

Guidance for Cardiothoracic Transplant Centers regarding SARS CoV-2 infection and COVID-19: March 15, 2020

We convened an international group of ISHLT members representing Infectious Diseases, Pulmonology, Cardiology, Cardiothoracic Surgery and Pharmacy to discuss frequently asked questions in the setting of the current pandemic caused by SARS-CoV-2 (virus) causing a disease termed COVID-19. At this time, there is very scant published information regarding COVID-19 in cardiothoracic transplant recipients. Current guidance is based on clinical experience and will be revised as more data becomes available.

1. Who is at risk of acquiring SARS-CoV-2 infection?

- Anyone presenting with one or more of these risk factors is at risk of acquiring SARS-CoV-2 infection:
 - Any travel or residence in an area in the preceding 14 days, where local SARS-CoV-2 transmission is known to occur.
 - Direct contact with known or suspected case of COVID-19 in the preceding 14 days
 - Severe COVID-19 disease occurs more frequently in patients aged 50 years and older and those with comorbidities (cardiovascular disease, diabetes mellitus, chronic respiratory diseases, hypertension, cancer). In immunocompetent hosts, severe disease can lead to acute respiratory distress syndrome (ARDS) and later in the course of disease, myocarditis.
 - At this time, it is unknown if cardiothoracic transplant recipients are at higher risk of acquiring SARS-CoV-2 infection or have higher likelihood of severe disease.

2. How can I try to prevent infection with SARS-CoV-2 in my patients?

If SARS-CoV-2 transmission is occurring within a community, and/or patients with COVID-19 are being cared for in their facility, we recommend that transplant centers consider minimizing medical facility visits by:

- Seeing only essential patients in clinic and reducing clinic volume by deferring outpatient visits for patients that are clinically well. Consider implementation of telemedicine approaches based on telephone or web contact, as locally available, with the aid of checklists to assess patients and also to screen for symptoms consistent with COVID-19. The remote contact should be noted formally and be part of the patient's clinical chart.
- Postponing routine surveillance heart and lung biopsies in patients that are more than 3-6 months from transplantation, have not had a prior episode of rejection, and are clinically stable.
- For patients who will be attending appointments in the clinic or hospital, consider pre-visit phone calls or other contact to ensure patients do not have current symptoms of COVID-19 and to remind them to alert the transplant program before presenting to the medical facility with active symptoms so they may be appropriately triaged.

- Screening for symptomatic patients prior to clinic arrival as per local guidelines and based on local prevalence of COVID-19.

Minimizing social interactions in the community:

- For patients with work or other activities that necessitate interactions with many people, we recommend medical leave or temporary reassignment to non-public facing work in order to minimize possible exposure. Work from home is strongly preferred.
- Basic precautions for transplant recipients and caregivers include staying at home and reducing contact with other people as much as possible. Stringent hand hygiene should be reinforced.
- Avoid non-essential travel.

3. How do I approach a cardiothoracic transplant recipient who has been in contact with someone diagnosed with COVID-19 disease in the past 2 weeks?

- We recommend home quarantine for 2 weeks in asymptomatic patients and testing for SARS-CoV-2 only if symptoms occur (or as per local public health guidelines).
- We recommend against routine testing for SARS-CoV-2 in asymptomatic patients, including when surveillance bronchoscopies are performed in lung transplant recipients.
- We recommend transplant centers performing surveillance biopsies consider deferring viral testing in asymptomatic patients to ensure viral laboratory resources remain available for testing symptomatic patients for SARS-CoV-2 and other viruses.

4. How do I approach management of a cardiothoracic transplant recipient with confirmed COVID-19?

- Patients with respiratory symptoms should have chest imaging, preferably chest computed tomography (CT) when available.
- Patients should be assessed for treatment based on disease severity:
 - o For mild disease, we recommend quarantine at home with frequent follow-up via telehealth modalities. Based on anecdotal experience, we suggest continuing maintenance immunosuppression.
 - o For moderate and severe disease, we recommend admission and assessment for treatment though evidence is anecdotal.
- Consider holding mycophenolate mofetil or azathioprine while admitted with severe/critical illness (with close monitoring for rejection)
- Consider therapy based on drug availability and disease severity. Several drugs have been used with some success in non-transplant patients with COVID-19 and there are ongoing trials investigating a variety of agents. Some of these drugs may be available on a compassionate use basis from the manufacturer as well. At this time, evidence for and against such agents remains weak and mostly anecdotal. Drugs that can be considered for treatment of COVID-19 in transplant recipients include chloroquine,

