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Post-acute sequelae of COVID-19 in solid organ transplant recipients

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Abstract

Background: Post-acute sequelae of COVID-19 (PASC), defined as prolonged symptoms following an episode of COVID-19, is not well-characterized in solid organ transplant recipients (SOTR). In this study, we aimed to assess the prevalence of PASC in SOTR, its descriptive characteristics, and associated risk factors.

Methods: We retrospectively identified SOTRs with acute COVID-19 between 06/01/2020 and 04/15/2022 and abstracted demographic and medical history, characteristics of acute COVID-19

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Karina Covarrubias carried out statistical analysis, and contributed to writing, review and editing.
Benjamin Chen was involved in investigation and data curation.
Rodrigo Barriola Rubarth in investigation and data curation.
Kelly Torosian in investigation and data curation.
Claudia Ramirez Sanchez in investigation and data curation.
Ajay Bharti was involved in conceptualization and data curation.
Victor DeGruttola oversaw the statistical analysis and methodology, and contributed to writing, editing and revision.
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illness, and COVID-19 vaccination status. We defined PASC as ongoing/ new symptoms present at 6 weeks or longer following acute COVID-19 diagnosis.

Results: Among 208 SOTRs with acute COVID-19, 72 (35%) developed PASC. Common symptoms were respiratory symptoms (67%), headache (40%), and difficulty concentrating (10%). Severe acute COVID-19 disease and presence of respiratory symptoms were associated with higher odds of PASC in multivariable analyses, while receipt of at least one COVID-19 vaccination prior to transplantation was protective.

Conclusion: We found that PASC occurs in about a third of SOTRs with acute COVID-19 and has similar symptoms as described previously in immunocompetent hosts. Pre-transplant vaccination may be protective. Further prospective multicenter studies are needed.

Keywords

COVID-19; Solid organ transplant; Long COVID; post-acute sequelae of COVID-19; immunocompromise

Introduction:

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic, causing the clinical syndrome of coronavirus disease 2019 (COVID-19), has infected millions of people worldwide. Post-acute sequelae of COVID-19 (PASC) is a clinical entity that appears at least four weeks after the onset of the initial illness. [1] Symptoms of PASC impact all organ systems and are variable.[2, 3] The prevalence of PASC has been reported between 26– 62% among the general population.[4, 5] With millions of people infected with SARS-CoV-2 globally, the potential impact of PASC is staggering.

Solid organ transplant recipients (SOTRs) are vulnerable to developing COVID-19 due to immunosuppression and sub-optimal immune response to COVID-19 vaccines.[6, 7] Prolonged viral shedding and protracted acute infection in SOTRs is well-described, which is similar to the experience at our center. [8, 9] However, one study suggested that SOTRs were less likely to develop PASC, considering the possibility of immunosuppression as a protective mechanism against PASC.[10] We conducted an exploratory study among SOTRs at our center to assess the frequency, symptoms and potential risk factors of PASC in this specific population.

Materials and Methods:

Setting:

This is a single center retrospective cohort study involving chart review.

Data collection:

We developed an internal electronic medical record (EMR) list in which SOTRs diagnosed with acute COVID-19 were added by the transplant team. This list was developed as part of clinical care to guide appropriate follow-up. After obtaining institutional review board (IRB) approval (#801965), we undertook chart review of SOTRs diagnosed with acute COVID-19

from 06/01/2020 to 03/01/2022. We included all SOTRs diagnosed with positive test results via positive polymerase chain reaction (PCR) or antigen test.

We collected the following information through EMR review: demographics, medical history, clinical details of acute COVID-19 infection, concomitant medications and medication changes, outcomes including development of PASC subsequent to the acute COVID-19 diagnosis, recurrent hospitalization/emergency room visits, and death with data recorded in RedCap. We reviewed all the details of acute COVID-19 as well as the medical record in the outpatient follow-up extending beyond at least 6 weeks from COVID-19 diagnosis.

