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Managing COVID-19-positive Solid Organ Transplant Recipients in the Community: What a Community Healthcare Provider Needs to Know

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Background. The current surge of coronavirus 2019 (COVID-19) cases in certain parts of the country has burdened the healthcare system, limiting access to tertiary centers for many. As a result, COVID-19-positive Solid Organ Transplant (SOT) recipients are increasingly being managed by local healthcare providers. It is crucial for community providers to understand disease severity and know if COVID-19-impacted SOT recipients have a different clinical course compared with COVID-19-negative SOT recipients with a similar presentation. **Methods.** We conducted a retrospective analysis on SOT recipients suspected to have COVID-19 infection tested during March 14, 2020–April 30, 2020. Patients were followed from time of testing to May 31, 2020. **Results.** One hundred sixty SOT recipients underwent testing: 22 COVID-19 positive and 138 COVID-19 negative. COVID-19-positive patients were more likely to have rapid progression of symptoms (median 3 vs 6 d, $P = 0.002$), greater hospitalizations (78% vs 64%, $P < 0.017$), and need for intensive care unit care (45% vs 17%, $P < 0.001$). Severe COVID-19 infection was not observed in patients on Belatacept for immunosuppression (30% vs 87%, $P = 0.001$). COVID-19 positive patients in the intensive care unit were more likely to have multifocal opacities on radiological imaging in comparison to those admitted to the medical floor (90% vs 11%). Survival probability was similar in both cohorts. **Conclusion.** COVID-19-infected SOT recipients have a propensity for rapid clinical decompensation. Local providers need to be work closely with transplant centers to appropriately triage and manage COVID-19 SOT recipients in the community.

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Coronavirus 2019 (COVID-19) has caused a global pandemic with staggering worldwide fatality. In the United States, COVID-19-associated case fatality is currently estimated at 5.3%.¹ It is now known that COVID-19 infections can manifest in a wide spectrum of clinical presentations ranging from asymptomatic to life-threatening presentations with multiorgan failures.² In the general population fever, cough, or fatigue at presentation is common, and the

literature published shows lymphopenia as a negative prognostic factor.^{2,3} Bilateral multifocal opacities on chest radiograph (CXR) are frequently observed in moderate to severe COVID-19 infection.²

Solid organ transplant (SOT) recipients are known to be at an increased risk for infections, emergency department visits, and hospitalizations, given their immunocompromised state and existing comorbidities, regardless of the time lapsed since transplant.⁴ Atypical clinical presentation and simultaneous infections with 2 or more organisms are not uncommon in transplant populations.⁵

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The differential diagnosis when evaluating SOT recipients for symptoms mimicking COVID-19 disease is vast and includes several infectious and noninfectious causes that are known to result in hospitalizations, readmission, and deaths in this population.⁶ It is presumed that COVID-19 infections in SOT recipients manifests with greater severity and results in significantly higher proportion of deaths.⁷⁻¹¹ Early published data show 16%–20% mortality among COVID-19-positive SOT recipients.¹⁰⁻¹³ Long-term SOT recipients (transplanted >3 years), particularly those with kidney transplants, are primarily managed by their local healthcare providers with limited expertise in caring for this vulnerable cohort. With the increasing cases in our region and with tertiary centers being at capacity, community providers are increasingly having to care for COVID-19 positive patients.¹⁴⁻¹⁷ Therefore, a better understanding of the COVID-19 disease spectrum in SOT recipients to identify those at risk for decompensation and appropriate triage is crucial for community providers. In this retrospective study, we examined SOT recipients suspected to have COVID-19 infection, who underwent testing for the same. The aim of this retrospective study was (1) to identify differences in susceptibilities; (2) to assess acuity of illness, clinical course; and (3) to ascertain differences in allograft and patient survival among SOT recipients with COVID-19 and those with another illness having similar presentations. Our goal is to utilize the information to create a framework assist community providers to successfully manage COVID-19 SOT recipients in the community.

MATERIALS AND METHODS

The study was conducted at several Emory University hospitals (Emory-Main Campus, Emory-Midtown, Emory-St. Joseph, Emory-DeKalb Medical and Emory-John's Creek). The study protocol was approved by the Emory University Institutional Review Board (Protocol Number: STUDY00000455). Informed consent process was waived owing to the retrospective and low-risk nature of the study. SOT recipients presenting with symptoms suspicious for COVID-19 and subsequently tested between March 14 and April 30, 2020 were included in the study. Testing was performed at a dedicated COVID-19 clinic, emergency room (ER) or in the hospital setting at above-mentioned Emory locations. In-hospital COVID-19 testing was done (1) upon transfer from outside hospital/ER or direct admission from Emory outpatient transplant clinic for COVID-19 concerning symptoms; (2) at new onset of fever or fever of unknown origin in a hospitalized patient; (3) for acute respiratory decompensation; or (4) before procedures/transplant surgery. Nasopharyngeal polymerase chain reaction (PCR) assays (local assay from Emory Medical Laboratories) was used for initial COVID-19 testing. COVID-19 PCR testing of bronchoalveolar lavage was done only if patients had a bronchoscopy. SOT recipients were enrolled into this study at the time of COVID-19 testing. Enrolled subjects were followed until May 15, 2020. Data were collected by manual chart review and transplant database queries.

