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Impact of Omicron on Lung Transplant Recipients: A Third COVID-19 Surge with Different Outcomes

To the Editor:

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B1.1.529 (Omicron) variant became the predominant variant in the United States in late 2021 (1). It is shown to be associated with lower severity of illness in the general population, particularly among the vaccinated, compared with the preceding variants (2). By December 19, 2021, the variant accounted for 92% of all coronavirus disease 2019 (COVID-19) cases in New York City (3). However, early data in solid organ transplant recipients continue to indicate higher severity of illness and mortality (6%) among lung transplant recipients (LTRs) (4). We aim to describe clinical and mortality outcomes in a larger cohort of LTRs infected with the Omicron variant and to provide a comparison to our center's prior cohorts of COVID-19–infected LTRs, which to our knowledge collectively represent the world's largest single-center experience (5, 6).

Methods

In this retrospective cohort study, we included all consecutive LTRs at our center who tested positive for SARS-CoV-2 via either polymerase chain reaction or rapid antigen testing between December 19, 2021,

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Table 1. Characteristics of the Omicron COVID-19 surge

	Mild (*n* = 59)	Moderate (*n* = 25)	Severe (*n* = 14)
Age, yr, median (IQR)	55 (43–65)	63 (50–70)	60 (58–67)
Sex, *n* (%)			
Male	29 (49)	12 (48)	8 (57)
Female	30 (51)	13 (52)	6 (43)
Transplantation indication, *n* (%)			
ILD	34 (58)	15 (60)	11 (79)
COPD	1 (2)	6 (24)	1 (7)
PH	2 (3)	0	0
Sarcoidosis	1 (2)	1 (4)	0
CF and non-CF bronchiectasis	17 (29)	1 (4)	1 (7)
Other*	4 (7)	2 (8)	1 (7)
Transplantation type, *n* (%)			
Single	24 (40)	16 (64)	11 (79)
Double	34 (58)	9 (36)	3 (21)
Multiorgan	1 (2)†	0	0
Years since transplantation, median (IQR)	5.1 (2.8–8.5)	4.1 (2.3–6.6)	2.9 (1.1–6.5)
Bronchiolitis obliterans syndrome stage, *n* (%)			
0	36 (61)	10 (40)	5 (36)
0p	15 (25)	7 (28)	3 (21)
1	7 (12)	7 (28)	0
2	1 (2)	0	5 (36)
3	0	1 (4)	1 (7)
History of prior COVID-19, *n* (%)	13 (22)	1 (4)	0
Vaccination status, *n* (%)			
None	6 (10)	3 (12)	2 (14)
Initial series	53 (90)	22 (88)	12 (86)
Pfizer (two doses)	30 (51)	13 (52)	4 (29)
Moderna (two doses)	19 (32)	4 (16)	7 (50)
J&J (one dose)	3 (5)	5 (20)	1 (7)
Other	1 (2)‡	0	0
Additional dose	42 (71)	17 (68)	12 (86)
Pfizer	24 (41)	11 (44)	4 (29)
Moderna	18 (31)	5 (20)	8 (57)
J&J	0	1 (4)	0
Symptomatic at time of testing, *n* (%)	53 (90)	22 (88)	14 (100)
Treatment, *n* (%)§			
None	13 (22)	0	1 (7)
Monoclonal antibody	35 (59)	5 (20)	1 (7)
Oral antiviral (Paxlovid)	12 (20)	1 (4)	0
Remdesivir without dexamethasone	—	6 (24)	0
Remdesivir plus dexamethasone	—	18 (72)	12 (86)
Other	—	0	5 (36)
Highest oxygen requirement, *n* (%)			
Mechanical ventilation	—	—	7 (50)
High-flow nasal cannula	—	—	4 (29)
Noninvasive ventilation	—	—	1 (7)
Nonrebreather	—	—	1 (7)
Nasal cannula	1 (2)‖	17 (68)	1 (7)
Room air	58 (98)	8 (32)	0
Length of admission, median (IQR)	—	6 (4–10)	20 (6.8–40.8)¶
Died (%)	0	3 (12)**	9 (64)

Definition of abbreviations: CF = cystic fibrosis; COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease 2019; ILD = interstitial lung disease; IQR = interquartile range; J&J = Johnson & Johnson; PH = pulmonary hypertension.