Definitions:

We defined PASC as symptoms lasting at least 6 weeks from the diagnosis of acute COVID-19 without an alternative etiology for those symptoms. The 6-week interval was chosen due to studies documenting longer viral shedding in immunocompromised patients vs. non-immunocompromised and concern that prolonged symptoms may potentially be related to ongoing viral replication rather than PASC.[11] Relapse occurred when a period of improvement or resolution in PASC symptoms was followed by a period of recurrent/worsening symptoms. We used the National Institutes of Health COVID-19 Treatment Guidelines to define severity of acute COVID-19: (i) mild illness included individuals with any sign or symptom of COVID-19, but no shortness of breath, dyspnea, or abnormal chest imaging; (ii) moderate illness included individuals with evidence of lower respiratory disease on exam or imaging, and with an oxygen saturation (SpO2) greater than 94% on room air; and (iii) severe illness was defined as SpO2 less than 94% on room air, ratio of arterial oxygen partial pressure (PaO2 in mmHg) to fractional inspired oxygen (PaO2/FiO2) was less than 300mmHg, respiratory rate greater than 30 breaths/minute, or greater than 50% lung infiltrates on imaging.[12] We defined COVID-19 variant era based on Center for Disease Control and Prevention (CDC) variant tracker: original virus and the alpha strain occurred prior to 6/20/2021; the Delta variant from 06/20/2021–12/19/2021; and the Omicron variant after 12/20/2021.[13]

PASC symptoms reported by the patient were categorized as mild (not interfering with activities of daily living, ADL), moderate (interfered with ADLs), severe (cannot perform ADL), or life threatening (requiring hospitalization).

Statistical methods:

Two sample tests were performed using the Wilcoxon test for continuous outcomes and the chi-squared test for binary or categorical outcomes (e.g. organ transplanted). The multivariable logistic regression model included factors related to acute COVID-19, as well as factors identified by literature review as associated with PASC; the model also included adjustment for gender as a potential confounder. Statistical analyses were conducted using logistic regression; hypothesis testing was based on the Wald test. Initial models included clinically pertinent variables and potential confounders. The Bayesian Information Criterion (BIC) was used to select the best fitting final models. We also conducted a mediation analysis to evaluate the extent to which the effect of pre-transplant vaccination on PASC

was mediated by disease severity. All of the regressions that comprise such an analysis were adjusted for the potential effect of confounding. A graphic illustrating the direct and mediated effects in this setting is provided in the supplementary materials. Statistical analysis was performed using STATA (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC).

Results:

Demographics:

Among the 224 SOTRs identified with acute COVID-19 during the study period, 16 died within 6 weeks of follow-up; four deaths were attributed to acute COVID-19 infection. Thus, 208 SOTR were alive at 6 weeks and included in the study. Among these, 72 (35%) had symptoms consistent with PASC at 6 weeks from diagnosis of acute COVID-19. SOTRs in both groups (PASC vs. no PASC) were similar in regard to age, gender, and ethnicity (Table 1). The median age of participants was similar: 54 years in the PASC group and 56 years in the non-PASC group. There were 31/72 (43%) women in the PASC group, and 44/136 (32%) in the non-PASC group.

Transplant History:

Neither time from transplant to acute COVID-19 diagnosis nor type of organ transplanted was associated with onset of PASC in univariable analyses (Table 1). Between 25% and 30% of patients were within the first year of transplant in both groups (Table 1).

Immunosuppression regimen at the time of acute COVID-19 infection was reviewed. The majority of SOTRs in both the PASC and non-PASC groups were on a combination of tacrolimus (90% versus 82%), mycophenolate mofetil (MMF) (58% versus 62%) and prednisone (67% versus 56%), respectively, as noted in Table 1. No specific immunosuppressive agent was associated with PASC in univariate analysis.

PASC symptoms, duration, and severity:

Among the 72 SOTR with PASC, respiratory symptoms were the most reported symptom of PASC occurring in 48/72 (67%) of participants, including shortness of breath (36/72) and cough (14/72) at 6 weeks (Figure 1). Of note, respiratory symptoms were considered part of the PASC symptomology when other diagnoses were excluded per chart review. Tiredness or fatigue was the second most common (32%). Each symptom, with the exception of difficulty concentrating/brain fog and anorexia, diminished over subsequent time frames. It is notable that lung transplant recipients reported respiratory symptoms more commonly than did other organ transplants: 9/18 (35%) lung recipients, compared with 12/65 (18%) liver transplant recipients, and 12/82 (15%) kidney transplant recipients. Other common symptoms included headaches (29/72, 40%), difficulty concentrating (7/72, 10%) and pain (4/72, 6%). Anosmia and/or dysgeusia was rare (2/72, 3%) at 6 weeks (Figure 1).