Definitions

Persons under investigation (PUI) were SOT recipients with COVID-19 suspicious symptoms who subsequently

underwent testing. Protocols aligned with Center for Disease Control (CDC) testing guidelines were applied for COVID-19 testing decisions.¹⁸ Concerning COVID-19 symptoms included fever, cough, sore-throat, shortness of breath, fatigue, headache, new loss of smell or taste, nausea/vomiting, or diarrhea.¹⁸ Fever was defined as a temperature greater than 37.5°C. Acuity at presentation was level of care (home, medical floor, or intensive care unit), and the patient was triaged to based on severity of presenting symptoms. The maximum level of acuity was the highest level of care required during the study duration. Concurrent infection was defined as the presence of 2 or more acute infections (viral, bacterial, or fungal) at the time of symptomatic presentation or emerging during the course of illness or hospital stay, diagnosed on laboratory testing (viral PCR testing, blood cultures, and stool or sputum samples). Lymphopenia was an absolute lymphocyte count less than 1000/ μ L on the automated white blood cell count (WBC) with automated differential. Diagnosis of acute kidney injury (AKI) was made based on (1) an increase in serum creatinine of greater than 0.3 mg/dl compared with baseline; (2) documented diagnosis in patients' problem lists by any provider; (3) nephrology consultation for AKI; or (4) need for renal replacement therapy documented during the study period.

Critically Ill SOT Recipients

To assess severity of illness and risk of mortality, sequential organ failure (SOFA) scores were calculated at the time of intensive care unit admission. SOFA scores (ranging from 0 to 24) are objective mortality prediction scores calculated based on degree of dysfunction of 6 organ systems (cardiovascular, respiratory, hepatic, renal, neurology, and coagulation).^{4,19} Higher SOFA score correlates to greater likelihood of in-hospital mortality.

Statistical Analysis

Statistical analysis was done using Microsoft Excel Data Analysis Pack. Means or medians with interquartile range (IQR) were used to express results, depending on whether data were normally distributed. Student's t-tests and ANOVA were used to compare the quantitative values with a normal distribution. Wilcoxon or Kruskal-Wallis test was used for variables without normal distribution. Chi-square and Fisher exact tests were used to evaluate categorical variables. Log rank tests were performed to compare survival probability. Statistical significance was determined by 2-tailed $P < 0.05$.

RESULTS

General Characteristics of COVID-19 tested SOT Recipients

Between March 14, 2020, and April 30, 2020, 173 adult SOT recipients were tested for COVID-19 (Figure 1). Thirteen asymptomatic SOT recipients tested before a procedure/surgery were excluded from the study. One hundred sixty SOT recipients were tested for COVID-19 symptoms, 22 were COVID-19 positive and 138 COVID-19 negative (Figure 2). Twenty-one COVID-19-negative patients were retested, given high clinical suspicion for COVID-19; of them, 1 tested positive and was included in the COVID-19 positive cohort. The median time between repeating the test was 8 days (IQR: 1–30 d) (Table 1).

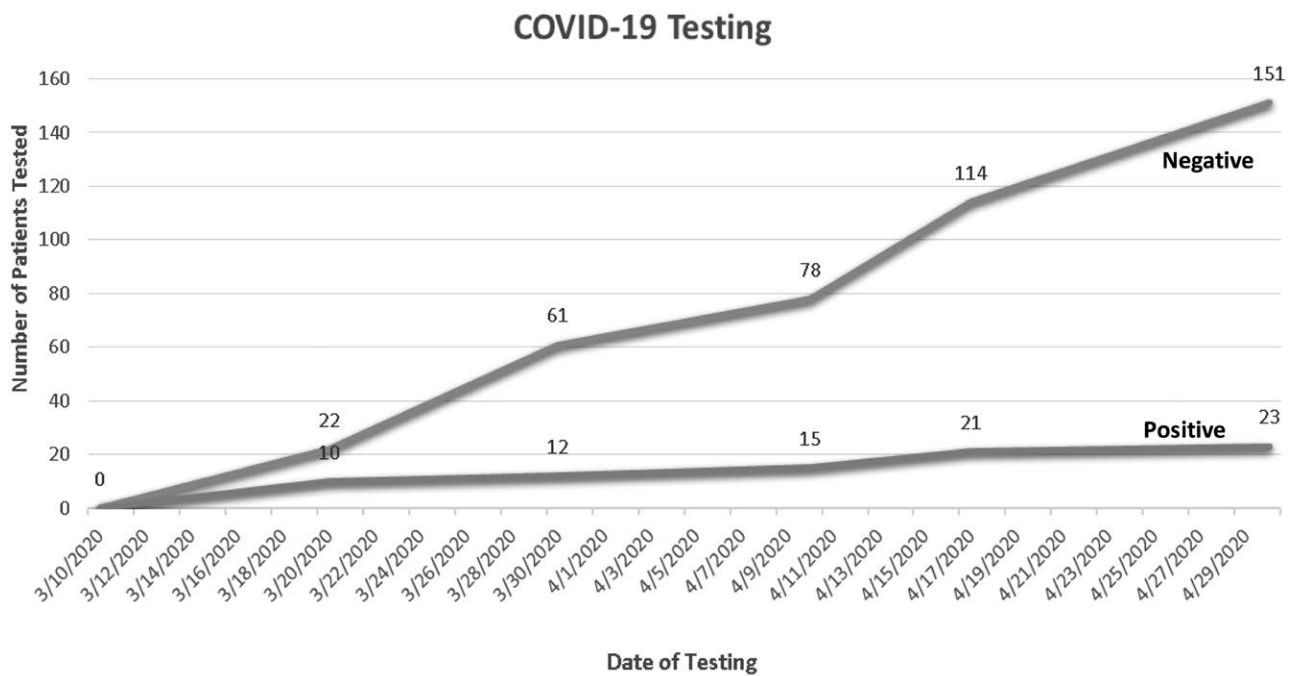


Figure 1. COVID-19 Testing Trends

FIGURE 1. COVID testing trends at Emory University between March 14, 2020, and April 30, 2020. *First testing done on March 14, 2020, and the last studied transplant was on April 30, 2020. COVID, coronavirus.

