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Management of Patients With Glomerulonephritis During the COVID-19 Pandemic: Recommendations From the Canadian Society of Nephrology COVID-19 Rapid Response Team

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Abstract

Purpose of program: This article will provide guidance on how to best manage patients with glomerulonephritis (GN) during the COVID-19 pandemic.

Sources of information: We reviewed relevant published literature, program-specific documents, and guidance documents from international societies. An informal survey of Canadian nephrologists was conducted to identify practice patterns and expert opinions. We hosted a national webinar with invited input and feedback after webinar.

Methods: The Canadian Society of Nephrology (CSN) Board of Directors invited physicians with expertise in GN to contribute. Specific COVID-19-related themes in GN were identified, and consensus-based recommendations were made by this group of nephrologists. The recommendations received further peer input and review by Canadian nephrologists via a CSN-sponsored webinar. This was attended by 150 kidney health care professionals. The final consensus recommendations also incorporated review by Editors of the *Canadian Journal of Kidney Health and Disease*.

Key findings: We identified 9 areas of GN management that may be affected by the COVID-19 pandemic: (1) clinic visit scheduling, (2) clinic visit type, (3) provision of multidisciplinary care, (4) blood and urine testing, (5) home-based monitoring essentials, (6) immunosuppression, (7) other medications, (8) patient education and support, and (9) employment.

Limitations: These recommendations are expert opinion, and are subject to the biases associated with this level of evidence. To expedite the publication of this work, a parallel review process was created that may not be as robust as standard arm's length peer review processes.

Implications: These recommendations are intended to provide optimal care during the COVID-19 pandemic. Our recommendations may change based on the evolving evidence.

Keywords

glomerulonephritis, infectious diseases, chronic kidney disease, inflammation

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Purpose

Kidney programs across Canada face challenges delivering care during the COVID-19 pandemic. Chronic kidney disease (CKD) and preexisting autoimmune diseases may increase the risk of COVID-19-related complications. In addition, physical distancing has impacted the ways in which health care providers deliver care.

To date, international and national nephrology societies have provided few, if any, recommendations for nondialysis care in the setting of the COVID-19 pandemic. In response

to this, the Canadian Society of Nephrology/Societe canadienne de nephrology (CSN/SCN) has created recommendations in an effort to provide optimal care to patients with glomerulonephritis (GN) while we ensure the safety of the health care team.

This document provides suggestions on how to provide the best possible care for patients living with GN during the COVID-19 pandemic. Patients with GN have health care needs that differ from those of patients with other forms of kidney disease, including CKD, end-stage kidney disease including transplantation. The care of other patients with kidney disease, including those with less advanced forms of CKD, is outside the scope of this document.

The recommendations outlined in this guidance document represent best practices based on information available at the time of writing on April 24, 2020.

Methods

In the context of the pandemic, individual regional programs rapidly developed policy. The CSN developed the COVID-19 rapid response team (RRT) by recruiting volunteers from within the CSN Board who identified other experts within the kidney community. Available COVID-19 documents from programs across the country were collected. Other national and international kidney agency literature and webinars were viewed for recommendations that could be applied to the Canadian environment. A review of the published literature was undertaken. A survey was conducted, April 9 to 15, 2020, of GN care provision in the era of COVID-19 in Canadian GN programs. Experts in the United Kingdom were contacted to provide experiential perspectives of GN care in the more advanced stages of the COVID-19 pandemic. Recommendations were developed based on the best judgment of the CKD and GN working groups, after consideration of known published peer-reviewed and non-peer-reviewed preprints, the CSN GN survey, guidelines from other jurisdictions, and input from infection control experts. Final revisions followed a public webinar of 150 kidney professionals sponsored by the CSN.

Context: Narrative Summary of CSN GN Care Survey Results; Current State as of April 2020

We surveyed 7 GN programs with representation from 6 provinces about GN clinic practices in the setting of the COVID-19 pandemic. In general, most programs have enacted similar approaches to the provision and delivery of GN care. No programs reported significant health care resource concerns at this time.

