Guidance on Coronavirus Disease 2019 (COVID-19) for Transplant Clinicians

Updated 16 March 2020

INTRODUCTION

This is the third update of Coronavirus Disease 2019 (COVID-19) Guidance from the TID Section of TTS. It is important to note that information about this disease and our understanding of this virus and its impact on transplantation is evolving rapidly so the guidance may change over time. We plan to regularly update the guidance as new information becomes available.

Since our initial guideline, COVID-19 has been declared a "public health emergency of international concern" and a pandemic by WHO. Further, the disease has been given the name Coronavirus Disease 2019 (COVID-19) and is caused by the virus named SARS CoV-2. As of 16 March 2020, there are 167,511 confirmed cases globally 151 countries (https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/). Ongoing community transmission has been noted in several countries in Europe, Asia and the United States.

As this is an emerging infection, we advise that, for decision making, careful attention to reports from local health authorities as well as review of updated data is essential.

EPIDEMIOLOGY

Initially limited to Wuhan, infection with COVID-19 is being reported from multiple Chinese cities

Recently, rates have been declining in China but increasing rapidly throughout Europe, Iran and the United States. Due to the change in locations experiencing local or national outbreaks, the relevant geographic exposure has expanded; the most up to date information can be found at relevant websites: https://www.arcgis.com/apps/opsdashboard/index.html#/bda7594740fd40299423467b48e9ecf6.

Special consideration should be given to countries with under resourced healthcare systems and high rates of travel and trade with China, Japan, South Korea and Iran; they may not be reporting cases for lack of diagnostic capacity.

GENERAL COMMENTS ON CLINICAL FEATURES OF RELEVANCE TO TRANSPLANT PHYSICIANS

Initial case series have been published that provide a picture of the clinical spectrum of COVID-19 from centers in Wuhan.[2,3] Imaging demonstrates pneumonia in the majority of patients that are hospitalized (75-100%). Patients with less severe infections may have lower rates of abnormalities. Further, there may be differences in indication for hospitalization around the world (China appears to be admitting the more severely ill patients while other countries are admitting all that are diagnosed for public health containment purposes).[4] Mortality appears to be age dependent, with the highest rates among older adults (Age 50-59: 1.3%, 60-69: 3.6%, 70-79: 8%, 80+: 14.8%).[5] There is a paucity of data on mild and asymptomatic infections which will alter these estimates.

Although many patients had co-morbidities in the reported series, data on transplant patients is limited; patients with cancer are more likely to have more severe disease (HR 3.56, 95% CI 1.65-7.69).[6] Hence a description of the disease in transplant recipients is still not available. Nevertheless the lymphocyte count was lower in those who required ICU care, and in those who perished.[2] It is not possible to tell if lymphopenia was a manifestation of a more severe form of disease, or if it predisposed to severe disease. Many transplant recipients have medication-induced lymphopenia. Particularly close attention should be paid to transplant patients with suspected or confirmed COVID-19 infection who are lymphopenic. Such attention may include admission (rather than care at home) and paying careful heed to oxygen saturation.

Among comorbidities of interest, more patients who required ICU care had cardiovascular diseases, compared with those who did not require ICU care.[2]

Patient-to-patient, and patient-to-healthcare worker infection were described and human-to-human transmission has been confirmed.[2,7] As such, strict infection prevention practices are essential.[8]

The mainstay of diagnostic testing is the use of PCR to detect presence of virus in samples collected from the respiratory tract of persons under investigation. Although viral load is generally highest early in the illness, an occasional case has been found with multiple initial negative swabs. Negative testing may occur early when patients are asymptomatic. (Personal communications, S Vasoo)

TRANSPLANT SPECIFIC RECOMMENDATIONS

GLOBAL COVID-19 GUIDANCE

The NOTIFY Library has developed a compendium of guidelines relevant to transplantation (https://www.notifylibrary.org/background-documents#SARS-CoV-2). As these are PDF documents, careful review of the primary organization website is recommended as guidance may change quickly.

DECEASED DONORS

Persons who returned from countries with >10 infected patients or who have been exposed to a patient with confirmed or suspected COVID-19 within 14 days should not be accepted as a donor. Likewise donors with unexplained respiratory failure leading to death should be excluded.

Where available, testing of upper and lower airway specimens by PCR/NAT of donors with concern for COVID-19 should be considered. Some national guidelines recommend routine testing of donors for SARS-CoV-2. Routine screening should only be performed in areas with significant ongoing community transmission to minimize the risk of false positive testing and organ wastage.

While the true risk of donor-derived transmission is unclear, RNAemia was reported in at least 15% in one case series.[9]

In a country with widespread community transmission, temporary suspension of the deceased donor program should be considered, especially when resources at the transplant center may be constrained.

A tiered suspension may also be considered (i.e. deferral of more elective transplants, i.e. kidney, pancreas and heart transplantation for patients with VADs).This was the approach in Toronto during the SARS outbreak in 2003.[10]

There is no clear reason to suspend deceased donor transplants in countries only experiencing sporadic cases of COVID-19 cases.

LIVING-RELATED TRANSPLANTS

Living donation should not be performed on either a donor or recipient who has returned from countries with >10 infected patients or who have been exposed to a patient with confirmed or suspected COVID-19 within 14 days. Donors should not be utilized if they have fever and/or respiratory symptoms unless SARS-CoV-2 is excluded.

