

Canadian Association of Paediatric Nephrologists COVID-19 Rapid Response: Guidelines for Management of Acute Kidney Injury in Children

Canadian Journal of Kidney Health and Disease
Volume 8: 1–17
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DOI: 10.1177/2054358121990135
journals.sagepub.com/home/cjk



Abdullah Alabbas^{1*}, Amrit Kirpalani^{2*}, Catherine Morgan¹,
Cherry Mammen³, Christoph Licht⁴, Veronique Phan⁵,
Andrew Wade⁶, Elizabeth Harvey⁴, Michael Zappitelli⁴,
Edward G. Clark⁷, Swapnil Hiremath⁷,
Steven D. Soroka⁸, Ron Wald⁹, Matthew A. Weir¹⁰,
Rahul Chanchlani^{11†}, and Mathieu Lemaire^{4,12†}

Abstract

Purpose: This article provides guidance on managing acute kidney injury (AKI) and kidney replacement therapy (KRT) in pediatrics during the COVID-19 pandemic in the Canadian context. It is adapted from recently published rapid guidelines on the management of AKI and KRT in adults, from the Canadian Society of Nephrology (CSN). The goal is to provide the best possible care for pediatric patients with kidney disease during the pandemic and ensure the health care team's safety.

Information sources: The Canadian Association of Paediatric Nephrologists (CAPN) COVID-19 Rapid Response team derived these rapid guidelines from the CSN consensus recommendations for adult patients with AKI. We have also consulted specific documents from other national and international agencies focused on pediatric kidney health. We identified additional information by reviewing the published academic literature relevant to pediatric AKI and KRT, including recent journal articles and preprints related to COVID-19 in children. Finally, our group also sought expert opinions from pediatric nephrologists across Canada.

Methods: The leadership of the CAPN, which is affiliated with the CSN, solicited a team of clinicians and researchers with expertise in pediatric AKI and acute KRT. The goal was to adapt the guidelines recently adopted for Canadian adult patients for pediatric-specific settings. These included specific COVID-19-related themes relevant to AKI and KRT in a Canadian setting, as determined by a group of kidney disease experts and leaders. An expert group of clinicians in pediatric AKI and acute KRT reviewed the revised pediatric guidelines.

Key findings: (1) Current Canadian data do not suggest an imminent threat of an increase in acute KRT needs in children because of COVID-19; however, close coordination between nephrology programs and critical care programs is crucial as the pandemic continues to evolve. (2) Pediatric centers should prepare to reallocate resources to adult centers as needed based on broader health care needs during the COVID-19 pandemic. (3) Specific suggestions pertinent to the optimal management of AKI and KRT in COVID-19 patients are provided. These suggestions include but are not limited to aspects of fluid management, KRT vascular access, and KRT modality choice. (4) Considerations to ensure adequate provision of KRT if resources become scarce during the COVID-19 pandemic.

Limitations: We did not conduct a formal systematic review or meta-analysis. We did not evaluate our specific suggestions in the clinical environment. The local context, including how the provision of care for AKI and acute KRT is organized, may impede the implementation of many suggestions. As knowledge is advancing rapidly in the area of COVID-19, suggestions may become outdated quickly. Finally, most of the literature for AKI and KRT in COVID-19 comes from adult data, and there are few pediatric-specific studies.

Implications: Given that most acute KRT related to COVID-19 is likely to be required in the pediatric intensive care unit initial setting, close collaboration and planning between critical care and pediatric nephrology programs are needed. Our group will update these suggestions with a supplement if necessary as newer evidence becomes available that may change or add to the recommendations provided.



Keywords

infectious disease, acute kidney injury, clinical practice guidelines, renal replacement therapy, pediatric nephrology

Received December 28, 2020. Accepted for publication January 4, 2021.

Introduction

Reports of children with symptomatic COVID-19 infections continue to grow. There are no clear data on the incidence of acute kidney injury (AKI) in children at this time because there are so few cases thus far. Below, we will present an overview of relevant pediatric data from China, Europe, and North America, a summary of similar data from adult studies, and a discussion on the evidence linking AKI with the new condition referred to as “multisystem inflammatory syndrome” (MIS). We will then introduce critical concepts for the safe management of pediatric patients diagnosed with AKI before presenting the detailed guidelines.

COVID-19 Infection and AKI: Pediatric Data From China

Four studies from China strongly suggest that pediatric COVID-19 is rare^{1,2} and rarely requires intensive care. In the largest (n = 72 314 cases), the Chinese Center for Disease Control and Prevention reported that ~2% of all cases were less than 18 years of age.¹ In a screening study of 745 children, 10 (1.3%) had confirmed AKI. Ten patients required admission to the hospital, but none required intensive care.³ The only center allowed to treat pediatric COVID-19 in the Wuhan region found 171 confirmed cases after testing 1391 children aged less than 16 years (12.3%); Of these, 3 required intensive care (1.7% of positive cases).⁴ All 3 patients had AKI

based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria and, importantly, all had preexisting conditions (hydronephrosis, leukemia, and intussusception).⁴ They were treated with plasma exchange and continuous kidney replacement therapy (CKRT), resulting in 1 complete recovery, 1 partial recovery, and 1 death.⁵