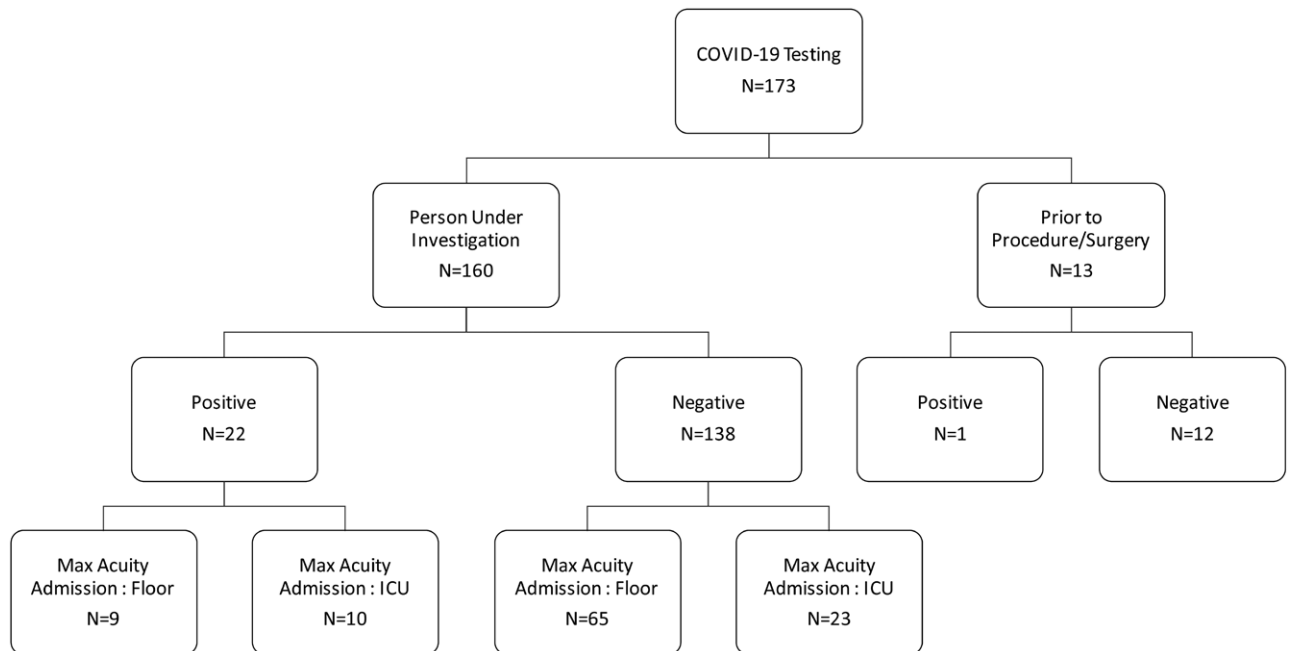


FIGURE 2. Schematic representation of COVID test results between March 14, 2020, and April 30, 2020. *Patients tested before procedure or surgery were excluded from the study. COVID, coronavirus.

Recipient age, sex, body mass index (BMI), race, comorbid conditions, smoking history, blood type, type of transplant, time since transplant, and maintenance immunosuppression were similar in both cohorts (Table 1). In the COVID-19-positive group, the median age was 55 years (IQR: 40–60 y), with 50% (11/22) being male and 59% (13/22) African American. In the COVID-19-negative cohort, the median age was 57 years (IQR: 44–65 y) with 54% (74/138) males, 51% (70/138) Caucasians, and 38% (54/138) African Americans.

Kidney transplant was the most common transplanted organ present in 64% (14/22) COVID-19-positive and 49% (68/138) of the COVID-19-negative group ($P = 0.33$). Among COVID-19 positive SOT recipients, 77% (17/22) versus 51% (70/138) in the COVID-19 negative group were transplanted for longer than 5 years, which was statistically significant ($P = 0.018$).

Time from symptom development to presentation was shorter in COVID-19 positive SOT recipients than in the COVID-19 negative group (median of 3 d [IQR: 1–7 d] vs

