Renal replacement therapy for acute kidney injury in intensive care

ABSTRACT

Acute kidney injury is a common occurrence on the intensive care unit and is associated with incremental risk of death and chronic kidney disease. Renal replacement therapy has become an essential tool in the intensive care management of patients with severe acute kidney injury and its use is rising. A basic understanding of renal replacement therapy is essential for all doctors treating acutely unwell patients. This article provides a brief overview of the principles and important considerations for the provision of renal replacement therapy for critically ill patients with acute kidney injury.

Acute kidney injury is a common occurrence on the intensive care unit, with up to 60% of patients being affected (Hoste et al, 2015). In hospitalized patients, acute kidney injury is associated with increased hospital mortality, length of stay and health-care costs, and is also an independent risk factor for chronic kidney disease (Chertow et al, 2005; Lafrance and Miller, 2010).

Renal replacement therapy has become an essential tool in the intensive care management of patients with severe acute kidney injury, and helps to correct metabolic derangements and fluid overload, and prevent the associated life-threatening complications. A basic understanding of renal replacement therapy is essential for all doctors treating acutely unwell patients, and this review provides a brief overview of renal replacement therapy commonly used in the intensive care unit.

Dr Thomas W Davies, ACCS Anaesthesia Speciality Trainee, Department of Critical Care, University College Hospital, London NW1 2BU

Dr Marlies Ostermann, Consultant in Nephrology and Intensive Care Medicine, Department of Critical Care, Guy's and St. Thomas' NHS Foundation Trust, London

Dr Edward Gilbert-Kawai, Speciality Registrar in Anaesthesia and Intensive Care Medicine, Department of Critical Care, University College Hospital, London

Correspondence to: Dr TW Davies (thomas.davies6@nhs.net)

Use and indications

Severe acute kidney injury results in the dysregulated homeostasis of fluid, potassium and acid–base status. Renal replacement therapy removes solutes and excess water, and thus provides supportive treatment, but does not replace any other functions of the kidney, i.e. resorption of amino acids, activation of vitamin D, production of erythropoietin or gluconeogenesis.

Around 5–10% of intensive care patients will receive renal replacement therapy during their stay, and the hospital mortality rate in such patients is around 50–60% (Susantitaphong et al, 2013; Hoste et al, 2015). The cause of acute kidney injury is often multi-factorial and complex in critically ill patients, but regardless of the underlying aetiology, if the renal injury cannot be easily rectified, and if the patient's primary condition has a reasonable degree of reversibility, then renal replacement therapy should be considered.

The indications for renal replacement therapy are not absolute, and several renal and non-renal factors play a role when considering whether renal replacement therapy should be started (*Table 1*). Notably, there are no universally accepted levels of urea, creatinine, potassium or pH at which to commence therapy.

Principles and techniques of renal replacement therapy

Renal replacement therapy can broadly be divided into intermittent or continuous techniques. Intermittent techniques include peritoneal dialysis and intermittent haemodialysis. Continuous renal replacement therapy includes continuous veno-venous haemofiltration, continuous veno-venous haemodialysis, and continuous veno-venous haemodiafiltration. Hybrid methods also exist such as sustained low-efficiency dialysis and slow continuous ultrafiltration, which attempt to combine the benefits of both intermittent and continuous methods. In the UK the most common methods used in intensive care are continuous veno-venous haemofiltration and continuous veno-venous haemodiafiltration, but continuous veno-venous haemodialysis is increasingly being used.

