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DQ (MFI 6360-25,824) 10-20 weeks post COVAX and all had episodes of high grade acute cellular rejection. One additional patient had rejection post COVAX without dnDSA. All 3 patients with dnDSA had robust response to the vaccine with antibodies to spike protein RBD of > 200 U/ml (Elecsys®). Eight vaccinated patients without dnDSA had anti-RBD testing, half had titres > 200 U/ml. In the historical pre COVAX cohort, 3 patients (9 %) demonstrated dnDSA (2022-25480 MFI), one of these had cellular rejection and one developed antibody mediated rejection.

Conclusion: One fifth of cardiac transplant recipients developed dnDSA in the weeks following COVAX, all associated with rejection. While no definitive conclusions may be drawn, we believe these data suggest the need for immunological surveillance after COVAX. This may be even more important after a booster dose.

Patient	Vaccination Post Transplant (weeks)	dnDSA HLA-DQ (MFI)	DSA Testing Post Vaccination (weeks)	COVID Spike Ab (U/ml)	COVID Spike Ab Testing Post Vaccination (weeks)	History of COVID-19 Prior to Vaccination
1	6	6360	13	244	12	no
2	3	2931	10	250	10	no
3	79	25824	20	218	16	no
4	32	none	18	>250	18	yes
5	14	none	12	>250	12	yes
6	4	none	5	>250	9	yes
7	3	none	8	>250	14	no
8	32	none	16	1.2	16	no
9	23	none	7	1	6	yes
10	23	none	5	0.6	0	yes
11	18	none	16	1.2	7	no
12	7	none	5	2.3	23	no
13	8	none	16	not tested	not tested	no
14	12	none	7	not tested	not tested	no
15	7	none	12	not tested	not tested	no
16	6	none	16	not tested	not tested	no

Ab (antibody), dnDSA (*de novo* donor specific HLA antibodies), MFI (luminex single antigen bead median fluorescent intensity)

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Regional Variation in COVID Vaccination Requirements for Potential Heart Transplant Recipients

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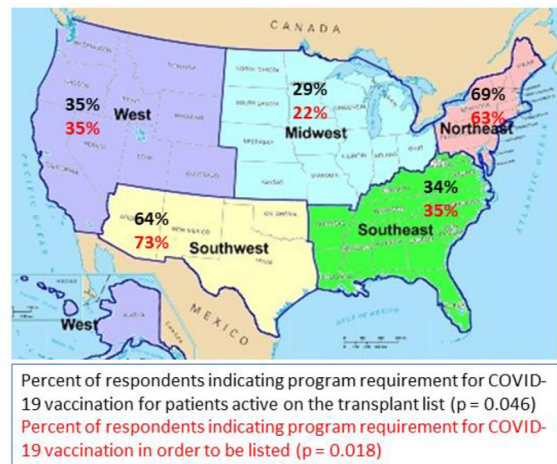
Purpose: As the COVID pandemic continues, transplant (Tx) and left ventricular assist device (LVAD) programs have been forced to contend with the challenges of vaccine hesitancy. To guide discussions regarding vaccine requirement, we sought to define provider perspectives and institutional policies.

Methods: We distributed a 5-question electronic survey from 9/17 - 9/24/21 to Tx and LVAD providers in the US.

Results: A total of 121 respondents completed the survey, which included Cardiologists (n=77), Cardiac Surgeons (n=12), Advanced Practice Providers and Coordinators (n=24), as well as other advanced heart failure team members (n=8). 113 responses included geographic data, which was converted to Midwest, Northeast, Southeast, Southwest and West for regional comparison. Statistically significant regional variation was noted in COVID vaccine requirements for patients in order to be listed for transplant and those that are active on the transplant list [Figure]. The highest

proportion of vaccine requirements for patients active on the transplant list were noted in the Northeast and Southwest (69% and 64%). The lowest proportion of vaccine requirements were noted in the Midwest, Southeast, and West (29%, 34%, and 35%). Providers in the Northeast were noted to have a significantly higher rate of requiring vaccination for patients active on the Tx list when compared to providers in all the other regions (69% vs. 37%, p=0.026) and a trend towards having a vaccination requirement to be listed (63% vs. 36%, p=0.057). There were no regional differences observed in requiring potential LVAD recipients or caregivers to be vaccinated. When asked if they would favor a vaccine requirement for these populations, the overwhelming majority of respondents answered in the affirmative, however there were no differences noted based on region.

