

CSN COVID-19 Rapid Review Program: Management of Acute Kidney Injury

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Abstract

Purpose: Severe acute kidney injury (AKI) is a potential complication of COVID-19-associated critical illness. This has implications for the management of COVID-19-associated AKI and the resulting increased need for kidney replacement therapy (KRT) in the intensive care unit (ICU) and elsewhere in the hospital. The Canadian Society of Nephrology COVID-19 Rapid Review Team has sought to collate and synthesize currently available resources to inform ethically justifiable decisions. The goal is the provision of the best possible care for the largest number of patients with kidney disease while considering how best to ensure the safety of the health care team.

Information sources: Local, provincial, national, and international guidance and planning documents related to the COVID-19 pandemic; guidance documents available from nephrology and critical care-related professional organizations; recent journal articles and preprints related to the COVID-19 pandemic; expert opinion from nephrologists from across Canada.

Methods: A working group of kidney specialist physicians was established with representation from across Canada. Kidney physician specialists met via teleconference and exchanged e-mails to refine and agree on the proposed suggestions in this document.

Key findings: (1) Nephrology programs should work with ICU programs to plan for the possibility that up to 30% or more of critically ill patients with COVID-19 admitted to ICU will require kidney replacement therapy (KRT). (2) Specific suggestions pertinent to the optimal management of AKI and KRT in patients with COVID-19. These suggestions include, but are not limited to, aspects of fluid management, KRT vascular access, and KRT modality choice. (3) We describe considerations related to ensuring adequate provision of KRT, should resources become scarce during the COVID-19 pandemic.

Limitations: A systematic review or meta-analysis was not conducted. Our suggestions have not been specifically evaluated in the clinical environment. The local context, including how the provision of acute KRT is organized, may impede the implementation of many suggestions. Knowledge is advancing rapidly in the area of COVID-19 and suggestions may become outdated quickly.

Implications: Given that most acute KRT related to COVID-19 is likely to be required initially in the ICU setting, close collaboration and planning between critical care and nephrology programs is required. Suggestions may be updated as newer evidence becomes available.

Keywords

COVID-19, AKI, dialysis, KRT, CRRT, critical care

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Purpose

Severe acute kidney injury (AKI) is a potential complication of COVID-19-associated critical illness. Patient volume related to COVID-19-associated AKI, as well as the unique features of this condition, has implications for the delivery of acute kidney replacement therapy (KRT).

Nephrology programs across the country are developing policies in this rapidly changing environment. The Canadian Society of Nephrology has synthesized guidance documents from the broader nephrology community in an effort to provide the best possible care to the largest number of patients with kidney disease while also ensuring the safety of the health care team.

Principles

The following principles guided our work to help ensure that decisions are ethically supported:

1. **Uncertainty:** An acknowledgment that clinicians and administrators are now working in a swiftly evolving environment, which will require decision-making with limited resources, and with levels of uncertainty that are higher than usual.
2. **Macro-allocation:** An acknowledgment that the local context and local government priorities will shape decision-making and that previously sacrosanct standards may need to be temporarily adjusted to maximize health outcomes for the greatest number of patients.
3. **Minimize net harm:** The idea of limiting the spread of disease and the disruption to the health care system.
4. **Reciprocity:** The idea that protecting health care workers from COVID-19 is not only an end in itself but also a goal that secondarily leads to maintained staffing levels for the delivery of care to patients with kidney disease.
5. **Fairness:** The idea that patients with kidney disease continue to receive appropriate treatments, regardless of their COVID-19 status, and the attempt to avoid outcomes that disproportionately impact those who are most vulnerable (eg, those of lower socioeconomic status).
6. **Proportionality:** The idea of keeping restrictions on staff and patients commensurate with the level of risk to public health.
7. **Respect for autonomy:** The idea that all plans should continue to reflect patient values and beliefs as much

as possible, granting that choices may be limited in a pandemic.

8. **Fidelity:** The need to maintain commitment to patients to provide necessary care, even through challenging times and when there is a degree of risk to providers.

Information Sources

The following key sources were reviewed and/or synthesized for the creation of this document:

Expert opinions and e-mails (Alberta, Nova Scotia, Quebec, British Columbia, and Ontario).

#NephJC (<http://www.nephjc.com/news/covidaki>).

Ontario Health: COVID-19 Supplemental Clinical Guidance #2: Acute Dialysis.

Ontario Health: Pandemic Planning Clinical Guideline for patients with chronic kidney disease.

BC Renal Agency: VCH/PCH COVID-19 Procedures and Protocols.

Public Health Agency of Canada: Clinical management of patients with moderate to severe COVID-19—Interim Guidance (April 2, 2020).

American Society of Nephrology: Webinar on hospital care and treatment options for COVID-19 positive patients with ESKD and AKI (April 2, 2020).