Finally, in a study focused on 2135 cases of pediatric COVID-19 (35% confirmed), the likelihood of critical disease (defined by the presence of life-threatening organ dysfunction) was highest in children aged less than 1 year (7/376, or ~1.9%) and substantially lower for the others (~0.3%-0.5%).⁶ Unfortunately, none of these studies provided data on AKI or kidney replacement therapy (KRT). One case report of a critically ill infant with COVID-19 reported mild AKI. The infant had a history of preexisting conditions (cardiac surgery and recurrent pneumonia).⁷ Furthermore, of 1065 cases from 18 studies, only 1 infant presented with pneumonia, complicated by shock and kidney failure, which required dialysis. Fortunately, the infant recovered with supportive treatment.⁸

COVID-19 Infection and AKI: Pediatric Data From Europe

Emerging data from European centers paint a similar picture. For example, Spanish investigators identified pediatric COVID-19 in ~1% of all confirmed cases from Madrid (41 of 4695). Of these, 4 patients (~10%) required intensive

¹Department of Paediatrics, Division of Nephrology, University of Alberta, Edmonton, Canada

²Department of Paediatrics, Division of Nephrology, Western University, London, ON, Canada

³Department of Paediatrics, Division of Nephrology, The University of British Columbia, Vancouver, Canada

⁴Department of Paediatrics, Division of Nephrology, University of Toronto, ON, Canada

⁵Department of Paediatrics, Division of Nephrology, Université de Montréal, Québec, Canada

⁶Department of Paediatrics, Division of Nephrology, University of Calgary, AB, Canada

⁷Division of Nephrology, Department of Medicine, Kidney Research Centre, Ottawa Hospital Research Institute, University of Ottawa, ON, Canada

⁸Division of Nephrology, Department of Medicine, Dalhousie University, Halifax, NS, Canada

⁹Division of Nephrology, St. Michael's Hospital and Department of Medicine, University of Toronto, ON, Canada

¹⁰Division of Nephrology, Department of Medicine, Western University, London, ON, Canada

¹¹Division of Pediatric Nephrology, Department of Pediatrics, McMaster Children's Hospital, McMaster University, Hamilton, ON, Canada

¹²Division of Nephrology, The Hospital for Sick Children, Toronto, ON, Canada

*These authors are co-first authors.

[†]These authors are co-senior authors.

Corresponding Authors:

Mathieu Lemaire, Division of Nephrology, The Hospital for Sick Children, 555 University Avenue, Toronto, ON, Canada M5G 1X8.

Email: mathieu.lemaire@sickkids.ca

Rahul Chanchlani, Division of Pediatric Nephrology, Department of Pediatrics, McMaster Children's Hospital, 1280 Main St W, Hamilton, ON, Canada L8N 3Z5.

Email: chanchlr@mcmaster.ca

care.² In Italy, ~1.2% of cases were children below 18 years of age. None of those patients died.⁹ Both studies reported no fatalities but did not include data on the incidence of AKI.

COVID-19 Infection and AKI: Pediatric Data From North America

A cross-sectional study from 46 US and Canadian pediatric intensive care units (PICUs) which focused on 1 month starting in mid-March 2020 revealed 48 cases of critical pediatric COVID-19 (none from Canada). Most of these patients (83%) had preexisting comorbidities, such as complex syndromes (46%) or requiring immunosuppression (23%). While the treating team did not use KRT (and there are no data on AKI incidence), 1 patient required extracorporeal membrane oxygenation and 2 patients (4%) died.¹⁰ Another multicenter cross-sectional study found a high prevalence of AKI among critically ill children with COVID-19 (44%). No child received dialysis. Most children with AKI had at least 1 comorbidity (n = 28, 60%). Three in the AKI group (6%) died.¹¹

In New York, a 16-year-old patient with COVID-19-associated rhabdomyolysis did not develop AKI, possibly because of early fluid therapy.¹² This condition has also been described in adult patients¹³ of whom a subset developed AKI.¹⁴⁻¹⁶

COVID-19 Infection and AKI: Brief Overview of Adult Data

Even in adults, AKI remains poorly defined for COVID-19 due to variations in testing rates, the case fatality rate, and the risk of other outcomes. The reported incidence of AKI across available preprints and published studies ranges from 0.5% to 39%¹⁷⁻²⁷ (Table 1). Studies that reported rates of COVID-19-related AKI primarily involved hospitalized patients with the majority requiring KRT. These data suggest that except for 2 studies that reported AKI stratified according to KDIGO criteria,^{25,26} published studies and preprints generally have focused on severe AKI requiring KRT (AKI-KRT) only.

Multisystem Inflammatory Syndrome and AKI

Of particular relevance to pediatrics is the emergence of the new condition associated with COVID-19, now referred to as reported MIS. In April 2020, physicians in London, England, reported a cluster of 8 children presenting with features similar to Kawasaki disease or toxic shock syndrome, 1 of whom required KRT.³¹ Common clinical features included gastrointestinal symptoms, rashes, mucous membrane changes, adenopathy, myocarditis, and fever lasting more than 5 days.³¹ Many of these children had exposure to severe

acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and several tested positive for SARS-CoV-2.³¹ After this initial publication, a team in Paris, France, reported the most extensive case series to date, describing 17 patients with apparent Kawasaki disease presenting over 11 days. From this group, 8 (47%) developed AKI and 14 (82%) had SARS-CoV-2 IgG antibodies.³² A team in Italy reported a 30-fold increase in the incidence of a Kawasaki-like disease categorized as MIS during the COVID-19 pandemic.³³ Multiple subsequent case reports of patients with MIS associated with SARS-CoV-2 describe varying degrees of end-organ involvement, including AKI.³⁴⁻³⁸ The pathophysiology of this syndrome remains unclear, and details of patients' clinical and biochemical markers related to AKI are scarce. Pediatric MIS remains an emerging entity, and measurement of incidence is challenging, though estimated to be less than 1% in children with COVID-19 infection.³⁹ As larger cohorts are available, the true incidence of AKI in this population may become more apparent.