Renal replacement therapy in the intensive care setting involves the use of an extracorporeal circuit to remove solutes and excess water from the blood and plasma. This

Table 1. Indications for initiation of renal replacement therapy

Renal indications	Rapidly evolving renal failure, or the development of uraemic complications (e.g. uraemic pericarditis or encephalopathy)
	Hyperkalaemia unresponsive to medical management
	Severe metabolic acidosis
	Oliguria or anuria resulting in fluid overload and diuretic-resistant pulmonary oedema
	Management of complex fluid balance, e.g. in cardiac failure
Non-renal indications	Drug toxicity, e.g. lithium
	Correction of electrolyte abnormalities, e.g. in hypernatraemia
	Temperature control (rarely performed nowadays because other methods work better)

circuit requires vascular access in the form of a large bore double lumen central venous catheter – often referred to as a 'vascath'. Blood is removed from the patient via the afferent limb of the catheter using roller pumps, and passed through a cylindrical synthetic semi-permeable polysulphone membrane consisting of multiple hollow fibres with pores throughout where filtration and/or dialysis takes place. The blood is then returned to the patient via the efferent limb of this catheter.

The fundamental aim of all renal replacement therapy techniques is the removal of unwanted solutes and water through a semi-permeable membrane using the processes of diffusion, convection or a combination of both. Diffusion describes solute transport across a semi-permeable membrane generated by a concentration gradient. Convection refers to bulk flow of solute across a semi-permeable membrane together with solvents (solvent drag), in a manner that is dependent on the transmembrane pressure and membrane characteristics, and independent of solute concentration.

Haemodialysis

Using the principle of diffusion, haemodialysis detoxifies the blood by running it through a semipermeable membrane bathed in a solution of pure water, electrolytes and salts, referred to as dialysate. Dialysate flows in the opposite direction to create a counter-current mechanism optimizing the concentration gradient between blood and dialysate at all times, thus enabling rapid diffusion of solute. Diffusion is more effective at removing low molecular weight molecules (<30 kDa) such as urea, creatinine, ions and ammonia.

Haemofiltration

Haemofiltration uses convection as the mechanism for detoxification of blood. The clearance of solute via convection depends on both the direction and magnitude of the transmembrane pressure. Increasing the flow rate will increase the volume of ultrafiltrate removed as effluent, and in turn increase solute clearance. The movement of solute across the semi-permeable membrane is also dependent on both the size of the molecule in question, the size of the pores in the membrane, the degree of protein binding and whether the substance is water soluble or not.

To effectively detoxify blood of solute by convection, large volumes of ultrafiltrate are needed, which leaves the circuit as waste (effluent). During this process, molecules like bicarbonate, magnesium, calcium and other essential electrolytes are also removed. This necessitates the return of a balanced crystalloid solution to the patient, in effect exchanging the waste ultrafiltrate with a replacement solution.

Haemodiafiltration

Haemodiafiltration is a combination of haemodialysis (diffusive clearance), and haemofiltration (convective clearance). Haemodialysis effectively becomes haemodiafiltration by increasing the transmembrane pressure and thereby increasing the ultrafiltration volume – and with it the convection of solutes. Diffusive clearance continues as previously described – down a concentration gradient maintained by the counter-current flow of dialysate. The removal of larger volumes of ultrafiltrate again necessitates volume replacement with a balanced crystalloid solution to maintain blood volume.

Choice of modality

There is no strong evidence to support use of one type of renal replacement therapy in intensive care over the others (*Table 2*), and no convincing survival advantages have been demonstrated (Rabindranath et al, 2007; Nash et al,

Table 2. Advantages and disadvantages of different modalities of renal replacement therapy

Modality	Advantages	Disadvantages
Intermittent haemodialysis	■ Allows more rapid removal of low molecular weight substances and toxins ■ Reduced anticoagulation exposure ■ Lower cost than continuous renal replacement therapy ■ More time for rehabilitation and mobilization	■ Hypotension with rapid fluid removal ■ Dialysis disequilibrium syndrome with risk of cerebral oedema ■ Usually not provided by intensive care unit team ■ More complex drug dosing ■ Possibly higher risk of long-term dialysis dependency ■ Loss of micronutrients
Sustained low efficiency dialysis	■ More haemodynamic stability than with intermittent haemodialysis ■ Decreased anticoagulation requirements ■ Time when not receiving treatment may be used for diagnostic or therapeutic procedures or rehabilitation	■ May not be tolerated by extremely unwell unstable patients
Slow continuous ultrafiltration	■ Gentler fluid removal and control of fluid balance in volume overload ■ Decreased anticoagulation requirements	■ No clearance of solutes or toxins ■ Can only be used in patient with fluid overload
Continuous renal replacement therapy	■ Haemodynamic stability as a result of gentler fluid removal ■ Continuous removal of toxins and better metabolic homeostasis ■ Gentler fluid removal and better control of fluid balance	■ Slower clearance of toxins ■ Need for anticoagulation ■ Risk of hypothermia ■ Higher costs than intermittent haemodialysis ■ Immobilization ■ Loss of micronutrients

