

Guidance from the International Society of Heart and Lung Transplantation regarding the SARS CoV-2 pandemic

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An international group of ISHLT members representing Infectious Diseases, Pulmonology, Cardiology, Cardiothoracic Surgery and Pharmacy was appointed by the Executive Board of the ISHLT to discuss frequently asked questions related to the current pandemic caused by SARS-CoV-2 (virus) causing the disease COVID-19. The group meets frequently to update this document as more data and experience become available. This guidance is pertinent to patients with chronic lung/ heart disease and transplant, mechanical circulatory support, and pulmonary vascular disease.

NEW INFORMATION IN THIS REVISION:

- [New section on ECMO](#)
- [Revised therapeutics](#)
- [Updated references](#)

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1. Are patients with chronic lung/heart disease and transplant, mechanical circulatory support, and pulmonary vascular disease at increased risk of acquiring SARS-CoV-2 infection?

At this time, it is unknown if specific patient populations are at higher risk of acquiring SARS-CoV-2 infection. Published data thus far do not suggest that patients with transplant, VAD, or pulmonary vascular disease (PVD) have a higher risk of acquiring the virus.(1) Currently, risk factors are assumed to be similar to those for any individual but risk may differ based upon location; local general recommendations apply. Updated map regarding disease prevalence can be seen on the [WHO website](#), [Johns Hopkins website](#); or other public health sources may be consulted to assess level of community transmission.

2. Are patients with chronic lung/ heart disease and transplant, mechanical circulatory support, and pulmonary vascular disease at greater risk of developing severe disease if infected by SARS-CoV-2?

In general, severe COVID-19 disease occurs more frequently with increasing age, in men, and in those with comorbidities, particularly cardiovascular disease including heart failure, hypertension, diabetes mellitus, cancer, renal disease, and chronic respiratory diseases.(2-4)

Recent National Health Services database analysis from England of >17 million people assessing risk factors for in-hospital COVID-19 deaths noted that SOT recipients, among other patient populations, were at increased risk [HR 4.27 (95% CI 3.20-5.70)].(5) In a recent case series of 28 heart transplant recipients (half had cardiac allograft vasculopathy) with COVID-19 from New York, approximately 70% required supplemental oxygen, 25% required mechanical ventilation; overall mortality was 25%.(6) Case fatality rates of predominantly abdominal SOT recipients in recent single center reports has varied between 9.5%-28% (7-10) which is similar to that reported for the general population though these are uncontrolled studies

3. How can I reduce the risk of infection with SARS-CoV-2 in my patients?

a. Minimize medical facility visits:

During this pandemic we recommend that centers minimize medical facility visits by:

- All patients:
 - Seeing only essential patients in clinic and reducing clinic volume by deferring outpatient visits for patients that are clinically well.
 - Implementation of telemedicine approaches based on telephone or web contact, as locally available, to assess patients' clinical stability and to screen for symptoms consistent with COVID-19. The remote contact should be noted formally and be part of the patient's medical record.
 - For patients who will be attending appointments in the clinic or hospital, consider pre-visit phone calls or screening questionnaires to ensure patients do not have current symptoms of COVID-19 and to remind them to alert the program before presenting to the medical facility with active symptoms so they may be appropriately triaged.
- Heart and lung transplant patients:

- We recommend deferring routine surveillance biopsies if clinically feasible in patients with stable allograft function and a low risk of rejection, until local resources and capacity allow. Such patients may include those that are > 3 months from transplant, have no recent history of rejection, and those that are not sensitized or with a positive cross match.
- For patients < 3 months post-transplant or with a history of recent rejection or at high risk for rejection, performing surveillance biopsies should be weighed against the risk of exposure to the patient and health care personnel.
- Surveillance biopsies and bronchoscopies may need to be further curtailed when local supply constraints limit availability of personal protective equipment.
- Clinically indicated testing should proceed considering factors such as time since transplant, clinical stability, and prior rejection history. Bronchoscopy should not be performed solely as a diagnostic test for COVID-19 due to virus aerosolization and risk of infection transmission to the medical team. If bronchoscopy is absolutely necessary for airway issues in lung transplant recipients, these should be done with appropriate protection for the bronchoscopist as directed by local recommendations and guidance.
- For lung transplant patients, in order to minimize exposure to the Pulmonary Function Test (PFT) laboratory personnel we recommend using home spirometry for routine monitoring of lung function rather than performing spirometry in the PFT lab. We recommend incorporation of home spirometry data into virtual outpatient visits, reinforcing expected home spirometry schedules, and establishing criteria for patients to notify the transplant team if there is a decline in the forced expiratory volume in 1 second (FEV1) of 10% over several readings.
- Pulmonary vascular disease
 - We recommend deferring routine right heart catheterizations and imaging if clinically feasible in patients with stable disease and a low risk of progression, until local resources and capacity allow.
 - Clinically indicated testing should proceed considering factors such as time since diagnosis, risk score severity, clinical stability, and recent history of right heart failure hospitalization