Frequency of Clinic Visits

Most programs are continuing their prescheduled clinic visits. Some programs are deferring follow-up of "routine" stable patients, as defined by usual follow-up greater than 3- to 6-month frequency. Some programs commented that routine care was not deferred as the duration of the pandemic is unknown and will likely continue to have an impact on care delivery in coming months.

Type of Visit

Clinic visits are almost universally being delivered virtually unless there is an urgent indication for in-person visit. Virtual visits are being delivered via telephone, video, and hosted video platforms. Significant barriers to video consultation have included lack of resources including Internet availability and computer technology to perform video visits. Although programs are adapting to the remote delivery of care, telephone call visits predominate at this time. For in-person clinic visits, local Infection Prevention and Control (IPAC) guidelines with respect to prescreening for symptoms and personal protective equipment are followed.

Blood Work Frequency

All programs are continuing to monitor blood work because it is essential for monitoring disease activity, treatment-related toxicities, and drug levels. Blood work is primarily performed in community laboratories with additional

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mechanisms in place to reduce risk of COVID-19 transmission, including physical distancing.

Multidisciplinary Care

All programs with preexisting multidisciplinary care are continuing to provide multidisciplinary care at this time. This is being provided virtually using the same platform (either telephone or video) as the physician visit.

Kidney Biopsies

Kidney programs have not provided guidance regarding kidney biopsy practice, which remains at physician discretion. Kidney biopsies continue to be performed in patients with urgent presentations, and where a tissue diagnosis is required to initiate or alter management. Elective kidney biopsies have generally been deferred. Telephone screening for COVID-19 symptoms is being performed before kidney biopsy procedures.

Challenges identified. The challenges include (1) potential supply chain disruptions for medications (notably hydroxychloroquine, but potentially other medications), (2) additional time required for telehealth visits, (3) communication challenges with telephone consultations with lack of nonverbal cues (this was noted to be more challenging with new patients), (4) making informed decisions regarding immunosuppression both with active and remission of GN, (5) lack of current knowledge of the effects of COVID-19 on the GN population.

Successes identified. The successes include (1) ability to continue to deliver care in a rapidly changing environment, (2) ability to continue to deliver multidisciplinary team care, (3) 1 provincial program has modified provincial drug dispensing to monthly to mitigate against the risk of drug shortages.

Recommendations

Scheduling Clinic Visits

1. We suggest that adherence to clinic visit schedules continue *where resources permit.*
2. We suggest that patients receive their clinic visit regardless of whether blood work is required or available.
3. We suggest that the center's plan for ongoing GN care be preemptively communicating to all GN patients
4. We suggest that consideration be given to increasing the interval between subsequent follow-up visits as clinical status permits.

Rationale. Continuing clinical care as previously scheduled will ensure patients continue to receive appropriate care, personalized advice regarding their immunosuppression, and the support of the clinical program in case of COVID-19 infection. Blood and urine tests are generally not routine in this population because they are required for assessment of disease activity, complications of therapy, and drug-level monitoring. Ongoing communication between care providers and patients is essential to avoid patient-initiated clinic visit cancelation with attendant risk of becoming lost to follow-up. A local or provincially developed letter to all patients with GN may be helpful.

Clinic Visit Type

1. We suggest that patients receive telehealth visits as permitted by local and provincial guidance unless an in-center visit is deemed required by the care team.[1,2]
2. We suggest, where resources permit, that in advance of the telehealth visit, patients are telephoned with instructions regarding blood and urine tests, preparing a current medication list, and performing blood pressure readings and weights (if required) in advance of their telehealth visit.
3. We suggest that patients be informed how to seek medical care in case of development of symptoms of COVID-19. This may include information regarding 911 for life-threatening symptoms, Emergency Room (ER), primary care provider, or GN clinic. We suggest that patients contact their GN clinic if they develop COVID-19 symptoms for advice on medications.
4. We suggest that patients who require an in-person visit receive a COVID-19 screening telephone call using local IPAC-guided questions.[1]
5. We suggest that patients who screen positive be directed to the most appropriate facility in keeping with local IPAC guidelines.