> Fluid overload is associated with adverse outcomes and increased mortality in patients with acute kidney injury.

2017). The superiority of continuous over intermittent techniques also remains debated, but current UK practice (and general international consensus) is that continuous renal replacement therapy is more appropriate for haemodynamically unstable patients and patients with acute brain injury who may not tolerate rapid fluctuations in fluid status and metabolic shifts (Kidney Disease: Improving Global Outcomes (KDIGO), 2012).

In the critically ill patient, continuous renal replacement therapy offers the theoretical advantages of more haemodynamic stability as a result of gentler fluid removal over a longer period, continuous control of fluid status and electrolytes, and better cerebral protection. The disadvantage of continuous renal replacement therapy is that the continuous nature necessitates immobilisation and anticoagulation which can have side effects.

Intermittent techniques, although preferred in the stable patient, can lead to rapid fluid and solute shifts causing haemodynamic instability in the critically ill patient, and an increased risk of cerebral oedema causing raised intracranial pressure (dialysis disequilibrium syndrome). Data from observational studies suggest that the use of continuous techniques for acute kidney injury may also result in reduced long-term dialysis dependence compared to intermittent haemodialysis (Wald et al, 2014).

Hybrid methods such as sustained low-efficiency dialysis have been developed in an attempt to achieve the best of both worlds, working for long enough time periods to ensure haemodynamic stability and good fluid and solute control, but short enough to allow rehabilitation and avoid the complications of continuous anticoagulation. Sustained low-efficiency dialysis is safe and effective in critically ill patients, but there is no evidence to suggest superiority over other techniques (Kitchlu et al, 2015). Slow continuous ultrafiltration is an alternative method of renal replacement therapy, used solely to control fluid balance in patients with volume overload via the removal of fluid through ultrafiltration. Owing to low blood flows, minimal solute clearance occurs and there is no need for dialysate or replacement fluid.

Considerations for continuous renal replacement therapy

Timing

The general criteria of when to initiate renal replacement therapy are outlined in *Table 1*, and normally it is started when one or more of these criteria is met. The optimal timing of when to initiate renal replacement therapy has become an area of debate with observational studies and single centre randomized controlled trials suggesting that early initiation may improve survival (Karvellas et al, 2011; Zarbock et al, 2016). However, larger multicentre randomized trials have shown no mortality benefit, and significantly reduced use of renal replacement therapy (and therefore associated complications), in the delayed initiation groups (Gaudry et al, 2016; Barbar et al, 2018). At present therefore, the decision to start renal replacement therapy should be made by the intensive care team, taking into account the severity and trajectory of the patient's illness and organ failure.

Anticoagulation

The physical contact of blood with the extracorporeal circuit activates the clotting cascade. In addition, a degree of haemoconcentration occurs within the filter as a result of fluid removal. This necessitates anticoagulation of the blood in the filter circuit to ensure efficient continuous renal replacement therapy.

Citrate is the recommended anticoagulant in the UK. It chelates calcium and thus inhibits the clotting cascade and platelet aggregation. Around 50% of citrate–calcium complexes are then removed in the effluent, which necessitates calcium replacement (and close monitoring of the calcium level to avoid hypocalcaemia). The remaining 50% of citrate–calcium complexes enter the systemic circulation where calcium is recycled, and citrate is metabolised to bicarbonate (Krebs cycle), mainly in the liver and muscle. Owing to the risk of accumulation, citrate should be used very cautiously in patients with severe liver failure or circulatory shock compromising muscle perfusion. The use of citrate results in strictly regional anticoagulation and therefore can reasonably be used in patients with high bleeding risk.