TABLE 1.**General characteristics of all patients tested for COVID-19**

Total (N = 160)	COVID-19 positive (N = 22)	COVID-19 negative (N = 138)	P
Testing location			
Outpatient COVID-19 clinic	5 (23%)	48 (35%)	
Emergency room	15 (68%)	66 (48%)	
Hospital	2 (9%)	24 (17%)	
Median age (IQR)	55 (40–60)	57 (44–65)	0.43
Male	11 (50%)	74 (54%)	0.73
BMI	27.3	26.8	0.69
Median follow-up (d)	36 (32–56)	39 (29–51)	0.7
Race, n (%)			0.41
Caucasian	8 (36%)	70 (51%)	
African American	13 (59%)	53 (38%)	
Hispanic	0	2 (2%)	
Asian	0	9 (6%)	
Unknown	1 (5%)	3 (2%)	
Other	0	1 (1%)	
Comorbid conditions			0.87
DM	8 (36%)	59 (43%)	
Coronary artery disease	3 (14%)	19 (10%)	
ESRD	3 (14%)	14 (10%)	
Malignancy	2 (9%)	19 (10%)	
Smoking history	6 (27%)	49 (36%)	0.45
Blood type, n (%)			0.25
O	8 (36%)	60 (44%)	
A	5 (23%)	48 (35%)	
B	3 (14%)	12 (9%)	
AB	2 (9%)	9 (6%)	
Unknown	4 (18%)	9 (6%)	
Type of Transplant, n (%)			0.33
Kidney	14 (64%)	68 (49%)	
Heart	4 (18%)	15 (11%)	
Liver	3 (14%)	34 (25%)	
Lung	1 (4%)	10 (7%)	
Combined	0	11 (8%)	
Time since transplant, n (%)			0.13
0–1 y	2 (9%)	28 (20%)	
1–5 y	3 (14%)	40 (29%)	
6–10 y	7 (32%)	34 (25%)	
>10 y	10 (45%)	36 (26%)	
Maintenance immunosuppression			0.64
Belatacept	4 (18%)	25 (18%)	
Other immunosuppression	18 (82%)	113 (82%)	
Median time to presentation in days (IQR)	3 (1–7)	6 (2–7)	<0.001
Acuity at presentation, n (%)			0.017
Home	5 (22%)	51 (37%)	
Floor	14 (64%)	76 (55%)	
ICU	3 (14%)	11 (8%)	
Max level of acuity, n (%)			<0.001
Home	3 (14%)	50 (36%)	
Floor	9 (41%)	65 (47%)	
ICU	10 (45%)	23 (17%)	
Clinical findings			
Fever	12 (55%)	66 (48%)	0.54
Pulmonary	17 (77%)	76 (55%)	0.05
GI symptoms	10 (45%)	54 (39%)	0.56
GU symptoms	2 (9%)	12 (9%)	0.71
CNS symptoms	0	33 (24%)	0.004
Other constitutional symptoms (malaise, myalgia, chills etc)	16 (72%)	93 (67%)	0.59
Concurrent infections	6 (27%)	10 (7%)	0.003
Total length of stay (IQR)	10 (4–12)	5 (3–10)	0.55
ICU length of stay (IQR)	7 (4–11)	4 (2–16)	0.29
Disposition (n = 106)	N = 19	N = 88	0.39
Discharged	14 (74%)	73 (83%)	
Pending	2 (10%)	5 (7%)	
Death	3 (16%)	9 (10%)	0.92
Median duration of follow-up in days (IQR)	36 (28–54)	37 (28–51)	0.53
Readmissions, n (%)	5 (26%)	11 (13%)	0.13

Bold indicates significant findings/results.

AKI, acute kidney injury; BMI, body mass index; CNS, central nervous system; COVID-19, coronavirus 2019; DM, diabetes mellitus; ESRD, end stage renal disease; GI, gastrointestinal; GU, genitourinary; ICU, intensive care unit; IQR, interquartile range.

6 d [IQR: 2–7 d], $P < 0.001$). Respiratory symptoms (cough or shortness of breath) were the most common presenting symptoms among COVID-19-positive patients. Seventy-seven percent (17/22) COVID-19-positive SOT recipients had pulmonary symptoms in comparison to 55% (76/138) COVID-19-negative subjects ($P = 0.05$). Fever at presentation was seen only in 55% (12/22) COVID-19-positive and 48% (66/138) of the COVID-19-negative patients ($P = 0.54$). At the time of initial presentation, COVID-19-positive SOT recipients were more likely to be hospitalized versus COVID-19-negative recipients (77% [17/22] vs 63% [87/138], $P = 0.017$). Of the SOT recipients not admitted at initial presentation, 40% (2/5) in the COVID-19-positive cohort compared with 2% (1/51) in the COVID-19-negative group required hospitalization for clinical worsening of symptoms. Additionally, 43% (6/14) COVID-19-positive subjects versus 16% (12/76) COVID-19-negative patients initially admitted to the floor ultimately transferred to the intensive care unit for acute decompensation. COVID-19-positive patients required a higher acuity of care ($P < 0.01$) with 45% (10/22) versus 17% (23/138) among the COVID-19-negative cohort having an intensive care unit course. The median length of hospital stay was 10 days (IQR: 4–12 d) versus 5 days (IQR: 3–10 d) between COVID-19-positive and COVID-19-negative cohorts, respectively ($P = 0.55$). The median length of intensive care unit stay was 7 days (IQR: 4–11 d) for COVID-19-positive and 4 days (IQR: 2–16 d) for COVID-19-negative SOT recipients ($P = 0.29$). Likelihood of concurrent infections was higher in the COVID-19-positive cohort compared with the COVID-19-negative arm (27% [6/22] vs 7% [10/138], $P = 0.003$). All enrolled patients had a minimum follow-up of 14 days from the day of testing. Median follow-up was 36 days (IQR: 28–51 d) for COVID-19-positive and 37 days (IQR: 27–54 d) for COVID-19-negative subjects ($P = 0.53$). During the study period, of the COVID-19-positive recipients needing hospitalization, 74% (14/19) were successfully discharged from the hospital with 26% (5/19) having a readmission. In the COVID-19-negative cohort, 83% (73/88) were successfully discharged and 13% (11/88) readmitted within the study period. The discharge diagnosis among hospitalized COVID-19 negative SOT recipients is listed in (Table 2). Mortality during the follow-up time was 16% (3/22) in COVID-19-positive and

10% (9/88) in COVID-19-negative patients ($P = 0.92$). There was no difference in the survival probability between the 2 cohorts (Figure 3). Transplant allograft loss was not seen in either cohorts during the study duration.

SOT Recipients With Maximum Acuity Admission to the Floor

COVID-19-positive and -negative SOT recipients with maximal acuity to the medical floor were similar in age, sex, BMI, comorbidities, smoking history, median time to presentation, and length of hospitalization. None (0/9) of the COVID-19-positive SOT recipients versus 85% (55/65) of the COVID-19-negative group were on Belatacept immunosuppression regimen ($P < 0.001$). Fifty-six percent (5/9) COVID-19-positive recipients had normal CXR with multifocal opacities on CXR seen in only 11% (1/9) COVID-19-positive and 9% (6/65) COVID-19-negative SOT recipients ($P = 0.72$). While mean WBC count was lower in COVID-19-positive (7×10^3 cells/ μ L) patients compared with the COVID-19-negative (9.8×10^3 cells/ μ L) cohort ($P = 0.013$), lymphopenia was only seen in 11% (1/9) COVID-19-positive but in 26% (17/65) COVID-19-negative patients ($P = 0.32$). AKI was noted in 56% (5/9) COVID-19-positive and 31% (20/65) COVID-19-negative patients ($P = 0.14$). No patients in either groups needed renal replacement therapy. One hundred percent of patients in both the groups were discharged within the study duration (Table 3).