American Society of Nephrology: Webinar on Overcoming Challenges to the Provision of Acute Dialysis for COVID-19 Positive Patients (April 30, 2020). Alhazzani W, Moller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: Guidelines on the Management of Critically Ill Adults with Coronavirus Disease 2019 (COVID-19). *Critical Care Medicine*. 2020 Mar 27 [Online ahead of print]. doi: 10.1097/CCM.0000000000004363.

Burgner A, Ikizler TA, Dwyer JP. COVID-19 and the Inpatient Dialysis Unit: Managing Resources During Contingency Planning Pre-Crisis. *Clinical Journal of the American Society of Nephrology*. April 3, 2020 [Online ahead of print]. doi: 10.2215/CJN.03750320.

Methods

A working group of kidney specialist physicians was established with representation from across Canada. Expert advice was sought and debated through e-mail exchanges. Five

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kidney physician specialists met via teleconference and exchanged e-mails to refine and agree on the proposed suggestions in this article.

Key Issues and Suggestions/ Considerations

Planning for Increased Capacity to Provide Acute KRT

We suggest working with ICU colleagues to plan for the possibility that up to 30% of critically ill patients with COVID-19 admitted to ICU will require acute KRT.

Rationale: Severe AKI related to COVID-19 appears mostly to affect critically ill patients with multiorgan failure.¹⁻⁵ This suggests that increased acute KRT capacity for patients with COVID-19, at least initially (and depending on the subsequent rate of recovery and death for patients that require it), will mostly be needed in ICU.

Because of variation in testing rates and the case fatality rate, the risk of other outcomes, such as AKI, is still poorly defined for COVID-19. The reported proportion of patients with COVID-19 who experience AKI, across available preprints and published studies, is 0.5% to 39%.¹⁻¹³ Studies were generally of patients hospitalized with COVID-19 and, in most studies that reported both outcomes, the proportion requiring KRT approximated the proportion with AKI. Two studies reported AKI stratified according to Kidney Disease: Improving Global Outcomes (KDIGO) criteria (Table 1).^{9,10} This suggests that most studies to date have focused on severe AKI requiring KRT (AKI-KRT). It is unclear to what extent KRT availability in different settings might have influenced the proportion reported as requiring KRT. It is notable that early studies from China reported very low rates of AKI.^{2,9,10} In contrast, a small study (n = 21) that included only patients admitted to ICU in Seattle who were generally elderly (mean age 70 years), and with co-morbidities, reported that 19% of included patients had AKI-KRT.⁴ Administrative data from the United Kingdom that included 6027 patients critically ill with confirmed COVID-19, reported that 24% required KRT.⁵ Table 1 (adapted from NephJC¹⁴) details preprints and published studies that have reported on the incidence of AKI in patients with COVID-19. Apart from the variation in the definition of AKI, there are regional differences in criteria for admission to ICUs; generalization to the Canadian setting should be made cautiously. Notably, a recent preprint indicates that, in New York, 34% of patients admitted to ICU with COVID-19 required KRT.¹⁵

Based on the available data, it seems prudent to plan for the possibility that acute KRT could be required for at least 30% of patients with COVID-19 admitted to the ICU. Although the timing of AKI after ICU admission is not clear, the short follow-up in all these studies suggests AKI follows

ICU admission quite quickly. As many ICU programs have plans to scale up the number of ventilated ICU beds (if required), parallel up-scaling for the provision of KRT should be strongly considered by nephrology programs. Designing such a plan requires an understanding of the local ICU COVID-19 plan (including physical layout and water supply for current and additional ICU beds) and currently available KRT resources (including machines (KRT machines \pm portable reverse osmosis machines, supplies, nursing [ICU and hemodialysis (HD)] and dialysis technician support).

Management of AKI and KRT

This section provides an overview of relevant considerations. We appreciate that there is wide variation in the relative responsibilities of nephrology and ICU programs in the management of KRT in patients in the ICU. Local circumstances should be taken into account in applying our suggestions. Close collaboration between nephrology and ICU programs at the local level will be required to plan for the potentially increased demands of the COVID-19 pandemic.

Fluid management

We suggest judicious fluid administration to target euvolemia and avoid fluid overload, bearing in mind the increased insensible losses expected for patients with persistent or recurrent fevers.

Rationale: The predominant clinical issue for critically ill patients with COVID-19 is acute respiratory distress syndrome (ARDS): we, therefore, recommend avoiding fluid overload.^{16,17} However, we recognize that assessing volume status may be challenging and a dogmatic approach to keeping patients “as dry as possible” should be avoided. Insensible losses in those with unremitting or recurrent fevers may be significantly increased¹⁸ and an overly aggressive approach to diuresis or ultrafiltration with KRT could carry potential increased risks of death¹⁹ and long-term cognitive impairment¹³ as a consequence of more frequent hypotensive episodes.^{13,20}

We suggest that, under most circumstances, direct examination of patients admitted to ICU with suspected or confirmed COVID-19 does not need to be routinely performed by the nephrology consultation service.