Rationale. In this document, we adhere to the World Health Organization's broad description of the term telehealth. Telehealth refers to the use of various types of information and communication technologies to deliver health care services where providers and patients are separated by distance.[3] Telehealth includes technologies such as telephone and web-based applications (eg, teleconsultations and teleconferences, e-mails, digital still images, videos), among others. Telehealth can provide patients with ongoing access to care while maintaining physical distancing, aiming to reduce the risk of COVID-19 transmission. Evidence for provision of GN care via telehealth is generalized from available literature including CKD clinic, general nephrology (of which 5.7% had chronic GN), diabetic nephropathy, and pediatric nephrology (of which 16% had nephrotic syndrome).[4-7]

Communication with patients prior to telehealth visits with reminders to have blood work completed, medication list prepared, and blood pressure and weights documented should improve both clinic efficiency and effectiveness. Recommended actions in case of COVID-19 infection may be disseminated to patients via a formal letter or communicated verbally at the time of telehealth visit. We suggest that GN clinic contact information should include usual contact telephone numbers as well as out-of-hours contact number and additional instructions, if needed. In-person visits should be reserved for patients requiring urgent assessment, to minimize exposure risk for both health care providers and patients.

Provision of Multidisciplinary Care

1. We suggest that multidisciplinary care continue to be provided as resources permit.
2. We suggest that care providers be physically distanced during all clinical encounters, for both in-person and telehealth visits (as local resources permit).[8]
3. We suggest that providers communicate when possible with one another via telephone calls, with secure e-mails or through electronic medical records, where available.
4. We suggest that paperwork generated during clinic visits (prescriptions, blood work, and other requisitions) be handled by as few individuals as possible.
5. We suggest that clinic documentation be continued in keeping with usual standard of care, and that information be conveyed to the primary care provider in keeping with usual practice.

Rationale. The use of telehealth to deliver CKD multidisciplinary care has previously been demonstrated to be noninferior to standard in-person care, with regard to the composite outcome of death, hospitalization, emergency department visits, and admission to skilled nursing facilities.[7] Usage of telehealth will allow for continued multidisciplinary care of this complex population.

Blood and Urine Tests

1. We suggest that patients continue to have blood and urine tests done before clinic appointments. This is based on current Canadian COVID-19 prevalence remaining low.
2. We suggest that blood and urine tests can be deferred to community laboratories where available, with consideration given to potential costs incurred in community laboratories. We suggest that drug-level monitoring (tacrolimus, cyclosporine) continue as required with the location determined by each center.
3. We suggest that systems should be established to follow up on laboratory values if a clinic visit is deferred in a time-sensitive manner.

Rationale. This advice is based on current Canadian COVID-19 prevalence rates remaining low. Laboratory management forms the cornerstone of monitoring for disease activity, treatment toxicity, and efficacy. LifeLabs and Dynacare have instituted policies to minimize infection risk. Some specialized tests, such as anti-phospholipase A2 receptor antibody, are available only through the hospital laboratory. Other tests (such as antineutrophil cytoplasmic antibody [ANCA]) may have their costs covered through the hospital laboratory, but billed to the patient when done at a private laboratory. Health care workers should be aware of local practices and constraints and make efforts not to increase direct costs for patients, especially without discussion of the issue in advance.

Home-Based Monitoring Essentials

1. We suggest that patients monitor their blood pressures at home (where resources permit), ideally using a Hypertension Canada Approved device.[9]
2. We suggest that patients with private drug insurance should receive prescriptions for home blood pressure monitoring cuffs. Patients older than 65 years may be eligible for provincial coverage depending on the province of residence. For patients who are unable to obtain access to home blood pressure monitoring, we suggest a referral to physical work to help patients access local resources.