b. Minimizing social interactions in the community:

- For patients with work or other activities that necessitate interactions with many people, we recommend working from home, if possible. For some patients, medical leave or temporary reassignment to non-public facing work in order to minimize possible exposure may be necessary
- Basic precautions for patients and their caregivers include staying at home and reducing contact with other people as much as possible.
- Stringent hand hygiene with soap and water or hand sanitizer should be reinforced.
- Avoid non-essential travel.

c. Ongoing medical therapies

- All prior disease-specific therapy or immunosuppression should be continued unless otherwise instructed.
- Immunosuppression: there is currently no evidence to suggest transplant patients are at greater risk of acquiring infection, thus immunosuppression should be continued unless otherwise indicated to discontinue or reduce doses.
- Angiotensin-converting enzyme inhibitors (ACEI)/Angiotensin receptor blockers (ARBs): Recent registry-based data demonstrate lack of an association between use of ACE-I or ARB with severe disease or mortality in patients diagnosed with COVID-19. At this time, patients receiving these drugs as part of heart failure treatment should continue their therapy.(4, 11)
- Pulmonary Hypertension (PH) therapy: There is some evidence that PH therapies, like endothelin antagonists, nitric oxide and prostacyclins may be beneficial in COVID-19 patients. However, in the absence of clinical evidence or progression in their primary disease, patients should not be advised to add or modify existing therapy.

4. When and how should patients with chronic lung/heart disease and transplant, mechanical circulatory support, or pulmonary vascular disease be tested and monitored for SARS-CoV-2?

Pending further evidence, the same rules apply to chronic lung/heart disease and transplant, mechanical circulatory support, or pulmonary vascular disease as to other individuals. Of note, recommendations regarding testing for SARS-CoV-2, quarantine, and proactive monitoring for asymptomatic patients may vary based on local policies, healthcare resources, and the phase and severity of the pandemic.

- a. Asymptomatic patient who has been in contact with a confirmed case of COVID-19:*
- For asymptomatic patients we recommend home quarantine for 2 weeks and testing for SARS-CoV-2 by PCR-based test only if symptoms occur (or as per local public health guidelines).
 - We recommend vigilance for development of symptoms by using telehealth options and self-monitoring at home (such as daily temperature checks, symptom diary etc.).
- b. Asymptomatic patients during this pandemic:*
- We do not recommend routine testing for SARS-CoV-2 via PCR- based tests in asymptomatic patients, including when bronchoscopies are performed.
 - For transplant centers continuing to perform surveillance biopsies, we recommend deferring routine viral testing in asymptomatic patients so that the resources in the viral laboratory are not strained unnecessarily.
- c. Testing in Symptomatic Patients:*
- Patients with symptoms of COVID-19 (fever, cough, headaches, myalgia, fatigue, nasal congestion, sudden loss of smell/ taste, diarrhea etc.) should be treated like any other patient considered at increased risk of developing severe disease as per

local guidelines.(1, 3, 12) The possibility of atypical presentations in transplant recipients, especially lack of fever, should be considered.(8, 13)

- Samples for testing should be taken as per local guidelines, usually nasopharyngeal and/or oropharyngeal swabs for PCR-based testing. Of note, tests may be negative even in individuals who later prove to be infected.(14) In this situation, computed tomography (CT) findings may assist in diagnosis, and repeat viral testing may be considered on an individual basis.(15, 16) Additionally, although the sensitivity of lower respiratory tract samples is higher than other sources, bronchoscopies carry a greater risk of aerosol spread of the virus, and thus diagnostic bronchoscopies are discouraged.(17)

5. How do I approach management of a patient with chronic lung/heart disease and transplant, mechanical circulatory support or pulmonary vascular disease with confirmed COVID-19?

