COVID-19 Critical Intelligence Unit

Evidence check

12 May 2020

Renal replacement therapies for COVID-19 positive patients in ICU

Rapid review question

What is the current evidence on the use of renal replacement therapies in intensive care units for patients with COVID-19?

In brief

- COVID-19 most frequently presents as mild respiratory illness and can generally be managed outside the hospital. About 20% of patients require hospitalisation, and of those, a quarter require intensive care.
- ICU patients typically require management of hypoxaemic respiratory failure or hypotension requiring vasopressor support. Acute kidney injury is a less common complication but is associated with a significant risk for mortality.
- Available data suggests that the prevalence of acute kidney injury in COVID-19 patients is around 3-9% and is more common in patients with severe disease, reported in up to 30% of critically ill or deceased patients.
- Studies have reported up to 25% of patients in intensive care units have required renal replacement therapy, and a meta-analysis within a letter reports the pooled incidence as 13%.
- The indications for continuous renal replacement therapy for acute kidney injury (of any aetiology) include hyperkalaemia metabolic acidosis volume overload, uraemic manifestations, or pericarditis. For COVID-19 patients, respiratory failure can be associated with fluid overload and require renal replacement therapy.
- Continuous renal replacement therapy is preferred over intermittent haemodialysis. This is because intermittent haemodialysis requires 1:1 nursing support. In intensive care units where nurses are trained in the use of continuous renal replacement therapy, haemodialysis nurses do not need to have direct contact with patients, thereby limiting healthcare staff exposure.
- A retrospective cohort study has shown that for COVID-19 patients, those receiving continuous renal replacement therapy (CRRT) was associated with a prolonged survival compared to non-CRRT group.
- There is emerging evidence that COVID-19 patients with acute respiratory distress syndrome are more likely to develop thrombotic complications that result in CRRT circuit clotting.

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Limitations

New evidence on this topic is emerging. The evidence is generally based on case studies and expert opinion and may differ due to stage and extent of the pandemic in different countries. Only full text articles available in English language were included in the evidence check. Considerations for renal replacement therapy in the context of COVID-19 are available, however these were out of scope for this review.

Background

COVID-19 most frequently presents as mild respiratory illness and can generally be managed outside the hospital. About 20% of patients require hospitalisation, and of those, a quarter require intensive care. ICU patients typically require management of hypoxaemic respiratory failure or hypotension requiring vasopressor support.(1) Acute kidney injury (AKI) is a less common complication but is associated with a significant risk for mortality.(2)

For patients with COVID-19, acute kidney injury may result from volume depletion (hypovolaemia), haemodynamic changes, viral infection leading directly to kidney tubular injury, thrombotic vascular processes, glomerular pathology or rhabdomyolysis.(3) Acute kidney injury is associated with haematuria, proteinuria and abnormal serum electrolyte levels (both increased and decreased serum sodium and potassium).(3)

Continuous renal replacement therapy (CRRT) is commonly used for critically ill patients with acute kidney injury to provide renal support. A variety of techniques that differ in their mode of solute clearance may be used.(4) CRRT has been shown to significantly lower mortality compared with conventional therapies for patients with acute kidney injury.(5, 6) CRRT has been has been successfully applied in the treatment of patients with SARS, MERS and sepsis.(7)

In COVID-19 patients, initial reports suggest the prevalence of acute kidney injury is around 3-9%.(8) Some studies of patients who were critically ill or deceased report rates of 25-29%.(9-11)

While thresholds for admission to ICU varies across jurisdictions, the proportion of COVID-19 patients receiving CRRT is higher in patients in ICU (18-25%) (12-16) compared to patients hospitalised outside the ICU (1-3%).(17-23) The Intensive Care National Audit and Research Centre's report on COVID-19 in critical care in the UK, reported about 31% of patients on ventilators and 4% of patients who were not on ventilators needed renal replacement therapy for AKI.(3)