SOT Recipients with Maximum Acuity Admission to the Intensive Care Unit

No differences in age, sex, BMI, comorbidities, smoking history, SOFA score, median length of hospitalization, or median length of intensive care unit stay were observed between COVID-19-positive and -negative groups. Thirty percent (3/10) COVID-19-positive versus 87% (20/23) COVID-19-negative SOT recipients were on Belatacept ($P = 0.001$). Both COVID-19-positive and -negative patients had similar symptoms at presentation ($P = 0.34$). Among the COVID-19-positive cohort 60% (6/10) had fever, 80% (8/10) reported pulmonary symptoms, and 50% (5/10) had gastrointestinal symptoms on presentation. Lower mean WBC was seen in the COVID-19-positive cohort compared with COVID-19-negative cohort (7.1×10^3 cells/ μ L vs 11×10^3 cells/ μ L, $P = 0.035$); however, lymphopenia was observed only in 50% (5/10) COVID-19-positive versus 39% (9/23) COVID-19-negative group ($P = 0.56$). Elevated inflammatory markers were more commonly seen in the COVID-19-positive arm. Both lactate dehydrogenase and D-Dimer were elevated in 80% COVID-19-positive patients versus COVID-19-negative patients having 30% (7/23) lactate dehydrogenase and 22% (5/23) D-Dimer elevation ($P = 0.01$). Multifocal opacities on imaging studies was seen in 90% (9/10) COVID-19-positive in-comparison to 35% (8/23) COVID-19-negative SOT recipients ($P = 0.05$). In the COVID-19-positive cohort, 90% (9/10) needed ventilator support, while 57% (13/23) COVID-19-negative SOT recipients needed ventilator support ($P = 0.06$). AKI was documented in 60% (6/10) COVID-19-positive and 65% (15/23) of COVID-19-negative patients ($P = 0.77$). Of them, 20% (2/10) COVID-19-positive and 35% (8/23) COVID-19-negative patients required renal replacement therapy ($P = 0.39$). Concurrent infections were higher in

TABLE 2.

Discharge diagnosis for hospitalized COVID-19-negative SOT recipients

Total (discharge + deaths) N = 82	
Pneumonia (community acquired, aspiration)	16 (19%)
GI infections (gastroenteritis, colitis, pancreatitis, cholangitis)	14 (17%)
Upper respiratory tract infection	12 (15%)
Sepsis/septic shock	8 (10%)
Bactremia	8 (10%)
Symptomatic rejection	7 (9%)
Fever of unknown origin	6 (7%)
Urinary tract infection	4 (5%)
CHF	3 (4%)
CNS infection (cerebral abscess)	2 (2%)
Other (abdominal wall cellulitis, PRES syndrome)	2 (2%)

CHF, congestive heart failure; CNS, central nervous system; COVID-19, coronavirus 2019; GI, gastrointestinal; SOT, solid organ transplant.

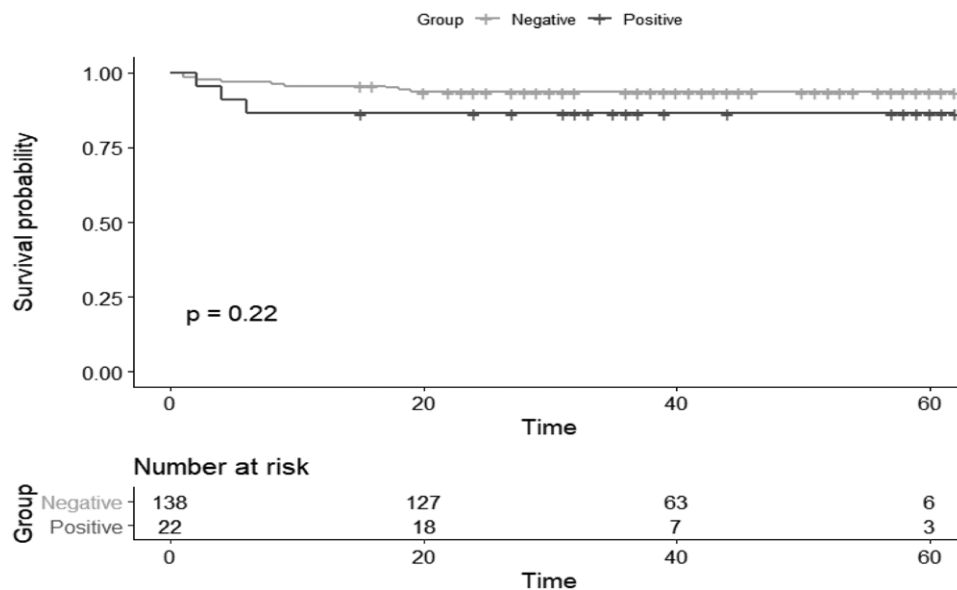


FIGURE 3. Survival probability between COVID-positive and COVID-negative cohorts. COVID, coronavirus.

the COVID-19-positive cohort with 50% (5/10) versus 17% (4/23) in the COVID-19-negative cohort ($P = 0.05$). Fifty percent (5/10) COVID-19-positive and 52% (12/23) COVID-19-negative patients were successfully discharged ($P = 0.97$). During the study period, mortality in both cohorts was 30% ($P = 0.75$) (Table 4).

