Canadian Society of Nephrology/ Société canadienne de néphrologie CSN/SCN

CANADIAN JOURNAL OF KIDNEY HEALTH AND DISEASE
Journal canadien de la santé et de la maladie rénale

Canadian Society of Nephrology COVID-19 Rapid Response Program—Rapid Communication

Canadian Journal of Kidney Health and Disease
Volume 7: 1–18

DOI: 10.1177/2054358120967845
journals.sagepub.com/home/cjk
SAGE

Management of Pediatric Kidney Transplant Patients During the COVID-19 Pandemic: Guidance From the Canadian Society of Transplantation Pediatric Group

Chia Wei Teoh[1,2,3], Marie-Michele Gaudreault-Tremblay[4,5], Tom D. Blydt-Hansen[6,7], Aviva Goldberg[8,9], Steven Arora[10,11], Janusz Feber[12,13], Valerie Langlois[1,2,3], Michelle Ruhl[14,15], Veronique Phan[16,17], Catherine Morgan[18,19], Philip Acott[20,21], and Lorraine Hamiwka[22,23] on behalf of the CST Paediatric Group

Abstract

Purpose of the program: To provide guidance on the management of pediatric kidney transplant patients during the COVID-19 pandemic.

Sources of information: Program-specific documents, preexisting, and related to COVID-19; documents from provincial, national, and international kidney transplant societies/agencies and organ procurement agencies; national and international webinars, including webinars that we hosted for input and feedback; with additional information from formal and informal review of published academic literature.

Methods: Challenges in the care of pediatric kidney transplant patients during the COVID-19 pandemic were highlighted within the Canadian Society of Transplantation (CST) Pediatric Group. It identified pediatric kidney transplant nephrologists (including a pediatric nephrologist ethicist) across the country and formed a workgroup. The initial guidance document was drafted and members of the workgroup reviewed and discussed all suggestions in detail via e-mail and virtual meetings. Disagreements were resolved by consensus. The document was reviewed by the CST Kidney Transplant Working Group, by the Canadian Society of Nephrology (CSN) COVID-19 Rapid Response Team (RRT), and an infectious disease expert. The suggestions were presented at an interactive webinar sponsored by CSN in collaboration with the CST and Canadian Association of Pediatric Nephrologists (CAPN), and attended by pediatric kidney health care professionals for further peer input. Final revisions were made based on feedback received. CJKHD editors reviewed the parallel process peer review and edited the manuscript for clarity.

Key findings: We identified 8 key areas of pediatric kidney transplant care that may be affected by the COVID-19 pandemic: (1) transplant activity, (2) outpatient clinic activity, (3) monitoring, (4) multidisciplinary care, (5) medications (immunosuppression and others), (6) patient/family education/support, (7) school and employment, and (8) management of pediatric kidney transplant patients who are COVID-19 positive. We make specific suggestions for each of these areas.

Limitations: A full systematic review of available literature was not undertaken for the sake of expediency in development of this guideline. There is a paucity of literature to support evidence-based recommendations at this time. Instead, these guidelines were formulated based on expert opinion derived from available knowledge/experience and are subject to the biases associated with this level of evidence. The parallel review process that was created to expedite the publication of this work may not be as robust as standard arms' length peer review processes.

Implications: These recommendations are meant to serve as a guide to pediatric kidney transplant directors, clinicians, and administrators for providing the best patient care in the context of limited resources while protecting patients and health care providers wherever possible by limiting exposure to COVID-19. We recognize that recommendations may not be

applicable to all provincial/local health authority practices and that they may not be delivered to all patients given the time and resource constraints affecting the individual provincial/local health jurisdiction.

Keywords
pediatric kidney transplant, pediatric nephrology, pediatric, kidney transplantation

Received September 24, 2020. Accepted for publication September 28, 2020.

Introduction

As of June 21, 2020, over 8.8 million cases of COVID-19 have been reported globally.[1] Children appear to be less commonly and less severely affected than adults, accounting for 1% to 5% of all COVID-19 cases and 0% to 1% of reported fatalities.[2-9] In Canada, 101 019 cases of COVID-19 have been reported. Of these, 6.97% were children ≤19 years of age, accounting for 1% of hospitalized patients, and 1% of patients admitted to intensive care, with no reported fatalities.[10]

The COVID-19 pandemic has challenged pediatric kidney transplant programs to provide safe and consistent care during this difficult and unprecedented time. While data are still emerging, it is presumed that children with chronic kidney disease and/or those who take immunosuppressive medications may be at increased risk for complications from COVID-19 infection. In addition, the implementation of necessary public health measures (ie, physical distancing, school and childcare closures, and restrictions on hospital services) has impacted the ways that health care providers deliver pediatric transplant care.

To date, national and international transplant societies have provided general guidance and recommendations for management of transplant programs and delivery of patient care during the COVID-19 pandemic—very few are specific to pediatric patients.

The Canadian Society of Transplantation (CST) Pediatric Group established a "virtual" working group of pediatric kidney transplant nephrologists to leverage the evolving experiences, protocols, and tools across Canada to develop a current snapshot of "best practices" which can be shared for the benefit of patients and care providers. Specific objectives of this working group are (1) to develop relevant interim guidance leveraging the pan-Canadian experience; (2) to facilitate real-time dissemination of interim guidance to pediatric kidney transplant programs; (3) to develop a collection of relevant external guidelines/recommendations and linkages to relevant literature; (4) to establish mechanisms for concurrent and rapid peer review; and (5) to solicit emerging needs through the CST, provincial organ procurement agencies, professional societies, and academic channels.

[1]Division of Nephrology, The Hospital for Sick Children, Toronto, ON, Canada
[2]Transplant & Regenerative Medicine Centre, The Hospital for Sick Children, Toronto, ON, Canada
[3]Department of Paediatrics, University of Toronto, ON, Canada
[4]Division of Nephrology, Montreal Children's Hospital, QC, Canada
[5]Department of Paediatrics, McGill University, Montreal, QC, Canada
[6]Division of Nephrology, BC Children's Hospital, Vancouver, Canada
[7]Department of Paediatrics, The University of British Columbia, Vancouver, Canada
[8]Division of Nephrology, The Children's Hospital of Winnipeg, MB, Canada
[9]Department of Paediatrics and Child Health, University of Manitoba, Winnipeg, Canada
[10]Division of Nephrology, McMaster Children's Hospital, Hamilton, ON, Canada
[11]Department of Paediatrics, McMaster University, Hamilton, ON, Canada
[12]Division of Nephrology, Children's Hospital of Eastern Ontario, Ottawa, Canada
[13]Department of Paediatrics, University of Ottawa, ON, Canada
[14]Division of Nephrology, Jim Pattison Children's Hospital, Saskatoon, SK, Canada
[15]Department of Paediatrics, University of Saskatchewan, Saskatoon, Canada
[16]Division of Nephrology, CHU Sainte-Justine, Montreal, QC, Canada
[17]Department of Paediatrics, University de Montreal, QC, Canada
[18]Division of Nephrology, Stollery Children's Hospital, Edmonton, AB, Canada
[19]Department of Paediatrics, University of Alberta, Edmonton, Canada
[20]Division of Nephrology, IWK Health Centre, Halifax, NS, Canada
[21]Department of Paediatrics, Dalhousie University, Halifax, NS, Canada
[22]Division of Nephrology, Alberta Children's Hospital, Calgary, Canada
[23]Department of Paediatrics, University of Calgary, AB, Canada

Corresponding Author:
Chia Wei Teoh, Division of Nephrology, The Hospital for Sick Children, 555 University Avenue, Toronto, ON, Canada M5G1X8.
Email: chiawei.teoh@sickkids.ca

Table 1. Ethical Principles That Guided the Decision-Making Process Underpinning the Guidance Provided Within This Document.

Principles	Description
Uncertainty	Acknowledge that clinicians and administrators are now working in a swiftly evolving environment which will require decision making with limited resources and greater uncertainty.
Macro-allocation	Acknowledge that the local context and local government priorities will shape decision making and that previous standards may need to be temporarily adjusted to maximize health outcomes for the greatest number of patients.
Minimize net harm	Includes limiting the spread of disease and disruption to the health care system.
Reciprocity	Protect our health care workforce from COVID-19 so staffing levels are maintained to deliver care to patients who by definition often require physical interventions, and as an objective in itself.
Fairness	Ensure that patients with kidney disease continue to receive appropriate treatments regardless of their COVID-19 status and avoid outcomes that disproportionately impact those who are most vulnerable (eg, lower socioeconomic status).
Proportionality	Keep restrictions on staff and patients commensurate with the level of risk to public health.
Respect for autonomy	Continue to reflect patient values and beliefs as much as possible, granting that choices may be limited in a pandemic.
Fidelity	Maintain commitment to patients to provide necessary care in challenging times and when there is a degree of risk to providers.

Note. COVID-19 = coronavirus disease 2019.

General care and public health practices should follow the most up-to-date provincial and national public health policies, but children with kidney transplants and those with chronic kidney disease have unique health care needs. The recommendations in this document provide suggestions on how to provide the best possible care for children living with kidney transplants during the COVID-19 pandemic.

The recommendations outlined in this document represent best practices based on available information from published literature and unpublished expert opinion, at the time of writing on June 1, 2020. We acknowledge that the data on COVID-19 are rapidly evolving, and these recommendations may need to be revised as new knowledge emerges.

Methods

During the COVID-19 pandemic, the CST Pediatric Group organized a working group of pediatric kidney transplant physicians across Canada. Available COVID-19 documents and experiences from programs across the country were collated. Other national and international kidney transplant literature and webinars were reviewed for recommendations that are applicable to the Canadian context. Experts from other countries were contacted to provide experiential perspectives of kidney transplant care during the COVID-19 pandemic. Recommendations were developed based on consensus of the working group, guided by available published peer-reviewed and non–peer-reviewed literature, guidelines from other jurisdictions, and input from transplant and infectious disease experts. The complete draft was reviewed by the entire CST Kidney Transplant Working Group and an infectious disease expert. Final revisions followed a public webinar of pediatric kidney professionals sponsored by the Canadians Society of Nephrology (CSN), in collaboration with the CST and Canadian Association of Pediatric Nephrologists (CAPN).