Conclusion: COVID vaccination requirements across LVAD and Tx programs vary by region, policies remain heterogeneous despite positive provider perspectives towards vaccination.



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Breakthrough Infections and Low Mortality Observed in Heart Transplant Recipients Infected with COVID-19 at UC San Diego

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Purpose: Management of COVID-19 has evolved over the course of the pandemic, with new therapies contributing to a decline in mortality in the general population. Immunosuppressed heart transplant (HT) recipients are at high risk of infection, but questions remain regarding their optimal management as these patients were excluded from many clinical trials on COVID-19 therapeutics and vaccines.

Methods: Retrospective search of electronic health records identified 41 HT recipients who tested positive for SARS-CoV-2 from February 1, 2020–October 13, 2021.

Results: Among the 41 HT recipients infected with SARS-CoV-2, 15 (36%) were monitored as outpatient, and of these, 4 received casirivimab/imdevimab and 1 received oral steroid. No COVID-19 related deaths were observed in this group. The remaining 26 patients (64%) were admitted for pneumonia or hypoxia. Five required admission to the intensive care unit (ICU), of which 3 required intubation and pressor support and 2 died (7.7% in-hospital mortality, 4.9% overall mortality). Of those admitted, 15 were treated with remdesivir and 7 received steroids. After vaccines were available in January 2021, 10 patients developed breakthrough COVID-19 occurring 2 weeks after the second Pfizer dose (n=6) and second Moderna dose (n=4). 8 of these patients were admitted for pneumonia or hypoxia and treated with COVID-19 directed therapies (4 received remdesivir, 2 received dexamethasone, 3 received casirivimab/imdevimab). 2 patients were monitored as outpatient where they received casirivimab/imdevimab. There was no severe illness or deaths observed in vaccinated patients.

Conclusion: We present 41 HT recipients at UCSD infected with COVID-19. By using outpatient isolation, monoclonal antibody infusions, and admission

for treatment of hypoxic patients with remdesivir and steroid, we have demonstrated a lower mortality from COVID-19 compared to other studies on HT recipients. No mortality was observed in the breakthrough cases.

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Characteristics and Outcome of COVID-19 Infection in Heart Transplantation Recipients in the Netherlands

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Purpose: Immunocompromised patients are at high-risk for complicated COVID-19 infection. The aim of this study is to describe the characteristics and outcome of heart transplantation (HTx) recipients infected with COVID-19 in the Netherlands.

Methods: All HTx patients with a COVID-19 infection between February 2020 and June 2021, proven by positive polymerase chain reaction-test or positive serology in one of the three heart transplant centers in the Netherlands were retrospectively included. The primary endpoint of this study is all-cause mortality.

Results: COVID-19 was diagnosed in 54/665 (8%) HTx patients, mean time from HTx was 11±8 years, mean age 53±14 years and 39% were female. Immunosuppressive therapy was reduced in 37%, 21 (39%) patients required hospitalization and all-cause mortality was 6%. Severe COVID-19 disease (hospitalized with ICU admission or mortality) was seen in 7 (13%) patients. Compared to patients with mild (not hospitalized) or moderate (hospitalized, no ICU admission) COVID-19 infection, patients with severe COVID-19 infection were generally older (p=0.007) and had a history of ischemic heart failure (p=0.004) more frequently. Compared to patients with moderate COVID-19 infection, severe COVID-19 patients were transplanted earlier and had a significantly higher body mass index (30±3 vs 26±3; p=0.01). Myocardial infarction, cellular rejection and pulmonary embolism were observed once in three different HTx patients. Physical complaints post-infection persisted with a median of 30 days (IQR 30-83 days) in 16 (39%) cases.

Conclusion: HTx patients are at increased risk for complicated COVID-19 infection with frequent hospitalization, but mortality is substantially lower than previously described.

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Efficacy and Safety of mRNA SARS-CoV2 Vaccination in Heart Transplant Recipients

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Purpose: Data on immunologic response to SARS-CoV2 vaccination in heart transplant recipients are scarce. We investigated the efficacy and safety of mRNA SARS-CoV2 vaccination in this patient population.