Treatment and Immunosuppression Management for COVID-19-positive SOT Recipients

No changes in immunosuppression regimen or COVID-19 treatment were provided to 100% (3/3) COVID-19-positive SOT recipients not requiring hospitalization. Immunosuppression was reduced in 47% (9/19) COVID-19-positive patients, with the antimetabolite agent being the first drug reduced or withdrawn. Directed COVID-19 treatment was decided in conjunction with infectious disease specialists. Forty-seven percent (9/19) COVID-19-positive patients were treated for COVID-19. Of these, 55% (5/9) were treated with azithromycin and hydroxychloroquine, while 45% (4/9) were treated with azithromycin alone. None of the patients met criteria to be enrolled in the Remdesivir trial. Tocilizumab was not considered for any patient given limited data on its benefit. One hundred percent (10/10) COVID-19-positive patients requiring intensive care unit-level care were treated with broad-spectrum antibiotics (Table 5).

DISCUSSION

We have described the experience at our institute during early COVID-19 pandemic and compared the risk of susceptibility, clinical presentation, and outcomes between COVID-19-positive SOT recipients and those with another illness presenting in a similar fashion. Our data suggest that COVID-19-positive SOT recipients are likely (1) rapid progression of symptoms; (2) higher likelihood of hospitalizations; (3) more severe illness needing intensive care unit care; and (4) more concurrent infections, in comparison to COVID-19-negative SOT recipients. The recent surge of COVID-19-positive cases in the southern and western states of the country has led to an increased demand for testing. While COVID-19 tests are more

readily available in most areas of the country, the global shortage of testing reagents/chemicals and limited equipment availability have caused significant backlogs, leading to prolonged turnaround times for results.²⁰⁻²³ Additionally, there have been reports of delays in testing appointment availabilities (more than a week) in certain areas, particularly in Georgia.²¹ This, combined with shortage of hospital beds and ventilators in this region¹⁴⁻¹⁷ has forced community healthcare providers to primarily rely on clinical findings, severity of presentation, and a high degree of clinical suspicion as a guide for offering COVID-19 testing, triage, and management (home isolation vs hospitalization) locally. It is therefore necessary for transplant centers to provide local facilities with resources and support to care for these patients until they have clinical improvement or can be transferred to a tertiary center.

Approximately, 40% of our COVID-19-positive SOT recipients required transfer to a higher level of care, which can adversely affect patient outcomes and also impact healthcare costs and burden available resources.²⁴ To minimize poor outcomes and optimize utilization of healthcare resources, identifying markers (clinical, laboratory, or radiological) to prognosticate infection severity in the COVID-19-positive SOT patient by community providers is critical but remains challenging.

Nonrespiratory clinical presentation of COVID-19 disease is increasingly being reported.²⁵⁻²⁷ While several of these manifestations are primarily due to the viral infection, others are secondary to inflammatory or immunologic sequelae.²⁵⁻²⁷ Previously published data in SOT recipients reported fever as the most common presenting symptom.⁸⁻¹¹ Chaudhary et al¹³ had 55% of SOT recipients with diarrhea on presentation, while 8.4% presented with altered mentation. In our study pulmonary symptoms were the most common presentation, while fever was observed only in 55% of our COVID-19-positive patients.

COVID-19 infection can trigger hyperinflammatory cascades, and it is postulated that lymphopenia observed among moderate and severe COVID-19 cases results from depletion of CD4 and CD8 T cells.²⁸ Lymphopenia and higher leukocyte counts have been identified as prognostic markers associated with severe COVID-19 illness.³ Contrary to this observation,

TABLE 3.
Characteristics of SOT recipients with maximal acuity admitted to the floor

Total N = 74 (%)	COVID-19 positive (N = 9)	COVID-19 negative (N = 65)	P
Age	53 (32–59)	60 (48–69)	0.2
Male	4 (44%)	39 (60%)	0.37
BMI	28.9	27.1	0.28
Comorbid conditions			0.29
DM	4 (44%)	31 (48%)	
Coronary artery disease	0	10 (15%)	
ESRD	0	9 (14%)	
Malignancy	0	10 (15%)	
Smoking history	2 (22%)	24 (37%)	0.39
Immunosuppression			<0.001
Belatacept	0	55 (85%)	
Other immunosuppression	9 (100%)	10 (15%)	
Median time to presentation in days (IQR)	3 (1–7)	3 (1–7)	
Clinical features			0.86
Fever	4 (44%)	30 (46%)	
Pulmonary symptoms	5 (56%)	28 (43%)	
GI symptoms	5 (56%)	27 (42%)	
GU symptoms	1 (11%)	11 (17%)	
CNS symptoms	0	8 (12%)	
Other constitutional symptoms (malaise, myalgia, chills etc)	6 (67%)	40 (61%)	
Laboratory findings			
Mean albumin	4	3.8	0.4
Mean WBC ($\times 10E3/\mu L$)	7	9.8	0.013
Lymphopenia	1 (11%)	17 (26%)	0.32
AKI	5 (56%)	20 (31%)	0.141
Radiological findings			0.72
Multifocal opacities	1 (11%)	6 (9%)	
Solitary lobe pneumonia	0	7 (11%)	
Normal	5 (56%)	32 (49%)	
Atelectasis	3 (33%)	15 (23%)	
Other (pleural effusion, pneumothorax, interstitial thickening)	0	5 (8%)	
Need for RRT	0	0	
Concurrent infections	1 (11%)	6 (9%)	0.86
Median length of hospital stay (IQR)	4 (1–10)	4 (2–7)	
Discharged	9 (100%)	65 ^a (100%)	

Bold indicates significant findings/results.

