Purpose: Multiple variants of SARS-CoV-2 have been documented throughout the COVID-19 pandemic. Mutations that lead to these variants can affect viral spread, disease severity, and the efficacy of vaccines and therapeutics. Lung transplant (LT) recipients (LTRs) are at high risk of COVID-19-related morbidity and mortality; however, disease severity may differ between SARS-CoV-2 variants. We sought to describe the clinical outcomes of LTRs with COVID-19 at different stages of the pandemic.

Methods: We performed a retrospective chart review of LTRs with COVID-19 and categorized them into 4 groups according to the prevalent variant on the date of the positive test. Chi-square and non-parametric binomial exact tests were used for comparative analyses.

Results: Since March 2020, 195 LTRs at our institute developed COVID-19; the median age was 66.6 years (58.7-72); 114 (58.5%) were male; 190 (97.4%) had received a bilateral LT; 106 (54.4%) had diabetes; 63 (32.3%) were obese; and 145 (74.4%) had chronic kidney disease with an eGFR <60. The most common immunosuppressive regimen included mycophenolate mofetil, tacrolimus, and prednisone (n=142; 72.8%). The median percent predicted FEV1 was 81% (IQR 63-96) and the median time from LT to COVID-19 diagnosis was 37.3 months (IQR 18.5-66.7). Rates of hospitalization, ICU admission, need for mechanical ventilation, and death were significantly lower for the Omicron variant than the original strain, the Alpha variant, and the Delta variant. However, there was no difference in length of hospital stay, development of extrapulmonary end-organ dysfunction, or persistent drop in spirometric flows (Table 1). Lastly, the utilization of vaccination and monoclonal antibodies grew over time and likely contributed to reduced COVID-19 severity in the latter part of the pandemic.

Conclusion: COVID-19 continues to drive morbidity and mortality among LTRs; however, the severity of disease is lower with the omicron variant.

Table 1

	Original Strain 03/01/2020-11/30/2020 N= 44 (22.6%)	Alpha Variant 12/01/2020-06/15/2021 N= 42 (21.5%)	Delta Variant 06/16/2021-11/30/2021 N= 20 (10.3%)	Omicron Variant 12/01/2021-08/08/2022 N= 89 (45.6%)	P value
COVID-19 Directed Treatment					
≥2 mRNA vaccines prior to COVID-19 diagnosis, no (%)	0 (0.0)	7 (16.7)	16 (80.0)	84 (94.4)	α p= <0.001 δ p= <0.001
Monoclonal antibody, no (%)	0 (0.0)	16 (38.1)	12 (60.0)	60 (67.4)	α p= <0.001 δ p= 0.092
Antiviral, no (%)	35 (79.5)	27 (64.3)	13 (65.0)	51 (57.5)	0.095
Clinical Outcomes					
Hospitalization, no (%)	33 (75.0)	32 (76.2)	15 (75.0)	33 (37.1)	h p=<0.001 α p= <0.001 δ p= <0.001
ICU admission, no (%)	16 (36.4)	13 (31.0)	6 (30.0)	12 (13.5)	h p= <0.001 α p= <0.001 δ p= <0.001
Length of hospitalization, days, median (IQR)	10 (5, 21.5)	8 (5, 23.25)	11 (5, 19)	10 (4.5, 16.5)	0.695
Mechanical ventilation, no (%)	9 (20.5)	12 (28.6)	5 (25)	6 (6.7)	h p= <0.001 α p= <0.001 δ p= <0.001
≥20% decline in FEV1 ≥3 months after COVID-19 diagnosis, no (%)	4 (9.1)	1 (2.4)	0 (0.0)	6 (6.7)	0.359
Heart failure (ejection fraction <45%), no (%)	2 (4.5)	2 (4.8)	2 (10.0)	1 (1.1)	0.239
Renal failure with need for dialysis, no (%)	7 (15.9)	4 (9.5)	3 (15.0)	8 (9.0)	0.612
Death due to COVID, no (%)	16 (36.4)	10 (23.8)	9 (45)	12 (13.5)	h p= <0.001 α p= 0.012 δ p= <0.001

h comparison between original strain and Omicron variant
α comparison between Alpha variant and Omicron variant
δ comparison between Delta variant and Omicron variant

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No Association Between BNT162B2 Vaccine and Graft Rejection Among Lung Transplant Recipients