Medical Management and KRT in AKI in Children With COVID-19

While acute respiratory distress syndrome (ARDS) is the predominant clinical issue for critically ill pediatric patients, it is crucial to acknowledge that the clinical presentation is variable in children with COVID-19.⁴⁰⁻⁴⁵ For those with AKI, the overarching goal is to avoid volume overload. There are no specific therapies for AKI in children with COVID-19, and traditional AKI management principles should guide clinical decision-making.

Unsurprisingly, volume overload appears to be the most likely indication for initiating acute KRT in these patients.^{43,45} There is insufficient evidence to recommend any particular KRT modality. As such, providers should individualize treatment options and use existing institutional protocols for KRT prescription to meet each patient's needs based on their clinical status. Given the burden of ARDS in these children, providers should anticipate difficulty with ventilation and prone positioning, limiting the feasibility of peritoneal dialysis (PD).

Risk Reduction and Resource Management of KRT During the COVID-19 Pandemic

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. Techniques that optimize physical distancing between providers and patients with COVID-19 should be balanced with providing the best

Table 1. Incidence and Outcomes for COVID-19 AKI in Adult Patients.

Study	Setting	Definition of AKI	Incidence of AKI	Need for KRT	Association with outcomes
Noncritical care setting					
Guan et al. ²⁵	Multicentre 552 hospitals 32 regions China	KDIGO	6/1099 (0.5%)	0.8%	NR
Wang et al. ¹⁷	Zhongnan Hospital, Wuhan, China	NR	2/102	0%	NR
Cheng et al. ²⁶	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 2/3 AKI associated with mortality.
Xiao et al. ²³	Hankou Hospital, Wuhan, China	KDIGO	55/287 (19%) Stage 1: 14% Stage 2/3: 5%	NR	Mortality: No AKI: 3% Stage 1: 7% Stage 2/3: 64%
Critical care setting					
Wang et al. ¹⁸	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. ¹⁷	Zhongnan Hospital, Wuhan, China	NR	3/36 (8%)	6%	NR
Chen et al. ¹⁹	Jin Yin-tan Hospital, Wuhan, China	Need for CKRT	9/23 (39%)	39%	NR
Arentz et al. ²⁰	Evergreen Hospital, Seattle, USA	KDIGO	4/21 (19%)	NR	NR
Yang et al. ²²	Jin Yin-tan Hospital, Wuhan, China	NR	15/52 (29%)	NR	NR
ICNARC ²¹	All critical care units from England, Wales and Northern Ireland	Need for "renal support"	1442/6027 (24%)	20%	NR
Joseph et al. ²⁹	University Hospital, Paris, France	KDIGO	All ICU patients: 81/100 (81%) with AKI 44/81 stage 1 10/81 stage 2 27/81 stage 3	13/100 (13%)	28/81 (35%) died with AKI. The severity of AKI was associated with mortality at day 28.
Chan et al. ²⁸	Mount Sinai COVID Informatics Center	KDIGO	All hospitalized: 1835/3993 (46%) with AKI Stage 1: 39% Stage 2: 19% Stage 3: 42%	347/1835 (19%)	In-hospital mortality was 50% among patients with AKI.
Fisher et al. ³⁰	New York City health system	KDIGO	All hospitalized: 1903/3345 (56%) Stage 1: 50% Stage 2: 20% Stage 3: 30%	164 (4.9%)	In the COVID-19-positive cohort, in-hospital death was 33.7% in those with AKI compared with 9.3% in those without AKI.

Source. Adapted from NephJC (<http://www.nephjc.com/news/covidaki>).

Note. AKI = acute kidney injury; KRT = kidney replacement therapy; KDIGO = Kidney Disease Improving Global Outcomes; NR = not reported; CKRT = continuous kidney replacement therapy; ICNARC = Intensive Care National Audit & Research Centre.

quality of care to patients. This includes the use of specialized equipment such as KRT extension tubing and remote dialysis technology, if available. Also, close coordination between nephrologists and intensivists minimizes the number of providers entering a patient room for routine assessments.

While current Canadian data do not suggest an imminent risk of KRT equipment shortage in children, providers should remain informed of up-to-date data and public health officials' recommendations. Should there be a significant rise in the incidence of severe pediatric COVID-19 disease at a local or national level, consideration should be given to

efficient resource allocation. These choices could include using intermittent hemodialysis (IHD) or shorter time CKRT sessions in the face of a CKRT machine shortage, redeployment of trained dialysis staff to intensive care units as needed, and consideration for the use of home dialysis machines or PD if experiencing an IHD machine shortage. At a broader health care level, should there be a rise in severe COVID-19 illness in adult patients, the treating team may have to consider reallocation of equipment, sharing of hospital space, or redeployment of staff to care for adult patients.

Canadian Association of Paediatric Nephrologists COVID-19 Rapid Response: Guidelines for Management of AKI in Children

Purpose

Acute kidney injury is a potential complication of COVID-19-associated critical illness in children. The burden of COVID-19-associated AKI, as well as the unique features of this condition, has implications for the delivery of acute KRT.