*Other indications include combined pulmonary fibrosis and emphysema and post–lung transplantation chronic lung allograft dysfunction.

†Multiorgan transplantation includes concomitant heart and double-lung transplantation.

‡One patient had mixed Moderna/Pfizer vaccines for the initial two-dose series.

§For monoclonal antibody therapy, one patient in the mild group received Regeneron in Florida, one in the moderate group received Eli Lilly, and the rest received sotrovimab. One patient in the mild group received both sotrovimab and Paxlovid. In the moderate group, two patients received sotrovimab before admission and then remdesivir during admission, two patients received sotrovimab before admission and then remdesivir and dexamethasone during admission, and one patient completed Paxlovid before admission and then received remdesivir and dexamethasone. One patient in the severe group received sotrovimab before admission and then solumedrol during admission. Four patients in the severe group received both remdesivir and dexamethasone. Other treatments included clinical trials, tocilizumab, and baricitinib.

‖One patient required a nasal cannula at baseline.

¶One patient was still admitted at the time of data collection.

**Two patients died after their index COVID-19 hospitalizations of complications related to COVID-19.

Table 2. Comparison among all three COVID-19 surges

	First Surge Cohort (*n* = 32)	Second Surge Cohort (*n* = 47)	Third Surge Cohort (*n* = 98)	*P* Value
Age, yr, median (IQR)	65 (51–69)	65 (57–72)	58 (44–67)	0.047
Sex, *n* (%)				
Female	16 (50)	25 (51)	49 (50)	0.97
Transplantation indication, *n* (%)				
ILD	15 (47)	28 (59)	60 (61)	0.31
Transplantation type				
Single	17 (53)	26 (55)	51 (52)	0.93
Years since transplantation, median (IQR)	5.6 (2–8.6)	4.3 (2–9.7)	4.8 (2.3–8.2)	0.59
Disease severity, *n* (%)				
Mild	5 (16)	16 (34)	59 (60)	<0.001
Moderate	14 (44)	18 (38)	25 (26)	0.093
Severe	13 (41)	13 (28)	14 (14)	0.005
Hospitalization, *n* (%)	27 (84)	31 (66)	39 (39)	<0.001
Mechanical ventilation, *n* (%)	10 (31)	7 (15)	7 (7)	0.002
Mortality, *n* (%)	11 (34)	8 (17)	12 (12)	0.016

Definition of abbreviations: COVID-19 = coronavirus disease 2019; ILD = interstitial lung disease; IQR = interquartile range.

and January 31, 2022. Patients were defined as having mild disease if they did not require hospitalization, moderate disease if they required hospitalization, and severe disease if they were admitted to an intensive care unit or a stepdown unit or required a nonrebreather mask, a high-flow nasal cannula, noninvasive ventilation, or mechanical ventilation. Positive cases were identified through the electronic health record and patient-reported information. Patient demographics and medical history were obtained from the electronic health record. The findings in this cohort were compared with findings from our center's first-surge (34 patients between March 19, 2020, and May 29, 2020) and second-surge cohorts (47 patients between November 1, 2020, and February 28, 2021) (5, 6).

Our treatment protocol was in accordance with our center's COVID-19 clinical guidelines. In patients with mild symptoms who had oxygen saturation > 94% and tested positive within 5–7 days of symptom onset, monoclonal antibodies (typically sotrovimab) and/or oral antivirals (Paxlovid [nirmatrelvir and ritonavir]) were used. Our protocol requires holding calcineurin inhibitors with frequent monitoring of calcineurin inhibitor concentrations while the patient completes Paxlovid. In patients who presented with oxygen saturation less than 94% on room air and/or required supplemental oxygen, dexamethasone 6 mg daily or an equivalent dose of corticosteroids was administered for total of 10 days or until hospital discharge, whichever was earlier. In addition, for patients with hypoxemia, remdesivir was used within 10 days of symptom onset, usually for a 5-day course.