Heparin is recommended as a second-line agent and is still widely used, but it is associated with a reduced filter lifetime, an increased filter failure rate, and an increased bleeding risk (Bai et al, 2015). Heparin is not recommended if the patient has an increased bleeding risk, impaired coagulation or is already receiving systemic anticoagulation (KDIGO, 2012).

Other alternatives include prostacyclin (epoprostenol), which is used if both citrate and heparin are contraindicated. Prostacyclin is a relatively weak anticoagulant and has vasodilatory properties which may affect haemodynamic stability during renal replacement therapy.

Administration of intermittent saline flushes into the circuit can help to reduce haemoconcentration but this is less effective than anticoagulants and increases the workload of the bedside staff.

Dosing

The optimal dose or intensity of continuous renal replacement therapy in patients with acute kidney injury is controversial. The dose is the amount of effluent fluid (ultrafiltrate) in ml/kg body weight/hour; standard dosing is around 25 ml/kg/hr. It had been postulated that increased intensity may result in improved outcome as a result of improved solute clearance, but large multicentre studies failed to detect any reduction in mortality with effluent flows of 35 ml/kg/hr, 40 ml/kg/hr and 70 ml/kg/hr when compared to the standard rate (Palevsky et al, 2008; Bellomo et al, 2009; Joannes-Boyau et al, 2013). Inadvertent losses of trace elements, water-soluble vitamins and essential drugs resulting in sub-therapeutic plasma levels (including antibiotics) are important risks of high dose renal replacement therapy.

Fluid balance and replacement

Fluid overload is associated with adverse outcomes and increased mortality in patients with acute kidney injury (Bouchard et al, 2009). During renal replacement therapy, a calculated proportion of the

ultrafiltrate is replaced with replacement fluid to maintain plasma electrolyte and acid–base homeostasis, and the desired net fluid balance. Bicarbonate ions are freely filtered during renal replacement therapy, so bicarbonate-based buffer solutions are often used as replacement fluid. Lactate-based fluids were previously used, with the lactate being metabolised to carbon dioxide and water, generating new bicarbonate ions via the Krebs cycle in the liver.

Fluid can be replaced before the filter (pre-dilution) and after (post-dilution). Pre-dilution reduces haemoconcentration and the incidence of premature filter clotting but results in less effective clearance of solute. A combination of both pre- and post-dilution is often used to help maintain the lifespan of the filter while achieving adequate solute clearance.

Drug dosing

The pharmacokinetics of drugs in patients on continuous renal replacement therapy is complex, making generalized recommendations difficult. The rate of drug removal on continuous renal replacement therapy is variable depending on the modality, the ultrafiltrate and dialysate flow rates, the type of semi-permeable membrane, the degree of protein binding of the drug, and the disease state of the patient.

Given the complexity of the above, under- and over-dosing of drugs has been reported. As such, recommendations for drug dosing should be made in conjunction with the intensive care unit pharmacy team who also take into account the degree of multiorgan dysfunction of the patient and the pharmacokinetic properties of the drug in question, including non-renal clearance.

Vascular access

Functional vascular access with adequate blood flow is essential for renal replacement therapy. A large bore double lumen catheter of appropriate length is required in a central vein as previously discussed. Kidney Disease: Improving Global Outcomes (2012) lists a preference for the site of vascular access as:

- First choice: right jugular vein
- Second choice: femoral vein
- Third choice: left jugular vein
- Last choice: subclavian vein with preference for the dominant side.

The right internal jugular is first choice because it allows improved delivery of renal replacement therapy (Parienti et al, 2010). The subclavian vein is rarely used because of difficulty using ultrasound-guided techniques and an increased risk of pneumothorax. There is also a perceived increased risk of vein stenosis which may compromise future venous access for long-term haemodialysis in those with premature development of end-stage renal failure after acute kidney injury (Schillinger et al, 1991).

