Acute kidney injury and kidney replacement therapy in adults

Opening Vignette

A 70-year-old man with hypertension, but no known chronic kidney disease, was found lying on the floor at home after a fall several hours earlier by family members. He had fever, productive cough and malaise for the past 3 days. He was brought by ambulance to the emergency department. On arrival, he had rapid, deep and laboured breathing. Vital signs measured at triage were as follows: temperature 39°C, pulse rate 120 beats/min, blood pressure 80/50 mmHg, respiratory rate 30 breaths/min and peripheral oxygen saturation 95% when receiving oxygen via a Venturi mask (inspired oxygen fraction 40%). Physical examination revealed generalised body tenderness and left basal crepitations. Bilateral consolidation was demonstrated on chest X-ray. Empirical broad-spectrum antibiotics were given for severe community-acquired pneumonia. The patient was intubated and mechanically ventilated as his respiratory failure worsened. Despite volume optimisation, vasopressor use and blood pressure normalisation, only a small amount of dark-coloured urine was produced over the next 6 h, followed by anuria for 12 h.

IDENTIFICATION OF ACUTE KIDNEY INJURY

Acute kidney injury (AKI) is the abrupt reduction of glomerular filtration rate over a period of 1 week or less.[1] If the reduction of glomerular function extends beyond 1 week, then the patient would have acute kidney disease (duration ≤3 months, inclusive of AKI) or chronic kidney disease (duration >3 months). The presence of AKI increases the risk of morbidity (long-term dialysis dependence) and mortality,[2] particularly in patients with multiple organ dysfunction. Global AKI incidence is 21.6% in adults, with a mortality of 23.9%.[3]

Diagnosis of AKI requires identification of AKI and its specific causes [Figure 1]. Acute kidney injury is commonly identified, and its severity assessed via serum creatinine elevation and decreased urine output [Box 1].[1] While using either creatinine or urine output criteria, the most severe stratum determines the overall severity of AKI. Although readily accessible, serum creatinine elevation is relatively insensitive to kidney injury. It is an intermittent measurement using blood draws and requires knowledge of 'baseline' creatinine. Ideally, baseline creatinine is available from the patient's medical record. Compared to serum creatinine, urine output is a more sensitive marker of kidney injury[4] and recovery (i.e., successful weaning from kidney replacement therapy [KRT]).[5] It can also be continuously measured via an indwelling urinary catheter, but will require close monitoring in the hospital. Urine output needs to be indexed against body weight. We use the actual body weight rather than the ideal body weight,

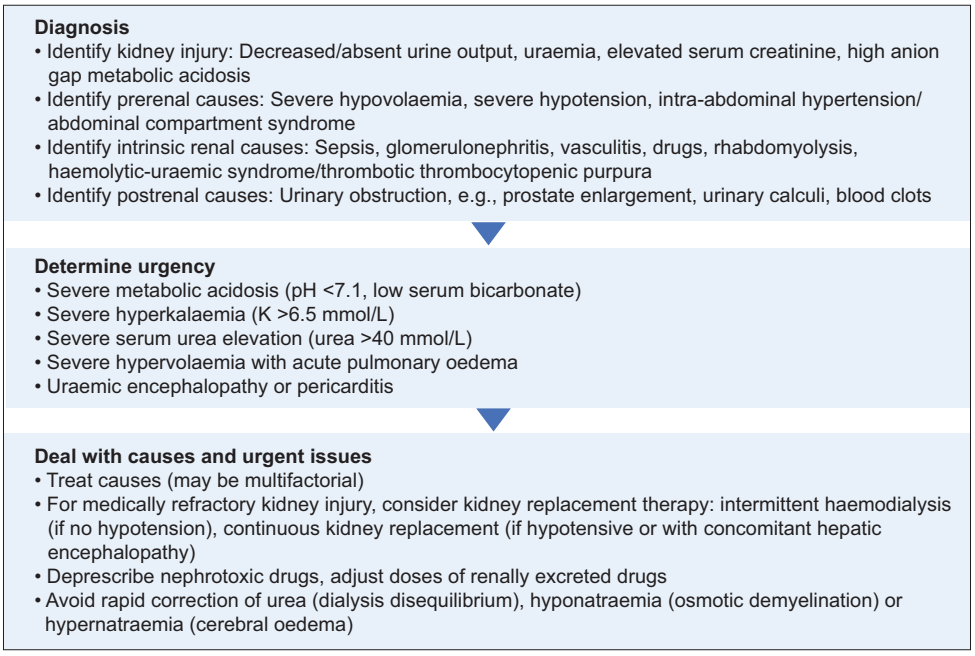

Figure 1: Chart shows the approach to acute kidney injury.

Box 1. Stage and management of AKI (KDIGO 2012).