Thirty-nine of the 72 (54%) had symptoms that persisted at least 12-weeks after diagnosis. Seventeen patients (24%) reported symptoms at 24 weeks.

Thirty-five of the 72 patients with PASC (49%) reported mild symptoms; 27/72 (38%) reported moderate symptoms; and 3/72 (4%) reported their symptoms as severe. Participants occasionally reported intermittent periods of symptomatology alternating with feeling well, termed as relapse. Fifteen of the 72 (21%) reported occasional or frequent relapses.

COVID-19 vaccination history:

Over one-third of participants had at least a single dose of COVID-19 vaccination prior to acute COVID-19 diagnosis in both groups (Table 1). In the PASC group, 23/72 (32%) had received two or more mRNA vaccines or one J&J vaccine. This was similar to the non-PASC group, among which 46/136 (34%) had received similar vaccination. We also noted that time from the latest COVID-19 vaccination to acute COVID-19 diagnosis was similar among both groups. Of interest, the number of SOTRs that had received at least one dose of a COVID-19 vaccination prior to transplant, was lower in the PASC vs. non-PASC group (9/72 (13%) vs. 34/136 (25%), p=.0.03). Among those SOTRs that received at least a single dose of COVID-19 vaccine prior to transplant 9/43 (21%) developed PASC, whereas 63/165 (38%) not vaccinated prior to transplant developed PASC (0=0.034).

Acute COVID-19 event:

Among those SOTRs who had been hospitalized for acute COVID-19, 48/102 (47%) developed PASC; among those not hospitalized 24/116 (21%) developed PASC (p<0.001). Of the 72 who developed PASC, 15 (21%) had been admitted to the intensive care unit (ICU) including 9 (13%), who required mechanical ventilation. Severity of acute COVID-19 as defined by NIH criteria was associated with development of PASC in univariate analysis: 12/15 patients (80%) with severe acute COVID-19 developed PASC, whereas 60/193 (31%) without severe disease developed PASC (p <0.001) (Table 2). PASC developed in 55/127 (43%) with respiratory symptoms during acute COVID-19 versus 17/81 (21%) without (p<0.001).

Treatment of acute COVID-19 consisted of remdesivir (65/208, 31%), steroids (64/208, 31%), and/or SARS-CoV-2 targeted monoclonal antibodies (72/208, 35%) (Table 2). PASC diagnosis was more common in patients that received remdesivir and steroids in univariate analysis; these patients also had more severe disease. Anti-SARS-CoV-2 monoclonal antibody administration was significantly associated with decreased development of PASC in univariate analysis. Discontinuation or reduction in mycophenolate dose during acute COVID-19 was not associated with PASC. Among those patients for whom mycophenolate was either held or reduced, 28/69 (41%) developed PASC, compared 41/69 (59%) who did not develop PASC (p=0.20).

Routine sequencing to identify variants of concern was not performed at our institution and so we estimated the relevant variant era based on the date of the acute illness, per CDC criteria.[13] There were no differences by variant era in the proportion of study participants who developed PASC.

Multivariable analysis:

Disease severity and presence of respiratory symptoms during acute COVID-19 illness were significantly associated with PASC. The odds of developing PASC among patients with respiratory symptoms were almost twice that of patients without these symptoms (OR= 2.08 95% CI 0.83 to 2.98, p=0.034). Severe acute COVID-19 increased the odds of developing PASC by 9-fold (OR 9.11, CI 2.38 to 34.90, p=0.001). Moderate severity of acute COVID-19 increased the odds of developing PASC by approximately 3-fold (OR 2.98, CI 1.39 to 6.38, p=0.005). The type of transplant organ was not associated with increased odds of developing PASC; but we note that the numbers of patients in different organ transplant categories were small. Neither treatment with remdesivir nor anti-SARS-CoV-2 monoclonal antibody treatment was associated with PASC in the multivariable analysis.