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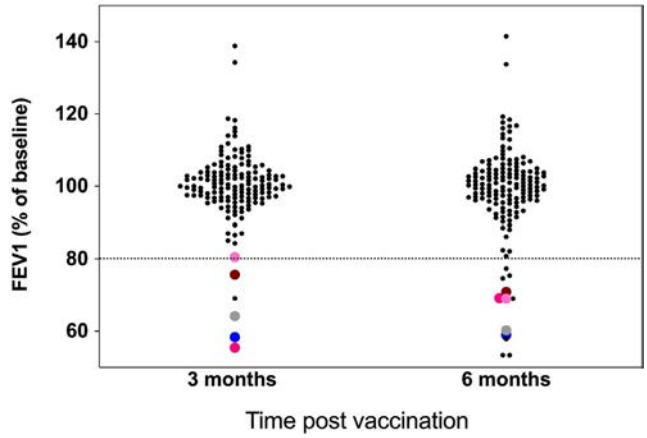
Purpose: Safety of the BNT162b2 vaccine has been described among the general population and solid organ transplant recipients (SOTR). Post vaccination development of donor specific antibodies (DSA) and organ rejection is a specific concern among SOTR. Yet data on effects of mRNA vaccine on the development of de novo DSA (ddDSA) and acute cellular rejection (ACR) in lung transplant recipients (LTR) is lacking. The purpose of this study is to describe the effect of the mRNA BNT162b2 vaccine on the development of ddDSA and prevalence of ACR episodes following vaccination.

Methods: A retrospective study including all LTR who participated in our observational prospective cohort study of immunogenicity following BNT162b2 vaccine. We collected data regarding demographics, documented ACR episodes, FEV1 decline and development of ddDSA between December 2020 and December 2021.

Results: Two doses of BNT162b2 mRNA vaccine were administrated to 168 LTR. Of them 139 patients received another booster dose. Median age was 60.5 years (IQR 49.25-67.75) and 33.3% were females. Median time from transplantation was 46.66 months (IQR 20.03-96.96). Among 139 patients who received three vaccine doses ACR episodes were documented in 4 patients (2.8%), similar to ACR rate documented within the six months preceding vaccine administration. DSAs were evaluated among 60 patients following two vaccine doses, none of whom developed ddDSA. Six patients had a positive DSA titer prior to vaccination, with no significant increase in mean fluorescence intensity (MFI) following vaccination. Lung function remained stable among the vast majority of our cohort with 94.6% demonstrating stable FEV1 following BNT162b2 vaccine (figure 1).

Conclusion: Despite previous concerns of possible graft targeted immune reactions to mRNA vaccines, the risk of ACR episodes and development of ddDSA after BNT162b2 vaccination among LTR is very low. Transplant centers should recommend appropriate vaccination for this immunosuppressed population.



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Vaccination with >2 Doses of Mrna Vaccines is Needed to Reduce Mortality Among Lung Transplant Recipients with Covid-19

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Purpose: Vaccination reduces COVID-19-related morbidity and mortality in the general population, however, the response to vaccination is attenuated among immunosuppressed lung transplant recipients (LTR). Boyarski et al noted that 61% of LTR had no serologic response to the first or second dose of mRNA vaccines, with an additional 31% only responding to the second dose. We sought to compare the impact of vaccination status on COVID-19-related morbidity and mortality in LTR.

Methods: We conducted a retrospective chart review of LTR with COVID-19 that did not receive Tixagevimab-Cilgavimab (Tix-Cil) prophylaxis. We compared outcomes based on vaccination status using chi-square and binomial exact tests.

Results: Between March 2020 and August 2022, 195 LTR developed COVID-19, 24 received Tix-Cil and were excluded from the analysis. The median age was 66.6 (58.8-71.9), 100 (58.5%) were male, 166 (97.1%) had a bilateral lung transplant, 91 (53.2%) had diabetes, 55 (32.2%) were obese, and 126 (73.7%) had chronic kidney disease with an eGFR <60. The most common immunosuppressive regimen included mycophenolate mofetil, tacrolimus, and prednisone (124 (72.5%)). The median percent predicted FEV1 was 78% (IQR 62, 94) and the median time from LT to COVID-19 diagnosis was 38.3 months (IQR 20.3, 66.9). LTR with COVID-19 that received at least 2 doses of the mRNA vaccines were less likely to be hospitalized compared to their unvaccinated counterparts. However, 2 vaccine doses alone did not reduce ICU admission, intubation, or mortality. LTR with COVID-19 that received >2 vaccines were less likely to be hospitalized, admitted to the ICU, or intubated, and had a lower mortality.