Guidelines on continuous renal replacement therapy in COVID-19

- The National Institute for Health and Care Excellence (NICE) has recently published guidance.(3) It notes that for COVID-19 patients:
    - Maintaining optimal fluid status (euvolaemia) is critical in reducing the incidence of acute kidney injury, but this can be difficult to achieve.
    - Treatments used to manage COVID-19 may increase the risk of acute kidney injury, for example diuretics if they have caused volume depletion.
    - Fever and increased respiratory rate increase insensible fluid loss.
    - Dehydration (often needing correction with intravenous fluids) is common on hospital admission and may develop during hospitalisation.
    - There is an increased risk of coagulopathy.
- The National Health Service (NHS) guidance states:

  - In all cases, maximal medical management should be considered before attempting renal replacement therapy, including appropriate dose loop binders, potassium binders and sodium bicarbonate.
  - The conventional indications to start renal replacement therapy include life-threatening hyperkalaemia, refractory fluid overload and severe metabolic acidosis.(24)
- The American society of nephrology guidelines recommend, in the intensive care unit, the preferred modality for renal replacement therapy is continuous renal replacement therapy or prolonged intermittent renal replacement therapy, also known as sustained low efficiency dialysis. Continuous renal replacement therapy machines are preferred over intermittent haemodialysis in the setting of isolation as intermittent haemodialysis requires 1:1 nursing support. In intensive care units where nurses are trained in the use of continuous renal replacement therapy, haemodialysis nurses do not need to have direct contact with patients, thereby limiting healthcare staff exposure.(25)

Methods (Appendix 1)

Databases and grey literature sources were searched on 29 April 2020. Recommendations on the care of hospitalised patients with COVID-19 and kidney failure requiring renal replacement therapy.

Results

Table 1: Renal replacement therapy in COVID-19 patients

Source	Advice	Source Link
Peer reviewed sources		
Effect of continuous renal replacement therapy on all-cause mortality in COVID-19 patients undergoing invasive mechanical ventilation: a retrospective cohort study *Pre peer review* Yang et al, 2020 (18)	• 22 (61.1%) patients received CRRT (CRRT group) and 14 cases (38.9%) were managed in conventional strategy (non-CRRT group). • The association between CRRT treatment and a reduced risk of mortality remained significant after adjusting for confounding factors in seven different models, with an adjusted hazard ratio (aHR) varying between 0.283 and 0.424. • Older age, higher levels of IL-1β, IL-2 receptor, hs-cTnI and NT-proBNP were independently associated with increased risk of mortality in patients with CRRT treatment.	https://www.medrxiv.org/content/10.1101/2020.03.16.20036780v1.full.pdf
Characterisation of Acute Kidney Injury in Critically Ill Patients with Severe Coronavirus Disease-2019 (COVID-19) *Pre-peer review* Rubin et al, 2020 (15)	• Single centre cohort study, 71 patients. • AKI was present in 8/71 (11%) patients. • AKI developed in a total of 57 out of 71 (80%) patients with 35% stage 1, 35% stage 2 and 30% stage 3 acute kidney injury; 10 out of 57 (18%) patients required renal replacement therapy. • On day seven after AKI onset, 6 (11%) patients remained dependent on renal replacement therapy, 9 (16%) had SCr >200 micromol/L, and 4 (7%) patients died.	https://www.medrxiv.org/content/10.1101/2020.05.06.20069872v1