Methods: In a retrospective single-center study we included 54 consecutive adult heart transplant recipients who received 2 doses of mRNA SARS-CoV2 vaccine between January 1 and June 30, 2021. All patients were followed for 112±28 days after the second dose. At the end of follow-up we measured humoral response to SARS-CoV2 by assessing total antibody levels to the receptor-binding domain of SARS-CoV2 spike (S) protein using anti-RBD immunoassay. Anti-S antibody serum levels ≥250 BAU/mL were considered protective. At the same time, cellular response was measured by the IFN-γ response to S-peptide stimulation of recipient T lymphocyte populations. Protective cellular response was defined as more than 0.3% of IFN-γ responsive T cells.

Results: Of 54 recipients, 44 (81%) were male with a mean age of 63±8 years and a mean time from transplantation of 6.6±4.0 years.

Immunosuppressive regimen consisted of tacrolimus (mean C0 level 7.4±1.7 μg/mL), mycophenolate mofetil (mean dose 2120±419 mg) and steroids (mean dose 2.5±0.9 mg). The majority of patients received BTN162b2 vaccine (83%), and 17% of recipients were vaccinated with mRNA-1273. During follow-up, a humoral response was present in 24 (44%) of the recipients (median anti-S serum level 35.5 BAU/mL). We found no difference in humoral response between patients receiving BNT162b2 and mRNA-1273 vaccine (median anti-S serum level 68.3 BAU/mL vs. 15.5 BAU/mL, P=0.81). Protective humoral response was observed in 6 (11%) of the recipients (median anti-S serum level 557 BAU/mL). A cellular response to vaccine was present in 3 (6%) of the recipients; all 3 displayed a protective level of response. No recipients developed simultaneous protective humoral and cellular responses. Recipient age was the only predictor of protective humoral response (55±11 years in responders vs. 65±8 years in nonresponders; P=0.01). In 3 (6%) recipients we found worsening of allograft function requiring hospital admission, which occurred within 1 month after receiving the second dose of vaccine.

Conclusion: In heart transplant recipients, mRNA SARS-CoV2 vaccination appears to be of limited efficacy and may, in some cases, be associated with worsening of allograft function.

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Impact of COVID-19 Vaccination After Orthotopic Heart Transplantation

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Purpose: The effect of COVID-19 vaccination in orthotopic heart transplant (OHT) patients is unknown. After OHT, patients are increased risk of COVID infection and hospitalization.

Methods: We retrospectively analyzed 119 patients who underwent OHT between 2017 and 2021. Eleven patients were excluded who died prior to the COVID outbreak in the United States.

Results: The mean age was 51 years (IQR 26). The known vaccination rate (partial or complete) was 83%. The overall infection rate was 14% (17 COVID cases were identified.) Five patients were infected prior to the availability of the COVID vaccine. Of the remaining 2 (16%) and 5 (42%) were in vaccinated and unvaccinated patients respectively. The hospitalization rate due to COVID infection or COVID-related complications such as supplemental oxygen use was 29%. All hospitalized subjects underwent changes in their antirejection therapies, and half required oxygen supplementation therapy at discharge. No COVID-related deaths were identified. There were 2 partially/fully vaccinated patients at the time of COVID infection. One patient had mild symptoms and did not require hospitalization while the other patient was asymptomatic.

Conclusion: Hospitalization rates were markedly higher in the OHT cohort compared to Kentucky state data (29% vs 4%.) Multiple factors contribute to this finding. Patients with OHT have more co-morbidities and after OHT and immunosuppressant therapy blunts host response to infection placing these patients at higher risk of complications. There was a higher vaccination rate in our OHT cohort compared to Kentucky state data (83% vs 61%). Breakthrough COVID infection was found in only 4% of OHT patients strongly supporting the efficacy of the vaccination in this immunosuppressant subgroup. While there were no COVID related deaths in our cohort, downstream complications related to immunosuppression changes and organ rejection detection require long term follow up. The vaccine has proved highly efficacious in this group and should be implemented up front, prior to transplantation. We suggest pre-transplant COVID-19 vaccination should become mandatory in patients being evaluated for OHT.

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Hemodynamic Effects of COVID-19 Vaccination in Hospitalized Patients Awaiting Heart Transplantation

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