Although formal definitions have been proposed for stratification, no consensus exists to date.(5) For the purpose of this document, patients with COVID-19 will be stratified into mild, moderate, and severe disease based on clinical triage as follows:

Mild	Mild symptoms, no shortness of breath or hypoxia
Moderate	Shortness of breath or hypoxia requiring supplemental oxygen via nasal cannula
Severe	Respiratory failure requiring intensive care unit admission. Need for ventilatory support, acute respiratory distress syndrome, circulatory collapse, acute kidney failure, cardiomyopathy, and/ or clinical syndrome compatible with cytokine storm

- Based on current literature, we recommend that patients should be assessed for treatment based on disease severity. Vigilance is important in all patients, especially if concern for increasing disease severity, usually noted 7-10 days into symptom onset. It is unclear if rejection rates or degree of pulmonary hypertension and/or right heart failure will be affected by the viral infection.
- General recommendations based on disease severity:
 - For mild disease, we recommend quarantine at home for 2 weeks with frequent follow-up via telehealth modalities to assess for worsening symptoms. There is currently no data to suggest a change in immunosuppression and we recommend continuing baseline maintenance immunosuppression.
 - For moderate and severe disease, we recommend admission for supportive care. For COVID-specific therapies, see recommendations below.

- As with all patients, we recommend caution when using non-invasive positive pressure ventilation and high-flow nasal cannulae because of the risk of viral spread via aerosolization, and early intubation should be considered depending upon local practices. Lung protective ventilation strategies are considered advantageous. Additionally, prone positioning during both mechanical ventilation and otherwise has been described to improve oxygenation.
- 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.
- Concomitant antibacterial or antifungal treatment can be considered for transplant recipients as per local center policy though rates of bacterial/fungal co- or superinfection are not well defined at this time.
- For transplant recipients, consider holding mycophenolate mofetil or azathioprine while admitted with moderate/ severe illness (with close monitoring for rejection).
- Ventricular assist device (VAD) recipients may safely be placed in a prone position if needed with special attention paid to the driveline to avoid tugging and skin trauma. Driveline exit site dressings may be changed when not prone.
- Specific pulmonary hypertension vasodilators should not be changed/stopped or titrated without prior consultation with a specialist. During active SARS-CoV-2 infection, consider avoiding inhaled epoprostenol due to risk of virus aerosolization.

- COVID-19 directed therapies

There are multiple (>600) ongoing clinical trials evaluating a variety of agents for treatment or prophylaxis of COVID-19. We strongly encourage investigators to facilitate inclusion of patients with chronic lung/heart disease and transplant, mechanical circulatory support and pulmonary vascular disease in clinical trials directed at COVID-19 so that data are available to guide future treatment recommendations. Guidance regarding treatment and diagnostics in the general population overall is updated regularly by the [Infectious Diseases Society of America](#); additional external resource by the American Society of Hospital Pharmacists listing drug dosage and summary of evidence is available at: [ASHP COVID-19 drug resources](#).

At this time there is no evidence to guide decisions regarding the use of COVID-19 treatment strategies in patients with thoracic transplant, VADs, or pulmonary vascular disease. Extrapolation of the limited published data to these populations should be done with caution, ideally in a clinical trial setting. Treatment of this population requires careful consideration of the following: drug availability, disease severity, patient co-morbidities, pertinent drug-drug interactions, and expected toxicities of the agents.

Drug interactions with transplant, pulmonary hypertension and cardiac medications are likely to be the most important consideration prior to initiating investigational treatment in suitable patients. An actively curated external resource addressing drug-drug interactions can be found at [COVID-19 drug interactions](#). This website collaboration has comprehensive tables of drug interactions between experimental COVID-19 treatments and transplant immunosuppressants, pulmonary hypertension and other advanced lung disease medications, antimicrobials (including anti-fungals) and other groups of medications commonly used in patients with transplant and advanced lung and heart disease.