Severity stage 1
- sCr increase from baseline within 7 days: 1.5–1.9 times
- Urine output criteria: <0.5 mL/kg/h for 6–12 h
- Other criteria: sCr increase of ≥26.5 μmol/L within 48 h
- General treatment:
  - Discontinue nephrotoxic drugs
  - Treat hyperglycaemia
  - Optimise haemodynamics
  - Manage the complications of AKI[a]

Severity stage 2
- sCr increase from baseline within 7 days: 2.0–2.9 times
- Urine output criteria: <0.5 mL/kg/h for ≥12 h
- General treatment:
  - Same as for severity stage 1
  - Check for changes in drug dosing of renally excreted drugs
  - Consider KRT[b]
  - Consider ICU admission

Severity stage 3
- sCr increase from baseline within 7 days: ≥3.0 times
- Urine output criteria: Anuria for ≥12 h, or <0.3 mL/kg/h for ≥24 h
- Other criteria: sCr increase to ≥353.6 μmol/L[c], or initiation of KRT or (in patients aged <18 years) decrease in eGFR[d] to <35 mL/min/1.73 m^2
- General treatment:
  - Same as for severity stage 2
  - Avoid subclavian catheters, if possible

[a]Hyperkalaemia: Consider intravenous insulin, oral exchange resins; metabolic acidosis: consider intravenous bicarbonate; hypervolaemia: consider diuretics; pulmonary oedema: consider oxygen supplementation, noninvasive or invasive mechanical ventilation. [b]Initiate kidney replacement therapy (KRT) in the presence of life-threatening conditions refractory to other medical management (e.g. severe metabolic acidosis, severe hyperkalaemia, severe drug toxicity, severe hypervolaemia), uraemic encephalopathy, uraemic pericarditis, or when urea is ≥40 mmol/L. [c]With serum creatinine (sCr) increase of ≥26.5 μmol/L within 48 h, or ≥1.5 times of baseline within 7 days. [d]Using the revised Schwartz formula, where eGFR (mL/min/1.73 m^2)=(36.5×height in cm) divided by creatinine in μmol/L. The estimated glomerular filtration rate (eGFR) criterion is introduced to account for acute kidney injury (AKI) in children with low muscle mass, who may not get a high sCr even if AKI is severe. KDIGO: Kidney Disease: Improving Global Outcomes (creatinine increase from baseline within 7 days, urine output criteria or other criteria may be used for severity staging)

as the former has higher sensitivity for the identification of AKI.[6]

CAUSES AND TREATMENT OF ACUTE KIDNEY INJURY

In the presence of oliguric AKI or postoperative AKI, hypovolaemia should not be assumed and indiscriminate fluid administration should be avoided. Instead, clinicians need to determine the specific causes of AKI, which can be divided into prerenal (reduced renal perfusion pressure), intrinsic renal (disease of the vessels, glomeruli or tubules within the kidneys) and postrenal (urinary flow obstruction) causes [Box 2]. Prerenal causes reduce blood flow into the kidney tissue, and may be due to circulatory shock and hypotension[7] (in turn contributed by hypovolaemia, vasodilation, acute heart failure), extrinsic renal artery compression from raised intra-abdominal pressure and renal artery stenosis. Intrinsic renal causes include atherosclerotic, infective, inflammatory and nephrotoxin-induced damage. Postrenal causes involve urinary outflow obstruction, which can occur at various levels and sites.

Box 2. Specific treatment for selected causes of AKI.

Mechanism & cause	Specific treatment
Prerenal	
Hypovolaemia	• Stop any blood loss • Volume expansion with crystalloids
Vasodilation	• Treat any sepsis with appropriate antimicrobials • Treat any adrenal insufficiency with corticosteroids • Volume expansion with crystalloids • Vasopressors, e.g., noradrenaline, vasopressin
Acute heart failure	• Treat coronary ischaemia (e.g., with revascularisation) • Diuretics for hypervolaemia • Inotropes, e.g., dobutamine, milrinone • Treat arrhythmia • Noninvasive or invasive mechanical ventilation • Mechanical circulatory support
Raised IAP	• Nasogastric tube drainage and gastric decompression • Rectal tube drainage and colonic decompression • Abdominal paracentesis for ascites • Remove constrictive abdominal dressings and binders • Sedation and analgesia to improve abdominal compliance • Correct hypervolaemia via diuresis or ultrafiltration • Consider surgical abdominal decompression if IAP >20 mmHg persistently
Intrinsic renal	
Sepsis	• Early and appropriate antimicrobials and source control • Volume expansion and vasopressors (e.g. noradrenaline) to keep the mean arterial pressure≥65 mmHg
Nephrotoxic drugs	• Stop causative drugs and use alternatives, e.g., NSAIDs causing acute interstitial nephritis, acyclovir causing crystal-induced AKI • Ensure volume repletion and good urine output for crystal-induced AKI
Thrombotic microangiopathy	• Ensure volume repletion • Antibiotics for diarrhoeal illness • Plasma exchange for thrombotic thrombocytopenic purpura
Rhabdomyolysis	• Stop any drugs (e.g., statins) that may lead to muscle breakdown • Infuse crystalloids to maintain good urine output, but avoid volume overload if the patient progresses to oliguria or anuria
Postrenal	
Urinary obstruction	• For bladder outlet obstruction (e.g., due to prostatic hyperplasia or cancer): urethral catheterisation or suprapubic catheterisation • For ureteral obstruction (e.g., due to metastatic cancer): percutaneous nephrostomy