To ensure that decision-making process underpinning the guidance provided within this document are ethically supported, we adhered to the following principles outlined in Table 1.

Narrative Summary of the Current State of Pediatric Kidney Transplant Programs Across Canada as of April 2020

We surveyed all 9 pediatric kidney transplant programs across 7 provinces: most programs have enacted similar approaches to the provision and delivery of care to pediatric kidney transplant patients and candidates. No programs reported significant health care resource concerns at the time.

Transplant Activity

Programs generally suspended living donor kidney transplantation and limited deceased donor kidney transplantation to those of highest need (medically urgent and/or highly sensitized) in the early stages of the pandemic. This included suspension of preemptive transplants, acknowledging that some children would need to start dialysis as they could not wait for preemptive transplants to be restarted. Programs also developed provincial/local guidance on a phased approach to resumption of kidney transplant activity based on very similar guiding principles. Programs developed donor and recipient COVID-19 screening and testing that were generally similar, consistent with national guidelines.[11]

No programs accepted donors or recipients who were confirmed or highly suspected to be COVID-19 positive, acknowledging that the risk of transmission of the virus through donor organs had not been established.

Outpatient Clinic Activity

Programs generally continued their scheduled transplant clinic visits. Few programs deferred follow-up of "routine" stable patients but many extended the usual follow-up frequency. Clinic visits were delivered virtually unless there were indications that necessitated in-person visits. Virtual visits were being delivered via telephone, video, and hosted video platforms. Barriers to virtual consultations included lack of computer technology and internet availability to perform virtual visits. All in-person clinic visits followed local Infection Prevention and Control (IPAC) guidelines with prescreening for symptoms and enhanced protection practices. Many centers also identified that they reached out to their patients (via telephone, e-mail, and other communication strategies) to inform them of the restrictions/policies that were enacted in their respective institutions to reduce the risk of exposure to SARS-CoV-2 during their in-person visits, and reassured them of the transplant clinic's ability to provide ongoing care.

Blood Work Monitoring

All programs continued essential blood work to monitor allograft function, treatment-related complications, and therapeutic drug levels, though the frequency of such testing was reduced for select stable patients in some programs. Blood work was performed both in community and hospital laboratories. While all hospitals enacted precautionary measures, some provinces had additional mechanisms in place to reduce risk of community COVID-19 transmission with designated community laboratories for immunocompromised patients.

Multidisciplinary Care

All programs with preexisting multidisciplinary care continued to provide care at the time. This was provided virtually using the same platforms used for virtual outpatient visits.

Kidney Biopsies

Urgent indication kidney allograft biopsies to establish etiology of allograft dysfunction continued to be performed. Elective/surveillance biopsies were generally deferred. One program had to ration the use of antibodies for immunofluorescence staining to those with most relevant clinical need due to supply concerns. Screening and testing for COVID-19 were performed prior to all procedures, for patients, while some programs also tested parents/caregivers.

Challenges Identified

Challenges identified include the following: (1) potential supply chain disruptions for medications especially immunosuppressive medications; (2) challenges with virtual visits: lack of technology/infrastructure to support telehealth, additional time required for virtual visits, inability to perform physical examination and communication challenges during virtual visits; (3) challenges with need for rapid reorganization of clinic infrastructure and resources to meet with demands of maintaining a low risk environment for in-person visits; (4) patient anxiety and fear of contracting COVID-19 by attending clinic visits and/or performing monitoring laboratory studies, leading to suboptimal monitoring and/or late presentation with complications; (5) lack of established knowledge to make informed decisions regarding immunosuppression management; (6) lack of knowledge of risks and effects of COVID-19 in the pediatric kidney transplant population; (7) lack of capacity to communicate with transplant patients en masse as recommendations change (eg, by website updates, group e-mails); (8) remuneration strategies in some jurisdictions that limit remuneration for virtual care visits.

Successes Identified

Successes identified include the following: (1) ability to continue delivering patient care in a rapidly changing environment; (2) ability of each center to provide timely communication with their patients/families in a rapidly changing environment; (3) no pediatric kidney transplant patients diagnosed with COVID-19 at the time of writing in Canada, and few reports internationally of significant complications in this population; (4) ability to quickly form a cohesive, working group of pediatric kidney transplant professionals from across the country to share evolving clinical experiences and knowledge, and to develop current consensus guidance on management of children with kidney transplants during the COVID-19 pandemic in the context of a rapidly evolving environment and evidence base; (5) ability to partner with other organ groups, adult care colleagues, and international colleagues to gather and respond to the best available evidence.

Recommendations

1. Transplant Activity

1.1. Pediatric kidney transplantation (deceased, living donor, and preemptive transplantation) should be considered an emergent or urgent life-saving procedure and be given priority for booking/rebooking when hospitals plan re-opening of their operating

rooms, inpatient, outpatient, laboratory, and imaging programs.

1.2. We suggest ongoing national collaboration to develop a unified approach to suspension/resumption of kidney transplant activity at each center based on careful consideration of risks versus benefits of transplantation based on these considerations:
  1.2.1. In general, the benefits of kidney transplantation outweigh the risks, and both life expectancy and quality of life are improved when compared with staying on/starting dialysis.
  1.2.2. The degree of community spread and active cases of COVID-19 locally may contribute to the risks and benefits at that particular site, so it may be reasonable for different sites to "re-open" at different rates and at different times.
  1.2.3. Availability of rapid and accurate COVID-19 testing on donors and recipients is essential to ensure timely identification of infected individuals to mitigate the risk of acquisition and transmission.
  1.2.4. Clear guidance/criteria for donor and recipient COVID-19 screening and testing should be provided by transplant centers in collaboration with their University, hospital leadership, organ procurement agency, and Public Health.
  1.2.5. Availability of hospital and health care system capacity for inpatient beds, intensive care beds, ventilators, diagnostic testing, staffing, and adequate personal protective equipment both in the pediatric center and the adult center (in the case of a living donor).
  1.2.6. Iatrogenic risk for COVID-19 acquisition and transmission should be minimized, with provision of a clear COVID-19-free pathway for hospital inpatient and outpatient care.
  1.2.7. Risks to living donors should be considered in any decisions regarding re-opening of living donor programs.
  1.2.8. Programs should strive for clear guidance/criteria for transplant activity suspension/modification taking the above considerations into account, and be prepared to review/change recommendations as new evidence emerges.

1.3. We recommend that only COVID-19 PCR negative donor and recipient pairs proceed to transplantation.

1.4. When possible, we recommend that living donor/recipient pairs self-isolate for 14 days leading up to the planned transplant surgery.

1.5. During the pandemic, we recommend that all potential recipients be informed at the time of organ offer, of the potential risk of contracting COVID-19 and associated risks of developing severe complications during the hospital stay and after discharge home. This informed consent should be clearly documented in the medical records (documentation of verbal consent as per exceptional distribution consent), acknowledging the paucity of clear evidence on transmission at this time.

1.6. We suggest that each jurisdiction and center develop a communication strategy to keep patients/families of those who are eligible and/or on the transplant waitlist informed.

1.7. We recommend that all health care professionals involved in organ donation and transplantation use appropriate personal protective equipment (PPE) and that health authorities ensure that sufficient PPE is available to these providers.
  1.7.1. We suggest that all health care professionals practice enhanced protection precautions while caring for donors and transplant recipients, according to local guidelines.
  1.7.2. We recommend that all health care professionals involved in organ donation and transplantation be provided with appropriate PPE and training on how to use the equipment.

Rationale

During the COVID-19 pandemic, transplant activity has been significantly curtailed[12] (1) to preserve hospital infrastructure and resources to allow treatment of COVID-19 patients, (2) to avoid iatrogenic immunosuppression when community or hospital exposure of SARS-CoV-2 infection to the transplant recipient remains possible, and (3) to allow programs time to develop appropriate procedures and testing to mitigate risk of iatrogenic transmission of SARS-CoV-2 infection to the transplant recipient.

Organ donation and transplantation is an essential life-saving and life-preserving medical intervention. A major effect of the temporary suspension of transplant activity is that potential deceased donor organs are not used. The longer that programs remain closed or operate at reduced capacity, the longer the predicted wait-time and associated mortality risk for recipients. Transplant organs are a finite time-sensitive resource, and once lost can no longer be recovered.

While it is currently too early to make decisions based on robust evidence, continually emerging evidence and anecdotal reports from other jurisdictions suggest that solid-organ transplant recipients who are immunosuppressed may be at increased risk of acquiring SARS-CoV-2 and develop more severe outcomes related to COVID-19.[13-28] These early reports are based on adult solid-organ transplant recipients with very limited data on pediatric recipients. Emerging and anecdotal reports from other jurisdictions suggest that children follow a relatively mild course of COVID-19 and have better outcomes when compared with adults.[2-9,29-34] An ongoing international survey initiated by the European Rare Kidney Disease Reference Network and supported by international pediatric nephrology societies suggests that

the incidence of COVID-19 in pediatric kidney transplant recipients is similar to the background incidence of COVID-19 in the general pediatric population.[35] Reports of COVID-19 in immunosuppressed children with kidney transplants have been few and far between. Currently available evidence suggests that this population is not at increased risk of severe COVID-19 disease.[36-39]

Given the currently available evidence, the system must balance the benefits of transplantation and the potential loss of organs, with the risks related to resource utilization and immunosuppression. In response to this, the Canadian Blood Services and Canadian Society of Transplantation in conjunction with provincial organ procurement agencies, adult/pediatric organ donation and transplant leaders across the country came together to develop a strategy for phased re-opening of transplantation activity in a safe and rational manner. The phased re-opening would be based on the guiding principles above with close coordination with public health, transplant institutions, and critical care planning.[11] Other jurisdictions have also taken similar approaches.[40,41]

When appropriate, self-isolation for a period of 14 days leading up to the transplant surgery will reduce the risk of exposure to SARS-CoV-2. This practice is only practical for living donor/recipient pairs and not for patients on the deceased donor waitlist. However, all donors and recipients should adhere strictly to public health measures (ie, physical distancing, masks, frequent hand hygiene) to reduce their risk of exposure to SARS-CoV-2.