QTc prolongation is another important consideration prior to initiating investigational treatments in patients with end stage heart and lung disease, post-transplant, VAD and PH. An actively curated external resource addressing risks of QTc prolongation with medications is available at <https://www.crediblemeds.org/>

Specific considerations for the use of current COVID-19 directed therapies under investigation in transplant patients include: (all off label uses or unlicensed medications):

- **Remdesivir** – antiviral agent with *in vitro* activity against SARS-CoV-2 and currently in multiple clinical trials. A prospective randomized placebo controlled trial from China did not show any clinical benefit with remdesivir use in hospitalized patients with COVID-19.(18) However, a press release from the National Institutes of Health funded clinical trial noted a significant reduction in time to recovery (though not mortality).(19) Remdesivir is available for use in the USA under an Emergency Use Authorization from the FDA in select hospitals as well as ongoing clinical trials; in Europe and Canada as part of clinical trials only, and currently unavailable in Australia. The risk of significant drug interactions with immunosuppressives, PH therapies, and anticoagulation is low, however there is a potential risk of a decreased tacrolimus, sirolimus and cyclosporine levels.
- **Interleukin-6 (IL-6) inhibitors** – IL-6, secreted by monocytes and macrophages, is considered to be a driver of the immunologic response to SARS-COV-2 in patients with severe disease and cytokine-release syndrome. There are two main agents in clinical trials currently assessing efficacy in COVID-19 - tocilizumab and sarilumab. Non-comparative data suggest efficacy and the drugs may be used off-label where available; however, we recommend treatment under the auspices of a clinical trial. (7) There are limited data regarding drug interactions at this time. The risk of significant drug interactions with immunosuppressives, PH therapies, and anticoagulation is low, however there is a potential risk of a decreased tacrolimus, sirolimus and cyclosporine levels.
- **Monoclonal interleukin-1 receptor antagonist** – Anakinra is an agent that may potentially combat cytokine release syndrome. Recent retrospective cohort from Italy suggested a survival advantage in 29 patients treated with anakinra. Prospective clinical trials are ongoing.(20) Risk of significant drug interactions with immunosuppressives, PH therapies, and anticoagulation is low.

- **Combination antivirals** with activity against human immunodeficiency virus (HIV) are under investigation as potential therapeutic option for COVID-19. However, in thoracic transplant recipients, we do not recommend lopinavir/ritonavir, darunavir/ritonavir and darunavir/cobicistat due to lack of evidence of efficacy in a recent randomized clinical trial and significant drug-drug interactions with immunosuppressive medications.(8) These combination antivirals also have significant interactions with medications used in patients with advanced cardiovascular and pulmonary disease (e.g. amiodarone) as well as having the potential to act synergistically with other baseline medications to prolong the QTc interval.
- **Antimalarials** –Chloroquine and hydroxychloroquine are under investigation for COVID-19 based on *in vitro* antiviral activity. **Several recent clinical trials and observational cohorts demonstrate lack of efficacy and known toxicity potential (including prolonging the QTc interval and attendant risk of arrhythmias)** and thus we recommend against empiric therapy in a non-clinical trial setting, especially in combination with other drugs that may increase the QTc interval such as macrolides (azithromycin, clarithromycin).(21-23) If pursued, such therapy should be accompanied by daily ECG monitoring to follow the QTc interval. The risk of significant drug interactions with immunosuppressives, PH therapies, and anticoagulation is low, however there is a potential risk of elevated cyclosporine levels in conjunction with hydroxychloroquine.(24) One potential risk that is not well described is that “loading doses” (eg 2,000mg in the first 24 hours) in patients with chronic kidney disease may carry the risk of accumulation and CNS excitation/seizures as well as suppression of bone marrow.(25)
- **Convalescent serum** - Small case series demonstrate feasibility of convalescent serum for treatment of severe COVID-19;(26, 27) randomized clinical trials are pending. Safety of use of convalescent serum in the patients with end-stage heart and lung disease, organ transplantation, and VADs has not been demonstrated and we recommend consideration of therapy only within the context of a clinical trial.
- **Prophylaxis:** Due to lack of evidence in addition to potential toxicity and drug interactions, we do not recommend prophylactic therapies (chloroquine, hydroxychloroquine, convalescent serum) outside of a clinical trial setting at this time.

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> and at <http://clinicaltrials.gov>; <https://www.clinicaltrialsregister.eu/ctr-search/search?query=covid-19> (European Union) and <https://www.nihr.ac.uk/covid-studies> (United Kingdom).

