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SARS-CoV-2 Vaccination in Heart and Lung Transplantation

Recommendations from the ISHLT COVID-19 Task Force

March 15, 2021

Several SARS-CoV-2 vaccines are approved for administration in various countries (Table 1) and are available to select populations based on local recommendations and regulations. These include mRNA-based vaccines (Moderna, Pfizer-BioNTech), those utilizing replication deficient viral vectors (Oxford-AstraZeneca, Johnson and Johnson, Sputnik V, Cansino), inactivated virus (Sinopharm, Sinopharm-Wuhan, Sinovac, Bharat) and protein subunits (Novavax, Vector Institute). Since none of the currently available vaccines are based on live replicating viral vectors, all are acceptable for transplant recipients. Thus, we recommend that transplant patients accept any of these vaccines made available to them.

Current efficacy data from clinical trials in immunocompetent hosts is variable as noted in Table 1 based on the type of vaccine used; however reported data in clinical trials thus far demonstrate 100% protection against severe COVID-19 related intensive care or death.[1-5] Real world observational data from Israel demonstrated 87% reduction in hospitalization related to COVID-19 after receipt of 2 doses of the Pfizer-BioNTech vaccine.[6] To date, nearly 350 million vaccine doses have been administered worldwide.[7] Common adverse events are local to the injection site and related to reactogenicity of the vaccine; importantly anaphylaxis is very rare ranging between 2.47-4.7 cases/million doses administered for the mRNA vaccines; 60% with anaphylaxis had a prior history of allergic reactions and no related death was reported.[8, 9] Rare serious adverse events with unclear association to vaccination are under evaluation, such as concerns regarding thrombotic events in a few patients that received the Oxford-AstraZeneca vaccine in Europe; however manufacturer review of >17 million doses does not indicate a serious safety signal.[10]

Efficacy data for SARS-CoV-2 vaccines in transplant recipients is lacking but emerging data are reassuring. The mRNA vaccines appear to demonstrate safety in the transplant population with no concern for rejection or other serious adverse events in the early period following administration.[11] Another analysis in transplant recipients has noted a reduced antibody response of 17% to the first of two mRNA vaccine doses. However, this is incomplete data lacking results on response to the second dose, with no description of Th1 cell response and no clinical data.[12] While this rate of immunogenicity appears lower than that noted in the general population, we do not yet have clinical efficacy data on rates of protection against severe illness or death in those transplant recipients that are fully vaccinated with longer term follow up. Rejection rates were not increased in this study. We expect that the risk of rejection will likely

remain low and not dissimilar to that observed in previous vaccine studies of adjuvanted zoster vaccine or high dose influenza vaccine in transplant recipients.[13, 14]

Serological correlates of immunity against COVID-19 as a measure of vaccine efficacy are unknown at this time. Commercially available serological tests that measure antibody response against SARS-COV-2 test for presence or absence of antibodies to the nucleocapsid and/ or spike protein in a qualitative fashion. Tests measuring only anti-nucleocapsid antibodies will not show evidence of immunogenicity after administration of vaccines that target only the viral spike protein; immunogenicity in response to such vaccines requires testing for anti-spike antibodies. At this time, an optimal titer cut-off for neutralizing antibodies remains unknown and vaccine efficacy cannot be defined adequately by a simple presence or absence of antibodies, which may be misleading. Additionally, neutralizing antibodies as well as a Th1 CD4+ and CD8+ T cell response contribute to immunity against SARS-CoV-2.[15] Testing for the latter is not readily available and such vaccine-related response in transplant recipients is unknown currently. Due to these uncertainties, we recommend against routine serological testing of patients after SARS-CoV-2 vaccination at this time; more research in this area is needed.