Rationale: Every interaction between a health care worker and a patient with suspected or confirmed COVID-19 requires personal protective equipment (PPE) and, even with its careful use, carries a risk of transmission of COVID-19. Every effort to minimize these interactions is justified. Information on physical findings should be sought from health care workers who have other reasons to enter the room. In addition to the usual chart-based data that inform

Table 1. Incidence and Outcomes for Acute Kidney Injury Associated With COVID-19.

Study	Setting	Definition of AKI	Proportion with AKI number/denominator (%)	Need for KRT (%)	Association with outcomes
Non-critical care setting					
Guan et al ⁹	Multicentre 552 Hospitals 32 regions China	KDIGO	6/1099 (0.5%)	0.8%	NR
Wang et al ²	Zhongnan Hospital, Wuhan, China	NR	2/102 (2%)	0%	NR
Cheng et al ¹⁰	Tongji Hospital, Wuhan, China	KDIGO	36/701 (5%) Stage 1 (2%) Stage 2 (1%) Stage 3 (2%)	NR	After adjustment for age, sex, disease severity, Stage 2 or 3 AKI associated with mortality
Xiao et al ⁷	Hankou Hospital, Wuhan, China	KDIGO	55/287 (19%) Stage 1 (14%) Stage 2 or 3 (5%)	NR	Mortality: No AKI: 3% Stage 1: 7% Stage 2 or 3: 64%
Critical care setting					
Wang et al ¹	Tongji Hospital, Wuhan, China	KDIGO	86/344 (25%) Stage 1 or higher	NR	Frequency of AKI (Stage 1 or higher) according to outcome: Survivors: 2.8% Died: 60.2%
Wang et al ²	Zhongnan Hospital, Wuhan, China	NR	3/36 (8%)	(6%)	NR
Chen et al ³	Jin Yin-tan Hospital, Wuhan, China	Need for continuous kidney replacement therapy	9/23 (39%)	39%	NR
Arentz et al ⁴	Evergreen Hospital, Seattle, USA	KDIGO	4/21 (19%)	NR	NR
Yang et al ⁶	Jin Yin-tan Hospital, Wuhan, China	NR	15/52 (29%)	NR	NR
ICNARC report on COVID-19 in critical care (May 8, 2020) ⁵	All critical care units from England, Wales and Northern Ireland	Need for "renal support"	1442/6027 (24%)	20%	NR
Chan et al ¹⁵	Mount Sinai Health System, New York, United States	KDIGO	All hospitalized: 1406/3235 (44%) Stage 1 (35%) Stage 2 (20%) Stage 3 (45%) Critically ill: 553/815 (68%) Stage 1 20% Stage 2 17% Stage 3 63%	Among critically ill 277/815 (34%)	In hospital mortality 45% for those with AKI (Stage 1 or higher); 7% in those without AKI

Note. AKI = acute kidney injury; KRT = kidney replacement therapy; KDIGO = Kidney Disease: Improving Global Outcomes; NR = not reported.

ultrafiltration prescription for KRT, close consultation with ICU colleagues and nurses will be required. Similarly, investigations that are part of the routine assessment of patients with AKI, including urinalysis and kidney ultrasonography, may be deferred, unless they are likely to influence management. Adopting these practices will decrease risk to health care workers, decrease risk of nosocomial transmission, and decrease the use of PPE, a scarce resource.

We recommend that starches, gelatins, and hypotonic crystalloids should not be used for resuscitation.

Rationale: Starches and gelatins should not be used for resuscitation^{16,17} because they have been shown in randomized trials to cause increased risk of death and AKI^{12,21}; markedly hypotonic solutions such as half-normal saline should not be used for resuscitation as they are less effective at increasing intravascular volume compared with isotonic solutions.¹⁶

Timing of initiation of KRT

We recommend that traditional indications for starting KRT apply to patients with COVID-19.

Rationale: In recent years, the optimal timing of KRT initiation for AKI in critically ill patients has been informed by several trials.²²⁻²⁴ Uncertainty prevails, and we await more definitive results from the STARRT-AKI trial.^{25,26} A 2020 systematic review and individual patient meta-analysis of 9 studies and nearly 2000 patients randomly allocated to earlier or later initiation found no benefit for earlier initiation, reporting risk ratio = 1.01 (95% CI = [0.91, 1.13], $P = .80$), in an analysis characterized by low heterogeneity ($I^2 = 0\%$) and generally low risk of bias.²⁷ In the context of the COVID-19 pandemic, with limited KRT resources, and the increased risk to health care workers associated with additional procedures, we recommend using traditional indications for timing of initiation KRT. It is possible that progressive volume overload will be the predominant trigger for the initiation of KRT in COVID-19 infections complicated by AKI.

Modality choice. Note: for the purposes of this document, slow low-efficiency dialysis (SLED) entails using a conventional HD machine to provide dialysis with the following adjustments: slow blood-flow rate (Qb) (ie, max 200 mL/min; slow dialysate flow rate (eg, Qd = 100 mL/min [or as low as machine allows] with a maximum of 300 mL/min). In addition, SLED involves using smaller-than-standard filters (eg, pediatric filter with 0.6 m² surface area) and treatment time of 6 to 10 hours.