6. Can my patient with chronic lung/heart disease be transplanted or undergo VAD placement during the current pandemic?

Decisions regarding transplantation or mechanical support 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, unless otherwise directed by regional or national authorities. This decision should be continually reassessed as conditions evolve and the center should consider the potential benefits and risks for the patient. The risk of receiving a transplant during the pandemic with ongoing community exposure, the risk of mortality if not transplanted, and the adequate and fair allocation of resources (particularly related to intensive care) should be considered. We do not recommend a general cessation of all transplant or VAD activity due to the COVID-19 pandemic solely to liberate resources for treating COVID-19 patients, as it is not certain that weighing of benefit and equity merits cessation of transplant/VAD in all programs though temporary cessation in the setting of an overwhelmed local healthcare system may be unavoidable.(28-30)

- Heart/ Lung Transplant

- While actively infected with SARS-CoV-2, we recommend foregoing transplantation and making the patient inactive on the waitlist.
- For patients with end stage heart or lung disease who contract COVID-19 while waitlisted and recover from illness, we recommend waiting at least 14 days after initial diagnosis AND two successive negative PCR-based tests at least 48 hours apart PRIOR to transplantation if possible as viral shedding has been demonstrated to occur following resolution of clinical symptoms; prolonged shedding up to 5 weeks in a minority of patients has been described.(31, 32) This timeframe is based on the higher acuity of heart and lung waitlisted patients and lesser opportunities for organ availability.
- Lung transplant specifically for COVID-19 related lung disease should be considered with grave caution in carefully selected cases following two negative PCR based tests as noted above, and after a sufficient observation period for natural recovery of lung function as is often seen after other viral causes of ARDS. Recent data indicate that myocarditis may occur at this stage, and thorough cardiac evaluation is warranted.(33)
- Induction therapy: current experience does not suggest a change in induction protocols with ongoing use of lymphocyte depleting agents if indicated, but it should be noted that COVID-19 is frequently associated with lymphopenia.
- When considering appropriate resource allocation in such settings, the expected need for prolonged postoperative care after a transplant in such patients should be weighed against the opportunity of liberating ICU capacity by performing the transplant.

- Mechanical circulatory support:

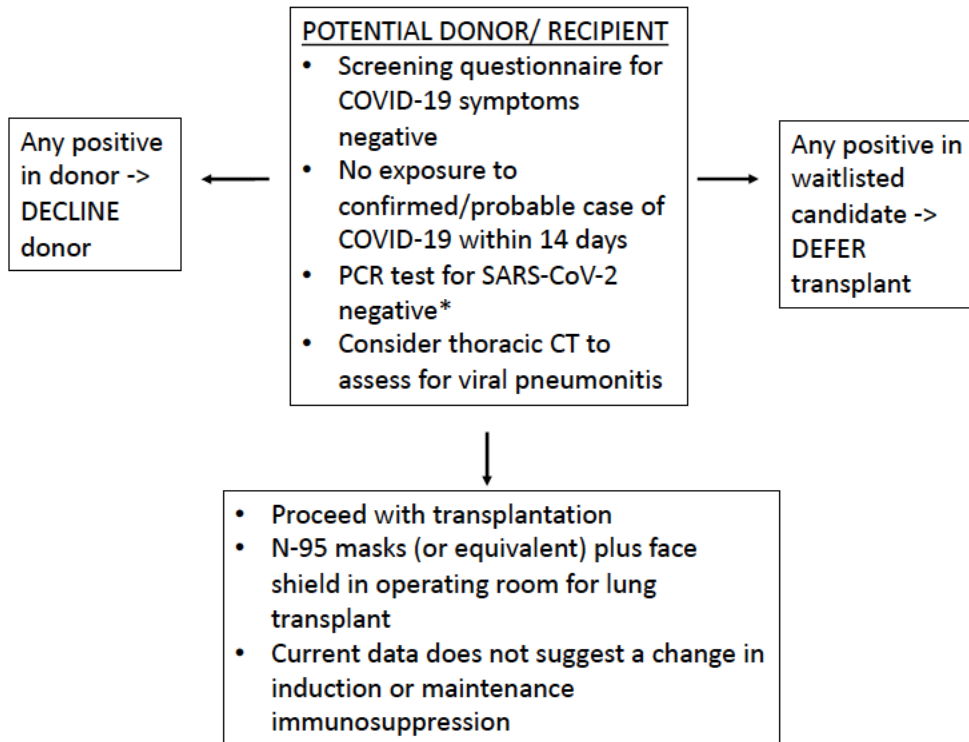
- Based on COVID-19 disease prevalence and resource availability at the local center, consider limiting VAD implantation to INTERMACS status 1-3 patients. For VAD patients who are otherwise stable and using their 30 days of prioritization (as allowed in the US), centers should consider deprioritizing until the pandemic abates.