AKI: acute kidney injury, IAP: intra-abdominal pressure, NSAIDs: nonsteroidal anti-inflammatory drugs

Initial workup of AKI requires careful physical examination augmented by point-of-care ultrasound.[8] Point-of-care echocardiography may reveal hypovolaemia (presence of small cardiac chambers), while abdominal ultrasound may reveal postrenal obstruction (presence of dilated renal calyces suggesting hydronephrosis or distended postvoid bladder suggesting bladder outlet obstruction). As AKI progresses in severity, prognosis worsens, necessitating therapeutic escalation [Box 1]. In general, patients require avoidance of nephrotoxins, reversal of specific causes and dose adjustment for renally excreted drugs. Also, KRT (also known as renal replacement therapy) should be considered and instituted when life-threatening conditions are present or when serum urea exceeds 40 mmol/L.[9]

INDICATIONS AND PRESCRIPTION OF KIDNEY REPLACEMENT THERAPY

The KRT is required when kidneys fail to perform critical homoeostatic functions, despite maximal medical therapy. These functions include regulating the blood volume, pH and electrolytes. When blood volume regulation fails despite diuretic use, left ventricular failure, acute pulmonary oedema and respiratory failure ensue. When pH and electrolyte regulation fail, severe acidaemia (pH <7.1) and severe hyperkalaemia ([K+] >6.5 mmol/L), can result in cardiac arrhythmia and arrest. To avoid these complications, KRT should be initiated when indications are present. In addition, to lessen the risk of mortality, KRT should also be considered when the blood urea rises to 40 mmol/L or above.[9]

Medical officers, residents and hospitalists working in high-dependency and intensive care settings would need to be familiar with KRT prescription [Table 1]. The key considerations are the choice of modality, the type of anticoagulation and the rate of fluid removal. The KRT options are either intermittent or continuous. Extracorporeal modalities include intermittent haemodialysis (IHD), prolonged intermittent KRT, sustained low-efficiency dialysis (SLED) and continuous KRT (CKRT). Another KRT modality that is less commonly used is peritoneal dialysis (PD). In practice, extracorporeal methods are more commonly used in non-resource-limited settings, and therefore, the discussion is focused on these methods. In extracorporeal therapy, the patient's blood is pumped through a semipermeable membrane (also known as the haemofilter or haemodialyser, depending on the technique of therapy). Water is moved across the membrane via ultrafiltration, while solutes are removed across the membrane via convection (i.e. haemofiltration) or diffusion (i.e. haemodialysis) or both (i.e. haemodiafiltration). Finally, the treated blood is returned to the patient [Figure S1, Supplemental Digital Appendix].

Intermittent techniques may predispose patients to intradialytic hypotension due to either rapid fluid removal or rapid osmotic shift. Even without active fluid removal, rapid solute clearance by itself can reduce plasma osmolality, leading to osmotic shift of water into the cells and hypotension. As such, for haemodynamically unstable patients, CKRT is preferred over intermittent KRT. The PD is another continuous form of KRT for AKI. Frequent PD exchanges are useful for acute fluid removal and solute clearance, though PD may be inferior to haemofiltration for treatment of infection-associated acute renal failure.[10]

Temporary vascular access can be quickly created by inserting a non-cuffed, non-tunnelled haemodialysis catheter into the internal jugular, femoral or subclavian vein. To facilitate blood flow, internal jugular and subclavian catheters need to be positioned such that their tips are at the junction of the superior vena cava and the right atrium; femoral catheters need to be positioned with their tips extending into the inferior vena cava. Usual catheter lengths are as follows: 16 cm for the right internal jugular site, 20 cm for the left internal jugular or subclavian site and 24 cm for the femoral site.

