

## **UK cardiothoracic transplantation service status update and guidance for managing a cardiothoracic transplant patient with COVID-19**

During COVID-19 pandemic, a reduction in donor organ availability, diversion of healthcare resources including critical care beds to COVID-19 and the unquantified risks of SARS-CoV-2 infection in transplant recipients have contributed to uncertainty for patients both pre and post-transplant. Transplant centres across the UK, supported by NHSBT, NHSE and ISHLT, have worked to reconfigure their services to allow transplantation to continue whilst minimising patient risk.

### **Are all lung transplant centres now open?**

- The decision whether or not to offer transplant during the COVID-19 period has been made at a local centre level, based on the rate of SARS-CoV-2 infection in the community and the availability of health care resources and has been continually reassessed as conditions evolved.
- All centres (adult and paediatric) are now open for transplant. New referrals are welcomed, but there may be a backlog at some centres following the recent COVID-19 surge. If local teams are concerned that their patient needs urgent assessment they should call to speak to one of the transplant physicians.
- Some lung transplant centres elected to transplant lower risk and more stable patients during the peak of the pandemic but have now activated all patients who have given their consent.
- Whilst fewer patients than normal have undergone lung transplant during the pandemic period, a number of successful lung transplants have recently been performed at centres across the UK.
- It is envisaged that transplant activity will increase, as it is appropriate and safe to do so, in the coming weeks and months.
- Activity may need to be evaluated if there is a second COVID-19 surge.

### **Is it safe to have a lung transplant now?**

- Although there have been no reported cases of transmission of SARS-CoV-2 via organ donation, as patients who need a transplant have significant health problems, require major surgery and are immuno-suppressed, there is a risk of contracting SARS-CoV-2 infection in hospital, but this risk must be balanced with the benefits of transplant and risk of dying on the wait list.
- In the early stages of the pandemic, a number of patients on the lung transplant waiting list elected to be placed “on hold” as the risk of undergoing a transplant during the COVID-19 outbreak could not be determined.
- The decision of whether individuals remain “active” on the transplant list is made jointly between patients and their transplant centres and should take into account the significant risk of missing the opportunity for transplantation.
- Infection control procedures are in place in all transplant centres to try and prevent COVID-19 infection in lung transplant recipients.

### **How are potential recipients screened for SARS-CoV-2?**

- Patients on the lung transplant wait list with a positive SARS-CoV-2 swab result will be temporarily suspended.
- At present, there is not enough evidence to suggest that molecular tests are useful to screen for SARS-CoV-2 in asymptomatic patients on the transplant list.

- In all patients for whom donor organs have been accepted, a PCR-based test for SARS-CoV-2 is performed prior to transplant and transplantation is not recommended if the potential recipient has a positive PCR-based test.
- The risks of a false negative PCR result are acknowledged and transplantation should only be considered for patients in the absence of recent exposure as well as absence of symptoms compatible with COVID-19 in the previous 2 weeks.
- For patients who have recovered from COVID-19, NHSBT recommend waiting 28 days after the onset of symptoms at initial diagnosis AND a negative PCR-based test PRIOR to transplant (see WHO recommendation on how to define a negative case).
- For patients with COVID-19 requiring ECMO, lung transplant candidacy should be with considered with extreme caution and if done at all, should only be in carefully selected cases in the setting of two negative PCR based tests a week apart, absence of myocarditis and other end organ dysfunction.

#### **How does the COVID-19 pandemic affect donor selection?**

- During the COVID-19 pandemic there has been an 80-90% reduction in the number of organs offered for donation however the number of potential organs being offered is now increasing.
- Transmission of SAR-CoV-2 from donor to recipient has not been reported as of yet but can be assumed to be possible.
- A national process ensures that each donor is confirmed SARS-CoV-2--free before organ donation.
- PCR-based donor testing for SARS-CoV-2 by nasopharyngeal/oropharyngeal swabs and endotracheal aspirate/bronchoalveolar lavage fluid is performed to minimise the risk of donation from positive donors.