In countries with widespread community transmission, temporary suspension of the living-donor kidney and liver transplant programs should be considered when donation can safely be deferred to a later date.

Where available, testing of upper and lower airway specimens by PCR/NAT of donors with concern for COVID-19 should be considered. Some national guidelines recommend routine testing of donors for SARS-CoV-2.

If transplantation is required as a life-saving procedure, it can be conducted with appropriate assessment of infection in door and recipient and with appropriate informed consent.

TRANSPLANT RECIPIENTS

Like all persons, transplant recipients should adhere to travel advisories issued by their respective health authorities/government bodies. This may necessitate postponing travel to countries with >10 infected patients.

Recipients should avoid travel to all locations where SARS-CoV-2 is currently circulating.

Transplant recipients should avoid all cruise ship travel.

TRANSPLANT RECIPIENTS RETURNING FROM ABROAD

There are two categories of patients here – those returning from a transplant performed abroad, and those returning from a holiday or work stint abroad. From an infection prevention viewpoint, both categories of patients may be managed similarly.

Teams should follow local health department guidelines for isolating, quarantining, testing, and monitoring returned travellers from endemic areas. Examples of such guidelines include (CDC: https://www.cdc.gov/coronavirus/2019-ncov/travelers/index.html; PHE: https://www.gov.uk/guidance/wuhan-novel-coronavirus-information-for-the-public#advice-for-travellers).

All patients who have returned from countries with >10 infected patients or have been exposed to a confirmed or suspected case of COVID-19 within the previous 14 days should avoid elective clinic visits and surgical procedures (including bronchoscopies in lung transplant patients). Plans should be in place to get required laboratory testing of such patients during the 14 days in such way as to avoid potential exposure of other patients.

Staff who have returned from countries with >10 infected patients or have been exposed to a confirmed or suspected case of COVID-19 within the last 14 days should follow hospital policies but should likely not care for transplant patients.

Transplant units should be prepared to receive patients who, for various reasons, have been abroad. They should be housed in single rooms with an attached bathroom, and all staff attending to them should be in full PPE, until infection with COVID-19 is ruled out. Close liaison is needed with other departments (eg, Radiology)

whose services are likely needed. An effort to re-arrange schedules may be needed to permit spatial and temporal separation of patients awaiting COVID-19 "rule-out". The incubation period, the asymptomatic shedder, negative PCRs early in the course of the disease combine to make "ruling out" a very difficult task.

Transplant patients with fever and/or respiratory symptoms should be instructed to call the transplant center and avoid presenting to the clinic without notifying the center in advance to avoid inadvertent exposures.

Transplant centers should develop guidelines for which symptomatic patients need evaluation, testing and management by the transplant center vs. which can remain at home with close telephonic follow-up.

Patients with suspected COVID-19 or who require testing to rule out COVID-19 should wear a surgical mask, be placed in isolation and have evaluation and testing coordinated with infection control or Transplant ID team, consistent with local policies.

Centers should develop testing algorithms for evaluation of patients with concern for SARS-CoV-2 infection. Examples of such algorithms are available (https://covid-19.uwmedicine.org/Screening%20and%20Testing%20Algorithms/4%20-%20Immunocompromised%20Patients%20-%20Protocol.pdf)
The situation is fluid, and all recommendations thus far are made on thin data. Preventing transmission from an infected patient to a healthcare worker is of essence. Careful attention to infection control precautions are essential. As more information becomes available, these guidelines will be updated.

HSCT GUIDANCE

There have been a number of guidance documents developed for HSCT patients. These will be updated over time so would consult the most up-to-date guidance.

- ESBMT: https://www.ebmt.org/ebmt/news/coronavirus-disease-covid-19-ebmt-recommendations-update-march-16-2020
- ASBMT: https://www.astct.org/connect/astct-response-to-covid-19

TREATMENT OF CASES

There is limited data on optimal treatment protocols and none have been clearly demonstrated to optimize outcomes. When considering potential therapies, it would be critical to recognize when there is drug-drug interactions (i.e. lopinavir-ritonavir) or may increase the risk of rejection (i.e. beta interferon).

Changes in immunosuppression are also not well studied in the transplant populations. Calibration of dose reduction has to balance consequences of rejection (i.e. easier to do with kidney transplants than heart transplantation).

OPERATIONAL CONSIDERATIONS

All transplant-related teams should develop plans to address the following key issues to reduce burden on the healthcare system and mitigate against interruption in care of transplant patients:

- Have a plan for physician and staff absences or furlows due exposure to patients with or team member illness with COVID-19.
- Identify team members who may be impacted by school closures.
- Determine who can work remotely and ensure they have the resources to do so.
- Develop messaging for candidates and recipients about how and when to contact the transplant center in case of illness.
- Develop guidance for candidates and recipients about risk mitigation, including limiting exposure to large crowds, hand hygiene and avoidance of sick exposures.
- Implement procedures to screen patients coming to clinic for fever and respiratory symptoms.
- Determine approaches to minimize exposure to the healthcare setting
    - Consider reduced frequencies of clinic visits and laboratory testing
    - Consider deferral of elective procedures (i.e. protocol biopsies) in stable patients
    - Consider delaying pre-transplant evaluations for patients who do not require immediate evaluation

KEY CHANGES SINCE LAST UPDATE:

- *Updated global epidemiologic data*
- *Global Guideline References*
- *Guidance for sick transplant candidates*
- *Advice for HSCT recipients*
- *Add Operational Consideration Guidance*

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