We suggest that, during the COVID-19 pandemic, nephrology programs should primarily continue to use the acute KRT modalities with which they have the most expertise.

Rationale: Clinical trials comparing continuous kidney replacement therapy (CKRT), intermittent HD, and SLED have not demonstrated improved survival with any 1 modality.^{28,29}

A sepsis-like syndrome, characterized by profound shock, and presumably related to high-levels of circulating cytokines (referred to as “cytokine storm”), has been reported as a frequent complication of COVID-19.^{8,30} KRT modalities that include convection, such as high-volume hemofiltration, are superior at removing larger molecules, such as cytokines; however, both pro- and anti-inflammatory cytokines are removed, and clinical outcomes are not improved in data from randomized trials of septic patients without COVID-19.^{31,32} In addition, high-volume hemofiltration involves the use of very large volumes of replacement solution, which could become scarce in the context of increased KRT use during the COVID-19 pandemic. In the absence of persuasive evidence of benefit for any particular modality, programs should use the KRT modalities with which they have the greatest expertise and those for which they have adequate staff.

We suggest not using hemoperfusion for patients with COVID-19.

Rationale: Some experts have suggested that hemoperfusion might be beneficial for patients with COVID-19, because of cytokine adsorption.^{33,34} At this time, the extent to which hemoperfusion might be beneficial for COVID-19 remains unclear and, to our knowledge, this has not yet been assessed in a randomized trial. The largest trial (n = 450) to assess the use of hemoperfusion in septic shock with high circulating endotoxin levels did not show an impact on 28-day mortality.³⁵

Dose of KRT

We suggest that the established minimum dose of continuous KRT (CKRT) should be used as a target during the COVID-19 pandemic.

Rationale: The RENAL³⁶ and ATN³⁷ trials demonstrated that higher doses of KRT do not provide an incremental survival benefit in patients with AKI; we suggest generalizing this to the management of patients with COVID-19-associated AKI. The control arms of these trials, and preceding observational evidence of worse outcomes at lower doses, have been used to establish the minimum dose of CKRT as 20 to 25 mL/kg/h of effluent. We recognize that it might become necessary to use lower doses of CKRT if dialysate and replacement solutions for CKRT become depleted (see below). Precise calculation of weight-based dosing at 20 to 25 mL/kg/h of effluent should be used, to maximize the number of patients who can be treated.

Vascular access

We recommend favoring the internal jugular (IJ) site for temporary HD catheter insertion.

Rationale: Given that many patients with COVID-19 will receive prone ventilation,^{16,17} IJ vascular access should be considered the first choice of temporary HD catheter insertion site in most circumstances.

We suggest that a temporary HD catheter (or dialysis catheter with a third infusion port) be inserted pre-emptively, at the IJ site, in patients with worsening kidney function who are thought likely to require prone ventilation, even in the absence of an acute indication for starting KRT.

Rationale: Although vascular access should not usually be inserted until a decision to initiate KRT is made, in patients with COVID-19, the high level of difficulty in successfully inserting a temporary HD catheter in a prone patient is a relevant consideration. In close consultation with the ICU team,

it may be advisable to insert a temporary HD catheter at the IJ site in patients with worsening kidney function before prone ventilation is started, even in the absence of an acute indication for starting KRT. Similarly, in patients with a high severity of illness, it may be optimal to have multiple procedures (including arterial and central venous catheter insertion) performed at the same time, immediately after intubation or ICU admission, to preserve PPE and limit the exposure of health care workers. In this circumstance, preemptive insertion of a temporary HD catheter (or of a triality catheter with additional port for medications) could also be considered for patients at risk of requiring KRT, even in the absence of an acute indication for it.

We recommend that temporary HD catheters are vigorously flushed with saline, and locked with citrate or heparin, immediately after placement.

Rationale: Many reports suggest that patients with COVID-19 have an exaggerated inflammatory response (“cytokine storm”)^{8,30} and are hypercoagulable.^{38,39} There are multiple anecdotal reports of KRT access clotting in this context. Other anecdotal reports indicate that some centers have experienced less catheter dysfunction in patients with COVID-19 on switching to a using a higher concentration of heparin for catheter locks than is typically used between KRT treatments (ie, 5000 vs 1000 U/mL).

Anticoagulation for KRT. In the context of the generalized hypercoagulability that has been reported in critically ill patients with COVID-19, there are multiple anecdotal reports of frequent KRT filter and catheter clotting.

We recommend routinely using higher than standard Qb for patients with COVID-19 according to the modality being used.

Rationale: Higher Qb will probably reduce the risk of clotting and does not confer a greater risk of hemodynamic instability.^{40,41}

We suggest, for patients with COVID-19 without a contraindication, using full-dose anticoagulation for KRT that includes a bolus through the filter with every new circuit.