Adequate protection of health care professionals will mitigate the risks of iatrogenic transmission of SARS-CoV-2 and help ensure the maintenance of adequate human resources pertaining to staffing and expertise. It is acknowledged that there is regional and institutional variability with respect to COVID-19 specific PPE and universal precaution practices. We suggest adhering to local provincial/institutional guidelines with the guiding principles outlined above.

2. Outpatient Clinic Activity

2.1. We suggest adhering to clinic visit schedules where resources permit.
  2.1.1. We suggest adhering to in-person visits when necessary for urgent issues, and for routine follow-up visits when vital signs measurement, growth parameters, relevant investigations, and physical examination are required.
    2.1.1.1. We suggest appropriate COVID-19 screening using local IPAC guidelines.
    2.1.1.2. We suggest patients who screen positive be directed to the most appropriate facility as per local IPAC guidelines.
  2.1.2. Where appropriate and when resources permit, we suggest patients are assessed via telemedicine or virtual visits to reduce the need for travel to/from clinic.
    2.1.2.1. Patients should be provided with clear instructions regarding blood work, performing blood pressure and/or weight measurements and preparation of a current medication list in advance of their telehealth visit.
  2.1.3. We suggest that a minimum of one parent or caregiver be allowed to accompany pediatric patients to their visits whenever possible.
2.2. We suggest an individualized approach regarding clinic visits based on clinical need/urgency and/or need for investigations.
2.3. We suggest centers consider increasing intervals between subsequent routine follow-up outpatient visits based on an individual patients' clinical status.
2.4. We suggest clear communication to all patients about the centers' plan for ongoing kidney transplant care.
2.5. We suggest providing patients/families with information on how to seek medical care in case of development of symptoms of COVID-19—this should include urgent/emergent and routine care plans.
2.6. We suggest providing patients/families with reassurances that they will receive appropriate medical/surgical care when indicated (including in-person visits).

Rationale

Maintaining continuity of care ensures that patients continue to receive adequate clinical assessment, personalized advice regarding immunosuppression, and access to the support of the transplant program in case of COVID-19 infection. Children with kidney transplants require ongoing assessment of allograft function, adequacy of immunosuppression, complications of chronic kidney disease and those related to therapy, viral load, and therapeutic drug level monitoring. Good communication between the health care team and patients/families is essential to avoid disruption of essential clinical care visits or becoming "lost to follow-up." Adhering to local IPAC guidelines for screening and utilization of enhanced protection measures will mitigate risks of transmission of SARS-CoV-2 in the clinical setting.

Telemedicine (telephone, web-based virtual care platforms, videoconferencing, and e-mail) can facilitate ongoing access to care while maintaining physical distancing with the aim of mitigating risks of transmission of SARS-CoV-2. Evidence supporting use of telehealth is extrapolated from literature for its application in provision of general nephrology, pediatric nephrology care,[42,43] and from other jurisdictions that have successfully implemented a telehealth strategy to manage transplant recipients during the COVID-19 pandemic.[44] Communication with patients prior to telehealth visits with reminders for completing blood work, measurement of blood pressure, weight and height, and preparation of medication list will help improve efficiency of telehealth visits. In-person

clinical visits are an essential component of care. However, in the context of the COVID-19 pandemic, with high levels of active community viral transmission or strain on hospital-based resources, in-person visits should be reserved for patients requiring urgent care or specialized investigations to minimize exposure risk for patients, families, and health care professionals. In this context, providing patients/families with reassurances that they will continue to receive appropriate medical/surgical care when indicated (including in-person/inpatient care) will allay their concerns about not being able to access care should they develop symptoms/signs suggestive of possible COVID-19 and will likely improve their truthfulness in reporting of symptoms.

3. Monitoring

3.1. Laboratory testing
- 3.1.1. We suggest that patients continue to have their routine laboratory studies, viral load testing, and therapeutic drug-level monitoring (tacrolimus, cyclosporine, mycophenolate) performed as determined by each center.
- 3.1.2. We recommend establishing a clear COVID-19-free pathway for in-hospital and community lab testing.
- 3.1.3. We suggest that laboratory studies be performed in testing facilities with established procedures to mitigate risk of infection (in-hospital and/or community laboratories).
- 3.1.4. We suggest establishing a system for timely follow-up on laboratory test results if a clinic visit is deferred/postponed.
- 3.1.5. In communities/areas with active community SARS-CoV-2 transmission, we suggest considering increasing the interval between routine monitoring laboratory studies, where clinical status permits (as determined by each center).

3.2. Home monitoring
- 3.2.1. Where resources and patient/family circumstances permit, we suggest that patients monitor their weight, height, and blood pressures at home using a calibrated device.
- 3.2.2. Other types of home monitoring should be considered based on each patient's needs or abilities.

3.3. Kidney biopsies
- 3.3.1. We suggest that urgent, for-cause kidney allograft biopsies continue to be performed as clinically indicated.
- 3.3.2. We suggest deferring surveillance/protocol kidney allograft biopsies that are not time-sensitive and where clinical status permits (as determined by each center).

3.4. We do not recommend testing of asymptomatic pediatric kidney transplant patients for COVID-19, unless directed by public health or as required in advance of admissions, procedures, and so on.

Rationale

Laboratory testing is essential for monitoring of ongoing allograft function, disease activity, treatment efficacy and toxicity, viral loads and therapeutic drug monitoring levels. While it is important that ongoing monitoring occurs in the context of the COVID-19 pandemic, we suggest a case-by-case need assessment and to consider increasing the interval between laboratory studies when appropriate. This assessment should balance the risk of infection and the strain on resource availability at testing sites (in-hospital and/or community laboratory) against the risk of potential morbidity by deviating from the standard of care. Establishing a clear COVID-19-free pathway for laboratory studies will help mitigate the risk of transmission of SARS-CoV-2. Home monitoring where appropriate can complement the required monitoring to enable the provision of necessary treatment and symptom management, as well as facilitate telehealth visits. While kidney biopsies are essential to diagnose the etiology of allograft dysfunction to inform treatment, we suggest that routine surveillance kidney allograft biopsies that are not time-sensitive (ie, annual surveillance biopsies after first year of transplant) be deferred when clinical status permits, based on the judgment of the individual center, with the aim of reducing exposure risks for patients, families, and health care professionals.

4. Multidisciplinary Care

4.1. We suggest that multidisciplinary care continue to be provided as resources permit.

4.2. When possible, we suggest that care providers perform telehealth assessments as resources permit.

4.3. When in-person visits are needed, we suggest that care providers practice physical distancing from patients/families and other providers, and/or use appropriate personal protective equipment when appropriate.

4.4. We suggest that communication between care providers be undertaken via telephone, secure e-mail, and/or secure virtual platforms.

4.5. We suggest that clinical documentation be continued as per usual standard of care, and information be conveyed to the primary care provider and other relevant health care professionals as per usual practice.

4.6. We suggest that the multidisciplinary team actively screen for risk factors for mental health and psychosocial problems secondary to the pandemic.

Rationale

Multidisciplinary care is essential to provide the care needs of children with chronic kidney disease and kidney transplants.

Strategic utilization of telehealth technology will allow for continued multidisciplinary care for this patient population. Evidence suggests that delivery of chronic kidney disease multidisciplinary care via telehealth is noninferior to in-person care.[45] Depression and anxiety are known to be common in children with chronic kidney disease.[46,47] Mental health concerns can be exacerbated by isolation from peers and the loss of purposeful routine that children with chronic health conditions have experienced during the COVID-19 pandemic.[48,49] We discuss these risks further in the section School, Daycare, Summer Camps, and Employment. These should actively be monitored during clinic visits. Where a large-group setting is not conducive to exploring mental health concerns, patients should be offered individual follow-up with a social worker or clinical psychologist.

5. Medications

5.1. Immunosuppression
- 5.1.1. We recommend that each center continue to determine the degree of immunosuppression required on a case-by-case consideration, to avoid under- or over-immunosuppression.
- 5.1.2. We suggest avoiding the use of lymphocyte-depleting induction agents.

5.2. Others
- 5.2.1. We suggest that ACE inhibitors and ARBs should not be routinely discontinued as a result of the COVID-19 pandemic.
- 5.2.2. We suggest that initiation or discontinuation of ACE inhibitors or ARBs should be performed at the clinical discretion of the individual physician.
- 5.2.3. We suggest that ACE inhibitors and ARBs should be temporarily suspended according to usual sick day guidance.

5.3. We recommend patients ensure they have a minimum 1 month supply of their immunosuppression and other medications available, with adequate prescription refills to allow for timely dispensing of medications.

Rationale

There is limited evidence in immunosuppressed children with kidney transplants to suggest that they may not be at increased risk of severe COVID-19 disease.[35-38] However, evidence from similar adult populations suggests an increased risk of acquiring COVID-19 and an increased risk of severe disease and undesirable outcomes.[13-18] Therefore, we recommend careful consideration of the degree of immunosuppression that is required in each child with a kidney transplant to avoid under- or over-immunosuppression. While no evidence is available to inform the risks associated with different induction agents, we recommend reconsideration of lymphocyte-depleting induction agents as lymphopenia in COVID-19 patients is associated with severe disease.[11,50,51] This would translate to the avoidance of "high-risk" transplants if they can be safely deferred. These considerations remain at the discretion of the clinician and the individual transplant program.

There has been much speculation of a possible association of severe COVID-19 disease with the use of angiotensin-converting enzyme inhibitors (ACEi) and angiotensin-receptor blockers (ARBs) as the spike protein of the SARS-CoV-2 virus uses angiotensin-converting enzyme 2 (ACE2) receptors for cell entry.[52,53] The relationship between viral protein binding to ACE2, renin-angiotensin-aldosterone system (RAAS) inhibition, and pathogenicity of the virus is complex and incompletely understood—and has been the subject of detailed reviews.[54,55] The current evidence suggests RAAS inhibition does not facilitate SARS-CoV-2 infection and/or more severe COVID-19 disease. We believe that further studies are required to definitively ascertain these risks. Therefore, we currently suggest that ACEi or ARBs should not be routinely discontinued due to COVID-19 and that any decisions to initiate/discontinue these medications should be subject to careful medical consideration led by the patient's physician—This position is supported by multiple specialty societies.[56-65]

6. Patient/Family Education/Support

6.1. When possible, we suggest that patient/family education be carried out via telehealth, supported by electronic education material.