7. How does the COVID-19 pandemic affect deceased donor and recipient selection at the time of organ offer?

Asymptomatic or pre-symptomatic viral shedding is well described with SARS-CoV-2 infection.(34, 35) Transmission of SARS-CoV-2 from donor to recipient has not yet been reported but is conceivable. The risk of viral transmission must be balanced against the risk to the recipient associated with not using the organ and losing an opportunity for transplant. Additionally, a waitlisted patient may be asymptotically infected at time of organ offer.

- If local testing strategy and rapid turn-around of PCR-based testing allow, we recommend testing for SARS-CoV-2 by nasopharyngeal/ oropharyngeal swab, sputum/ tracheal aspirate, or bronchoalveolar lavage; latter two are reported to have higher viral loads and thus higher sensitivity of test results.(17) BAL should only be performed if it is safe to do so within a closed ventilatory circuit with adequate personal protective equipment available. In the absence of evidence-based effective treatment, we recommend avoiding transplantation from PCR+ donors and deferring transplant on PCR+ waitlisted candidates.
- Donor or candidate with an exposure to a confirmed/ probable case of COVID-19 within past 14 days should be avoided as patients may be in an incubation phase.
- Donor or candidate with a clinical syndrome compatible with COVID-19, regardless of known exposure within the past 14 days, should be avoided
- A thoracic CT scan may show signs of SARS-CoV-2 infection even before development of symptoms or positive PCR and thus should be considered for donor and candidate assessment. This is based on availability of adequate personal protective equipment and other resources. If CT imaging is suggestive of a viral pneumonitis, we recommend foregoing transplant.
- Regardless of donor screening, the center should have a discussion of risk-benefit with the recipient regarding transplantation during the ongoing pandemic.

Figure 1 delineates screening pathway for donor and recipient screening at time of organ offer.



* Recommended prior to transplant based on testing availability; naso/oropharyngeal, sputum/tracheal aspirate or bronchoalveolar lavage sample (latter not recommended unless closed ventilatory circuit and adequate PPE supplies).

8. How do we protect healthcare workers (HCW) during donor and recipient procedures at the time of transplantation?

Data regarding COVID-19 in HCWs from China, Europe, and the US indicate that HCWs form a substantial proportion of patients with COVID-19, ranging from 3.8% in China overall (majority in Wuhan);(36); 30% in an outbreak linked to a long-term care facility in Washington state, US (37); and 9% in Italy overall (38). Nosocomial sources of infection include, not just the donor and recipient transmission, but also transmission from hospital personnel with asymptomatic/ pre-symptomatic infection. Thus, possible transmission of infection to the clinical transplant team is a distinct possibility, especially in the setting of lung transplantation, in which organ retrieval and transplant surgery itself are considered aerosol generating procedures. Data regarding infection risk during these specific procedures is lacking at this time.

a) Procurement travel:

- The minimum number of personnel should be involved in the procurement team and related travel to reduce the risk of infection to the HCWs.
- When possible, it is strongly recommended that organs should be procured by a local recovery team in order to reduce travel-related risk.
- Team members should use surgical mask during transportation.
- Consider screening questionnaire assessing COVID-19 symptoms of the procurement team prior to commencing travel.

b) *Donor and transplant surgery:*

- Appropriate PPE should be available for the procurement team on site either provided by the local organ procurement organization, the donor hospital, or carried by the procurement team according to their institutional guidelines. This should be negotiated in advance of commencing travel.
- N-95 masks (or equivalent) should be worn by all team members in the operating room during lung retrieval and lung transplantation; face shield is suggested as well. We recommend avoiding donor bronchoscopies in the operating room; if performed, only the bronchoscopist should be in the room with airborne precautions.
- Standard surgical masks are considered sufficient for heart retrieval and transplantation, along with suggested face shield if no lung retrieval is being performed in the same donor).
- Where available, negative pressure operating room should be used for lung surgical procedures.