Pre-transplant vaccination was associated with reduced odds of developing PASC in univariate analysis. As this was the only variable in the model that occurred temporally prior to acute COVID-19 diagnosis, we investigated its role in a separate multivariable model which included acute COVID-19 disease severity. In the best fitting model selected by BIC, pre-transplant vaccination was associated with lower odds of PASC (OR 0.39, 95% CI 0.16 to 0.95, p=0.037), while accounting for disease severity in the model. Moderate severity of acute COVID-19 was associated with 3.5-fold increase in odds of PASC (OR 3.52, 95% CI 1.64 to 7.52), whereas severe acute COVID-19 was associated with 12-fold increase in odds of PASC in this model (OR 12.07, 3.19 to 45.58, p<0.001) (Table 3b and Supplement).

To further investigate these relationships, we performed a mediation analysis (details in Supplement), which showed a direct effect of both pre-transplant vaccination and disease severity of acute COVID-19 on development of PASC. Thus, pre-transplant vaccination had an additional independent protective effect on PASC incidence in our study, though additional confirmation is needed with larger studies.

Healthcare utilization: Hospital length of stay during acute COVID-19 was reflective of disease severity, with a median of 6 vs. 5 days in the PASC and non- PASC groups respectively (p =0.018). The median length of stay in the ICU was longer in the PASC vs. non- PASC group (14 vs. 5 days, p=0.023). Among survivors, the number of outpatient healthcare visits were similar among both groups with a median follow up visit of one in each group.

Discussion:

We demonstrated that almost a third of SOTRs that survived at least 6 weeks following diagnosis of acute COVID-19 developed PASC. Severe disease and presence of respiratory symptoms during the acute COVID-19 illness were significantly associated with development of PASC in our multivariable analysis though overall burden of disease was high even among those without severe disease. Additionally, pre-transplant vaccination was observed to be protective of PASC development when investigated in multivariable analysis; and this additional protective effect was independent of pre-transplant vaccination's effect on acute COVID-19 disease severity.

Studies assessing PASC in immunocompetent people report development of PASC in 26–62%.[4, 5, 14] Some variability may be related to differences in definitions of the syndrome, with some of these studies defining PASC as lasting at least 4 weeks and others as lasting up to 6 months. We used 6 weeks as the cut-off in our definition of PASC as prior data suggest that COVID-19 related viral shedding and symptomology may be prolonged in immunocompromised hosts. [1, 8, 11] In our study, PASC occurred in 34.6% of SOTRs with acute COVID-19 that survived to at least 6 weeks. Among those with PASC, 45% of patients reported symptoms that lasted 6–12 weeks.

PASC symptoms described by our patients are similar to those described in immunocompetent people.[15] Respiratory symptoms were the most commonly reported across all time periods from 6 to 24 weeks. [16] Psychological symptoms, including depression, confusion, anxiety, and difficulty concentrating were all reported, but were less common in our cohort than described in the general population.[17] Underreporting of psychological symptoms may be a limitation of chart review, as these are not commonly asked for in review of systems by all medical providers.

Certain symptoms of acute COVID-19 in SOTRs were significant predictors of PASC in the multivariable analysis. Respiratory symptoms had an increased odds of developing PASC. Respiratory symptoms, which includes both shortness of breath and cough, are frequently seen in more severe disease, but the effect of symptoms on development of PASC remained significant even when accounting for severe acute COVID-19 disease. Anosmia/dysgeusia were not commonly reported in our population but have been found in non-hospitalized population to be associated with PASC.[18–20] The fact that no other symptoms were significant in the development of PASC in our population bears further investigation. In one study of kidney transplant recipients, the number of symptoms in acute COVID-19 illness was the only independent risk factor identified with development of PASC.[21]

Severe presentation of acute COVID-19 appeared to be a strong predictor for the development of PASC. Severe acute COVID-19 was also more likely to be associated with respiratory symptoms, remdesivir use, and hospitalization in our cohort. Disease severity remained an independent predictor in the multivariable model; although some studies have demonstrated an association between acute COVID-19 disease severity and persistent symptoms, they also note that mild acute COVID-19 may be associated with PASC.[16–18, 22] Based on our multivariable analysis, both severe acute COVID-19 and presence of respiratory symptoms at the index illness independently increased the odds of developing PASC.