6.2. We suggest providing patients/families with information on how to seek medical care in case of development of symptoms of COVID-19—this should include urgent/emergent and routine care plans.

6.3. We suggest that patients continue to receive education about their diagnosis, ongoing clinical status, and treatment plan.

6.4. We suggest compilation of clinically vetted information, maintained by professional organizations/societies to be shared with patients where appropriate.

6.5. COVID-19-specific educational resources:
- https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19.html
- https://www.cps.ca/en/tools-outils/covid-19-information-and-resources-for-paediatricians
- https://www.cst-transplant.ca/COVID-19_Information.html
- https://profedu.blood.ca/en/organs-and-tissues/covid-19-update-organ-donation-and-transplantation-services
- https://tts.org/index.php?option=com_content&view=article&id=692&Itemid=115
- https://www.myast.org/covid-19-information
- https://tts.org/ipta-about/ipta-presidents-message/146-uncategorised/ipta/ipta-about/701-ipta-paediatric-information-on-covid-19

- https://www.who.int/emergencies/diseases/novel-coronavirus-2019
- https://www.cdc.gov/coronavirus/2019-ncov/index.html
- https://resources-covid19canada.hub.arcgis.com/
- https://kidney.ca/COVID-19-How-to-Protect-Yourself
- https://publications.msss.gouv.qc.ca/msss/fichiers/2020/20-210-166W.pdf (from Institut national d'excellence en santé et en services sociaux, INESS)

Rationale

Providing patients/families with accurate and up-to-date information about their clinical status and treatment plan reinforces good self-management. During the COVID-19 pandemic, it is important to provide patients/families with accurate, vetted, and up-to-date information about how COVID-19 may impact their health and ongoing access to care. Pediatric transplant programs should consider reinforcing this with written information and links to specific resources maintained by professional organizations/societies.

7. School, Daycare, Summer Camp, and Employment

7.1. We advise that children with kidney transplants and their close caregivers/family members take extra precautions and continue to practice enhanced protective precautions (ie, frequent hand hygiene, physical distancing, masking) to minimize exposure to SARS-CoV-2.

7.2. We recommend that schools, local/provincial school authorities, daycares, summer camps, and employment facilities actively take precautionary measures to mitigate risks of SARS-CoV-2 transmission in their local environment (ie, masking policy, physical distancing, encouragement of proper hand hygiene practices, policy for staff/participant nonattendance/self-isolation if symptomatic).

7.3. We recommend that schools, local/provincial school authorities, daycares, summer camps, and employment facilities implement active screening measures to assess risk of SARS-CoV-2 transmission (ie, symptom and/or temperature screening among staff/participants).

7.4. We suggest that schools, local/provincial school authorities, daycares, summer camps, and employment facilities maintain active surveillance of their COVID-19 infection rates among their staff, participants, and local community to keep patients/families informed, as well as to facilitate informed decisions about attendance for kidney transplant recipients.

7.5. We recommend that the decision to return to school, daycare, summer camp, and/or work be considered on a case-by-case basis, with particular consideration of their immunosuppressive burden, exposure risk inherent to their school and/or environment, and the presence of other comorbid conditions, psychosocial concerns, and/or learning needs, and be guided by the epidemiology of COVID-19 cases in the community and by public health (see also Table 2).

Rationale

In response to the COVID-19 pandemic, many countries have implemented school and daycare closures as a physical distancing measure to reduce the rates of community transmission to avoid the risk of overwhelming available health care resources. While evidence about its contribution to transmission control is generally lacking, recent rapid systematic reviews highlighted preliminary findings that children and young adolescents were less susceptible to SARS-CoV-2, suggesting their relatively smaller role in transmission of the virus[66] and suggested that school closures alone would prevent between 2% and 4% of deaths from COVID-19.[67]

We recognize that the necessary implementation of physical distancing measures during the COVID-19 pandemic will likely lead to unintended consequences on the mental health and well-being of children.[68,69] Children will invariably be affected by concerns and anxiety related to the risks posed by the pandemic on their own health, safety, and need for protection. These concerns can exacerbate preexisting trauma, adversity, and disparities. For many children and their families, the pandemic may have led to new loss, grief, and trauma, as well as adversity related to their isolation, economic hardship, and unmet basic needs which increases the risk for emotional and physical abuse at home. A recent rapid review of the psychological impact of quarantine highlighted increased anger, confusion, and posttraumatic stress symptoms, as well as substance abuse in those under quarantine.[70] Depression and anxiety are known to be common in children with chronic kidney disease.[46,47] Mental health concerns can be exacerbated by isolation from peers and the loss of purposeful routine that children with chronic health conditions have experienced during the COVID-19 pandemic.[48,49] These mental health risks must also be considered when counseling patients on the timing of returning to school, daycare, summer camp, and/or employment.

We do not currently have evidence to confirm that pediatric kidney transplant recipients are at higher risk for more severe COVID-19. These suggestions are made on the basis that children with kidney transplants who are immunosuppressed, particularly those with higher degree of immunosuppression (eg, recent transplantation, recent treatment of acute rejection, lymphopenia), and those with medical comorbidities (eg, obesity, diabetes mellitus, chronic lung/heart disease) may be at increased risk for acquiring COVID-19 and suffering from related complications when compared with the general pediatric population. We advise that

Table 2. Suggested Risk Stratification for Pediatric Kidney Transplant Recipients Who May Be at Increased Risk for Severe COVID-19.

	High risk	Moderate risk	Low risk
Degree of immunosuppression	High level of immunosuppression: • Within initial 6 months post-kidney transplant • Undergoing treatment for acute rejection (high-dose steroids, thymoglobulin, rituximab)	Stable and tapering level of immunosuppression: • Within 6-12 months post-kidney transplant • Within 3-6 months post-treatment for acute rejection OR Increased level of immunosuppression (ie, for treatment of donor-specific antibodies)	Stable and low level of immunosuppression: • Beyond 1st year post-transplant on low baseline immunosuppression • Beyond 6 months post-treatment for acute rejection
Medical stability	Unstable allograft function with increased likelihood for increasing level of immunosuppression (ie, for acute rejection, donor-specific antibodies)	Stable and improving allograft function, on tapering level of immunosuppression Low likelihood for need to increase level of immunosuppression	Stable allograft function
Comorbidities	Unstable, multiple, or severe comorbidities: • Obesity • Diabetes mellitus • Chronic lung or cardiac disease • Neurologic and neurodevelopmental conditions • Rheumatologic diseases • Inflammatory bowel disease • Inherited metabolic disorders • Hematologic disorders • Severe liver diseases • Severe kidney diseases Concurrent immunocompromising condition (ie, treatment of malignancy/ PTLD, primary immunodeficiency) Conditions suggesting increased net state of immunosuppressed state (ie, lymphopenia, concomitant CMV)	Stable or improving stability of comorbidities	No comorbidities
Ability to adhere to enhanced precautions in school	Unable to consistently adhere to optimal physical distancing, frequent hand hygiene practices, and/or wearing face covering	Unable to consistently adhere to optimal physical distancing, frequent hand hygiene practices, or wearing a face covering BUT otherwise considered "low risk"	Able to consistently adhere to optimal physical distancing, frequent hand hygiene practices, and wearing a face covering
Local COVID-19 activity[a]	High level of active community spread	Moderate level of active community spread	Stable and low level of active community spread

Note. COVID-19 risk stratification for pediatric kidney transplant recipients based on risk factors for severe COVID-19 in adults, emerging risk factors for severe COVID-19 in children, and extrapolation of risk factors from other respiratory viruses. CMV = cytomegalovirus.
[a]Degree of COVID-19 activity (high, moderate, low) as defined by local public health authorities.

