally, so intravenous fluids are frequently required. Standard practice is to replace the previous hour's urine output with the next hour's IV input. Serum electrolytes should be measured at least daily. Ringer's lactate or 0.9% saline with potassium supplementation are the usual crystalloids of choice.

Prevention of further AKI and the development of chronic kidney disease

Patients who have suffered an AKI are at increased risk of further episodes and of developing chronic kidney disease (CKD). They should ideally be reviewed yearly by a healthcare provider, with a thorough history and clinical examination, serum biochemistry (urea, creatinine and electrolytes) and urinalysis to monitor kidney and urinary tract health. Patients should be advised to drink enough fluids to maintain regular passage of urine, to avoid dehydration and to avoid taking substances or medications that are nephrotoxic (e.g. NSAIDs). They should be advised that if they experience a reduced urine output, difficulties urinating or haematuria, this should prompt a visit to their physician.

CONCLUSION

This article provides an overview of the major causes of acute kidney injury and the underlying pathophysiology. It describes how to detect and treat AKI in a timely and effective manner. A clear understanding of these concepts is essential when working with critically ill patients, as a good practical knowledge of the assessment and management of the patient with an AKI is vital in improving both the short and long term prognosis of patients.

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