As blood is pushed and perfused through the haemofilter/haemodialyser, thrombosis at the intra-arterial side of the membrane (termed 'membrane clotting' and detected by increased filter pressure) and caking of the membrane pores (termed 'membrane clogging' and detected by increased transmembrane pressure) gradually occur. To improve duration of patency (generally termed 'filter life'), anticoagulation should be used. Regional citrate anticoagulation is particularly useful as it does not increase systemic bleeding risk and results in a longer filter life compared to systemic heparin anticoagulation (median filter life span 47 vs. 26 h, $P < 0.001$).[11] Nonetheless, anticoagulation needs to be used with caution in some patients. For instance, systemic heparin anticoagulation is contraindicated in patients who are actively bleeding or who have type II heparin-induced thrombocytopenia, while regional citrate anticoagulation should be carefully applied in patients with liver failure or circulatory shock.[12]

Some adjustments to the usual KRT prescription would be required for patients with severe hyponatraemia (Na <125 mmol/L) or severe hypernatraemia (Na >155 mmol/L). As KRT solutions have sodium concentrations of 140 mmol/L, the usual KRT will equilibrate the patient's serum sodium concentration to 140 mmol/L. Patients with severe hyponatraemia will be at risk of osmotic demyelination, while patients with severe hypernatraemia will be at risk of cerebral oedema. For IHD, the dialysate sodium concentration can usually be set between 130 and 150 mmol/L. For CKRT, modified dialysate or replacement fluid can be prepared every 24 h by injecting either hypertonic (3% or 20%) NaCl or sterile water into the fluid bag, keeping the fluid sodium concentration within 10 mmol/L of the patient's starting sodium level [Table S1, Supplemental Digital Appendix].[13]

Table 1. Prescription of kidney replacement therapy.

Domain & selected choice	Advantages	Requirements and considerations
Mode, dose		
Intermittent HD	• High efficiency • Possibility of anticoagulation-free protocol	It can be done using a pre-existing arteriovenous access; usually over 2–4 h. If fluid is removed, rapid rate of fluid removal requires haemodynamic stability. Not suitable for patients at risk of raised intracranial pressure, due to compensatory cerebral vasodilation when the mean arterial pressure drops and shift of water to the intracellular space when the solute is rapidly removed.
Iso-UF or sequential ultrafiltration	• Allow higher UF rate without change in solute concentration • Possibility of anticoagulation-free protocol	It can be done using a pre-existing arteriovenous access. Iso-UF followed by intermittent HD allows higher fluid removal rate.
SLED	• Moderate efficiency • Possibility of anticoagulation-free protocol	Usually over 8–12 h, and with lower blood flow rate and dialysate flow rate compared to intermittent HD. If fluid is removed, lower fluid removal rate poses less risk of haemodynamic compromise in critically ill patients. Not suitable for patients at risk of raised intracranial pressure
CVVHD, CVVH, CVVHDF	• Haemodynamic stability. • Better fluid and solute control than intermittent HD in haemodynamically unstable patients • Suitable for patients at risk of raised intracranial pressure	CKRT over 24–72 h (longer filter life with anticoagulation protocol), delivering an effluent flow rate of 20–25 mL/kg/h. Preferable in patients with haemodynamic instability, cerebral oedema, severe hypo- or hypernatraemia or hepatic encephalopathy. CVVHD and CVVHDF modes allow increasing dialysate rate to remove excess citrate (in patients with citrate accumulation).
Peritoneal dialysis	Avoids the need for vascular access or anticoagulation	Challenge of peritoneal dialysis catheter placement in critically ill patients.
Anticoagulation		
Anticoagulation free	No increased bleeding risk	Suitable for patients with impaired coagulation.
Regional citrate anticoagulation	No increased bleeding risk	Suitable for CVVHD, CVVH or CVVHDF. May be used with caution in patients with liver failure or circulatory shock.
Systemic heparin anticoagulation	Some increased bleeding risk	Suitable for intermittent HD, iso-UF, SLED, CVVHD, CVVH and CVVHDF.
Net fluid removal rate		
0 mL/h (even balance)	Lower risk for patients with haemodynamic instability	Suitable for patients with unstable haemodynamics.
>0 mL/h or >0 L	Correction of hypervolaemia	For example: 1–2 L over 4–8 h for HD/SLED; 25–50 mL/h for CVVHD/CVVHDF/CVVH
Dialysate and/or replacement fluid for CKRT		
Decreased fluid Na concentration	Avoids osmotic demyelination if fluid Na is kept <10 mmol/L above the patient's Na	Modify dialysate or replacement fluid Na by injecting free H_2O into the fluid bag, adjusting fluid Na to within 10 mmol/L of the patient's starting Na [see Table S1, Supplemental Digital Appendix]. Done for patients with severe hyponatraemia (Na <125 mmol/L), as the usual fluid Na is 140 mmol/L.
Increased fluid Na concentration	Avoids cerebral oedema if fluid Na is kept <10 mmol/L below the patient's Na	Modify dialysate or replacement Na by injecting hypertonic (3% or 20%) NaCl into the fluid bag, adjusting fluid Na to within 10 mmol/L of the patient's starting Na [see Table S1, Supplemental Digital Appendix]. Done for patients with severe hypernatraemia (Na >155 mmol/L), as the usual fluid Na is 140 mmol/L.