Rationale: Initiation of KRT with full-dose anticoagulation, including a bolus, should be considered, in consultation with ICU colleagues, in the absence of overt contraindications. Anecdotal reports suggest that higher than standard boluses and infusion rates may be required to maintain circuit patency.

We suggest, for patients with COVID-19 already on systemic anticoagulation, using a bolus of anticoagulation through the filter when starting KRT (or a new circuit).

Rationale: As above.

We suggest, for patients on CKRT with an element of hemofiltration, minimizing the post-filter component of the total effluent rate.

Rationale: Limiting hemoconcentration may reduce the risk of circuit clotting.

We recommend that programs with experience using regional citrate anticoagulation for CKRT consider using it preferentially for patients with COVID-19.

Rationale: Anecdotal reports suggest that regional citrate anticoagulation is generally effective in preventing circuit clotting in patients with COVID-19.

We suggest that programs with experience using regional citrate anticoagulation for CKRT, consider using regional citrate anticoagulation plus additional systemic anticoagulation (eg, heparin bolus and infusion), when clotting of the extra-corporeal circuit prevents delivery of prescribed dialysis.

Rationale: We recognize that there is no evidence regarding the potential benefits or harms of this intervention; the citrate anticoagulation is regional and its intent is not to produce systemic anticoagulation. In a time of resource constraint, it is particularly important to deliver dialysis efficiently, a full treatment as prescribed, with a single setup. We make this suggestion to facilitate that goal, recognizing its unknown effectiveness and unknown harms, and recognizing the need for close collaboration with other disciplines, close monitoring for bleeding, and particular awareness of the possibility of pulmonary hemorrhage complicating the respiratory disease.

We suggest that programs that do not have experience using regional citrate anticoagulation protocols for CKRT not implement them immediately.

Rationale: Given that implementing regional citrate anticoagulation protocols is complex under normal circumstances, in the context of other pandemic-related demands, for programs that do not currently use regional citrate anticoagulation, it is not advisable to start this immediately.

We suggest that low molecular weight heparin may be considered for CKRT anticoagulation in patients with COVID-19.

Rationale: Some centers in the United States have reported less clotting with the use of low-molecular-weight-heparin protocols for CKRT than they were previously experiencing using unfractionated heparin in patients with COVID-19. In

similar circumstances, low-molecular-weight-heparin, already in widespread use for outpatient intermittent HD and nocturnal dialysis, could be used for CKRT or for acute intermittent HD or SLED. This requires close collaboration with other disciplines to develop or adapt dosing protocols, recognition by the whole team that the anticoagulation effect may be prolonged beyond the end of dialysis, and recognition that quantification of its effect, if needed (eg, if bleeding occurs) is by anti Xa level rather than by partial thromboplastin time (PTT).

Prevention of intradialytic hypotension during intermittent HD and SLED

We suggest adjusting the intermittent KRT prescription to optimize hemodynamic tolerance of fluid removal.

Rationale: Given that the primary consideration in many cases may be management of fluid overload, various measures can be considered to improve hemodynamic tolerance of fluid removal during intermittent KRT treatments. Adjustments to the intermittent HD prescription that may be considered include use of cool dialysate ($\leq 35.5^{\circ}\text{C}$); use of higher dialysate sodium concentration (eg, 145 mmol/L); switch from intermittent HD to SLED to reduce hourly ultrafiltration rate. Overall, there is limited evidence in this area. A quasi-experimental “before-after” study that included 121 critically ill patients who underwent 537 intermittent HD sessions showed that implementation of guidelines recommending the use of cool dialysate and higher dialysate sodium concentration was associated with less-frequent intradialytic hypotension.⁴¹

Isolated ultrafiltration (ultrafiltration without dialysis) is sometime suggested as a method to promote hemodynamic stability: during HD, the removal of urea in the intravascular compartment creates a reverse osmotic gradient toward the interstitium that may reduce refilling (the movement of salts and water from extracellular and intracellular compartments to the intravascular space that is critical to the maintenance of circulating volume during dialysis). This does not occur in isolated ultrafiltration. However, direct evidence on this question is limited to a single study of 6 stable patients treated with outpatient HD, all men, mean age 59 years, excluding patients with evidence of autonomic insufficiency.⁴² Fluid targets were the same in each group, fluid removal was similar, and post dialysis blood pressures similar. We are not aware of studies in critically ill patients that have directly assessed this intervention.²⁰ This intervention, then, is supported by weaker evidence than the other interventions suggested and has the potential for harm. If ultrafiltration time is substituted for HD time it limits the delivered dose of dialysis; underdialysis is known to be associated with mortality in patients with critical illness.^{43,44} If ultrafiltration time is added to HD time, it increases the resources (particularly staff) required for treatment and increases the possibility of clotting and the need for a second setup.