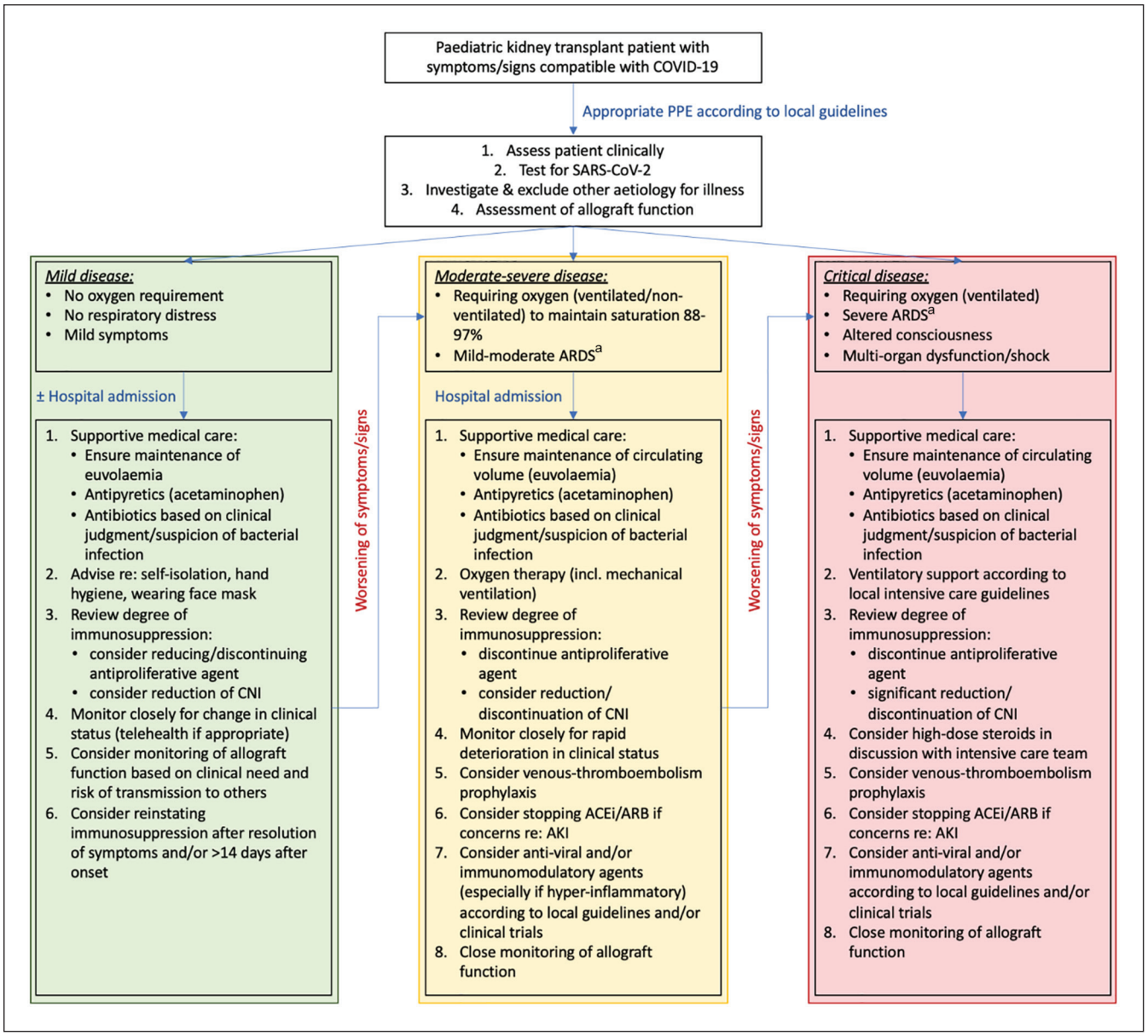

Figure 1. Suggested algorithm of management of pediatric transplant recipients with suspected/confirmed COVID-19.
Note. COVID-19 = coronavirus disease 2019; PPE = personal protective equipment; SARS-CoV-2 = Severe Acute Respiratory Syndrome Coronavirus 2; ARDS = acute respiratory distress syndrome; CNI = calcineurin inhibitors; ACEi = angiotensin-converting enzyme inhibitors; ARB = angiotensin-receptor blockers; AKI = acute kidney injury.
[a]ARDS definition as per Pediatric Acute Respiratory Distress Syndrome criteria.[74]

children with kidney transplants, and their close caregivers/families continue to practice enhanced protective precautions and take a cautious approach to the resumption of physical/in-person activities.[71] We recommend that questions pertaining to the suitability for children with kidney transplants to return to school, daycare, summer camps, and/or employment physically should be considered on a case-by-case basis, with particular consideration of their immunosuppressive burden, exposure risk inherent to their school and/or environment and the presence of other comorbid conditions, psychosocial concerns, and/or learning needs. Suitability should be guided by the epidemiology of COVID-19 cases in the community and by public health.[72,73]

8. Management of Pediatric Kidney Transplant Patients Who Are COVID-19 Positive (see also Figure 1)

8.1. General Principles

8.1.1. We recommend that health care professionals managing patients with suspected/confirmed COVID-19 use appropriate personal

protective equipment (PPE) according to local, provincial, and national guidelines.

8.1.2. We recommend appropriate isolation of patients with suspected/confirmed COVID-19 in all clinical settings (inpatient, intensive care unit, outpatient, emergency department); ideally within a specific COVID-19 unit that is separate from other areas with non-COVID-19 patients.

8.1.3. We recommend that patients with symptoms suggestive of COVID-19 be tested according to local guidelines. Health care professionals should be aware that children may present with atypical symptoms (eg, gastrointestinal symptoms, skin rash or skin lesions), and thus should have a high level of suspicion

8.1.4. We recommend that clinical care decisions for patients be assessed on a case-by-case basis with consideration of patient/family resources, local hospital resources, local guidelines, and in consultation with the multidisciplinary care team with relevant expertise (ie, pediatric transplant, infectious diseases, rheumatology, hematology).

8.1.5. We recommend close monitoring/follow-up of patients (asymptomatic or with mild symptoms) who are managed as outpatients utilizing telehealth (telephone, video calls) for development/worsening of symptoms (tachypnea, respiratory distress, hypoxia) and/or allograft dysfunction that may warrant hospital admission.

8.1.6. We recommend that health care professionals managing pediatric kidney transplant recipients maintain a high index of suspicion and be aware of atypical presentations of COVID-19 in children (eg, gastrointestinal symptoms, multisystem hyperinflammatory syndrome) to make timely diagnoses.

8.2. Immunosuppression management

8.2.1. We recommend that decisions about reduction or discontinuation of immunosuppression for kidney transplant recipients who are COVID-19 positive be considered on a case-by-case basis with close clinical assessment, consideration of the overall degree of immunosuppression, and in consultation with local kidney transplant and infectious diseases experts.

8.2.2. We suggest consideration of initial reduction or discontinuation of antiproliferative agents (mycophenolate mofetil or azathioprine) in mild-to-moderate COVID-19.

8.2.3. We suggest consideration of reduction or discontinuation of calcineurin inhibitors (tacrolimus or cyclosporine) in moderate-to-severe COVID-19 or if there is progressive clinical deterioration.

8.2.4. If immunosuppression is reduced or discontinued, we suggest that the decision on when to reinstate be considered on a case-by-case basis upon clinical assessment of recovery of symptoms, and in consultation with local kidney transplant and infectious diseases experts.

8.3. Considerations for antiviral or additional agents

8.3.1. Currently, there is no definitive evidence to support the efficacy of specific antiviral or additional agents for treatment of COVID-19 in pediatric kidney transplant recipients.

8.3.2. We suggest consideration of systemic corticosteroids in consultation with the intensive care team in severe or critical COVID-19, if there is progressive clinical deterioration or if patients require ventilatory support.

8.3.3. We suggest that the use of these agents be considered in conjunction with local guidelines and practice, emerging evidence or as part of clinical trials.

8.3.4. If antiviral treatment is used, we suggest close monitoring for potential adverse outcomes and therapeutic drug levels due to possible drug-drug interactions.

Rationale

This represents a consensus opinion of a group of pediatric transplant professionals, based on limited evidence base for COVID-19 in children and in pediatric transplant recipients (mostly adult patients).[41,75-80] We suggest that these recommendations be used in conjunction with provincial and/or institutional guidelines. We recommend that caution be exercised when making decisions about immunosuppression adjustment, in consultation with the pediatric kidney transplant team.

Each patient should be carefully considered when presenting with symptoms suspicious for COVID-19. The majority of pediatric patients have mild symptoms and may not require admission.[3,4,6-9,29-34] Reports of COVID-19 in immunosuppressed children with kidney transplants have been few and far between. Currently available evidence suggests that this population is not at increased risk of severe COVID-19 disease.[35-39] However, clinicians should be aware that there have been reports suggesting that transplant recipients may present with atypical symptoms (eg, gastrointestinal symptoms).[81] There have also been reports where children present with dermatologic manifestations (eg, chilblains, vasculitic rash)[82-86] and a pediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS).[87,88]

There are currently no evidence-based reports to support specific adjustments to immunosuppressive medications in relation to COVID-19. Reported clinical experience and expert opinion suggests the initial reduction or discontinuation

of antiproliferative agents (ie, mycophenolate mofetil, azathioprine) in patients with mild-to-moderate COVID-19, extrapolated from the approach for clearance of other viral pathogens.[89] The suggestion for continuation of calcineurin inhibitors (CNIs—tacrolimus and cyclosporine) unless patients develop moderate-to-severe or progressively worsening COVID-19 is based on in vitro evidence that suggests that coronaviridae replication may require intact immunophilin pathways and that CNIs inhibit coronavirus replication.[90-92] It has to be emphasized that the decision to continue/discontinue any immunosuppression lies with the clinician, guided by provincial/local guidelines, with consideration of their potential benefit versus their ongoing immunosuppressive effect.

There is currently limited evidence to support the efficacy of a specific antiviral and/or immunomodulatory agent for the treatment of COVID-19 in adults, and no evidence in children.[93,94] There are currently several antiviral agents being used/studied: (1) remdesivir[95-98]; (2) lopinavir-ritonavir ± ribavirin[99,100]; (3) chloroquine/hydroxychloroquine ± azithromycin.[101-106] Preliminary results from a double-blind, randomized, placebo-controlled trial suggest that intravenous remdesivir may be effective in shortening the time to recovery in adults hospitalized with COVID-19, although no adult or pediatric kidney transplant recipients were included.[98] A randomized, double-blind, placebo-controlled trial assessing hydroxychloroquine use as post-exposure prophylaxis also showed that its use within 4 days of exposure did not prevent COVID-19 illness.[107] Certain patients with COVID-19 and acute respiratory distress syndrome (ARDS) develop hyperinflammatory syndromes which resemble secondary hemophagocytic lymphohistiocytosis (HLH) and CAR-T cell therapy associated cytokine release syndrome (CRS). Raised inflammatory markers (C-reactive protein, ferritin, d-dimer and interleukin-6) is associated with more severe disease and worse prognosis.[108,109] Anakinra (anti-IL1 receptor antagonist) and Tocilizumab (anti-IL6 receptor antagonist) are established treatments for HLH and CRS which have been used to treat the hyperinflammatory syndrome associated with severe COVID-19.[110-114]

There is emerging evidence to suggest that systemic corticosteroid use may be beneficial in hospitalized adults with severe COVID-19 who required oxygen or invasive mechanical ventilation. Preliminary results from the RECOVERY trial group suggest that the use of dexamethasone (dose of 6mg daily for up to 10 days) in hospitalized adults with COVID-19 who required oxygen or invasive mechanical ventilation was associated with lower 28-day mortality.[115] Informed by evidence from 8 randomized trials (including 7184 participants), the World Health Organization (WHO) recommends the use of corticosteroids in severe and critical COVID-19: systemic corticosteroids reduced 28-day mortality in adults with critical COVID-19 (absolute effect estimate 87 fewer deaths per 1000 patients, 95% confidence interval [CI] 124 to 41 fewer deaths per 1000 patients) and in adults with severe disease (absolute effect estimate 67 fewer deaths per 1000 patients, 95% CI 100 to 27 fewer deaths per 1000 patients).[116-122] In contrast, systemic corticosteroid use was found to potentially increase the risk of death in patients without severe COVID-19 (absolute effect estimate 39 more deaths per 1000 patients, 95% CI 12 fewer to 107 more deaths per 1000 patients).[116] The use of systemic corticosteroids for 7 to 10 days in the treatment of COVID-19 was not associated with increased risk of adverse events beyond increasing the incidence of hyperglycemia (absolute effect estimate 46 more per 1000 patients, 95% CI 23 to 72 more per 1000 patient) and hypernatremia (26 more per 1000 patients, 95% CI 13 to 41 more per 1000 patients).[116] At the time of writing, there are no randomized controlled trials specifically informing the use of systemic corticosteroids in adult or pediatric solid-organ transplant recipients with COVID-19. Systemic corticosteroids may be associated with prolonged viral shedding in the immunocompromised host.[123] Their use should be considered in pediatric kidney transplant patients with severe or critical COVID-19 who are progressively worsening or requiring mechanical ventilation, in consultation with the pediatric intensive care team.