CKRT: continuous kidney replacement therapy, CVVH: continuous venovenous haemofiltration (blood flow 100–250 mL/h), CVVHD: continuous venovenous haemodialysis (blood flow 100–250 mL/h), CVVHDF: continuous venovenous haemodiafiltration (blood flow 100–250 mL/h), HD: haemodialysis (blood flow 200–250 mL/h, dialysate flow 400–500 mL/h), Iso-UF: isolated ultrafiltration (blood flow 200–250 mL/h), SLED: sustained low-efficiency dialysis (blood flow 100–150 mL/h, dialysate flow 200–300 mL/h)

As such, for patients with severe hypo- or hypernatraemia, CKRT is recommended.

Some other adjustments to the usual KRT prescription may be required in the following scenarios. For patients with severe uraemia (e.g. urea >60 mmol/L) who are at risk of dialysis disequilibrium syndrome (reverse osmotic shift due to rapid urea clearance leading to cerebral oedema), the urea clearance rate should be slowed down by either short duration intermittent dialysis using low blood flows or with CKRT. For patients with low electrolyte levels (hypokalaemia, hypophosphataemia, hypomagnesaemia), the dialysate or replacement fluid should contain the relevant electrolytes to avoid further lowering of electrolyte levels. For patients with hypocalcaemia who do not require regional citrate anticoagulation, the dialysate or replacement fluid should contain calcium to avoid worsening hypocalcaemia.

As the patient improves, KRT should be de-escalated. If KRT is still needed and the patient can be taken off vasopressors and inotropes, then CKRT should be switched to intermittent KRT. Compared to CKRT, use of intermittent KRT would decrease the cost of care and facilitate early mobilisation. When urine output improves, a trial of KRT cessation should be done, with initial close monitoring of pH and electrolytes.

TROUBLESHOOTING OF KIDNEY REPLACEMENT THERAPY

After initiating KRT, frontline clinicians should be ready to solve one or more of the following problems: persistent metabolic acidosis or hyperkalaemia (related to inadequate KRT dose), premature filter clotting/clogging, intradialytic hypotension, citrate overload, citrate accumulation (also known as citrate toxicity) and type II heparin-induced thrombocytopenia [Table 2].

Although staff training and protocols have enabled a complex intervention like KRT to be successfully initiated in high-dependency and intensive care units, KRT may be interrupted due to premature filter clotting/clogging. The KRT interruptions can be detrimental in several ways, including loss of clotted blood in the circuit, reduced therapy time and effectiveness, increased nursing workload from frequent filter changes, increased costs and aggravating shortages of KRT consumables. Filter clotting occurs when thrombosis occurs at the intra-arterial side of the membrane, marked by a sharp rise of filter pressure drop, calculated as the pressure difference between the prefilter pressure and the return pressure. Filter clogging occurs when proteinaceous material blocks the membrane pores, and is marked by increased transmembrane pressure, calculated as the pressure difference between the blood and dialysis compartments. Both filter clotting and clogging have common causes and may be considered together. An approach to filter clotting/clogging requires a systematic search for access, anticoagulation and prescription problems.

Table 2. Troubleshooting of kidney replacement therapy.

Problem	Cause	Possible solutions
Persistent metabolic acidosis or hyperkalaemia	Inadequate KRT dose	• Treat underlying causes • Increase effluent flow rate: increase ultrafiltration flow rate in CVVH or CVVHDF; increase dialysis dose in CVVHD or CVVHDF
Premature filter clotting/clogging (sharp rise of FPD/TMP, with <48 h of filter lifespan)	Catheter malfunction (sharp drop of access pressure)	• Fix catheter kinking • Improve the volume status to reduce vessel wall collapse onto catheter side holes • Exchange with catheter of an appropriate length
	Insufficient anticoagulation	• Use anticoagulation, e.g., RCA or systemic heparin • Optimise anticoagulation, e.g., increase the citrate dose for RCA
	Suboptimal prescription	• Reduce filtration fraction (i.e. ultrafiltration flow rate divided by plasma water flow rate) while keeping the KRT dose constant • Decrease ultrafiltration flow rate when using CVVH or CVVHDF, or by switching from CVVH to CVVHD • Increase plasma water flow rate by increasing the blood flow rate or by increasing the proportion of prefilter versus postfilter replacement fluid when using CVVH or CVVHDF
Intradialytic hypotension	Excessive fluid removal rate	• Reduce or cease fluid removal • Fluid replacement if hypovolaemia
	Non-dialysis-related cause	• Stop any blood loss • Vasopressors (e.g. noradrenaline) to keep the mean arterial pressure ≥65 mmHg
Citrate overload (indicated by tCa/iCa ≤2.5, with metabolic alkalosis)	Excessive citrate dosing and citrate metabolism not overwhelmed	• Decrease citrate load, e.g., by decreasing blood flow rate or citrate flow rate or by targeting a lower citrate dose • Increase citrate clearance by increasing dialysis dose
Citrate accumulation (citrate toxicity) (indicated by tCa/iCa >2.5, with metabolic acidosis)	Citrate metabolism severely impaired and overwhelmed	• Decrease citrate load, e.g., by decreasing blood flow rate or citrate flow rate or by targeting a lower citrate dose • Increase citrate clearance by increasing dialysis dose • Use non-citrate anticoagulation strategy, e.g., no anticoagulation or systemic heparin
Type II heparin-induced thrombocytopenia	Antiplatelet factor 4/ heparin autoantibodies that activate platelets to cause arterial and venous thromboses	• Stop all forms of heparin, including low-molecular-weight heparin • In the presence of thrombosis and warfarin use, administer intravenous vitamin K to reverse warfarin and halt further protein C depletion • Start anticoagulation with direct thrombin inhibitors or factor Xa inhibitors • Regional citrate anticoagulation is not useful