Reducing infection risk to health care workers involved in providing KRT

Whenever possible, we recommend preferentially using KRT modalities that reduce the number of health care workers exposed to patients with COVID-19, to decrease risk to health care workers, risk of nosocomial transmission, and use of PPE.

Rationale: Preferentially using KRT modalities that reduce health care worker exposure to patients with COVID-19 has to be considered within the local context of how the provision of KRT is organized (eg, if SLED provided by ICU nurses compared with provided by an additional nurse from the HD unit; whether SLED can be provided to more than 1 patient at a time for cohorted patients with a single dialysis nurse) and with respect to resource availability at that time.

We suggest assessing if the use of tubing extensions can allow for KRT machines to be operated by health care workers at a greater distance from patients with COVID-19, or outside the isolation room.

Rationale/comments: The use of extension tubing (blood line extensions between patient and KRT machines, or water line extensions from reverse osmosis [RO] units to KRT machines) may reduce infection risk by allowing nurses to operate the KRT machine at a further distance from the patient or potentially outside of the patient’s isolation room depending on the layout of the room. The use of extension tubing should be considered with several caveats. First, blood extension tubing may result in more frequent triggering of pressure alarms. Second, the lack of visual surveillance of the whole extracorporeal circuit may increase the risk of undetected blood leak. Third, increased exposure to the extracorporeal circuit may increase the risk of clotting. Fourth, increased blood cooling as it passes through the longer tubing may provoke hypothermia. Fifth, extra tubing connections returning blood from the KRT machine to the patient increase the risk of undetected air leaks and, thus, air embolism. Last, tubing extensions pose a tripping hazard and could result in trauma to the patient’s vascular access. Some centers have reported using extensions to operate machines outside patient isolation rooms. This might facilitate cohorting of several patients to receive dialysis with a single HD nurse, which may be useful if staff become a constrained resource. Note that when CKRT is provided with the machine placed outside the room, effluent bags containing contaminated fluid will be situated in the otherwise “clean” space.

We recommend routinely using remote-control features of KRT machines, where available.

Rationale/comments: Although few machines are equipped with this technology at present, the use of a remote-control

feature may reduce infection risk by allowing control of a KRT machine in an isolation room from outside the room.

Considerations if KRT-Related Resources Become Limited During the COVID-19 Pandemic

There is an expectation that significant additional ICU capacity will be required to care for patients with COVID-19 in the context of the current pandemic. Given that 25% or more of critically ill patients with COVID-19 may require KRT, the ability for programs to scale up the provision of KRT in the ICU setting is also necessary. Planning should consider that specific KRT-related resources may become scarce in the context of the pandemic. Planning considerations vary depending on how acute KRT is provided at the level of individual programs (eg, if a program routinely uses CKRT or SLED; whether SLED is routinely provided by ICU nurses or HD nurses). The following subsections outline considerations specific to various potential KRT-related shortages.

Delaying the need for KRT

We recommend that pre-emptive KRT (ie, before an acute indication is present) should not be used.

Rationale/comments: See section on *Timing of Initiation*, above.

We suggest that, in the context of an overall shortage of KRT resources, clinicians consider using high-dose diuretics (including serial nephron blockade through the use of loop and thiazide-type diuretics together) and off-label use of potassium-binding resins to delay the need for KRT, depending on the clinical context and resource availability.⁴⁵

Rationale: No direct data are available on the use of conventional or novel potassium binders in patients who are critically ill.⁴⁶ In outpatients, an increased risk of intestinal ischemia and thrombosis for users of sodium polystyrene sulfonate (SPS, Kayexalate), compared with non-users, has been noted in observational research: the increased risk was 5.6 events per thousand patient-years in stable outpatients, but the hazard ratio was 4.9 (95% CI = [1.1, 22.3]).⁴⁷ The team should be alert to the possibility that this incremental risk may be higher in patients with COVID-19 because of the higher baseline risk of thrombosis; they should also be aware that because of this tendency, the occurrence of intestinal thrombosis in a patient treated with potassium binders should not necessarily be attributed to the use of the binder.

Shortage of CKRT machines

We recommend, in the context of a shortage of CKRT machines, using intermittent HD in patients in whom

intradialytic hypotension is likely to be manageable with increased vasopressor dosing.

Rationale/comments: This needs to be weighed according to the extent to which there is a shortage of HD nurses if a separate HD nurse is required for intermittent HD in the ICU. In addition, this approach involves exposing additional nursing staff to COVID-19 infection risk and increased PPE consumption.

We suggest, in the context of a shortage of CKRT machines, using intermittent HD machines to do SLED for hemodynamically unstable patients.

Rationale/comments: SLED is defined in the section pertaining to *Modality Choice*, above. Even when SLED is provided using the smallest filter available, due to its increased efficiency relative to CKRT, the prescription should be tailored to avoid precipitating hypokalemia and/or hypophosphatemia. This involves using a dialysate potassium concentration of 3 or 4 mmol/L even in the context of significant pre-SLED hyperkalemia. As well, a phosphate additive should be used if the patient's pre-SLED phosphate concentration is in the low-normal range or lower. Using SLED rather than CKRT also carries the potential issue of having to deploy more HD nurses to the ICU and the increased COVID-19 risk exposure and PPE use which that entails.