Convalescent plasma has also been used in the treatment of patients with severe COVID-19.[124,125] A living Cochrane systematic review that included 4 controlled studies (1 RCT with 103 participants [55 received convalescent plasma] which was stopped early, 3 controlled non-randomized intervention studies [NRSI] with 236 participants [55 received convalescent plasma]) failed to confirm the efficacy of convalescent plasma in treatment of patients with COVID-19.[124,126-129] The risk ratio for all-cause mortality was 0.89 (95% CI, 0.61-1.31) from one NRSI (21 participants); hazard ratio for prolongation of time to death was 0.74 (95% CI, 0.30-1.82) from one RCT (103 participants) and 0.46 (95% CI, 0.22-0.96) from one NRSI (95 participants); and the risk ratio of clinical symptom improvement at 28 days was 1.20 (95% CI, 0.80-1.81) from one RCT (103 participants). The adverse effects reported in the studies included in the Cochrane review were death (4/15 classified as possibly related to transfusion), anaphylaxis, transfusion-associated dyspnea, and transfusion-related acute lung injury.[126] Currently, there is no evidence to support the use of convalescent plasma in the treatment of COVID-19 in pediatric kidney transplant recipients. The various antiviral and immunomodulatory agents are subject to ongoing clinical trials.

Antiviral therapy is likely to yield most benefit in the initial phase of illness. Immunomodulatory therapy may only be indicated if there is clear evidence of a hyperinflammatory state and likely yield most benefit in the later phase of illness. However, pending the results of randomized clinical trials, the risks and benefits of these approaches are unknown. The decision on their use in pediatric kidney transplant recipients should be carefully considered on a case-by-case basis in conjunction with local, regional, and national guidelines and in consultation with relevant pediatric infectious disease, respirology,

rheumatology, hematology, immunology, and pediatric kidney transplant specialists. When used, we recommend close monitoring for possible adverse effects and drug-drug interaction with the patient's immunosuppression.[130,131] We suggest that the use of these agents be considered within a clinical trial setting.

Limitations

A full systematic review of available literature was not undertaken for the sake of expediency in development of this guideline. There is a paucity of literature to support evidence-based recommendations at this time. Suggestions and recommendations were formulated from expert opinion, based on available knowledge and experience, and are subject to the biases associated with this level of evidence. The parallel review process that was created to expedite the publication of this work may not be as robust as standard arms' length peer review processes.

Implications

These recommendations are meant to serve as a guide to pediatric kidney transplant directors, clinicians, and administrators for providing the best patient care in the context of limited resources while protecting patients and health care providers wherever possible by limiting exposure to COVID-19. We recognize that these suggested practices may not be applicable to all provincial and local health authority practices and that they may not be delivered to all patients given the time and resource constraints affecting the individual provincial and local health jurisdiction.

Acknowledgments

CST Paediatric Kidney Transplant Working Group: Chia Wei Teoh, Tom D. Blydt-Hansen, Marie-Michelle Gaudreault-Tremblay, Michelle Ruhl, Aviva Goldberg, Janusz Feber, Steven Arora, Philip Acott, Valerie Langlois, Lorraine Bell, Bethany Foster, Veronique Phan, Catherine Morgan, Julian Midgley, and Lorraine Hamiwka.

Ethics Approval and Consent to Participate

Not applicable

Consent for Publication

Not applicable

Availability of Data and Materials

Not applicable

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

Chia Wei Teoh https://orcid.org/0000-0002-5994-0799

Janusz Feber https://orcid.org/0000-0002-3687-6691

References

1. Center for Systems Science and Engineering (CSSE) at Johns Hopkins University (JHU). COVID-19 Dashboard 2020. https://coronavirus.jhu.edu/map.html. Accessed October 15, 2020.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese Center for Disease Control and Prevention. *JAMA*. 2020;323:1239-1242.
3. CDC Covid-Response Team. Coronavirus disease 2019 in children—United States, February 12-April 2, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(14):422-426.
4. Tagarro A, Epalza C, Santos M, et al. Screening and severity of coronavirus disease 2019 (COVID-19) in children in Madrid, Spain. *JAMA Pediatr*. https://jamanetwork.com/journals/jamapediatrics/fullarticle/2764394. Accessed October 15, 2020.
5. Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. *JAMA*. 2020;323:1335.
6. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. *Pediatrics*. 2020;145:e20200702.
7. Lu X, Zhang L, Du H, et al. SARS-CoV-2 infection in children. *N Engl J Med*. 2020;382(17):1663-1665.
8. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr*. 2020;109(6):1088-1095.
9. Centers for Disease Control and Prevention. Coronavirus disease 2019 (COVID-19)—Information for pediatric healthcare providers 2020. https://www.cdc.gov/coronavirus/2019-ncov/hcp/pediatric-hcp.html#anchor_1587145914005. Accessed October 15, 2020.
10. Government of Canada. Coronavirus disease 2019 (COVID-19): epidemiology update 2020. https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html. Accessed October 15, 2020.
11. Canadian Blood Services. Consensus guidance for organ donation and transplantation services during COVID-19 pandemic. https://profedu.blood.ca/en/organes-et-tissus/covid-19-update-organ-donation-and-transplantation-services. Accessed October 15, 2020.
12. Kumar D, Manuel O, Natori Y, et al. COVID-19: a global transplant perspective on successfully navigating a pandemic. *Am J Transplant*. 2020;20:1773–1779.
13. The Columbia University Kidney Transplant Program. Early description of coronavirus 2019 disease in kidney transplant recipients in New York. *J Am Soc Nephrol*. 2020;31:1150–1156.

14. Fernandez-Ruiz M, Andres A, Loinaz C, et al. COVID-19 in solid organ transplant recipients: a single-center case series from Spain. *Am J Transplant*. 2020;20:1849–1858.
15. Montagud-Marrahi E, Cofan F, Torregrosa JV, et al. Preliminary data on outcomes of SARS-CoV-2 infection in a Spanish single centre cohort of kidney recipients. *Am J Transplant*. 2020;20:2958–2959.
16. Pereira MR, Mohan S, Cohen DJ, et al. COVID-19 in solid organ transplant recipients: initial report from the US epicenter. *Am J Transplant*. 2020;20:1800–1808.
17. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and kidney transplantation. *N Engl J Med*. 2020;382:2475–2477.
18. Nair V, Jandovitz N, Hirsch JS, et al. COVID-19 in kidney transplant recipients. *Am J Transplant*. 2020;20:1819–1825.
19. Ali Husain S, Dube G, Morris H, et al. Early outcomes of outpatient management of kidney transplant recipients with coronavirus disease 2019. *Clin J Am Soc Nephrol*. 2020;15:1174–1178.
20. Alberici F, Delbarba E, Manenti C, et al. A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV2 pneumonia. *Kidney Int*. 2020;97(6):1083-1088.
21. Devresse A, Belkhir L, Vo B, et al. COVID-19 infection in kidney transplant recipients: a single-center case series of 22 cases from Belgium. *Kidney Med*. 2020;2:459–466.
22. Kates OS, Fisher CE, Stankiewicz-Karita HC, et al. Earliest cases of coronavirus disease 2019 (COVID-19) identified in solid organ transplant recipients in the United States. *Am J Transplant*. 2020;20:1885–1890.
23. Crespo M, Mazuecos A, Rodrigo E, et al. Respiratory and gastrointestinal COVID-19 phenotypes in kidney transplant recipients. *Transplantation*. 2020;104:2225–2233.
24. Caillard S, Anglicheau D, Matignon M, et al. An initial report from the French SOT COVID Registry suggests high mortality due to Covid-19 in recipients of kidney transplants [published online ahead of print August 24, 2020]. *Kidney Int*. doi:10.1016/j.kint.2020.08.005.
25. Ali T, Al-Ali A, Fajji L, et al. Coronavirus disease-19: disease severity and outcomes of solid organ transplant recipients: different spectrum of disease in different populations? [published online ahead of print August 24, 2020]. *Transplantation*. doi:10.1097/TP.0000000000003433.
26. Elias M, Pievani D, Randoux C, et al. COVID-19 infection in kidney transplant recipients: disease incidence and clinical outcomes. *J Am Soc Nephrol*. 2020;31:2413–2423.
27. Felldin M, Softeland JM, Magnusson J, et al. Initial report from a Swedish high-volume transplant center after the first wave of the COVID-19 pandemic [published online ahead of print August 20, 2020]. *Transplantation*. doi:10.1097/TP.0000000000003436.
28. Molnar MZ, Bhalla A, Azhar A, et al. Outcomes of critically ill solid organ transplant patients with COVID-19 in the United States [published online ahead of print August 26, 2020]. *Am J Transplant*. doi:10.1111/ajt.16280.
29. Yasri S, Wiwanitkit V. Clinical features in pediatric COVID-19. *Pediatr Pulmonol*. 2020;55(5):1097.
30. Qiu H, Wu J, Hong L, Luo Y, Song Q, Chen D. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis*. 2020;20:689–696.
31. Zhong Z, Zhang Q, Xia H, et al. Clinical characteristics and immunosuppressant management of coronavirus disease 2019 in solid organ transplant recipients. *Am J Transplant*. 2020;20:1916–1921.
32. Castagnoli R, Votto M, Licari A, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. *JAMA Pediatr*. 2020;174(9):882-889. doi:10.1001/jamapediatrics.2020.1467.
33. Shekerdemian LS, Mahmood NR, Wolfe KK, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian pediatric intensive care units. *JAMA Pediatr*. 2020;174:1–6.
34. Zachariah P, Johnson CL, Halabi KC, et al. Epidemiology, clinical features, and disease severity in patients with coronavirus disease 2019 (COVID-19) in a children's hospital in New York City, New York. *JAMA Pediatr*. 2020:e202430.
35. Marlais M, Wlodkowski T, Vivarelli M, et al. The severity of COVID-19 in children on immunosuppressive medication. *Lancet Child Adolesc Health*. 2020;7:E17–E18.
36. Minotti C, Tirelli F, Barbieri E, Giaquinto C, Donà D. How is immunosuppressive status affecting children and adults in SARS-CoV-2 infection? a systematic review. *J Infect*. 2020;81:e61–e66.
37. Bush R, Johns F, Acharya R, Upadhyay K. Mild COVID-19 in a pediatric renal transplant recipient. *Am J Transplant*. 2020;20:2942-2945.
38. Angeletti A, Trivelli A, Magnasco A, et al. Risk of COVID-19 in young kidney transplant recipients. Results from a single-center observational study. *Clin Transplant*. 2020;34:e13889.
39. Melgosa M, Madrid A, Alvárez O, et al. SARS-CoV-2 infection in Spanish children with chronic kidney pathologies. *Pediatr Nephrol*. 2020;35:1521-1524.
40. Chung SJ, Tan EK, Kee T, et al. Practical considerations for solid organ transplantation during the COVID-19 global outbreak. *Transplant Direct*. 2020;6(6):e554.
41. National Institute for Health and Care Excellence (NICE). COVID-19 rapid guideline: renal transplantation. https://www.nice.org.uk/guidance/ng178. Accessed October 15, 2020.
42. Trnka P, White MM, Renton WD, McTaggart SJ, Burke JR, Smith AC. A retrospective review of telehealth services for children referred to a paediatric nephrologist. *BMC Nephrol*. 2015;16:125.
43. Rohatgi R, Ross MJ, Majoni SW. Telenephrology: current perspectives and future directions. *Kidney Int*. 2017;92(6):1328-1333.
44. Zhao Y, Wei L, Liu B, Du D. Management of transplant patients outside hospital during COVID-19 epidemic: a Chinese experience. *Transpl Infect Dis*. 2020:e13327.
45. Ishani A, Christopher J, Palmer D, et al. Telehealth by an interprofessional team in patients with CKD: a randomized controlled trial. *Am J Kidney Dis*. 2016;68(1):41-49.