Nephrology programs across the country are developing policies in this rapidly changing environment. The Canadian Association of Paediatric Nephrologists (CAPN), in close collaboration with the Canadian Society of Nephrology (CSN), has synthesized guidance documents from the broader pediatric nephrology community to provide the best care to the largest number of children with kidney disease while also ensuring the safety of the health care team.

Principles

The following principles guided our work:

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 levels of uncertainty that are higher than usual.
2. Macroallocation—an acknowledgment that the local context and local government priorities will shape decision-making. Those previous sacrosanct standards may need to be temporarily adjusted to maximize health outcomes for the most significant number of patients.
3. Minimize net harm—limit the spread of disease and the disruption to the health care system.
4. Reciprocity—protect our health care workforce from COVID-19, and secondarily, so that staffing levels needed for the delivery of care to patients who, by

definition, require physical interventions are maintained.

5. Fairness—ensure that patients with kidney disease continue to receive appropriate treatments, regardless of their COVID-19 status and avoid outcomes that disproportionately affect those most vulnerable (eg, lower socioeconomic status).
6. Proportionality—keep restrictions on staff and patients commensurate with the level of risk to public health.
7. Respect for autonomy—continue to reflect patient and family values and beliefs as much as possible, granting that choices may be limited in a pandemic.
8. Fidelity—maintain commitment to patients to provide necessary care, even through challenging times and when there is a degree of risk to providers).

Information Sources

CSN COVID-19 Rapid Review Program: Management of Acute Kidney Injury⁴⁶

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 2nd, 2020).

Alhazzani 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*. 2020 Apr 3 [Online ahead of print]. doi: 10.2215/CJN.03750320.

Methods

The CAPN, which is affiliated with the CSN, solicited a team of clinicians and researchers with expertise in pediatric AKI and acute KRT. The goal was to adapt the recently developed Canadian adult COVID-19-related AKI guidelines⁴⁶ for pediatric-specific settings. These included specific

COVID-19-related themes that are relevant to AKI and KRT in a Canadian setting, as determined by a group of pediatric nephrologists. The revised pediatric guidelines were reviewed by a group of experts in pediatric AKI and acute KRT. We then held a Webinar, hosted by CAPN to invite pediatric nephrologists and other health care workers around the country to review the guidelines and provide feedback before the document was finalized.

We reproduced the guidance of the adult AKI continuous renal replacement therapy working group verbatim, unless the pediatric group intended a change, in which case this is highlighted. The adult rationale is reproduced either verbatim or condensed. We added, where available, pediatric context and considerations, and justify our differences from the adult AKI guidance. For many questions, no pediatric-specific data were available and no specific considerations applied. We have chosen to reproduce the adult guidelines in their entirety and include the adult nephrologists who wrote them on our writing team. We chose this approach rather than writing a document about the differences. The article would be easy to read for pediatric nephrologists and would stand alone as a useful reference and resource.

Key Issues and Suggestions/Considerations

Planning for Capacity to Provide Acute KRT

We suggest planning for a 25% to 30% increase in the acute pediatric KRT capacity even though the prevalence of pediatric COVID-19 is low. This would help provide flexibility to allocate resources to adult centers as needed based on how the pandemic evolves over time.

Rationale/comments. Report of children with symptomatic COVID-19 infections is growing. At this time, there are no precise data to suggest the incidence of AKI in this population. This is likely related to the low incidence and severity of this disease in children as previously discussed above.

Lipton et al from Columbia University published an editorial commentary on the role of pediatric nephrologists in managing adults with AKI due to COVID-19. The authors share their mutually beneficial experience of pediatric to adult redeployment. The capacity of the PICU was expanded by 50% (from 41 to 60 beds), and all levels of pediatric providers worked on the front line in response to the growing demand during the pandemic. This specifically helped off-load the volume of adults requiring CKRT at the adult hospital.⁴⁷

At present, COVID-19 rates in Canada are increasing after a previous downtrend. Should there be a reemergence of severe COVID-19 hospitalization rates in adults requiring increased KRT needs, consideration should be given to redeploying staff and reallocating equipment from pediatric

centers to support adult patients requiring KRT, provided severe pediatric COVID-19 incidence remains unchanged.

Management of AKI and KRT

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

Fluid Management

These Suggestions are Aligned With Adult AKI Guidance, Except Where the Reason for the Change Is Discussed

We suggest judicious fluid administration to target euvolemia and avoid fluid overload while factoring that insensible losses may be very high in patients with persistent or recurrent fevers

Rationale (from adult AKI guidance). The predominant clinical issue for critically ill patients with COVID-19 is ARDS: We, therefore, recommend avoiding fluid overload.⁴⁰⁻⁴⁵ 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 increased,⁴⁸ and an overly aggressive approach to diuresis or ultrafiltration with KRT could carry potential increased risks of death⁴⁹ and longer term cognitive impairment⁵⁰ as a consequence of more frequent hypotensive episodes.^{50,51}

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). 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 ultrafiltration prescription for KRT, close consultation with PICU 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 thought to influence clinical management. Adopting these practices will decrease risk to health care workers, decrease the risk of nosocomial transmission, and decrease PPE use, a scarce resource.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). Starches and gelatins should not be used for resuscitation^{40,41} because they have been shown in randomized trials to cause an increased risk of death and AKI in adults^{52,53}; 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.⁴⁰

Pediatric context. We did not find pediatric-specific data.