We recommend, in the context of a shortage of CKRT machines at centers that use both CKRT or SLED for hemodynamically unstable patients, preferentially using SLED.

Rationale/comments: This suggestion needs to be weighed according to the extent to which there is a shortage of HD nurses if a separate HD nurse is required for SLED in the ICU.

We suggest, in the context of a shortage of CKRT machines, consider using CKRT machines to provide shorter sessions of CKRT for 2 patients in 24 hours.

Rationale/comments: Essentially, this involves using 1 CKRT machine for 10 hours on 2 patients daily (or 6 hours for 3 patients), realistically estimating 2 hours for moving and cleaning the machine between treatments. One can consider running higher than usual effluent rates (eg, 45-50 mL/kg/h) if there is no expectation of a shortage of CKRT fluid supplies.

Shortage of CKRT solutions (replacement fluid/dialysate)

We recommend, in the context of a shortage of CKRT solutions (fluids), having a lower threshold for using intermittent HD in patients in whom hemodynamic instability is likely to be manageable with increased vasopressor dosing.

Rationale/comments: As detailed in the preceding section, this suggestion needs to be weighed according to the extent to which there is a shortage of HD nurses if a separate HD nurse is required for intermittent HD in the ICU. In addition, this approach involves exposing additional nursing staff to COVID-19 infection risk and increased PPE consumption.

We recommend, in the context of a shortage of CKRT solutions (fluids), using conventional HD machines to do SLED in hemodynamically unstable patients.

Rationale/comments: As detailed above, SLED entails utilizing $Q_b \text{ max} = 200 \text{ mL/min}$; $Q_d = 100 \text{ mL/min}$ (or as low as machine allows) with a maximum of 300 mL/min . One should also consider using smallest filter available (eg, pediatric filter with 0.6 m^2 surface area) and treatment time of 6 to 10 hours. This carries the potential issue of having to deploy HD nurses to the ICU and the increased COVID-19 risk exposure and PPE use which that entails. In addition, one needs to consider and account for increased risks of disequilibrium, hypokalemia, and hypophosphatemia during treatment.

We recommend, in the context of a shortage of CKRT solutions (fluids), in centers that use both CKRT and SLED for hemodynamically unstable patients, favoring the use of SLED.

Rationale/comments: As detailed in the preceding section, this suggestion needs to be weighed according to the extent to which there is a shortage of HD nurses if a separate HD nurse is required for SLED in the ICU.

We suggest, if there is a shortage of CKRT solutions (fluids), using a lower dose of CKRT (eg, $10\text{-}15 \text{ mL/kg/h}$) once metabolic control has been achieved.

Rationale/comments: This maximizes the number of patients who can be treated, but requires attention to the possibility that underdialysis (ie, failure to deliver standard targets) may lead to excess mortality, as suggested by observational data.

We suggest, if there is a shortage of CKRT solutions, that centers consider producing CKRT solutions locally.

Rationale/comments: A recent publication reports one such strategy.⁴⁵ The successful use of intermittent HD machines to generate CKRT solution has also previously been reported.⁴⁸ Careful attention and planning is required to address issues related to sterility,⁴⁹ endotoxin levels,^{48,50} storage, and bridging incompatible tubing connections. Locally made solutions should be used as dialysate (rather than as replacement fluid) to reduce the risk of direct introduction of potentially-contaminated fluids into the bloodstream.

Shortage of intermittent HD/SLED capability (nurses and/or machines)

We suggest, in the context of a shortage of capacity for intermittent HD or SLED, that centers consider redeploying resources by decreasing the frequency of dialysis for selected stable outpatients treated with maintenance HD patients, as outlined in the CSN COVID-19 Rapid Response Team recommendations for outpatient HD.⁵¹

Rationale/comments: Redeployment of trained dialysis staff from outpatients to critically ill patients is intended to maximize the number of surviving patients.

We recommend, in the context of a shortage of capacity for intermittent HD or SLED machines, that centers review and consider using outdated, but still operable, dialysis machines and portable RO units.

Rationale/comments: Doing this early enables an accurate understanding of available resources.

We recommend, in the context of a shortage of staff for intermittent HD or SLED, dialysis-trained staff be redeployed from other areas to provide necessary support.

Rationale/comments: Prior to redeployment, an assessment of the total number of dialysis-trained staff and the machines with which they have experience working with should be undertaken.

We suggest, in the context of a shortage of machines for intermittent HD or SLED, that centers consider using any available home HD machine stockpile.

Rationale/comments: Although this maximizes available resources, we recognize that staff training will likely be necessary for the use of machines outside their usual setting in each program.

We suggest, in the context of a shortage of machines for intermittent HD or SLED, that centers consider whether home HD patients who use their machines on alternate days would be willing to share a machine, allowing the return of a machine to the program for acute KRT.