Source	Advice	Source Link
Peer reviewed sources		
Acute kidney injury in hospitalized patients with coronavirus disease 2019 (COVID-19): A meta-analysis (in a letter) Ng et al. 2020 (26)	• The risk of AKI in all hospitalised patients seemed to be low with a pooled incidence rate of 3%. • This risk increases to 19% when patients are admitted to the ICU. • Correspondingly, the need for RRT in all hospitalised patients was low, with a pooled incidence of 2%. • In ICU, the need for RRT increased to 13%.	https://www.sciencedirect.com/science/article/pii/S0163445320302802?via%3Di hub
COVID-19 and Acute Kidney Injury requiring Kidney Replacement Therapy: A Bad Prognostic Sign. Shekhar et al. 2020 (27)	• Out of 50 patients admitted to the hospital with COVID-19, 13 (26%) developed AKI. • At the end of study period, 1 patient remained hospitalised, 10 (90%) patients died and one patient was discharged home with resolution of AKI. • Findings suggest poor prognosis despite continuous kidney replacement therapies in patients who develop AKI with COVID-19.	https://www.medrxiv.org/content/10.1101/2020.05.08.20096040v1
High risk of thrombosis in patients in severe SARS-CoV-2 infection: a multicentre prospective cohort study Helms et al. 2020 (12)	• 150 COVID-19 patients were included. • 28 of 29 patients (96.6%) receiving continuous RRT experienced circuit clotting. • The median lifespan of an RRT circuit was 1.5 [1.0; 2.0] days, compared to 3 days recommended by the manufacturer. The total number of circuits used was 141 for 230 days of continuous RRT (4.9 devices/patient). • In comparison with non-COVID-19 ARDS patients (n=145), confirmed COVID-19 ARDS patients (n=77) developed significantly more thrombotic complication. • The median length of stay in ICU was 9.6 ± 4.2 days and mortality rate was 8.7%, with 101 patients (67.3%) still intubated at the time of data analysis.	https://www.esicm.org/wp-content/uploads/2020/04/863_author_proof.pdf

Source	Advice	Source Link
Peer reviewed sources		
Veno-venous Extracorporeal Membrane Oxygenation for Severe Pneumonia: COVID-19 Case in Japan Taniguchi et al. 2020 (28)	• CRRT used to remove excessive water and improve metabolic acidosis in a patient on ECMO.	https://onlinelibrary.wiley.com/doi/full/10.1002/ams2.509
Expert recommendations on blood purification treatment protocol for patients with severe COVID-19: Recommendation and consensus Yang et al. 2020 (29)	• Severe COVID-19 combined with AKI or severe electrolyte and acid-base balance disorders, CRRT is recommended as first-line treatment, which should be initiated immediately. • Volume overload that is refractory to diuretics. • Severe hyperkalemia (>6.5 mmol/L). • AKI of KDIGO standard grade ≥2. • Serum inflammatory mediator levels greater than five times the normal upper limit. • For simple volume overload and acute pulmonary oedema, slow continuous ultrafiltration (SCUF) is recommended. • High volume hemofiltration (HVHF) for removing inflammatory mediators. • For patients with severe COVID-19 with severe ARDS, ECMO with CRRT is recommended.	https://www.sciencedirect.com/science/article/pii/S2095882X20300372#bib9

Impending Shortages of Kidney Replacement Therapy for COVID-19 Patients
 	
Goldfarb et al. 2020 (30)
	• Challenges described in the study due to surge of COVID-19 patients with AKI:
	  ○ Reduced numbers of trained staff available for CRRT, including machine maintenance staff addressing machine dysfunction in a timely fashion.
	  ○ Temporary loss of nephrologists.
	  ○ Unanticipated shortages for consumable continuous kidney replacement therapy (CKRT) supplies.
		https://cjasn.asnjournals.org/content/clinjasn/early/2020/04/27/CJN.05180420.full.pdf

Source	Advice	Source Link
Peer reviewed sources		

	• Interventions described in the study:
	  ○ Purchased more dialysis machines.
	  ○ Accelerated venovenous hemofiltration.
	  ○ Use of acute peritoneal dialysis, a modality rarely used in American ICUs in recent years, to remove pressures from CKRT supply and haemodialysis staff.
	  ○ Trained more staff to assist with CKRT and peritoneal dialysis.
	  ○ Contingency plans placed for resources and consumables.	

Providing care to patients with acute kidney injury and COVID-19 infection: Experience of front line nephrologists in New York
 	
Fisher et al. 2020 (31)
	• Interventions described to manage increased demand in CRRT
	  ○ Treatment times were reduced and dialysate flow rates were increased to convert CRRT to prolonged intermittent renal replacement treatments (PIRRT).
	  ○ PIRRT was performed for 6-12 hour treatments with effluent flow rates of 40-50ml/kg/hr. This permitted use of one machine for 2-3 patients, with time for disinfection in between patients.
	  ○ Perfusionists, who ordinarily manage extracorporeal membrane oxygenation procedures, were reassigned and assumed the role of PIRRT management during the day.
	  ○ A non-validated bivalirudin protocol was initiated with close monitoring of partial thromboplastin time (PTT) to resolve the issue with frequent clotting on CRRT despite therapeutic heparin infusion (PTT 2x normal).
		https://kidney360.asnjournals.org/content/kidney360/early/2020/05/05/KID.0002002020.full.pdf