Timing of Initiation of KRT

We recommend that traditional indications for starting KRT should be used in patients with COVID-19

Rationale (from adult AKI guidance). In recent years, several trials provided evidence regarding the optimal timing of KRT initiation for critically ill patients with AKI.⁵⁴⁻⁵⁶ For example, STARRT-AKI trial did not show any benefit of starting KRT early among critically ill adults.^{57,58} A recent systematic review of nearly 2000 patients from 9 studies randomly allocated to earlier or later initiation found no benefit for earlier initiation.⁵⁹ In the context of the COVID-19 pandemic, with limited KRT resources, we recommend using traditional indications to decide on the timing of KRT initiation. We anticipate that volume overload will be the predominant trigger to start KRT in COVID-19 patients with AKI.

Pediatric context. Observational studies have yielded mixed results regarding outcomes of early compared with late initiation of KRT in critically ill children.⁶⁰⁻⁶³

Modality Choice

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

Rationale (from adult AKI guidance). Clinical trials comparing CKRT, IHD, and sustained low-efficiency dialysis (SLED) have not demonstrated improved survival with any particular modality.^{64,65} 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^{24,66} including reports of “hyperinflammatory shock” related to multi-inflammatory syndrome in children.^{31-33,35-37,67}

Kidney replacement therapy modalities that include convection, such as high-volume hemofiltration, are superior at removing larger molecules, such as cytokines; however, both proinflammatory and anti-inflammatory cytokines are removed. To date, randomized trials of septic AKI patients

without COVID-19 demonstrate no additional benefit with convective-based therapies.^{68,69} Also, 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.

Pediatric context. Pediatric literature does not suggest a survival benefit attributable to 1 specific CKRT modality over another in critically ill children.^{70,71} During the CAPN COVID-19 Rapid Response Team Webinar, a clear consensus emerged about this issue. In the absence of evidence of benefit for any particular modality, individual centers should use KRT modalities based on local expertise.

We suggest not using hemoperfusion for COVID-19 patients

Rationale (from adult AKI guidance). COVID-19 patients who require KRT may, in theory, benefit from hemoperfusion because it adsorbs circulating cytokines.⁷²⁻⁷⁴ However, no data are supporting this specific case use. A large trial (n = 450 adult patients) did not reveal any impact on 28-day mortality when hemoperfusion was prescribed to patients with septic shock and high circulating endotoxin levels.⁷⁵

Pediatric context. There are no large trials in pediatrics evaluating this modality.

Dose of KRT

We suggest that the treating team prescribes the established minimum dose of CKRT during the COVID-19 pandemic

Rationale (from adult AKI guidance). The RENAL⁷⁶ and ATN⁷⁷ trials demonstrated that higher doses of KRT do not provide incremental survival benefits for AKI patients. On that basis, we suggest that the treating team should not prescribe higher dialysis doses to patients with COVID-19-associated AKI. Instead, the target dose of CKRT should be 2000 to 2500 mL/1.73 m²/hr of clearance (dialysis fluid rate and/or replacement fluid rate). We recognize that it might be necessary to use lower doses of CKRT if dialysate and replacement solution stocks are limited (see below). To limit solution usage, the treating team should prescribe only the necessary dose of CKRT.

Pediatric context. Because of children’s highly variable body weight, we recommend that the treating team should calculate the precise dialysis dose needed for each child.

Vascular Access

We recommend favoring the internal jugular site for temporary hemodialysis catheter insertion

Rationale. Given that many patients with COVID-19 will receive prone ventilation,^{40,41} internal jugular (IJ) vascular access should be considered the first choice of the temporary HD catheter insertion site in most circumstances.

Pediatric context. We did not find pediatric-specific data.

We suggest that a temporary hemodialysis catheter (or trialysis catheter with a third infusion port) be inserted preemptively, 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 (from adult AKI guidance). While 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 PICU team, it may be advisable to insert an 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. A nontunneled catheter may be used in older children, whereas for younger, smaller patients, a tunneled catheter is preferable. Similarly, in patients with 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 PICU 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 trialysis catheter with an 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.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). Many reports suggest that patients with COVID-19 have an exaggerated inflammatory response (“cytokine storm”)^{24,31,66,67} and are hypercoagulable.^{78,79} There are multiple anecdotal reports of KRT access clotting in this context. Other anecdotal reports in adults indicate that some centers have experienced less catheter dysfunction in patients with COVID-19 upon switching to using a higher concentration of heparin for catheter locks than is typically used between KRT treatments (ie, 5000 U/mL vs 1000 U/mL).

Pediatric context. We did not find pediatric-specific data. However, in pediatrics, the risk of clot-related catheter dysfunction is greater due to lower blood flow rates used, and hypercoagulability may further exacerbate this risk.

Blood Priming and Anticoagulation for KRT

In the context of the generalized hypercoagulability that has been reported in critically ill COVID-19 patients, there are

multiple anecdotal reports of frequent KRT filter and catheter clotting.

We suggest using standard institutional protocols for blood priming extracorporeal circuits for children with COVID-19 starting on IHD or CKRT (pediatric guidance only—no parallel statement in adult AKI guidance)

Pediatric rationale. There is insufficient evidence to recommend any changes to standard blood priming practices in children. After a discussion at the CAPN COVID-19 Rapid Response Team Webinar, there was consensus that the decision to use a blood prime should be made on an individualized basis based on existing protocols.