Rationale/comments: There are potential barriers to this approach including the near-inevitability of a breach in patient confidentiality and the potential for COVID-19 transmission between patients who have agreed to share machines. As above, staff training on the unfamiliar machine will also likely be necessary.

We suggest, in the context of a shortage of capacity for intermittent HD or SLED, shortening SLED duration to 6 hours, permitting the treatment of 3 patients daily.

Rationale: This schedule allows 2 hours for moving and cleaning the machine between patients.

We suggest, in the context of a shortage of capacity for intermittent HD or SLED, that centers consider whether 1 nurse can supervise 2 or more machines simultaneously, for patients who are located close together and who have the same isolation status; start and stop times can be staggered.

Rationale: If machines are available but HD nurses are limited, this will maximize benefits.

We suggest, in the context of a shortage of capacity for intermittent HD or SLED, at centers where SLED is the modality typically used for hemodynamically unstable patients and it is usually provided by ICU nurses (which is not widely done), use SLED rather than intermittent HD for hemodynamically stable patients.

Rationale/comments: This can be done to reduce HD nursing needs and PPE use (if ICU resources allow).

We suggest, in the context of shortage of capacity for intermittent HD or SLED, that centers consider building capacity for KRT in community hospitals that have maintenance HD units but where acute KRT is not routinely provided in ICU.

Rationale/comments: Staffing issues need to be carefully considered as well as the potential need for additional KRT machines and RO units.

Use of Acute Peritoneal Dialysis to Meet AKI-KRT Needs During the Pandemic

We suggest, in the context of an acute shortage of other KRT modalities, using acute peritoneal dialysis (PD) if necessary.

Rationale/comments: Acute PD can successfully be used to treat critically ill patients in a variety of settings.⁵² General guidelines for the use of PD in AKI have previously been reported.¹¹ Many considerations would be involved in the decision to use acute PD, including the following:

- Depending on the center, nephrologists, surgeons, or interventional radiologists may perform acute PD catheter insertion. Early planning with those specialists is warranted if resources for non-PD KRT modalities are likely to become scarce during the COVID-19 pandemic.
- Nursing exposure to COVID-19 infection risk (and PPE use) would be best limited using automated PD (cycler).

- PD may be more complicated in patients who require prone ventilation, with problems with pressure effects affecting filling and the risk of abrasion and traction at the new exit site. However, successful acute use in a prone patient has been reported.⁵³
- Lower dialysate volumes, compared with higher dialysate volumes, have several potential advantages in this setting: they may enable better ventilation because of lower intra-abdominal pressure; they may reduce the risk of peri-catheter leak, an important consideration because catheters will be used soon after insertion. Clinicians need to be alert to the possibility of underdialysis when lower volumes are used.

COVID-19 Drug Dosing for Patients With Kidney Dysfunction

We suggest adjusting the dose of medications used to treat COVID-19 in patients with low glomerular filtration rate of any cause and in patients who are treated with maintenance dialysis.

Rationale/comments: This consideration is not specific to patients with AKI. Currently, no medications have been approved in Canada for treatment of COVID-19. Nonetheless, many medications are being used off-label or through clinical trials. Given that this is a rapidly changing area in which there is currently minimal evidence, we suggest referring to continuously updated online resources such as the #NephJC AKI blog¹⁴ that detail kidney function dosing considerations for medications that have been suggested as potential therapies for COVID-19.

Limitations

There are many important limitations to this work. First, because of time constraints and the rapidly evolving information in this field, systematic review or meta-analysis was not possible. Second, none of the suggestions have been specifically evaluated in the clinical environment. Third, we are unable to anticipate the many ways in which the dynamic local context, including the details of organization of care for patients with AKI and the magnitude of the clinical need, will affect the implementation of our suggestions. Fourth, we did not address any ethical issues with respect to the need to triage KRT related resources if rationing were to be required. Finally, knowledge is advancing rapidly in this area; our suggestions may be rapidly outdated. We recognize the importance of other curated sources of evidence and advice (eg, #NephJC blog, available at <http://www.nephjc.com/news/covidaki>) in this rapidly changing environment.

Implications

We explicitly recognize that we may not be able to deliver care to all patients, that is, in keeping with current Canadian best practices, and suggest practical methods of maximizing benefits for the greatest number of patients. Acute KRT secondary to COVID-19 is likely to be initially required in the ICU setting; close collaboration and planning between critical care and nephrology programs at the local level is required. Suggestions included in this document will require updating as newer evidence becomes available. As part of our knowledge translation strategy, the manuscript will be available on the CSN Web Site⁵¹ as a preprint and when published. Members of the CSN, Canadian Association of Nephrology Nurses and Technologists (CANNT), and the Canadian Association of Nephrology Administrators (CANA) will receive an e-mail to this effect. Preliminary suggestions were shared with these groups during a CSN-hosted webinar on 2020 April 18.

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