CVVH: continuous venovenous haemofiltration, CVVHD: continuous venovenous haemodialysis, CVVHDF: continuous venovenous haemodiafiltration, FPD: filter pressure drop, calculated as the pressure difference between the prefilter pressure and the return pressure, iCa: ionised serum calcium, KRT: kidney replacement therapy, RCA: regional citrate anticoagulation, tCa: unadjusted total serum calcium, TMP: transmembrane pressure, which is the pressure gradient across the filter membrane, calculated as the pressure difference between the blood and dialysis compartments

Another important problem is intradialytic hypotension, which has been associated with increased mortality among critically ill patients.[14] To manage this, a key step is to avoid anchoring bias, which is to refrain from pinning the cause of hypotension on KRT alone. Non-KRT causes need to be considered, including hypovolemia/haemorrhage (which may be exacerbated or unmasked by fluid removal during KRT), sepsis, cardiac dysfunction, pericardial tamponade, tension pneumothorax and pulmonary embolism.[7]

Finally, anticoagulation is a double-edged sword. While it can prolong filter lifespan, adverse events can occur. For regional citrate anticoagulation, excess citrate in the patient's blood can be metabolised by hepatic and muscle cells to bicarbonate, leading to citrate overload (indicated by a ratio of unadjusted total calcium [tCa] to ionised calcium [iCa] ≤2.5) and metabolic alkalosis. However, in a minority of patients with liver failure and circulatory shock, citrate metabolism is severely impaired.[12] Excess citrate then remains as an acid and binds free serum calcium, leading to citrate accumulation (also known as citrate toxicity, indicated by tCa/iCa >2.5), hypocalcaemia, metabolic acidosis and eventually cardiac complications.[15] When using systemic heparin, bleeding and type II heparin-induced thrombocytopenia with thrombosis may occur. In both cases, systemic heparin needs to be stopped and alternative anticoagulation needs to be considered. For bleeding, either regional citrate anticoagulation or no anticoagulation can be used. For heparin-induced thrombocytopenia, given ongoing thrombosis, another systemic anticoagulation method (e.g. direct thrombin inhibitors) is required and regional citrate anticoagulation is not enough.

TAKE HOME MESSAGES

1 Acute kidney injury is the abrupt reduction of glomerular filtration rate over a period of 1 week or less, identified via creatinine elevation and/or decreased urine output.
2 Specific causes of AKI can be divided into prerenal (reduced renal perfusion pressure), intrinsic renal (disease of the vessels, glomeruli or tubules within the kidneys) and postrenal (urinary flow obstruction) causes.
3 In general, patients with AKI require avoidance of nephrotoxins, reversal of specific causes and dose adjustment for renally excreted drugs. The KRT should be considered and instituted when life-threatening conditions are present or when serum urea exceeds 40 mmol/L.
4 Problems related to KRT include the following: persistent metabolic acidosis or hyperkalaemia, premature filter clotting/clogging, intradialytic hypotension, citrate overload, citrate accumulation toxicity and type II heparin-induced thrombocytopenia.

Closing Vignette

Further blood investigations revealed the following: creatinine kinase 75,000 U/L, urea 22 mmol/L, creatinine 250 µmol/L, pH 7.15, serum bicarbonate 11 mmol/L, serum ionised calcium 0.74 mmol/L. The patient was diagnosed with stage III AKI secondary to sepsis and rhabdomyolysis, and rhabdomyolysis-associated hypocalcaemia. As he required vasopressor support, continuous venovenous haemodiafiltration, regional citrate anticoagulation and intravenous calcium replacement were commenced. Clinical improvement, resolution of rhabdomyolysis and recovery of urine output occurred over the next 4 days and KRT was then stopped. In addition, the patient was extubated and transferred to the general ward for further monitoring.