Patients were followed until death or study end (April 30, 2022) to allow 90-day follow-up. Continuous and categorical variables were compared using the *t* test and one-way analysis of variance, respectively.

This study was approved by the Columbia University Human Research Protection Office and the Institutional Review Board.

Results

We identified 98 LTRs who tested positive for SARS-CoV-2 between December 19, 2021, and January 31, 2022 (Table 1). The patients had a median age of 58 years, and 51% were men. They underwent single-lung transplantation (52%), most commonly for interstitial lung disease (61%), and were a median of 5.8 years post-transplantation. Fourteen patients (14%) had previously been infected with SARS-CoV-2 (10 of 14 patients [71%] had received their initial vaccines and a booster, 2 of 14 patients [14%] had received their initial vaccines without a booster, and 2 of 14 patients [14%] were not vaccinated). Eleven percent of the entire cohort were unvaccinated. Eighty-nine percent had received two doses of the messenger ribonucleic acid COVID-19 vaccines or one dose of a viral vector vaccine, and 72% had received an additional booster vaccine before their COVID-19 diagnoses. One patient had also received Evusheld before COVID-19 diagnosis and had mild symptoms. Baseline characteristics are reported in Table 1.

Sixty percent of the patients had mild, 26% moderate, and 14% severe COVID-19. Thirty-nine percent were hospitalized, and 31 patients (31% of the cohort) received oxygen supplementation, including 7 patients (7%) who required mechanical ventilation. Ninety-one percent (26 patients) of those who required supplemental oxygen therapy received dexamethasone or equivalent corticosteroids. Of those patients with mild symptoms, 78% were treated with either monoclonal antibodies or oral antiviral medications. Treatment and clinical outcomes are also reported in Table 1.

The 90-day mortality rate in this cohort was 12%. This is in comparison with the mortality rates of 34% and 17% in the first- and second-surge cohorts, respectively (5, 6). The present Omicron cohort exhibited lower proportions of severe disease and hospitalization compared with the prior two cohorts (5, 6). Comparative outcomes from all three COVID-19 cohorts at our center are reported in Table 2.

Discussion

Despite the lower mortality rate in this cohort of LTRs infected by the SARS-CoV-2 Omicron variant compared with the two prior COVID-19 cohorts at our center, COVID-19 continues to cause significant morbidity and mortality. Our findings show that LTRs remain at increased risk of severe disease and mortality from the Omicron variant compared with the general population and compared with mortality of other common respiratory infections in

solid organ transplant recipients, including influenza and respiratory syncytial virus (7, 8). Notably, the patients who developed severe COVID-19 continue to have high associated mortality of 64% at 90 days.

The proportions of patients with asymptomatic disease at the time of COVID-19 diagnosis were 10% and 12% in the mild and moderate groups, respectively. In the first two surges, most of the patients included in the studies, particularly the moderate and severe groups, were symptomatic at the time of diagnosis. Only one patient (severe disease) in the first surge was asymptomatic at the time of testing. In the second surge, 25% of the patients with mild disease were asymptomatic, whereas all the of moderate and severe patients were symptomatic at the time of testing (5, 6). More than 70% of the cohort (85% in the severe COVID-19 group) contracted COVID-19 after having received an additional COVID-19 vaccine booster. These findings lend support to the observed suboptimal vaccine immunogenicity response to the Omicron variant among immunocompromised patients described in early studies (9, 10). We acknowledge the limitations when comparing different COVID-19 cohorts at our center throughout the pandemic. Many challenges uniquely present during the first surge of spring 2020, including the novelty of the disease with limited prior knowledge, expertise, testing, and treatments, scarcity of healthcare resources together with the lack of vaccines, and concrete guidelines on preventive measures for the public, all resulted in the higher illness severity in the first surge. We hypothesize that the additive effects of the changes in these factors and the decreased virulence of the Omicron variant all contributed to the lower COVID-19–associated mortality over time at our center.

In summary, despite major improvements in outcomes in the past two years, COVID-19 continues to be associated with significant mortality among LTRs. As mask mandates have been lifted, it is important for LTRs to continue to wear masks and practice distancing to prevent infection. Continued research for more effective pre- and postexposure prophylactic therapies is also needed for this population. ■

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