Rationale. Having tools to monitor blood pressure and weights is essential to facilitate telehealth visits and enable the provision of important disease-modifying therapy and appropriate symptom management. Patients with GN should be supplied with these basic tools, regardless of socioeconomic status.

Medication—Immunosuppression

1. We suggest that treatment be provided according to current best practice guidelines in patients with active acute GN.[10-12] This will involve consideration of underlying diagnosis, kidney biopsy findings, degree of renal dysfunction, risk of progressive loss of kidney function, level of proteinuria, morbidity of untreated nephritic and nephrotic syndromes, and underlying comorbidities.
2. We suggest that significant treatment reductions or changes be deferred until postpandemic to mitigate the risk of disease relapse, flare, or progression requiring re-induction in clinically stable patients.

There is a significant risk of disease relapse, flare, or progression with cessation or interruption of immunosuppressive regimens.[1,13-16]

3. We suggest that treatment decisions with regard to continuing or modifying immunosuppression be individualized in the event of COVID-19 infection.[17]
4. We recommend that patients already treated with hydroxychloroquine should continue uninterrupted. Hydroxychloroquine remains under investigation for the treatment of COVID-19.[18,19]
5. We suggest that the geographic location of administration of intravenous immunosuppression will continue to be based on local best practices. This may involve the use of infusion centers outside the hospital setting. We suggest adhering to local IPAC policies, and that infusion centers be made aware of patients' immunocompromised condition.[2]
6. We recommend that patients have at least 1 month's supply of medications available and, where appropriate, adequate prescription refills to allow for timely dispensing of immunosuppression.[20]

Rationale. We do not currently know the risk of acquiring COVID-19 in patients with GN. Initial reports have indicated an increased risk of intensive care unit admission and requirement for mechanical ventilation in those with preexisting CKD.[21] Reports of patients with GN are sparse. Registries of rheumatology patients, including rheum-covid.org and UKIVAS, have reported COVID-19 infection in patients with lupus and ANCA-associated vasculitis, but we do not yet have reports of clinical outcomes or specifically kidney outcomes.[22] In a single-center study of patients with either rheumatologic or inflammatory bowel disease, 14 of 86 patients required hospitalization with an increased risk identified in those treated with corticosteroids, methotrexate, and hydroxychloroquine.[23] Limited data are available on the effect of COVID-19 on those who are receiving immunosuppression for GN.[17] There is, however, a well-described risk of increased severity and/or frequency of other infections.[24,25]

Induction therapy decisions will include consideration of underlying diagnosis, kidney biopsy findings, degree of kidney dysfunction, level of proteinuria, and underlying comorbidities. There is little evidence to guide appropriate medication changes in this rapidly evolving clinical setting. In kidney transplant recipients with severe infections, strategies reported have included reduction/withdrawal of antimetabolites followed sequentially by other immunosuppression.[26] These strategies remain investigational and at the discretion of the physician based on clinical status.

Medication—Other

1. We recommend continuing angiotensin-converting enzyme inhibitor/angiotensin receptor blockers (ACEi/ARBs) as prescribed. The interaction between the renin-angiotensin-aldosterone system (RAAS) system and COVID-19 by virtue of the binding of the virus to ACE-2 has generated theories of both potential harm and benefit of RAAS inhibitor use during the pandemic. Observational studies have found no significant increase in the risk of positive COVID-19 test, severe COVID-19 infection, and death in hospital from COVID-19.[27-29]
2. We suggest that ACEi and ARBs should be temporarily suspended in accordance with usual sick day rules.[30,31]
3. We suggest that the decision to start ACEi or ARBs, given the increased need for monitoring and potential for side effects,[32] be individualized, taking into account the patient's clinical context and the current local epidemiology of COVID-19. This risk may be outweighed in individual circumstances.[33] In the treatment of GN, ACEi/ARBs form the cornerstone of conservative management with potential to reduce the requirement for immunosuppression through reduction in proteinuria.