9. Recommendations for ECMO:

Extracorporeal Membrane Oxygenation (ECMO) should be considered in patients with critical COVID-19 disease who fail conventional measures to improve hypoxemia and should not deviate from the usual indications per Extracorporeal Life Support Organization (ELSO).(39) Considerations during a pandemic are inherently different due to limited hospital capacity and several factors ought to be weighed in making a decision to judiciously offer this resource-intensive mode of support. These include availability of PPE, space, equipment and personnel to initiate, maintain and decannulate ECMO patients. More stringent inclusion/exclusion criteria, including age, frailty and single organ involvement, may be necessary as determined by hospital capacity and local guidelines.

Cannulation process should occur preferably at the bedside to avoid exposure of personnel and surfaces in the operating room or catheterization lab. Femoro-femoral or femoro-internal jugular venovenous support using large (>23 Fr) multistage drainage cannula and single stage return cannula provide optimal flows.

Ongoing care on ECMO should follow existing guidelines and be based on optimal supportive care to maximize outcomes.(40-42) Centers should follow institutional anticoagulation ECMO protocols with a consideration to more intense therapy in light of the hypercoagulable state typical of these patients. Along these lines, low ECMO flows should be avoided. Weaning from ECMO ought to follow existing guidelines and decannulation should be performed with PPE precautions, as indicated.(39)

VA ECMO may be required in patients with COVID-19 who decompensate hemodynamically as a result of cytokine storm and/or myocardial dysfunction. Similarly, patients with classical indications for VA ECMO including acute myocardial infarction, cardiogenic shock, regardless of COVID-19 status may require support.

10. How do we discuss palliative care considerations in patients with cardiothoracic transplant, pulmonary vascular disease and VAD?

While advance care planning is an essential element of care for patients with advanced heart and lung disease, the SARS-CoV2 pandemic has brought a greater urgency to this process. Patients with advanced heart/lung disease are likely at higher risk of death if they acquire severe COVID-19 disease, and may not have the option of ICU care in hospitals forced to ration these services during pandemic surges.(43) Higher transplant waiting list mortality may also be expected as transplant volumes are reduced during the pandemic, and the availability of bridging therapies such as mechanical ventilation or ECMO may be restricted. Moreover, due to pandemic visitor restrictions, patients may be unaccompanied by support persons during hospitalizations, even during critical illness when discussions of goals of care are required.

- We recommend engaging patients with advanced heart and lung disease (referred or listed for transplant, PAH, VADs, and post-transplant patients with severe chronic allograft dysfunction) and their support persons in advance care planning discussions prior to hospitalization. This can occur during virtual visits with the clinical team and/or through referral to Palliative Care.
- Palliative care discussions should include the usual general considerations as well as the specific pandemic considerations noted above. Patients ineligible for bridging to transplant should be made aware of this, to inform their advance care planning.
- During hospital admissions, we recommend attempting to involve support persons in discussions around goals of care through video or phone calls.

Additional resources to assist with advance care planning discussions can be found at the following links: https://respectingchoices.org/wp-content/uploads/2020/03/Proactive_Care_Planning_Conversation_COVID-19.pdf
<https://www.vitaltalk.org/guides/covid-19-communication-skills/>

11. How do we get more knowledge regarding SARS-CoV-2 infection in patients with cardiothoracic transplant, pulmonary hypertension and VAD?

We request that all centers performing cardiothoracic transplantation and VADs collect key data of the course of disease in recipients who develop COVID-19, as per local regulatory guidelines. These data should at a minimum 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)
- occurrence, treatment and outcome of acute and chronic rejections
- outcome.

Clinical, laboratory and radiological findings would also be helpful.

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.

Specifically, the group identifies the following research questions that should be prioritized:

1. Presentation and symptoms in thoracic transplant and VAD recipients infected with SARS-CoV-2 compared to appropriate controls.
2. Disease progression and prognosis in thoracic transplant and VAD recipients infected with SARS-CoV-2 compared to compared to appropriate controls.
3. Effects of adjustment of immunosuppressive medication and risk of acute rejection and graft dysfunction in SARS-Cov-2 infected thoracic transplant recipients.
4. Effects of experimental antiviral and anti-inflammatory medication on survival and risk of acute rejection and graft dysfunction in SARS-Cov-2 infected thoracic transplant and VAD recipients.
5. Risk of severe or lethal COVID-19 in patients with VAD or pulmonary vascular disease compared to recently transplanted patients to determine whether this particular group of patients should have higher priority for transplant in the current situation.
6. Assessment of acquisition of specific protective immunity by thoracic transplant and VAD recipients.

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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payment to individual; Abiomed: Consultant; payment to individual;

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