In aggregate, we believe that the benefits of receiving SARS-CoV-2 vaccination outweigh the risk and endorse vaccination for transplant recipients, once the early period (1-3 months) following transplantation has passed and immunosuppression is stabilized. Transplant patients should continue to use a face mask and maintain social distancing as recommended until further data on vaccine efficacy is available for this population. We recommend vaccination of transplant candidates and immunocompetent household members as a priority, particularly in those situations where a close care provider is needed for the transplant recipient. We also recommend the enrollment of cardiothoracic transplant recipients in vaccine trials or registries where available to assess vaccine efficacy, dosing intervals, need for booster shots, transplant-related adverse events such as rejection and potential change in circulating donor specific antibodies, and long-term effects of vaccination.

SPECIFIC RECOMMENDATIONS

Timing of SARS-CoV-2 vaccination:

1. We recommend vaccination of all transplant candidates to allow for development of an effective immune response to the vaccine prior to transplantation.
2. In the post transplantation setting, the ideal timing of vaccination is uncertain. We recommend delaying vaccination at least 1 month from transplant surgery and at least 3 months from use of T-cell depleting agents such as anti-thymocyte globulin or specific B-cell depletion agents such as rituximab (which may require a longer deferral period).
3. Patients who are transplanted in between vaccine doses, should delay the 2nd dose until at least 1 month after the transplant surgery if no T-cell/B-cell depleting agent was used for induction, or at least 3 months after the transplant surgery if a T-cell/B-cell depleting agent was used for induction.

4. We recommend following manufacturer guidelines regarding dosing interval between the first and second vaccine doses until transplant specific data is available.
5. We recommend continuing stable maintenance immunosuppressive regimens, including anti-proliferative agents (such as mycophenolate mofetil) in patients that are receiving SARS-CoV-2 vaccination. We do not recommend alteration of immunosuppression specifically around vaccination as the risk of rejection may be greater with a reduction in immunosuppression.
6. Transplant recipients with prior COVID-19 should receive vaccination after clinical resolution of the infection or as per local regulations/ guidelines.
7. Vaccination should be delayed by 3 months in patients that received monoclonal antibodies for COVID-19.

Choice of SARS-CoV-2 vaccine:

1. All currently available vaccines, as noted in Table 1, do not use a live replicating viral vector and thus we consider these to be safe in transplant recipients.
2. We do not recommend any specific vaccine for transplant recipients. Patients should receive whichever vaccine is available to them based on local regulations and distribution policy.

Serological testing:

1. We recommend against routine testing of SARS-CoV-2 serology following vaccination as correlates of immunity are unclear. Additionally, many current serological assays test for nucleocapsid antibody only which will not detect anti-spike antibodies that are expected following vaccination with the vaccines that target the virus spike protein.

Daily Activities:

1. Fully vaccinated transplant recipients should continue to mask and practice social distancing based on local transmission rates of SARS-CoV-2 until more data on vaccine efficacy are available. Vaccinated transplant recipients should continue to follow local guidelines as applicable to the highest-risk community members.

Prioritization:

1. We recommend vaccine prioritization for transplant candidates particularly those accepted on the waitlist.
2. We recommend prioritization of immunocompetent household members of patients that are at increased risk of poor outcome from COVID-19, including patients with obesity, older age, underlying cardiopulmonary disease and transplant candidates and recipients.

Table 1. SARS-CoV-2 vaccinations available globally, as of March 15, 2021.

Manufacturer	Type	Vaccine efficacy reported in clinical trials	Prevention of severe disease leading to hospitalization or death in clinical trials
Pfizer/BioNTech	mRNA	95%	100%
Moderna	mRNA	94.5%	100%
Sputnik V	Ad26/Ad5	91.4%	100%
AstraZeneca	ChAdOx1	60-85%	100%
Johnson & Johnson	Ad26	57-72%	100%
Cansino	Ad5	66%	100%
Sinopharm	inactivated	79.6-86%	100%
Sinovac	Inactivated	50.1%	100%
Sinopharm-Wuhan	inactivated	?	?
Bharat	inactivated	?	?
Vector Institute	protein	?	?
Novavax	protein	86-96%	100%

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