The femoral vein is preferred to the left internal jugular as it is associated with less malfunction, and is no longer thought to be linked with a high risk of catheter-related bloodstream infections, except in patients with raised body mass index (Parienti et al, 2008, 2010). It is important that the tip of the catheter is positioned in a high flow portion of the vessel. As such, it is recommended to insert a 15 cm catheter in the right internal jugular, 20 cm catheter in the left internal jugular and 25 cm catheter in the femoral vein (Huriaux et al, 2017).

Discontinuation of therapy and prognosis

Renal replacement therapy usually continues until the patient shows signs of recovery of native renal function or the goals of overall care change. There is a paucity of studies evaluating the process of weaning or providing guidance on ideal markers that predict sufficient renal recovery. Deciding the optimal time to wean acute renal replacement therapy is complex and should be individualized in critically ill patients.

Renal recovery may be demonstrated by an increase in urine output, an improvement of creatinine clearance, and/or urea excretion on steady state renal replacement therapy, or after a short period off renal replacement therapy (filter holiday). Of these, urine output is probably the most well studied, and has been used in two large trials as a marker to wean renal replacement therapy (Gaudry et al, 2016; Zarbock et al, 2016). Retrospective data showed that patients with a spontaneous urine output over 400 ml/day while on renal replacement therapy had an 80% chance of successful discontinuation (Uchino et al, 2009).

A proportion of patients will not be able to be weaned off the filter, so will need input from the renal team to enable discharge from intensive care and provide ongoing renal replacement therapy (Wald et al, 2014). In the longer term, between 4 and 15% of patients who received renal replacement therapy for acute kidney injury on intensive care unit will require long-term renal replacement therapy at 2 years (Ishani et al, 2009).

KEY POINTS

- The mortality associated with acute kidney injury is high.
- The fundamental aim of all techniques of renal replacement therapy is removal of unwanted solutes and water through a semi-permeable membrane via diffusion (dialysis) and/or convection (filtration).
- Continuous modes of renal replacement therapy are predominantly used in intensive care units.
- The optimal timing for initiation of renal replacement therapy remains unknown; early initiation is not associated with improved survival.
- Anticoagulation is required during continuous renal replacement therapy; citrate is the recommended first choice agent, although heparin is still commonly used in the UK.
- Increased intensity or dose of continuous renal replacement therapy is not associated with improved survival.

Supportive measures during renal replacement therapy

In patients receiving renal replacement therapy, nutritional status may be affected by the removal of amino acids, trace elements, glucose and water-soluble vitamins (Berger et al, 2004). During continuous renal replacement therapy, amino acid losses of 10–15 g/day have been reported, and up to 80% of patients had below-normal levels of at least one important micronutrient (thiamine, pyridoxine, ascorbic acid, folate, zinc or copper) (Scheinkestel et al, 2003; Kamel et al, 2018). The most recent guideline by the European Society for Clinical Nutrition and Metabolism recommends delivering 1.3 g/kg protein equivalents per day gradually, together with trace elements and water-soluble vitamins (Singer et al, 2019). In patients with insufficient oral intake, enteral feeding within 24–48 hours of acute illness is recommended. When enteral nutrition is contraindicated, parenteral nutrition should be considered.

CURRICULUM CHECKLIST

This article addresses the following requirements from the general internal medicine training curriculum:

- Delivering effective resuscitation and managing the acutely deteriorating patient.
- Managing medical problems in patients in other specialties and special cases.
- Managing an acute unselected take.

In patients receiving citrate-based continuous renal replacement therapy, it is important to remember that citrate contributes to the daily caloric load.

Conclusions

Acute kidney injury is associated with significant mortality and morbidity. Renal replacement therapy can prevent the life-threatening complications of severe acute kidney injury. Continuous techniques provide more haemodynamic stability than intermittent techniques, so are preferred in intensive care units. A basic understanding of factors to consider when using continuous renal replacement therapy is essential for any doctor treating acutely unwell patients. **BJHM**

Conflict of interest: none.