46. Kang NR, Ahn YH, Park E, et al. Mental health and psychosocial adjustment in pediatric chronic kidney disease derived from the KNOW-Ped CKD study. *Pediatr Nephrol*. 2019;34(10):1753-1764.
47. Moreira JM, Bouissou Morais Soares CM, Teixeira AL, Simoes ESAC, Kummer AM. Anxiety, depression, resilience and quality of life in children and adolescents with pre-dialysis chronic kidney disease. *Pediatr Nephrol*. 2015;30(12): 2153-2162.
48. Golberstein E, Wen H, Miller BF. Coronavirus disease 2019 (COVID-19) and mental health for children and adolescents *JAMA Pediatr*. 2020;174:819–820.
49. Liu JJ, Bao Y, Huang X, Shi J, Lu L. Mental health considerations for children quarantined because of COVID-19. *Lancet Child Adolesc Health*. 2020;4(5):347-349.
50. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Internal Medicine*. 2020;180:934–943.
51. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323:1061-1069.
52. Ni L, Ye F, Cheng ML, et al. Detection of SARS-CoV-2-specific humoral and cellular immunity in COVID-19 convalescent individuals. *Immunity*. 2020;52(6). doi:10.1016/j.immuni.2020.04.023.
53. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181(2):271–280.e8
54. Sparks MA, South A, Welling P, et al. Sound Science before quick judgement regarding RAS blockade in COVID-19. *Clin J Am Soc Nephrol*. 2020;15(5):714-716.
55. Vaduganathan M, Vardeny O, Michel T, McMurray JJV, Pfeffer MA, Solomon SD. Renin-angiotensin-aldosterone system inhibitors in patients with covid-19. *N Engl J Med*. 2020;382(17):1653-1659.
56. European Society of Hypertension. Statement of the European Society of Hypertension (ESH) on hypertension, Renin-Angiotensin System (RAS) blockers and COVID-19 2020. https://www.eshonline.org/spotlights/esh-statement-covid-19/. Accessed October 15, 2020.
57. The International Society of Hypertension. A statement from the International Society of Hypertension on COVID-19 2020. http://ish-world.com/news/a/A-statement-from-the-International-Society-of-Hypertension-on-COVID-19. Accessed October 15, 2020.
58. High Blood Pressure Research Council of Australia. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? 2020. https://www.hbprca.com.au/wp-content/uploads/2020/03/HBPRCA-Statement-on-COVID-19-and-BP-medication-17.03.20.pdf. Accessed October 15, 2020.
59. Hypertension Canada. Hypertension Canada's statement on: hypertension, ACE-inhibitors and angiotensin receptor blockers and COVID-19 2020. https://hypertension.ca/wp-content/uploads/2020/03/2020-30-15-Hypertension-Canada-Statement-on-COVID-19-ACEi-ARB.pdf. Accessed October 15, 2020.
60. Canadian Cardiovascular Society. Guidance from the CCS COVID-19 rapid response team 2020. http://www.ccs.ca/images/Images_2020/CCS_CHFS_Update_COVID__CV_medications_Mar20.pdf. Accessed October 15, 2020.
61. HFSA/ACC/AHA statement addresses concerns re: using RAAS antagonists in COVID-19 2020. https://www.acc.org/latest-in-cardiology/articles/2020/03/17/08/59/hfsa-acc-aha-statement-addresses-concerns-re-using-raas-antagonists-in-covid-19. Accessed October 15, 2020.
62. European Society of Cardiology. Position statement of the ESC council on hypertension on ACE-inhibitors and angiotensin receptor blockers 2020. https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang. Accessed October 15, 2020.
63. The Renal Association UK. The renal association, UK position statement on COVID-19 and ACE inhibitor/angiotensin receptor blocker use 2020. https://renal.org/covid-19/ra-resources-renal-professionals/renal-association-uk-position-statement-covid-19-ace-inhibitorangiotensin-receptor-blocker-use/. Accessed October 15, 2020.
64. British Cardiovascular Society and British Society for Heart Failure. Treatment of patients with ACEi or ARB in relation to COVID-19 2020. https://mailchi.mp/bcs/bcs-newswire-795910?e=a26a153410. Accessed October 15, 2020.
65. American Society of Pediatric Nephrology. Position statement on COVID-19 and ACE inhibitor and angiotensive receptor blocker use in children with hypertension and kidney disease 2020. https://www.aspneph.org/covid-19-information/. Accessed October 15, 2020.
66. Viner RM, Mytton OT, Bonell C, et al. Susceptibility to and transmission of COVID-19 amongst children and adolescents compared with adults: a systematic review and meta-analysis. Medrxiv; 2020. doi:10.1101/2020.05.20.20108126.
67. Viner RM, Russell SJ, Croker H, et al. School closure and management practices during coronavirus outbreaks including COVID-19: a rapid systematic review. *Lancet Child Adolesc Health*. 2020;4(5):397-404.
68. Humphreys KL, Myint MT, Zeanah CH. Increased risk for family violence during the COVID-19 pandemic. *Pediatrics*. 2020;146:e20200982.
69. Silliman Cohen RI, Bosk EA. Vulnerable youth and the COVID-19 pandemic. *Pediatrics*. 2020;146:e20201306.
70. Brooks SK, Webster RK, Smith LE, et al. The psychological impact of quarantine and how to reduce it: rapid review of the evidence. *Lancet*. 2020;395(10227):912-920.
71. Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet*. 2020;395:1973-1987.
72. The Hospital for Sick Children T. COVID19: recommendations for school reopening. 2020. http://www.sickkids.ca/PDFs/About-SickKids/81407-COVID19-Recommendations-for-School-Reopening-SickKids.pdf
73. Downes KJ, Danziger-Isakov LA, Cousino MK, et al. Return to school for pediatric solid organ transplant recipients in the United States during the COVID-19 pandemic: expert opinion on key considerations and best practices [published online ahead of print August 4, 2020]. *J Pediatric Infect Dis Soc*. 2020. doi:10.1093/jpids/piaa095.