^a Two deaths following hospital discharge in the COVID-19-negative group.

AKI, acute kidney injury; BMI, body mass index; CK, creatinine kinase; CNS, central nervous system; COVID-19, coronavirus 2019; DM, diabetes mellitus; ESRD, end stage renal disease; GI, gastrointestinal; GU, genitourinary; IQR, interquartile range; LDH, lactate dehydrogenase; SOFA, sequential organ failure score; SOT, solid organ transplant; RRT, renal replacement therapy; WBC, white cell count.

in our study, moderate-severely ill COVID-19-positive SOT patients had lower WBC counts compared with COVID-19-negative SOT recipients, and lymphopenia was seen only in 50% of the severely ill COVID-19-positive patients.

At our institution, CXR is the first-line imaging study used for assessing COVID-19 PUIs. CXR is known to have a low sensitivity (~69%) for diagnosing COVID-19 infection.²⁹ The presence of bilateral multifocal opacities has been identified as an independent predictor for intubation.³⁰ In previously published COVID-19 data among SOT recipients, almost all hospitalized patients were found to have multifocal opacities.^{9–11} While we observed multifocal opacities in 90% COVID-19 SOT recipients requiring intensive care unit care, only 11% of SOT recipients admitted to the medical floor had these findings. Multifocal opacities likely represent an advanced stage of COVID-19 infection, and its presence even in clinically stable COVID-19-positive SOT recipients without severe symptoms

should be taken into consideration when triaging to minimize adverse patient outcomes. Further analysis in larger cohorts of COVID-19-positive SOT recipients is necessary to better utilize radiological findings for risk stratification.

At the Emory Transplant Center, approximately 400 solid organ transplants are performed every year.³¹ We observed considerably low moderate/severe COVID-19 infection in our SOT recipients during the early months of the pandemic compared to that reported in early data from New York.¹⁰ This could be due to early shelter-in-place that was effective in Georgia since April 4, 2020. Reports have also identified older age as a risk factor for severe COVID-19 illness in SOT recipients.¹⁰ Older age increases likelihood of infections and illnesses in all transplants patients, and we did not observe increased susceptibility to COVID-19 illness among our older patients. There have been several reports on increased susceptibility to COVID-19 infection and associated mortality in the

TABLE 4.**Characteristics of SOT recipients with maximal acuity admitted to the intensive care unit**

Total (N = 33)	COVID-19 positive (N = 10)	COVID-19 negative (N = 23)	P
Age	59 (46–61)	63 (54–67)	0.36
Male	6 (60%)	12 (52%)	0.68
BMI	26.1	25.6	0.84
Comorbid conditions			0.56
DM	3 (30%)	13 (57%)	
Coronary artery disease	3 (30%)	4 (17%)	
ESRD	3 (30%)	4 (17%)	
Malignancy	2 (20%)	5 (22%)	
Smoking history	3 (30%)	11 (48%)	0.34
SOFA score	7	7	0.7
Immunosuppression			0.001
Belatacept	3 (30%)	20 (87%)	
Other immunosuppression	7 (70%)	3 (13%)	
Clinical features			0.34
Fever	6 (60%)	6 (26%)	0.06
Pulmonary symptoms	8 (80%)	13 (57%)	
GI symptoms	5 (50%)	9 (39%)	
GU symptoms	1 (10%)	1 (4%)	
CNS symptoms	0	9 (39%)	
Other constitutional symptoms (malaise, myalgia, chills etc)	6 (60%)	11 (48%)	
Laboratory findings			
Mean albumin	3.64	3.52	0.56
Mean WBC ($\times 10E3/\mu L$)	7.13	11	0.035
Mean platelets ($\times 10E3/\mu L$)	214.7	192.7	0.57
Lymphopenia	5 (50%)	9 (39%)	0.56
AKI	6 (60%)	15 (65%)	0.77
Inflammatory markers			0.01
Elevated transaminase	5 (50%)	12 (52%)	
Elevated troponins	6 (60%)	8 (35%)	
LDH elevation	8 (80%)	7 (30%)	
Elevated CK	4 (40%)	3 (13%)	
Elevated Ddimer	8 (80%)	5 (22%)	
Radiological findings			0.05
Multifocal opacities	9 (90%)	8 (35%)	
Solitary lobe pneumonia	0	3 (13%)	
Normal	1 (10%)	3 (13%)	
Atelectasis	0	5 (22%)	
Other (pleural effusion, pneumothorax, interstitial thickening)	0	4 (17%)	
Ventilator support	9 (90%)	13 (57%)	0.06
Median duration of intubation (d)	6 (3–8)	1 (0–6)	0.71
Pressor support	7 (70%)	12 (52%)	0.34
RRT support	2 (20%)	8 (35%)	0.39
Concurrent-infections	5 (50%)	4 (17%)	0.05
Median length of hospital stay (IQR)	11 (7–19)	14 (5–27)	0.54
Median length of ICU stay (IQR)	7 (4–10)	4 (2–17)	0.29
Disposition			0.97
Discharge	5 (50%)	12 (52%)	
Pending	2 (20%)	5 (22%)	
Death	3 (30%)	7 ^a (30%)	0.75

Bold indicates significant findings/results.

^a One death following hospital discharge in the COVID-19-negative group.

AKI, acute kidney injury; BMI, body mass index; CK, creatinine kinase; CNS, central nervous system; COVID-19, coronavirus 2019; DM, diabetes mellitus; ESRD, end stage renal disease; GI, gastrointestinal; GU, genitourinary; ICU, intensive care unit; IQR, interquartile range; LDH, lactate dehydrogenase; SOFA, sequential organ failure score; SOT, solid organ transplant; RRT, renal replacement therapy; WBC, white cell count.