We suggest using standard institutional protocols to determine blood flow rates (Qb) for children with COVID-19 starting on IHD or CKRT (differs from adult AKI guidance, which suggests higher than standard Qb)

Pediatric rationale. Higher Qb may reduce the risk of clotting^{80,81}; however, there is insufficient evidence to recommend routine use of higher Qb in patients with COVID-19. Moreover, children receiving regional citrate anticoagulation (RCA) using a higher Qb may result in more citrate accumulation and associated complications. Routine assessment of the filter and transmembrane pressure should be done to adjust Qb and anticoagulation appropriately.

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

Rationale (from adult AKI guidance). Initiation of KRT with full-dose anticoagulation, including a bolus of heparin, should be considered, in consultation with PICU 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. Providers should continue to follow their existing institutional protocols.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). As above.

Pediatric context. We did not find pediatric-specific data.

We suggest, for patients on CKRT with an element of hemofiltration, minimizing the postfilter component of the total effluent rate

Rationale (from adult AKI guidance). Limiting hemoconcentration may reduce the risk of circuit clotting.

Pediatric context. We did not find pediatric-specific data.

We suggest that programs with experience using RCA for CKRT consider using RCA based on the clinical status of each patient with COVID-19 (differs from adult AKI guidance which suggests using citrate plus heparin when clotting prevents delivery of prescribed dialysis)

Pediatric context. Anecdotal reports suggest that RCA is generally effective in preventing circuit clotting in COVID-19 patients. Citrate may also prolong circuit lifetime in pediatric patients on CKRT.⁸²

We suggest that programs that do not have experience using RCA protocols for CKRT not implement them immediately

Rationale (from adult AKI guidance). Implementing RCA protocols is complex under normal circumstances; programs that do not already use this approach regularly should consider other anticoagulation modalities during the pandemic.

Pediatric context. We did not find pediatric-specific data.

We suggest that low-molecular-weight heparin be considered for CKRT anticoagulation in children with COVID-19 only by providers who already have experience using it (differs from adult AKI guidance, which does not mention the need for expertise)

Rationale (from adult AKI guidance). Some centers in the United States have reported less clotting with the use of low-molecular-weight heparin (LMWH) protocols for CKRT than they were previously experiencing using unfractionated heparin in patients with COVID-19. In similar circumstances, LMWH is already in widespread use for outpatient IHD and nocturnal dialysis in adults. There have been reports of successful use in chronic HD in children as well.^{83,84} With this experience, there is a consideration that LMWH could be used for CKRT or acute IHD 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 impact if needed (eg, if bleeding occurs) is by the anti-Xa level rather than by partial thromboplastin time (PTT).

Pediatric context. There are no studies of LMWH use in CKRT in children: Because of this, caution and close monitoring should be used. We suggest that only centers with experience using LMWH in CKRT consider its use during the COVID-19 pandemic.

Prevention of Intradialytic Hypotension During Intermittent KRT

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

Rationale (from adult AKI guidance). Given that the primary consideration in many cases may be fluid overload management, various measures can be considered to improve hemodynamic tolerance of fluid removal during intermittent KRT

treatments. Adjustments to the IHD 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), increasing time on IHD, or switching from IHD to CKRT to reduce the hourly ultrafiltration rate. Overall, there is limited evidence in this area.⁸¹ A quasi-experimental “before-after” study that included 121 critically ill patients who underwent 537 IHD sessions showed that implementation of guidelines recommending cool dialysate and higher dialysate sodium concentration was associated with less-frequent intradialytic hypotension.⁸¹

Isolated ultrafiltration (ultrafiltration without dialysis) is a method that may promote hemodynamic stability. During hemodialysis (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 problem 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 were men with a mean age of 59 years.⁸⁵ Fluid targets were the same in each group, so were fluid removal and postdialysis blood pressures. We are not aware of studies in critically ill patients that have directly assessed this intervention.⁵¹ It is perhaps ill-advised to substitute ultrafiltration time for HD time because it may reduce the dialysis dose delivered. Indeed, underdialysis is associated with higher mortality risk in critically ill patients.^{86,87} Adding ultrafiltration time to HD time would increase resource needs (particularly staff time) and will increase the risk of clotting the system.

Pediatric context. We did not find pediatric-specific data.

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, provided that centers have the expertise and support to manage the chosen modality (differs from adult AKI guidance in explicit recognition of the need for expertise and resources)

Rationale (from adult AKI guidance). 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 PICU nurses is compared with that provided by an additional nurse from the HD unit; whether SLED can be provided to more than 1 patient at a time for cohorts of patients with a single dialysis nurse) and concerning resource availability at that time.

Pediatric context. We did not find pediatric-specific data.

We suggest routinely using remote control features of KRT machines, where available

Rationale (from adult AKI guidance). 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.

Pediatric context. We did not find pediatric-specific data.

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

Current Canadian data do not suggest an imminent threat of increasing acute KRT needs in children due to COVID-19. However, there is an expectation that significant additional PICU capacity might be required to care for children with COVID-19 in the current pandemic context. 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 PICU nurses or HD nurses routinely provide SLED.). The following subsections outline the considerations specific to various potential KRT-related shortages.

Delaying the Need for KRT

We recommend that preemptive KRT (ie, before an acute indication is present) should not be used

Rationale (from adult AKI guidance). See the section on *Timing of Initiation* above.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). No direct data are available on the use of conventional or novel potassium binders in critically ill children and especially infants.^{88,89} In outpatients, an increased risk of intestinal ischemia, thrombosis for users of sodium-polystyrene-sulfonate (Kayexalate), compared with nonusers, 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% confidence intervals: 1.1-22.3).⁹⁰ The team should be alerted 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.