74. The Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. *Pediatr Crit Care Med*. 2015;16(5):428-439.
75. British Transplantation Society and the Renal Association. Guidance on the management of transplant recipients diagnosed with or suspected of having COVID19. https://bts.org.uk/wp-content/uploads/2020/05/Clinical-management-of-transplants-and-immunosuppression-updated-1st-May-FINAL-svg-002.pdf. Accessed October 15, 2020.
76. Ritschl PV, Nevermann N, Wiering L, et al. Solid organ transplantation programs facing lack of empiric evidence in the COVID-19 pandemic: a by-proxy society recommendation consensus approach. *Am J Transplant*. 2020;20:1826–1836.
77. Indian Society of Pediatric Nephrology. Coronavirus disease 2019 (COVID-19): information for caregivers and health care personnel managing children with renal diseases. http://www.ispnonline.org/pdf/COVID-19_and_children_with_renal_diseases_ISPN_Doc.pdf. Accessed October 15, 2020.
78. Alberici F, Delbarba E, Manenti C, et al. Management of patients on dialysis and with kidney transplant during SARS-COV-2 (COVID-19) pandemic In Brescia, Italy. *Kidney Int Rep*. 2020;5:580–585.
79. Lopez V, Vazquez T, Alonso-Titos J, et al. Recommendations on management of the SARS-CoV-2 coronavirus pandemic (Covid-19) in kidney transplant patients. *Nefrologia*. 2020;40:265–271.
80. Royal College of Paediatrics and Child Health. COVID-19—clinical management of children admitted to hospital with suspected COVID-19 2020. https://www.rcpch.ac.uk/sites/default/files/generated-pdf/document/COVID-19—clinical-management-of-children-admitted-to-hospital-with-suspected-COVID-19.pdf. Accessed October 15, 2020.
81. Guillen E, Pineiro GJ, Revuelta I, et al. Case report of COVID-19 in a kidney transplant recipient: does immunosuppression alter the clinical presentation. *Am J Transplant*. 2020;20:1875-1878.
82. Andina D, Noguera-Morel L, Bascuas-Arribas M, et al. Chilblains in children in the setting of COVID-19 pandemic. *Pediatr Dermatol*. 2020;37:406–411.
83. Castelnovo L, Capelli F, Tamburello A, Faggioli PM, Mazzone A. Symmetric cutaneous vasculitis in COVID-19 pneumonia. *J Eur Acad Dermatol Venereol*. 2020;34(8):e362-e363.
84. Joob B, Wiwanitkit V. Chilblains-like lesions in children following suspected COVID-19 infection. *Pediatr Dermatol*. 2020;37:437–440.
85. Piccolo V, Neri I, Filippeschi C, et al. Chilblain-like lesions during COVID-19 epidemic: a preliminary study on 63 patients. *J Eur Acad Dermatol Venereol*. 2020;34:e291-e293.
86. Recalcati S, Barbagallo T, Frasin LA, et al. Acral cutaneous lesions in the time of COVID-19. *J Eur Acad Dermatol Venereol*. 2020;34:e346-e347.
87. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet*. 2020;395:1607-1608.
88. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19 2020. https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19. Accessed October 15, 2020.
89. Maggiore U, Abramowicz D, Crespo M, et al. How should I manage immunosuppression in a kidney transplant patient with COVID-19? An ERA-EDTA DESCARTES expert opinion. *Nephrol Dial Transplant*. 2020;35(6):899-904.
90. Willicombe M, Thomas D, McAdoo S. COVID-19 and calcineurin inhibitors: should they get left out in the storm. *J Am Soc Nephrol*. 2020;31:1145-1146.
91. Carbajo-Lozoya J, Muller MA, Kallies S, Thiel V, Drosten C, von Brunn A. Replication of human coronaviruses SARS-CoV, HCoV-NL63 and HCoV-229E is inhibited by the drug FK506. *Virus Res*. 2012;165(1):112-117.
92. Pfefferle S, Schopf J, Kogl M, et al. The SARS-coronavirus-host interactome: identification of cyclophilins as target for pan-coronavirus inhibitors. *Plos Pathog*. 2011;7(10):e1002331.
93. Chiotos K, Hayes M, Kimberlin DW, et al. Multicenter initial guidance on use of antivirals for children with COVID-19/SARS-CoV-2 [published online ahead of print April 22, 2020]. *J Pediatric Infect Dis Soc*. doi:10.1093/jpids/piaa045.
94. Siemieniuk RA, Bartoszko JJ, Ge L, et al. Drug treatments for covid-19: living systematic review and network meta-analysis. *BMJ*. 2020;370:m2980.
95. Grein J, Ohmagari N, Shin D, et al. Compassionate use of remdesivir for patients with severe COVID-19. *N Engl J Med*. 2020;382:2327-2336.
96. Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet*. 2020;395(10236):1569-1578.
97. National Institutes of Health. NIH clinical trial shows Remdesivir accelerates recovery from advanced COVID-19 2020. https://www.nih.gov/news-events/news-releases/nih-clinical-trial-shows-remdesivir-accelerates-recovery-advanced-covid-19. Accessed October 15, 2020.
98. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19—preliminary report. *New England Journal of Medicine*. 2020;383:992-994.
99. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med*. 2020;382(19):1787-1799.
100. Hung IF-N, Lung K-C, Tso EY-K, et al. Triple combination of interferon beta-1b, lopinavir–ritonavir, and ribavirin in the treatment of patients admitted to hospital with COVID-19: an open-label, randomised, phase 2 trial. *Lancet*. 2020;395:1695–1704. doi:10.1016/S0140-6736(20)31042-4.
101. Geleris J, Sun Y, Platt J, et al. Observational study of hydroxychloroquine in hospitalized patients with Covid-19. *N Engl J Med*. 2020;382:2411-2418.
102. Chen Z, Hu J, Zhang Z, et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. https://publons.com/publon/31023519/. Accessed October 15, 2020.

103. Mahevas M, Tran VT, Roumier M, et al. Clinical efficacy of hydroxychloroquine in patients with covid-19 pneumonia who require oxygen: observational comparative study using routine care data. *BMJ*. 2020;369:m1844.
104. Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. *BMJ*. 2020;369:m1849.
105. Borba MGS, Val FFA, Sampaio VS, et al. Effect of high vs low doses of chloroquine diphosphate as adjunctive therapy for patients hospitalized with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection. *JAMA Network Open*. 2020;3(4):e208857.
106. Huang M, Tang T, Pang P, et al. Treating COVID-19 with chloroquine. *J Mol Cell Biol*. 2020;12(4):322-325.
107. Boulware DR, Pullen MF, Bangdiwala AS, et al. A randomized trial of hydroxychloroquine as postexposure prophylaxis for Covid-19. *N Engl J Med*. 2020;383:517-525.
108. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395(10229):1054-1062.
109. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020;46(5):846-848.
110. Allam SR, Dao A, Madhrira MM, et al. Interleukin-6 receptor antagonist therapy to treat SARS-CoV-2 driven inflammatory syndrome in a renal transplant recipient. *Transpl Infect Dis*. 2020:e13326.
111. Aouba A, Baldolli A, Geffray L, et al. Targeting the inflammatory cascade with anakinra in moderate to severe COVID-19 pneumonia: case series. *Ann Rheum Dis*. 2020;79(10):1381-1382.
112. Dimopoulos G, de Mast Q, Markou N, et al. Favorable anakinra responses in severe Covid-19 patients with secondary hemophagocytic lymphohistiocytosis. *Cell Host Microbe*. 2020;28:117–123.e1.
113. Capra R, De Rossi N, Mattioli F, et al. Impact of low dose tocilizumab on mortality rate in patients with COVID-19 related pneumonia. *Eur J Intern Med*. 2020;76:31-35.
114. Luo P, Liu Y, Qiu L, Liu X, Liu D, Li J. Tocilizumab treatment in COVID-19: a single center experience. *J Med Virol*. 2020;92(7):814-818.
115. Recovery Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19—preliminary report. *N Engl J Med*. 2020.
116. Lamontagne F, Agoritsas T, Macdonald H, et al. A living WHO guideline on drugs for covid-19. *BMJ*. 2020;370:m3379.
117. WHO Rapid Evidence Appraisal for COVID-19 Therapies Working Group. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19: a meta-analysis. *JAMA*. 2020;324(13):1330-1341.
118. Tomazini BM, Maia IS, Cavalcanti AB, et al. Effect of dexamethasone on days alive and ventilator-free in patients with moderate or severe acute respiratory distress syndrome and COVID-19: the CoDEX randomized clinical trial. *JAMA*. 2020;324(13):1-11.
119. Dequin PF, Heming N, Meziani F, et al. Effect of hydrocortisone on 21-day mortality or respiratory support among critically ill patients with COVID-19: a randomized clinical trial. *JAMA*. 2020;324(13):1-9.
120. Writing Committee for the R-CAPI, Angus DC, Derde L, et al. Effect of hydrocortisone on mortality and organ support in patients with severe COVID-19: the REMAP-CAP COVID-19 corticosteroid domain randomized clinical trial. *JAMA*. 2020;324(13):1317-1329.
121. Corral L, Bahamonde A, Arnaiz delas Revillas F, et al. GLUCOCOVID: a controlled trial of methylprednisolone in adults hospitalized with COVID-19 pneumonia. medRxiv. https://www.medrxiv.org/content/10.1101/2020.06.17.20133579v1.full.pdf. Accessed October 15, 2020.
122. Jeronimo CMP, Farias MEL, Val FFA, et al. Methylprednisolone as adjunctive therapy for patients hospitalized with COVID-19 (Metcovid): a randomised, double-blind, phase IIb, placebo-controlled trial [published online ahead of print August 12, 2020]. *Clin Infect Dis*. doi:10.1093/cid/ciaa1177.
123. Ogimi C, Greninger AL, Waghmare AA, et al. Prolonged shedding of human coronavirus in hematopoietic cell transplant recipients: risk factors and viral genome evolution. *J Infect Dis*. 2017;216(2):203-209.
124. Duan K, Liu B, Li C, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proc Natl Acad Sci U S A*. 2020;117(17):9490-9496.
125. Shen C, Wang Z, Zhao F, et al. Treatment of 5 critically ill patients with COVID-19 with convalescent plasma. *JAMA*. 2020;323(16):1582-1589.
126. Piechotta V, Chai KL, Valk SJ, et al. Convalescent plasma or hyperimmune immunoglobulin for people with COVID-19: a living systematic review. *Cochrane Database Syst Rev*. 2020;7:CD013600.
127. Li L, Zhang W, Hu Y, et al. Effect of convalescent plasma therapy on time to clinical improvement in patients with severe and life-threatening COVID-19: a randomized clinical trial. *JAMA*. 2020;324(5):460-470.
128. Liu STH, Lin H-M, Baine I, et al. Convalescent plasma treatment of severe COVID-19: a matched control study. medRxiv. https://www.medrxiv.org/content/10.1101/2020.05.20.20102236v1. Accessed October 15, 2020.
129. Zeng QL, Yu ZJ, Gou JJ, et al. Effect of convalescent plasma therapy on viral shedding and survival in patients with coronavirus disease 2019. *J Infect Dis*. 2020;222(1):38-43.
130. Bartiromo M, Borchi B, Botta A, et al. Threatening drug-drug interaction in a kidney transplant patient with Coronavirus disease 2019 (COVID-19). *Transpl Infect Dis*. 2020;22(4):e13286.
131. Elens L, Langman LJ, Hesselink DA, et al. Pharmacologic treatment of transplant recipients infected with SARS-CoV-2: considerations regarding therapeutic drug monitoring and drug-drug interactions. *Ther Drug Monit*. 2020;42(3):360-368.