Bai M, Zhou M, He L et al. Citrate versus heparin anticoagulation for continuous renal replacement therapy: an updated meta-analysis of RCTs. Intensive Care Med. 2015 Dec;41(12):2098–2110. https://doi.org/10.1007/s00134-015-4099-0

Barbar SD, Clere-Jehl R, Bourredjem A et al; IDEAL-ICU Trial Investigators and the CRICS TRIGGERSEP Network. Timing of renal-replacement therapy in patients with acute kidney injury and sepsis. N Engl J Med. 2018 Oct 11;379(15):1431–1442. https://doi.org/10.1056/NEJMoa1803213

Bellomo R, Cass A, Cole L et al; RENAL Replacement Therapy Study Investigators. Intensity of continuous renal-replacement therapy in critically ill patients. N Engl J Med. 2009 Oct 22;361(17):1627–1638. https://doi.org/10.1056/NEJMoa0902413

Berger MM, Shenkin A, Revelly JP, Roberts E, Cayeux MC, Baines M, Chioléro RL. Copper, selenium, zinc, and thiamine balances during continuous venovenous hemodiafiltration in critically ill patients. Am J Clin Nutr. 2004 Aug 01;80(2):410–416. https://doi.org/10.1093/ajcn/80.2.410

Bouchard J, Soroko SB, Chertow GM, Himmelfarb J, Ikizler TA, Paganini EP, Mehta RL; Program to Improve Care in Acute Renal Disease (PICARD) Study Group. Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury. Kidney Int. 2009 Aug;76(4):422–427. https://doi.org/10.1038/ki.2009.159

Chertow GM, Burdick E, Honour M, Bonventre JV, Bates DW. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. J Am Soc Nephrol. 2005 Nov;16(11):3365–3370. https://doi.org/10.1681/ASN.2004090740

Gaudry S, Hajage D, Schortgen F et al; AKIKI Study Group. Initiation strategies for renal-replacement therapy in the intensive care unit. N Engl J Med. 2016 Jul 14;375(2):122–133. https://doi.org/10.1056/NEJMoa1603017

Hoste EAJ, Bagshaw SM, Bellomo R et al. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. Intensive Care Med. 2015 Aug;41(8):1411–1423. https://doi.org/10.1007/s00134-015-3934-7

Huriaux L, Costille P, Quintard H, Journois D, Kellum JA, Rimmelé T. Haemodialysis catheters in the intensive care unit. Anaesth Crit Care Pain Med. 2017 Oct;36(5):313–319. https://doi.org/10.1016/j.accpm.2016.10.003

Ishani A, Xue JL, Himmelfarb J, Eggers PW, Kimmel PL, Molitoris BA, Collins AJ. Acute kidney injury increases risk of ESRD among elderly. J Am Soc Nephrol. 2009 Jan;20(1):223–228. https://doi.org/10.1681/ASN.2007080837

Joannes-Boyau O, Honoré PM, Perez P et al. High-volume versus standard-volume haemofiltration for septic shock patients with acute kidney injury (IVOIRE study): a multicentre randomized controlled trial. Intensive Care Med. 2013 Sep;39(9):1535–1546. https://doi.org/10.1007/s00134-013-2967-z

Kamel AY, Dave NJ, Zhao VM, Griffith DP, Connor MJ Jr, Ziegler TR. Micronutrient alterations during continuous renal replacement therapy in critically ill adults: a retrospective study. Nutr Clin Pract. 2018 Jun;33(3):439–446. https://doi.org/10.1177/0884533617716618

Karvellas CJ, Farhat MR, Sajjad I, Mogensen SS, Leung AA, Wald R, Bagshaw SM. A comparison of early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury: a systematic review and meta-analysis. Crit Care. 2011;15(1):R72. https://doi.org/10.1186/cc10061

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. https://doi.org/ 10.1038/kisup.2012.1