#### **How does COVID-19 affect lung transplant recipients?**

- At present, it is unknown if cardiothoracic transplant recipients are at higher risk of acquiring SARS-CoV-2 infection or have higher likelihood of severe disease
- The mortality risks of COVID-19 in a solid organ transplant recipient in the early post-transplant period have not been adequately quantified but are likely to be significant.
- The largest recent epidemiological study of electronic records of 17 million NHS patients showed that people with any solid organ transplant had 4 times the risk of dying with COVID-19 compared to the general population independent of all other known risk factors (such as age, gender, ethnicity, obesity). Given that the infection fatality rate from COVID-19 in the general population is estimated to be 0.5-1% these data suggest that the infection fatality rate from COVID-19 in solid organ transplant recipients could be in the region of 2-4% although this is likely to vary substantially depending on co-morbidities and age. NHSBT keeps a weekly updated record of solid organ transplant patients that require hospital admission for COVID-19 (a subgroup with at least moderate disease severity). So far, approximately 1 in 4 solid organ transplant patients who required hospital admission for COVID-19 have died (somewhat higher in lung transplant recipients).
- Beyond the early post-transplant period, it appears reasonable to suggest that lung transplant recipients may be at increased risk of severe infection particularly if they have established lung damage (from either native lung or as a result of chronic lung allograft dysfunction) or if they require oxygen or non-invasive ventilation post-transplant.
- Immunosuppression reduction may form an important part of the COVID-19 infection management approach but this may have subsequent potential detrimental long-term effects on allograft function and outcomes.

## How to approach management of a cardiothoracic transplant recipient with confirmed COVID-19

- UK patients listed for a transplant or under post-transplant follow-up with suspected or confirmed COVID-19 must be reported to NHSBT.
- Local hospitals should inform the transplant centre of any pre or post-transplant patients with suspected or confirmed COVID-19 at an early stage.
- Cardiothoracic transplant recipients may present with atypical symptoms because of immunosuppression and may not have typical fever; gastrointestinal symptoms may be more frequent. COVID testing should be considered in all post-transplant patients presenting to their local with symptoms. Patients with respiratory symptoms should have chest imaging, preferably chest computed tomography (CT) when available.
- Disease severity is determined on clinical (e.g. oxygen saturation), radiological and spirometry testing if available. In selected cases, transbronchial lung biopsy may be required to confirm the presence of viral pneumonitis and exclude other pathology such as allograft rejection. Please liaise with the transplant centre for advice.
- Patients should be assessed for treatment based on disease severity:
- **For mild disease:**
  - quarantine at home with frequent follow-up via telehealth modalities.
  - based on anecdotal experience, maintenance immunosuppression should be continued.
- **For moderate and severe disease:**
  - admit for assessment and treatment, though evidence is anecdotal.
  - decisions regarding the cessation of mycophenolate mofetil or azathioprine while admitted with severe/critical illness should be made only in liaison with the patient's transplant centre (with close monitoring for rejection).
  - in highly selected cases (and only following advice from the transplant centre) immunosuppression may temporarily be discontinued.
- Treatment options that can be considered include azithromycin, dexamethasone, intravenous immune globulin, convalescent serum from persons recovered from COVID-19, remdesivir, and tocilizumab. The latter 2 drugs have been used with some success in the setting of ARDS.
- Caution is recommended if considering the use of lopinavir/ritonavir, darunavir/ritonavir and darunavir/cobicistat due to known significant drug-drug interactions with immunosuppressive medications. This should be discussed with the transplant centre.
- Transplant centres have developed 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.

### Additional guidance can be accessed via the following links:

- <https://www.odt.nhs.uk/information-for-patients/coronavirus-faqs/>
- <https://www.odt.nhs.uk/deceased-donation/covid-19-advice-for-clinicians/>
- <https://nhsbt-dbe.blob.core.windows.net/umbraco-assets-corp/18300/nhsbt-bts-consent-guidance-covid-19-26320.pdf>
- <https://community.ishlt.org/HigherLogic/System/DownloadDocumentFile.ashx?DocumentFileKey=e48794c6-d4b3-cef4-2e53-dbcbb50b6a12&forceDialog=0>

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