Treatment of COVID-19 did not affect the development of PASC. Although remdesivir, anti-SARS-CoV-2 monoclonal antibody, and steroids were all significantly associated with PASC in univariate analysis, these were not associated in the multivariable model when controlling for acute COVID-19 disease severity and presence of respiratory symptoms. Although a protective effect of anti-SARS-CoV-2 monoclonal antibody treatment has been theorized in studies of PASC, its benefit among hospitalized patients is unknown.[23] It should be noted that all patients in our study who received remdesivir were hospitalized, whereas most patients treated with anti-SARS-CoV-2 monoclonal antibody were outpatient;

hospitalization appeared to be a proxy for severity of acute COVID-19 disease in these patients. Our study did not include patients treated with oral antivirals as our center did not use these agents in transplant recipients during the time-period of the study, nor did it include patients treated with tixagevimab-cilgavimab as this was not available to patients at UCSD during the study time-period.

Of particular interest was the finding that patients that had received at least one dose of COVID-19 vaccination prior to transplant had significantly reduced odds of developing PASC. We speculate that this could be related to a more robust immune response to COVID-19 vaccination in the pre-transplant period. Mediation analysis suggested an effect of pre-transplant vaccination on PASC development that is independent of its effect on modulation of disease severity of acute COVID-19. This important preliminary finding should be further investigated in multicenter prospective cohorts. This finding may provide an additional reason for transplant candidates to receive COVID-19 vaccination while on the waitlist.

Our study has several limitations including the fact that this was single center and retrospective in nature. It is possible that patients with mild acute COVID-19 did not report their illness to our transplant center and the study may be biased to those with more symptomatic illness, thus impacting the generalizability of our results. Additionally, symptoms may not have been recorded in the same manner in the medical record of different patients, and there may have been a difference in clinical presentation based on various COVID-19 eras. Symptoms of PASC were abstracted from the medical record and thus mild and/or psychological symptoms, such as anosmia or “brain fog”, may be underreported in our study. We noted collinearity among several predictors that are associated with hospitalization, such as acute COVID-19 disease severity, nature of acute COVID-19 treatment and respiratory symptoms. For example, the use of remdesivir was solely in the inpatient setting during the study period, though later we have used remdesivir in the outpatient setting as well. As a result, it is not possible to isolate the effect of hospitalization itself on PASC. Finally, our study lacked a comparison group of non-immunocompromised patients. Therefore, we cannot speculate whether immunomodulating drugs have a protective effect or impact on PASC duration. In terms of vaccination status, we reviewed the medical record in the “Immunizations” section of the electronic health record, which has bidirectional data sharing with the state immunization registry; however, we cannot confirm that 100% of vaccinations were noted.

In conclusion, we found that one third of SOTRs that survived an episode of acute COVID-19 developed PASC. In our cohort, acute COVID-19 disease severity and presence of respiratory symptoms increased the odds of developing PASC. Both pre-transplant vaccination and reduction in acute COVID-19 disease severity appear independently to reduce the risk of PASC, thus further increasing the impetus for pre-transplant COVID-19 vaccination. Further research is needed with larger, multicenter, and prospective cohorts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data availability statement:

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Abbreviations:

BIC	Bayesian Information Criterion
CDC	Centers for Disease Control and Prevention
COVID-19	Coronavirus disease 2019
FiO2	fraction of inspired oxygen
ICU	Intensive care unit
IRB	institutional review board
J&J	Johnson and Johnson
NIH	National Institutes of Health
PaO2	partial pressure of oxygen
PASC	Post-acute sequelae of COVID-19
SpO2	capillary oxygen saturation
SARS	CoV-2 severe acute respiratory syndrome coronavirus-2
SOTR	solid organ transplant recipients