Pediatric context. We did not find pediatric-specific data.

Shortage of CKRT Machines

We recommend, in the context of a shortage of CKRT machines, using IHD in patients in whom intradialytic hypotension is likely to be manageable with increased vasopressor dosing

Rationale (from adult AKI guidance). 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 IHD in the PICU. Also, this approach involves exposing additional nursing staff to COVID-19 infection risk and increased PPE consumption.

Pediatric context. We did not find pediatric-specific data.

We recommend, in the context of a shortage of CKRT machines, using IHD machines to do prolonged HD session or SLED for hemodynamically unstable patients (differs from adult AKI guidance in mentioning prolonged HD as an alternative to SLED)

Rationale (from adult AKI guidance). Prolonged IHD sessions or SLED would require the HD nurse to be in the PICU. This carries the potential issue of having to deploy more HD nurses to the PICU and the increased COVID-19 risk exposure and PPE use which that entails.

Pediatric context. We did not find pediatric-specific data.

We recommend, in the context of a shortage of CKRT machines at centers that use CKRT, prolonged HD or SLED for hemodynamically unstable patients, preferentially using prolonged HD or SLED (differs from adult AKI guidance in mentioning prolonged HD as an alternative to SLED)

Rationale (from adult AKI guidance). 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 PICU.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). This involves using 1 CKRT machine for 10 hours on 2 patients daily (or 6 hours for 3 patients), realistically estimating 2 hours to move and clean the machine between treatments. One can consider running higher-than-usual effluent rates if there is no expectation of a shortage of CKRT fluid supplies.

Pediatric context. We did not find pediatric-specific data.

Shortage of CKRT replacement fluid or dialysate

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

Rationale (from adult AKI guidance). 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 IHD in the PICU. Also, this approach involves exposing additional nursing staff to COVID-19 infection risk and increased PPE consumption.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). As detailed above, 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 high risks of disequilibrium, hypokalemia, and hypophosphatemia during treatment.

Pediatric context. We did not find pediatric-specific data.

We suggest, in the context of a shortage of CKRT solutions (fluids), in centers that use both CKRT and prolonged HD (or SLED) for hemodynamically unstable patients, favoring the use of prolonged HD (or SLED) if adequate staffing is available

Rationale (from AKI guidance). 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 HD (or SLED) in the PICU.

Pediatric context. We did not find pediatric-specific data.

We suggest, if there is a shortage of CKRT solutions (fluids), using a lower dose of CKRT (eg, 10-15 mL/kg/hr) once metabolic control has been achieved

Rationale (from AKI guidance). 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 (ref).

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from AKI guidance). A recent publication reports 1 such strategy.⁹¹ The successful use of IHD machines to

generate CKRT solution has also previously been reported.⁹² Careful attention and planning are required to address sterility,⁹³ endotoxin levels,^{92,94} 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. Centers considering locally made solutions should plan their preparation to ensure adequate quality control before these solutions are used.

Pediatric context. We did not find pediatric-specific data.

Shortage of IHD/SLED Capability (Nurses and/or Machines)

We recommend, in the context of a shortage of capacity for IHD 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 HD⁹⁵

Rationale (from adult AKI guidance). Redeployment of trained dialysis staff from outpatients to critically ill patients may be required with the intention to maximize the number of surviving patients.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). Doing this early enables an accurate understanding of available resources in the event of reallocation to adult units if needed. Providers should remain up to date with their available equipment during the COVID-19 pandemic.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). Before redeployment, an assessment of the total number of dialysis-trained staff and the machines with which they have experience working should be undertaken. If there is a shortage for children, this may require staff redeployment from other areas of the pediatric center. However, it may be more likely that a shortage occurs in adults requiring pediatric staff's redeployment to adult centers. Institutions should be prepared to provide readily available training for acute HD nursing should this need arise.

Pediatric context. We did not find pediatric-specific data.

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

Rationale (from adult AKI guidance). While 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.

Pediatric context. We did not find pediatric-specific data.

We suggest, in the context of a shortage of machines for IHD 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 device to the program for acute KRT

Rationale (from adult AKI guidance). This suggestion has been made in adult nephrology guidelines. This approach has potential barriers, 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 an unfamiliar machine will also likely be necessary. These machines may also be considered for allocation to adult patients if needed.

Pediatric context. It must be noted that home HD is less common in children than adults, and in discussion with experts during the CAPN COVID-19 Rapid Response Team Webinar, there were no providers currently caring for any patients on home HD. However, it was felt that this suggestion would still be valid for consideration in the event of a machine shortage if such an option were available.

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

Rationale (from adult AKI guidance). This schedule allows 2 hours to move and clean the machine between patients.

Pediatric context. We did not find pediatric-specific data.

We suggest, in the context of a shortage of capacity for IHD or SLED, that centers consider whether 1 nurse can supervise 2 or more machines simultaneously for older children who are cooperative, located close together and have the same isolation status; start and stop times can be staggered (differs from an adult by the inclusion of the idea of older children who are cooperative)

Rationale (from adult AKI guidance). If machines are available, but HD nurses are limited, this will maximize benefits.

Pediatric context. We did not find pediatric-specific data.

We suggest, in the context of a shortage of capacity for IHD or SLED, at centers where SLED is the modality typically used for

hemodynamically unstable patients, and it is usually provided by PICU nurses (which is not widely done), using SLED rather than IHD for hemodynamically stable patients

Rationale (from adult AKI guidance). This can be done to reduce HD nursing needs and PPE use (if PICU resources allow).