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Conflicts of interest

See KC is a member of the SMJ Editorial Board, and was thus not involved in the peer review and publication decisions of this article.

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Supplemental digital content

Appendix at https://links.lww.com/SMJ/XXX

REFERENCES

1. Lameire NH, Levin A, Kellum JA, Cheung M, Jadoul M, Winkelmayer WC, *et al*. Harmonizing acute and chronic kidney disease definition and classification: Report of a Kidney Disease: Improving Global Outcomes (KDIGO) Consensus Conference. Kidney Int 2021;100:516-26.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Kidney Int Suppl 2012;2:1-138.
3. Susantitaphong P, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, Koulouridis I, *et al*. World incidence of AKI: A meta-analysis. Clin J Am Soc Nephrol 2013;8:1482-93.
4. Macedo E, Malhotra R, Bouchard J, Wynn SK, Mehta RL. Oliguria is an early predictor of higher mortality in critically ill patients. Kidney Int 2011;80:760-7.
5. Katulka RJ, Al Saadon A, Sebastianski M, Featherstone R, Vandermeer B, Silver SA, *et al*. Determining the optimal time for liberation from renal replacement therapy in critically ill patients: A systematic review and meta-analysis (DOnE RRT). Crit Care 2020;24:50.
6. Katayama S, Koyama K, Goto Y, Koinuma T, Tonai K, Shima J, *et al*. Body weight definitions for evaluating a urinary diagnosis of acute

kidney injury in patients with sepsis. BMC Nephrol 2018;19:101.
7. See KC. Management of circulatory shock and hypotension. Singapore Med J 2022;63:239-44.
8. Lau YH, See KC. Point-of-care ultrasound for critically-ill patients: A mini-review of key diagnostic features and protocols. World J Crit Care Med 2022;11:70-84.
9. Gaudry S, Hajage D, Martin-Lefevre L, Lebbah S, Louis G, Moschietto S, *et al*. Comparison of two delayed strategies for renal replacement therapy initiation for severe acute kidney injury (AKIKI 2): A multicentre, open-label, randomised, controlled trial. Lancet 2021;397:1293-300.
10. Phu NH, Hien TT, Mai NT, Chau TT, Chuong LV, Loc PP, *et al*. Hemofiltration and peritoneal dialysis in infection-associated acute renal failure in Vietnam. N Engl J Med 2002;347:895-902.
11. Zarbock A, Kullmar M, Kindgen-Milles D, Wempe C, Gerss J, Brandenburger T, *et al*. Effect of regional citrate anticoagulation vs systemic heparin anticoagulation during continuous kidney replacement therapy on dialysis filter life span and mortality among critically ill patients with acute kidney injury: A randomized clinical trial. JAMA 2020;324:1629-39.
12. Kindgen-Milles D, Brandenburger T, Dimski T. Regional citrate anticoagulation for continuous renal replacement therapy. Curr Opin Crit Care 2018;24:450-4.
13. Ostermann M, Dickie H, Tovey L, Treacher D. Management of sodium disorders during continuous haemofiltration. Crit Care 2010;14:418.
14. Silversides JA, Pinto R, Kuint R, Wald R, Hladunewich MA, Lapinsky SE, *et al*. Fluid balance, intradialytic hypotension, and outcomes in critically ill patients undergoing renal replacement therapy: A cohort study. Crit Care 2014;18:624.
15. Schneider AG, Journois D, Rimmele T. Complications of regional citrate anticoagulation: Accumulation or overload? Crit Care 2017;21:281.

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SMC CATEGORY 3B CME PROGRAMME