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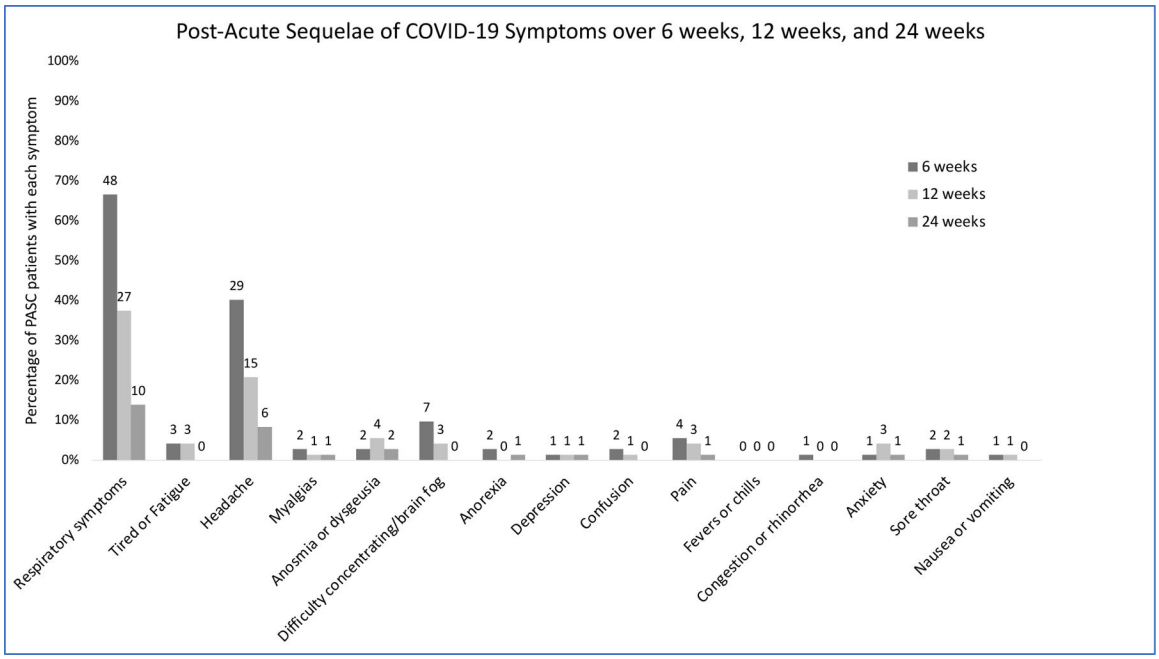

Figure 1.

Presence of post-acute sequelae of COVID-19 (PASC) symptoms at 6, 12, and 24 weeks after COVID-19 infection.

Table 1.

Demographics and baseline characteristics of the study population.

	PASC (n= 72)	Non-PASC (n= 136)	p-value
Demographics			
Median age in years, (IQR)	54 (46–65)	56 (45–64)	0.63
Female gender, %	31 (43.1%)	44 (32.6%)	0.14
Race, %			0.21
White	43 (59.7%)	82 (60.3%)	
Black	7 (9.7%)	6 (4.4%)	
Asian	4 (5.6%)	9 (6.6%)	
Other/decline to state	18 (25.0%)	39 (28.7%)	
Hispanic ethnicity, %	42 (58.3%)	79 (58.1%)	0.97
Transplant Details			
Within one year of transplant, %	18 (25.0%)	40 (29.4%)	0.50
Median time since transplant in months (IQR)	38 (11–74)	33 (13–72)	0.89
Organ transplanted, %			0.43
Kidney	20 (27.8%)	45 (33.1%)	
Liver	19 (26.4%)	38 (27.9%)	
Heart	14 (19.4%)	30 (22.1%)	
Lung	12 (16.7%)	11 (8.1%)	
Multiorgan	7 (9.7%)	12 (8.8%)	
Immunosuppression, %:			
Tacrolimus	65 (90.3%)	111 (81.6%)	0.10
MMF	42 (58.3%)	84 (61.8%)	0.63
Prednisone	48 (66.7%)	76 (55.9%)	0.13
Sirolimus	8 (11.1%)	17 (12.5%)	0.78
Cyclosporine	5 (6.9%)	17 (12.5%)	0.22
Azathioprine	0	5 (3.7%)	0.1
Tocilizumab	0	3 (2.2%)	0.2
COVID-19 Vaccination status			
At least two mRNA vaccines or one J&J vaccine (any time pre- or post-transplant)	23 (31.9%)	46 (33.8%)	0.78
Any vaccine dose prior to COVID-19, %	25 (34.7%)	50 (36.8%)	0.77
At least one vaccine dose prior to transplant, %	9 (12.5%)	34 (25%)	0.034
Days from last vaccine dose to COVID-19, (IQR)	192 (121–276)	258 (143–296)	0.12