Conclusion: Two doses of mRNA vaccines reduced COVID-19-related hospitalization among LTR with COVID-19; additional vaccine doses were needed to reduce risk of ICU admission, intubation, and death.

Table1

COVID-19 Outcomes	Unvaccinated or <2 doses n=87	2 doses n=50	>2 doses n=34	Unvaccinated vs 2 doses p-value	Unvaccinated vs >2 doses p-value	2 doses vs >2 doses p-value
Baseline characteristics						
Age, median (IQR)	65.4 (58.0, 71.1)	68.3 (58.9, 72.8)	67.2 (60.1, 72.0)	0.073	0.237	0.824
Immunosuppressive Regimen includes ntiproliferative, no (%)	65 (74.7)	38 (76.0)	21 (61.8)	1.000	0.184	0.224
Months from Transplant to COVID-19, median (IQR)	37.4 (18.5, 61.7)	48.1 (22.5, 70.7)	36.2 (21.2, 68.8)	0.341	0.582	0.120
Treatment at COVID-19 Diagnosis, no. (%)						
Monoclonal antibody therapy)	18 (20.7)	29 (58.0)	22 (64.7)	**<0.001**	**<0.001**	0.650
Antiviral therapy	62 (71.3)	29 (58.0)	20 (58.8)	0.134	0.201	1.000
Increased dose of corticosteroids	70 (80.5)	48 (96.0)	31 (91.2)	**0.019**	0.184	0.644
Clinical Outcomes: Unadjusted Analysis, no. (%)						
Hospitalized	64 (72.7)	30 (60)	14 (41.2)	**0.035**	**<0.001**	**0.020**
Admitted to ICU	27 (31.0)	13 (26.0)	4 (11.8)	0.275	**0.008**	**0.038**
Intubated	18 (20.7)	10 (20.0)	2 (5.9)	0.535	**0.018**	**0.023**
Deceased	26 (29.9)	15 (30.0)	4 (11.8)	0.547	**0.012**	**0.012**

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Use of Tixagevimab and Cilgavimab (Evusheld) and Subsequent Outcomes of SARS-CoV-2 Infections in Lung Transplant Recipients

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Purpose: The protection of solid organ transplant recipients from infection has been challenging throughout the Coronavirus disease (COVID-19) pandemic. In 2022, tixagevimab and cilgavimab (Evusheld) was introduced as a means of providing passive antibodies and augmenting the vaccine immune response in immunocompromised patients. We aimed to assess the efficacy of Evusheld in reducing the incidence of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection in lung transplant recipients.

Methods: We conducted a single center, retrospective, observational cohort study examining SARS-CoV-2 incidence in 289 lung transplant recipients from January 2022 through July 2022. Manual chart extraction was utilized to collect dates of Evusheld administration, SARS-CoV-2 vaccination, and SARS-CoV-2 infection, as well as demographic and clinical data. Exact logistic regression models were used to compare incidence of SARS-CoV-2 infection and hospitalization rates between lung transplant recipients who received versus did not receive Evusheld.

Results: Of the 289 lung transplant recipients, 136 (47.1%) received Evusheld during the study period. The incidence of SARS-CoV-2 infection in transplant recipients who received Evusheld was 8.1% (or 11/136), compared to 34.0% (or 52/153) among those who did not receive Evusheld. Controlling for the number of SARS-CoV-2 vaccines received, the odds of a SARS-CoV-2 infection was approximately 83% lower for patients who received Evusheld (*OR*=0.18, 95% CI: 0.08 to 0.38, p<0.001). Further, the rate of hospitalization was available for 62 of 63 (98.4%) patients with a SARS-CoV-2 infection. Among these patients, no patient in the Evusheld group required hospitalization; conversely, 12 of 51 (23.5%) patients who did not receive Evusheld required hospitalization (*OR*=0.39, 95% CI: 0.00 to 2.38, p=0.21).

Conclusion: Evusheld administration was associated with significant efficacy in the prevention of SARS-CoV-2 infection in lung transplant recipients.

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