Pediatric context. We did not find pediatric-specific data.

We suggest, in the context of a shortage of capacity for IHD or SLED, that centers consider building capacity for KRT in community hospitals or other pediatric centers that have maintenance HD units but where acute KRT is not routinely provided in PICU

Rationale (from adult AKI guidance). Staffing issues need to be carefully considered and the potential need for additional KRT machines and RO units.

Pediatric context. We did not find pediatric-specific data.

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

We suggest, in the context of an acute shortage of other KRT modalities, using acute PD if necessary

Rationale (from adult AKI guidance). Acute PD can successfully be used to treat critically ill patients in various settings.^{96,97} PD was the modality of choice in KRT in pediatric patients until the development of CKRT machines.⁹⁸ General guidelines for the use of PD in AKI have previously been reported.^{96,99} Many considerations would be involved in the decision to use acute PD, including the following:

- Depending on the center and nephrologists, surgeons and/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 by using a cycler/automated PD.
- Given that volume control may often be the primary concern in COVID-19 patients with AKI, higher glucose concentration solutions may be required (eg, starting with 2.5%/2.36% glucose solutions and then titrating according to achieved ultrafiltration).
- Peritoneal dialysis may be more complicated in patients who require prone ventilation, although its acute use in a predisposed patient has previously been reported to have been successful.¹⁰⁰ We would suggest using another dialysis modality if feasible, as PD would increase the intra-abdominal pressure which may accelerate the need for ventilation.¹⁰¹

- Lower dialysate volumes with shorter dwell times offer several potential advantages in this setting. Low volumes may enable better ventilation relative to larger volumes, limiting pericatheter leaks as catheters are used shortly after insertion.

Pediatric context. Pediatric patients tend to be high transporters allowing higher ultrafiltration.¹⁰²

COVID-19 Drug Dosing for Patients With Kidney Dysfunction

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

Rationale (from adult AKI guidance). This consideration is not specific to patients with AKI. Currently, no medications have been approved in Canada for the treatment of COVID-19. Nonetheless, many drugs are being used off-label or through clinical trials. Given that this is a rapidly changing area, we suggest referring to continuously updated online resources that detail kidney function dosing considerations for potential therapies for COVID-19 (such as the #NephJC AKI blog).¹⁰³

Pediatric context. We did not find pediatric-specific data.

Limitations

There are many significant limitations to this work. Several important considerations were outlined in the adult AKI guidance and are reproduced here. 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 cannot anticipate the many ways in which the dynamic local context, including the details of the 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 concerning the need to triage KRT-related resources if rationing were to be required.

Further limitations apply to these pediatric AKI considerations. We have reproduced the adult guidance and rationale throughout, often verbatim, for consistency, and highlighted areas where there are specific pediatric considerations. However, there is a lack of pediatric AKI and KRT data in children with COVID-19 infections; more research is needed. Finally, knowledge is advancing rapidly in this area; our suggestions may quickly be 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

Best practices may not be delivered to all patients, given time constraints, resource constraints, and local health authority priorities. The priority is to maximize benefits for the greatest number of patients. Given that most acute KRT related to COVID-19 is initiated in the PICU setting, close collaboration and planning between critical care and pediatric nephrology programs at the local level are required. Suggestions included in this document may need updating as newer evidence becomes available. As part of our knowledge translation strategy, the article will be hosted on the CSN/CAPN Web site.^{104,105} Members of the CSN, CAPN, Canadian Association of Nephrology Nurses and Technologists (CANNT), and the Canadian Association of Nephrology Administrators (CANA) will receive an e-mail to this effect.

Ethics Approval and Consent to Participate

Not applicable, this work did not involve human subjects.

Consent for Publication

All authors provided consent for publication.

Availability of Data and Materials

Not applicable, as original data was not collected for this study.

Acknowledgments

We would like to acknowledge the following individuals for providing feedback on these guidelines during the Canadian Association of Paediatric Nephrologists (CAPN) COVID-19 Rapid Response Team Webinar: Shehab Ahmed, Walaa Al-Shammasi, Hanan Alkanani, Areefa Alladin, Ghadah Almahr, Weiam Almainan, Sami Bahar, Anke Banks, Laura Betcherman, Jannie Co, Allison Dart, Janis Dionne, Joanne Grimmer, Swapnil Hiremath, Laura Hornby, Maria Pia Rosati, Sara Rodriguez Lopez, Mohammed Salah Faheem Kasem, James Tjon, Mahdi Farah, and Morteza Ahmadi. The CAPN COVID-19 Rapid Response Team includes Mathieu Lemaire, Rahul Chanchlani, Cal Robinson, Michelle Ruhl, Amrit Kirpalani, Abdullah Alabbas, Damien Noone, Chia Wei Teoh, Valerie Langlois, and Veronique Phan. The Steering Committee includes Mathieu Lemaire and Rahul Chanchlani.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iDs

Abdullah Alabbas  <https://orcid.org/0000-0003-2312-7541>

Edward G. Clark  <https://orcid.org/0000-0002-6767-1197>
 Swapnil Hiremath  <https://orcid.org/0000-0003-0010-3416>
 Steven D. Soroka  <https://orcid.org/0000-0002-7278-1702>
 Ron Wald  <https://orcid.org/0000-0003-4411-8169>

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