[a]There were not enough data to perform statistical tests of significance.

Table 2.

Characteristics of COVID-19 symptoms, hospitalization, and management among solid organ transplant recipients with post-acute sequelae of COVID-19 (PASC) and those without PASC.

	PASC (72)	No PASC (136)	p-value
Acute symptoms during COVID-19, %			
Fever, chills	36 (50.0%)	83 (61.0%)	0.13
Shortness of breath, cough	55 (76.4%)	72 (52.9%)	<0.001
Gastrointestinal	15 (20.8%)	22 (16.2%)	0.40
Upper respiratory tract symptoms	7 (9.7%)	19 (14.0%)	0.38
Headache	24 (33.3%)	44 (32.4%)	0.89
Anosmia/dysgeusia	5 (6.9%)	7 (5.1%)	0.60
Fatigue	29 (40.3%)	50 (36.8%)	0.62
Myalgia	11 (15.3%)	19 (14.0%)	0.80
Hospitalized, %	48 (66.7%)	54 (39.7%)	<0.001
Intensive care unit (ICU), %	15 (20.8%)	6 (4.4%)	<0.001
On mechanical ventilation	9 (12.5%)	1 (0.7%)	<0.001
Hospitalization length of stay in days, median (IQR)	6 (5–16)	5 (3–8)	0.018
ICU length of stay in days, median (IQR)	14 (5–34)	5 (2–5)	0.023
Severity of acute COVID-19, %			<0.001
Mild	40 (55.6%)	116 (85.3%)	
Moderate	20 (27.8%)	17 (12.5%)	
Severe	12 (16.7%)	3 (2.2%)	
Asymptomatic, %	5 (6.9%)	13 (9.6%)	0.52
Treatment, %			
Remdesivir	37 (51.4%)	28 (20.6%)	<0.001
Steroids	33 (45.8%)	31 (22.8%)	<0.001
Anti-SARS-CoV-2 antibody	17 (23.6%)	55 (40.4%)	0.015
Cessation or reduction in mycophenolate dose, %	28 (38.9%)	41 (30.1%)	0.20
Predominant variant era, %			0.74
Original and alpha	51 (72.2%)	88 (64.7%)	
Delta	8 (11.1%)	19 (14.0%)	
Omicron	12 (16.7%)	29 (21.3%)	
Year of acute COVID-19 diagnosis, %			0.56
2020	26 (36.11%)	47 (34.6%)	
2021	36 (50.0%)	62 (45.6%)	
2022	10 (13.9%)	27 (19.9%)	

Table 3a.

Results of multivariable analysis with post-acute sequelae of COVID-19 (PASC) as the outcome.

Variables	Odds Ratio	95% CI	p value
Gender (Female)	1.58	0.83 to 2.98	0.162
Moderate acute COVID-19 disease	2.98	1.39 to 6.38	0.005
Severe acute COVID-19 disease	9.11	2.38 to 34.90	0.001
Respiratory symptoms	2.08	1.06 to 4.09	0.034

Table 3b.

Results of multivariable logistic regression model with PASC as the outcome and incorporating gender (potential confounder), severe acute COVID-19 and pre-transplant vaccination.

	Odds Ratio	95% CI	p-value
Gender (female)	1.66	0.87 to 3.13	0.121
Moderate acute COVID-19 disease	3.52	1.64 to 7.52	0.001
Severe acute COVID-19 disease	12.07	3.19 to 45.58	<0.001
Vaccinated prior to transplant	0.39	0.16 to 0.95	0.037