Kitchlu A, Adhikari N, Burns KEA et al. Outcomes of sustained low efficiency dialysis versus continuous renal replacement therapy in critically ill adults with acute kidney injury: a cohort study. BMC Nephrol. 2015 Dec;16(1):127. https://doi.org/10.1186/s12882-015-0123-4

Lafrance JP, Miller DR. Acute kidney injury associates with increased long-term mortality. J Am Soc Nephrol. 2010 Feb;21(2):345–352. https://doi.org/10.1681/ASN.2009060636

Nash DM, Przech S, Wald R, O'Reilly D. Systematic review and meta-analysis of renal replacement therapy modalities for acute kidney injury in the intensive care unit. J Crit Care. 2017 Oct;41:138–144. https://doi.org/10.1016/j.jcrc.2017.05.002

Palevsky PM, Zhang JH, O'Connor TZ et al; VA/NIH Acute Renal Failure Trial Network. Intensity of renal support in critically ill patients with acute kidney injury. N Engl J Med. 2008 Jul 03;359(1):7–20. https://doi.org/10.1056/NEJMoa0802639

Parienti JJ, Thirion M, Mégarbane B et al; for Members of the Cathedia Study Group. Femoral vs jugular venous catheterization and risk of nosocomial events in adults requiring acute renal replacement therapy: a randomized controlled trial. JAMA. 2008 May 28;299(20):2413–2422. https://doi.org/10.1001/jama.299.20.2413

Parienti JJ, Mégarbane B, Fischer MO et al; Cathedia Study Group. Catheter dysfunction and dialysis performance according to vascular access among 736 critically ill adults requiring renal replacement therapy: A randomized controlled study. Crit Care Med. 2010 Apr;38(4):1118–1125. https://doi.org/10.1097/CCM.0b013e3181d454b3

Rabindranath K, Adams J, Macleod AM, Muirhead N. Intermittent versus continuous renal replacement therapy for acute renal failure in adults. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD003773. https://doi.org/10.1002/14651858.CD003773.pub3

Scheinkestel CD, Adams F, Mahony L, Bailey M, Davies AR, Nyulasi I, Tuxen DV. Impact of increasing parenteral protein loads on amino acid levels and balance in critically ill anuric patients on continuous renal replacement therapy. Nutrition. 2003 Sep;19(9):733–740. https://doi.org/10.1016/S0899-9007(03)00107-2

Schillinger F, Schillinger D, Montagnac R, Milcent T. Post catheterisation vein stenosis in haemodialysis: comparative angiographic study of 50 subclavian and 50 internal jugular accesses. Nephrol Dial Transplant. 1991;6(10):722–724. https://doi.org/10.1093/ndt/6.10.722

Singer P, Blaser AR, Berger MM et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr. 2019 Feb;38(1):48–79. https://doi.org/10.1016/j.clnu.2018.08.037

Susantitaphong P, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, Koulouridis I, Jaber BL; Acute Kidney Injury Advisory Group of the American Society of Nephrology. World incidence of AKI: a meta-analysis. Clin J Am Soc Nephrol. 2013 Sep 06;8(9):1482–1493. https://doi.org/10.2215/CJN.00710113

Uchino S, Bellomo R, Morimatsu H et al. Discontinuation of continuous renal replacement therapy: A post hoc analysis of a prospective multicenter observational study. Crit Care Med. 2009 Sep;37(9):2576–2582. https://doi.org/10.1097/CCM.0b013e3181a38241

Wald R, Shariff SZ, Adhikari NKJ et al. The association between renal replacement therapy modality and long-term outcomes among critically ill adults with acute kidney injury: a retrospective cohort study. Crit Care Med. 2014 Apr;42(4):868–877. https://doi.org/10.1097/CCM.0000000000000042

Zarbock A, Kellum JA, Schmidt C et al. Effect of early vs delayed initiation of renal replacement therapy on mortality in critically ill patients with acute kidney injury. JAMA. 2016 May 24;315(20):2190–2199. https://doi.org/10.1001/jama.2016.5828