Online Quiz: https://www.sma.org.sg/cme-programme

Deadline for submission: 6 pm, 05 January 2024

Question	True	False
1. Acute kidney injury (AKI) is the abrupt reduction of kidney tubular function over a period of 1 week or less.		
2. Compared to serum creatinine, urine output is a more sensitive marker of kidney injury and recovery.		
3. Stage III AKI can be diagnosed when the duration of anuria exceeds 12 h in a patient with AKI.		
4. Prerenal AKI is always due to hypovolaemia.		
5. Raised intra-abdominal pressure can lead to AKI.		
6. For patients with AKI, kidney replacement therapy (KRT) should be considered when serum urea exceeds 40 mmol/L.		
7. Intermittent modes of KRT may predispose patients to intradialytic hypotension due to rapid solute clearance, even without fluid removal.		
8. Intermittent modes of KRT are not suitable for patients at risk of raised intracranial pressure.		
9. A non-cuffed right internal jugular dialysis catheter would usually have a length of 24 cm.		
10. During continuous venovenous haemofiltration, the main mechanism of solute clearance is via diffusion.		
11. For continuous KRT, regional citrate anticoagulation results in a longer filter life compared to systemic heparin anticoagulation.		
12. Without prescription modification, KRT may lead to osmotic demyelination in patients with severe hyponatraemia (serum Na <125 mmol/L).		
13. If KRT is still needed and the patient can be taken off vasopressors and inotropes, then continuous KRT should be switched to intermittent KRT.		
14. When urine output improves, a trial of KRT cessation should be done, with initial close monitoring of pH and electrolytes.		
15. Filter clotting occurs when thrombosis occurs at the intra-arterial side of the membrane, marked by increased transmembrane pressure.		
16. Intradialytic hypotension worsens mortality in critically ill patients.		
17. Intradialytic hypotension is always due to excessive fluid removal.		
18. For regional citrate anticoagulation, excess citrate in the patient's blood may result in either metabolic acidosis or alkalosis.		
19. For regional citrate anticoagulation, citrate accumulation is identified by the ratio of total albumin-adjusted calcium to ionised calcium ≤ 2.5.		
20. For heparin-induced thrombocytopenia, regional citrate anticoagulation can be used instead of systemic heparin anticoagulation for continuous KRT.		

APPENDIX

Figure S1. Modes of acute kidney replacement therapy.

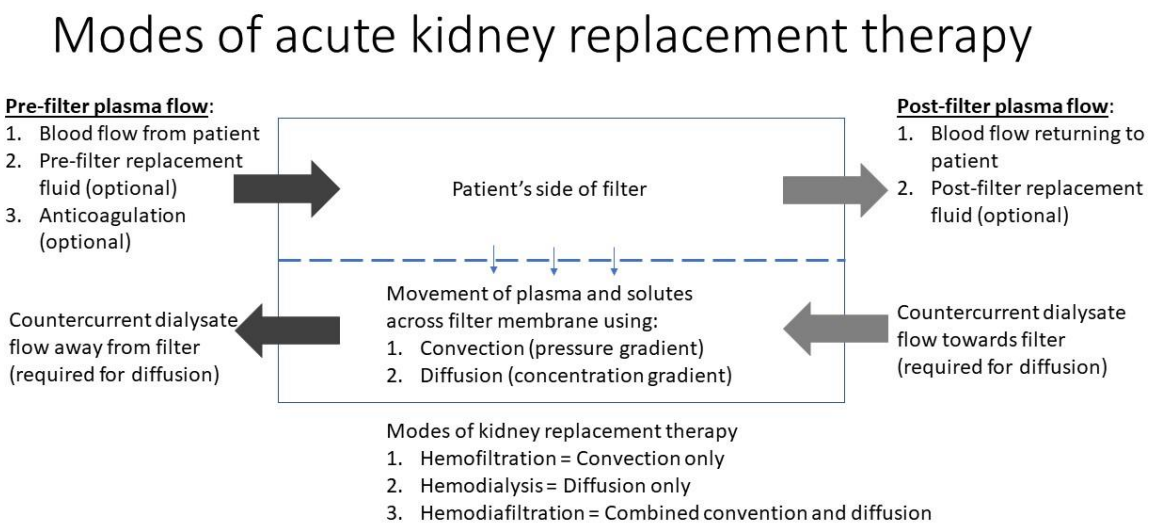

Table S1. Modification of fluid bag for CKRT when patients have severe hyponatremia or severe hypernatraemia.

Volume (ml) of sterile water added to 5L fluid bag	Final [Na+] in 5L fluid bag after adding sterile water (mmol/L)	Volume (ml) of 3% NaCl added to 5L fluid bag	Final [Na+] in 5L fluid bag after adding 3% NaCl (mmol/L)	Volume (ml) of 20% NaCl added to 5L fluid bag	Final [Na+] in 5L fluid bag after adding 20% NaCl (mmol/L)
0	140	0	140	0	140
100	137	68	145	8	145
150	136	82	146	9	146
200	135	96	147	11	147
250	133	109	148	12	148
300	132	124	149	14	149
350	131	138	150	15	150
400	130	152	151	17	151
450	128	166	152	18	152
500	127	180	153	20	153
550	126	195	154	21	154
600	125	209	155	23	155
650	124	224	156	24	156
700	123	239	157	26	157
750	122	253	158	28	158
800	121	268	159	29	159
850	120	283	160	31	160
900	119	298	161	32	161
950	118	313	162	34	162
1000	117	328	163	35	163
1050	115	344	164	37	164
1100	114	359	165	38	165
1150	114	374	166	40	166
1200	113	390	167	41	167
1250	112	405	168	43	168
1300	111	421	169	45	169
1350	110	437	170	46	170

[Na+]: Sodium concentration

CKRT: Continuous kidney replacement therapy