African American populations.^{32–35} This increased propensity was not observed in our study.

The optimal approach to immunosuppression adjustment in COVID-19 SOT recipients has not yet been defined.

Immunosuppression reduction is common practice in critically ill SOT recipients and was also applied to our COVID-19-positive cohort. At our center, Belatacept is the principal maintenance immunosuppression in kidney

TABLE 5.**Management of hospitalized COVID-19-positive SOT recipients**

Total hospitalized (N = 19)	Floor (N = 9)	ICU (N = 10)
Immunosuppression reduction	3 (33%)	6 (60%)
COVID-19 treatment	2 (22%)	7 (70%)
Broad-spectrum antibiotics	2 (22%)	10 (100%)

COVID-19, coronavirus 2019; ICU, intensive care unit; SOT, solid organ transplant.

transplant recipients, and several patients receive Belatacept at local infusion centers. We did not observe any statistically significant difference in the likelihood of COVID-19 infections among our Belatacept population. While a significant portion of COVID-19-positive patients in the intensive care unit were not on Belatacept, given our small sample size, we cannot presume that patients on Belatacept are less prone to COVID-19 infections. However, it can be inferred that continuing Belatacept infusions in patients during COVID-19 pandemic does not confer increased susceptibility to COVID-19 infection if social distancing is practiced. More research is needed to better assess the impact of immunosuppression on COVID-19 infection.

As the pandemic continues and hospitals remain at near capacity in some regions, we are forced to ration care at tertiary centers and rely more heavily on community healthcare providers to care for SOT recipients. In the current scenario, a clear channel of communication between transplant centers and local providers as well as a collaborative management is critical for favorable outcomes. At our transplant center, given that a majority of our SOT recipients have a kidney transplant, we have incorporated a weekly COVID-19 newsletter sent to all nephrologists in our region providing updated information on COVID-19 in SOT recipients and our hospital status (hospitalized cases, surgeries, center operations, etc.). We have also created a protocol to provide community nephrologist guidance for appropriate triage and immunosuppression management (Table S1, SDC, <http://links.lww.com/TXD/A292>).³⁶⁻³⁹ Similar communication practices adopted by other transplant centers and community providers will alleviate concerns of local providers caring for SOT recipients in the community while utilizing all available resources in the best manner.

The unique aspect of our work is that it contributes to increase awareness of COVID-19 disease in SOT recipients among local providers and gives them a perspective of the disease course by providing comparison to a similar immunocompromised cohort. To date, most discussion on COVID-19 outcomes in SOT recipients have been in-comparison to the general population with COVID-19, who are immunocompetent. By having a comparable group with similar presenting symptoms who ultimately have a different disease process, we attempted to get more clarity on clinical outcomes in COVID-19-infected SOT recipients compared with other SOT recipients. It is reassuring that we did not observe any difference in survival probability between our COVID-19-positive and -negative cohorts. Regardless of the disease severity, typical clinical and laboratory findings of COVID-19 infection might be absent in COVID-19-positive SOT recipients. We highlighted this wide variability of presentation and successfully showcased the need for specific guidelines for testing and to triage COVID-19-positive SOT recipients that can

be useful to local providers. Our study emphasizes the need to maintain a higher degree of suspicion, close monitoring, and lower threshold for COVID-19 testing in SOT recipients. Having a median follow-up period of >30 days is valuable to our understanding of COVID-19 outcomes beyond the initial acute phase. While readmissions were not statistically significant, it was 2-fold higher than those observed in the COVID-19-negative cohort. Larger cohort studies with longer follow-ups are necessary to better define mid long-term outcomes in COVID-19 SOT recipients. To our knowledge, no study has reported COVID-19 outcomes in SOT recipients on Belatacept. We did not observe increased COVID-19 infections or worse outcomes in patients on Belatacept. Therefore, continuing belatacept infusion in the community during this pandemic, if safely done, is acceptable.

We acknowledge the limitations of our study. Our small sample size is not representative of all SOT recipients. Large multicenter study from different geographic regions with long follow-up time is necessary to better grasp the extent of COVID-19's effect on SOT recipients. It can also help identifying prognostic markers in SOT recipients, thereby allowing for better triage and identification of SOT recipients at risk for sudden decompensation, which is a key to improve outcomes. Nasopharyngeal PCR is known to have variable testing sensitivity and likelihood for false negatives results. This could have led to underestimating and misclassifying cases. It is possible that our COVID-19-negative cohort may have included patients who had COVID-19 infection with a false negative test result. Developing more accurate diagnostic assays would help with this regard. We did not measure T-cell subsets to assess for depletion in any of the critically ill COVID-19 patients. Larger studies to determine if COVID-19-positive SOT have less severe lymphopenia than that observed in COVID-19 patients in the general population is required. While most SOT recipients in the COVID-19-negative cohort primarily had an infectious diagnosis, a small subset had noninfectious causes. Collectively, considering them in the COVID-19-negative cohort could have skewed our results. However, we identified our comparable group only based on presenting symptoms and clinical suspicion for COVID-19, and in our opinion, these noninfectious causes contribute considerably to hospitalizations and patient survival in SOT recipients. Including patients based on clinical symptoms replicates a scenario often faced in this population and serves as a reminder to our community providers that SOT recipients present with atypical signs and symptoms, and therefore, greater vigilance is needed while caring for this vulnerable population.

In conclusion, transplant-specific guidelines for COVID-19 testing, maintaining a higher degree of clinical suspicion, close monitoring, and utilizing imaging studies for risk stratification are necessary to identify COVID-19-positive SOT recipients at risk of deterioration early in their clinical course in the community. Transplant centers need to work in close conjunction with local community providers to successfully care for COVID-19 SOT recipients in the event of limited resource availability.

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