Considerations for Providing Haemodialysis to Patients with Suspected or Confirmed COVID-19 in Acute Care Settings (32)	• Based on a patient's clinical status and the facility's resources, clinicians can decide to provide either intermittent haemodialysis or CRRT to patients requiring haemodialysis. • In the intensive care unit (ICU), CRRT is usually managed by an ICU nurse; due to this, use of CRRT may help limit the number of healthcare professionals exposed to the patient.	https://www.cdc.gov/coronavirus/2019-ncov/hcp/dialysis/dialysis-in-acute-care.html

Source	Advice	Source Link
Peer reviewed sources		
	• For ICU patients with end-stage renal disease with a dialysis fistula or graft, clinicians can weigh the risks and benefits of placing a dialysis catheter for CRRT (in order to limit exposure to healthcare professionals) or performing intermittent haemodialysis.	
Recommendations on the care of hospitalized patients with COVID-19 and kidney failure requiring renal replacement therapy(33)	• Indications to start RRT are similar to other patients with AKI. • Accumulating evidence suggests that a delayed RRT initiation is safe. • If available at an institution, the preferred modality for RRT in critically ill patients is CRRT or PIRRT, also known as sustained low efficiency dialysis (SLED). • CRRT machines, if available, are preferred over intermittent hemodialysis (IHD) in setting of biocontainment/isolation, as IHD requires 1:1 hemodialysis nursing support. • In ICUs where ICU nurses are all trained and competent on the use of CRRT, haemodialysis nurses do not need to have direct contact with patients, thereby limiting healthcare staff exposure. • IHD can also be performed in patients with critical illness if CRRT and PIRRT equipment are not available. • If patient surge overwhelms CRRT capacity at an institution, consideration should be given to using CRRT machines for prolonged intermittent treatments with higher flow rates (e.g. 10 hours instead of continuous at 40-50 ml/kg/h) and then using the machine for another patient after terminal cleaning as per institutional policies.	https://www.asn-online.org/g/blast/files/Handouts_Webinar_4.21.20.pdf
Clinical guide for renal replacement therapy options in critical care during the coronavirus pandemic 15 April 2020 (24)	• In all cases, maximal medical management should be considered before attempting RRT. • A facility should assess its available capacity and match this to patients according to need. • A conservative approach to using RRT may preserve consumable stocks.	https://www.england.nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/04/C0298-speciality-guide-clinical-guide-for-renal-replacement-therapy-

Source	Advice	Source Link
Peer reviewed sources		
		options-in-critical-care-v1.1.pdf

Appendix

PubMed search terms

((("Renal replacement Therapy"[Title/Abstract] OR "Renal replacement Therapy"[MeSH Terms] OR "sustained low efficiency dialysis"[Title/Abstract] OR "intermittent dialysis"[Title/Abstract] OR "Continuous dialysis"[Title/Abstract]) AND (2019-nCoV[title/abstract] or nCoV[title/abstract] or covid-19[title/abstract] or covid19[title/abstract] or "covid 19"[title/abstract] OR "coronavirus"[MeSH Terms] OR "coronavirus"[title/abstract])) AND (2019:2020[pdat])

(((("Renal replacement Therapy"[Title/Abstract] OR "Renal replacement Therapy"[MeSH Terms] OR "sustained low efficiency dialysis"[Title/Abstract] OR "intermittent dialysis"[Title/Abstract] OR "Continuous dialysis"[Title/Abstract])) AND (((((("critical care"[Title/Abstract]) OR ("critically ill"[Title/Abstract])) OR ("intensive care"[Title/Abstract])) OR (ICU[Title/Abstract])) OR ("Acute Kidney Failure"[Title/Abstract]))

Google search terms

TRIP Google Scholar & Organisational websites were searched using key words continuous renal replacement therapy, intermittent haemodialysis or sustained low efficiency dialysis, acute kidney injury and COVID-19

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