Rationale. The interactions between the RAAS and SARS-CoV-2, by virtue of the binding of the virus to ACE-2, have generated theories of both potential harm and benefit of RAAS inhibitor use during the pandemic. Evidence supporting or refuting these theories is lacking; we agree with the Canadian Cardiovascular Society and multiple other relevant societies, that ACEi and ARBs should not be discontinued as a result of the COVID-19 pandemic.[27,28,34,35]

Patient Education/Support

1. We suggest that usual sick day rules be reinforced during telehealth consultations, including explicit advice on specific medications that should be temporarily suspended for that individual patient, should they become unwell.
2. We suggest that patients requiring education about their diagnosis and treatment plan receive education delivered virtually during the patient encounter and further supported by electronic or paper tools. Where access to Internet and electronic devices is limited, we suggest mailing education materials or conveying the information by telephone.
3. We suggest compiling, reviewing, and curating lists of information from Web Sites maintained by professional organizations, and patient-driven online forums, and sharing these with patients where appropriate.
4. We suggest that patients with GN be given clear guidance on who they should contact if any concerns arise. Patients should be advised to contact the clinic team, in keeping with usual practice, for changes in clinical status. Contact numbers that are accessible

during weekdays may be different than weekend contact numbers, and all patients should be made aware of them. We suggest a dedicated contact telephone number that is routinely answered/monitored during office hours be made available and be easily accessible on the hospital Web Site or available on the information letter that some centers may choose to send.

Rationale. Programs may consider reinforcing sick day advice with existing written patient information leaflets.[30] This is of particular relevance in those prescribed long-term corticosteroids, immunosuppression, ACEi/ARBs, and diuretics.[1,31]

Glomerulonephritis educational resource examples include the following:

1. cansolveckd.ca/gnregistry/about-gn
2. https://www.ontariorenalnetwork.ca/en/about/our-work/glomerulonephritis
3. nephcure.org

COVID-19-specific educational resource examples include the following:

- https://www.era-edta.org/en/covid-19-news-and-information/
- kidneycareuk.org/news-and-campaigns/coronavirus-advice/
- bcrenalagency.ca/health-info/prevention-public-health/novel-coronavirus-(covid-19)
- ontario.ca/page/2019-novel-coronavirus
- https://www.canada.ca/en/public-health/services/diseases/coronavirus-disease-covid-19.html

Employment

We suggest a case-by-case approach when considering the question of whether patients with GN should refrain from work or school. Modified work/learning practices including working/attending remotely are generally recommended.

Consideration should be given to the following:

- Cumulative immunosuppressive burden
- Chronic kidney disease G category
- Exposure risk inherent in their occupation
- Concomitant comorbidities (eg, diabetes, hypertension, cardiovascular disease)[36]
- Patients may require supportive letters to assist with the establishment of safe working/learning environments.

Future Directions

Observational data on disease-specific risk morbidity and mortality due to COVID-19 infection in patients with GN are needed to assist in guiding treatment recommendations and provide patient-specific estimates of the risks of immunosuppression in the context of the COVID-19 pandemic. We need to determine the impact of COVID-19 serological testing on future immunosuppression decisions. In addition, the approach to COVID-19 Immunization (if/when available) will require clarity in this population.

Limitations

A full systematic review of available literature was not attempted for the sake of expediency in developing this guidance. In addition, recommendations and suggestions outlined here have not been formally proven in clinical environments, and we recognize that local context may impede their implementation.

Implications

These suggestions are meant to serve as a guide for providing the best patient care we can in a limited resource environment while protecting patients and health care providers wherever possible by limiting exposure to COVID-19. We recognize that these suggested practices may not be delivered to all patients, given time constraints, resource constraints, and local health authority priorities.

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Information Sources

On behalf of the Canadian Society of Nephrology Renal COVID-19 Rapid Response Team, information sources include the following:
https://www.lifelabs.com/covid-19-updates/
https://www.dynacare.ca/important-notices/covid-19-important-information.aspx

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