hydroxychloroquine, intravenous immune globulin, convalescent serum from persons recovered from COVID-19, remdesivir, high dose steroids, and tocilizumab. The latter 2 drugs have been used with some success in the setting of ARDS. We recommend caution if considering the use of lopinavir/ritonavir, darunavir/ritonavir and darunavir/cobicistat due to known significant drug-drug interactions with immunosuppressive medications.

- Centers may develop local guidelines on criteria for proceeding with extracorporeal membrane oxygenation (ECMO) use in carefully selected patients based on availability of ECMO and availability of critical care resources.
- Information on COVID-19 related clinical trials can be found at the World Health Organization International Clinical Trials Registry Platform at <http://apps.who.int/trialsearch/default.aspx>.

5. Can my patient with end stage heart/lung disease be transplanted during this pandemic?

- We suggest proceeding with transplantation in the absence of recent exposure as well as absence of symptoms compatible with COVID-19 in the previous 2 weeks. Although the risk of a false negative remains, if timing and testing availability allows, we suggest PCR-based test for SARS-CoV-2 be performed prior to transplant on patients for whom an organ is accepted.
- If proceeding with transplantation, current experience does not suggest a change in induction protocols with ongoing use of lymphocyte depleting agents if indicated.
- For patients who have recovered from COVID-19, we recommend waiting 14 days after initial diagnosis AND two successive negative PCR-based tests a week apart PRIOR to transplantation (see WHO recommendation on how to define a negative case).
- We recommend foregoing transplantation if a patient has a positive PCR-based test for SARS-CoV-2.
- For patients with COVID-19 requiring ECMO, lung transplant consideration should be with grave caution and if done at all, only in carefully selected cases in the setting of two negative PCR based tests a week apart and absence of myocarditis.
- Considerations regarding non-urgent transplantation should be made on a local center level based on rate of SARS-CoV-2 infection in the community and availability of health care resources; this should be continually reassessed as conditions evolve.

6. How does the COVID-19 pandemic affect donor selection?

Transmission of SAR-CoV-2 from donor to recipient has not been reported as of yet but can be assumed to be possible.

- While the eventual goal would be to have all donors screened for SARS-CoV-2, screening should be calibrated to availability of testing and incidence of COVID-19 cases. Additionally, the false negative rate of testing, especially in asymptomatic individuals is unclear at this time.

- In case donor testing is available, we recommend PCR-based donor testing for SARS-CoV-2 by nasopharyngeal/ oropharyngeal swabs or bronchoalveolar lavage fluid and to avoid transplantation from positive donors.
- If donor testing is not available, as is the case in many areas currently, we recommend avoiding donors with a history of:
 - o Travel to or residing in an area in the preceding 14 days, where local SARS-CoV-2 transmission is occurring
 - o Exposure to a confirmed or probable case of COVID-19 within past 14 days
 - o Compatible clinical syndrome regardless of known exposure within the past 14 days

We request that all centers performing heart and/or lung transplantation collect key data of the course of disease in recipients who develop COVID-19. These data should at a minimum should include: gender and age, transplant date, date of proven COVID-19 infection, date of hospital admission, date of organ replacement therapy or ventilatory support, specific treatment (if any), change to immunosuppression (if any), and outcome. The collaborative effect of collecting such data could at a later time allow our community to compile evidence beyond the anecdotal, to the benefit of future patients. The possibilities of presenting accumulated data in real time on the ISHLT website are currently being explored.

Additional guidance is also available from the following resources:

WHO SARS-CoV-2 dashboard

<https://experience.arcgis.com/experience/685d0ace521648f8a5beeeee1b9125cd>

CDC: <https://www.cdc.gov/coronavirus/2019-ncov/index.html>

ECDC <https://www.ecdc.europa.eu/en/covid-19/all-reports-covid-19>

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