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ABSTRACT

Background. Solid organ transplant (SOT) recipients are a complex, immunocompromised population in whom greater coronavirus disease 2019 (COVID-19) mortality has been reported compared with the general population.

Methods. We examined a retrospective cohort of 58 SOT recipients with first-wave COVID-19, comparing patients with severe and nonsevere illness. Additionally, SOT recipients are compared with general patients with first-wave COVID-19.

Results. Organs transplanted included 38 kidneys, 8 livers, 5 hearts, and 3 pancreases. Average SOT recipient age was 57.4 years; 62% were male; 46.6% were African American 36.2% were white. Comorbidities included hypertension (86%), chronic kidney disease (86%), diabetes mellitus (50%), coronary artery disease (26%), and chronic obstructive pulmonary disease (14%). Twenty patients had severe COVID-19 (34.5%) and 38 had nonsevere disease (65.5%). Severe disease was more common in older SOT recipients with comorbidities and was associated with cough, dyspnea, pneumonia, C-reactive protein >10 mg/L, and platelet count <150/μL. Sex, race, body mass index, time from transplant, baseline immunosuppression, and diagnosis month did not differ among those with severe and nonsevere COVID-19. Seventy percent of SOT recipients were hospitalized vs 27.2% of general patients with COVID-19 and inpatient SOT recipients had a higher mechanical ventilation rate. Though a trend toward longer length of stay, higher intensive care unit admission, and greater inpatient mortality was observed (19.5% vs 14.8%), these differences were not significant.

Conclusions. The severe acute respiratory syndrome coronavirus 2 has greatly impacted SOT recipients. One-third of our SOT recipients seen during the first wave had severe illness with associated standard risk factors for poor outcome. Compared with general first-wave patients, more SOT recipients were hospitalized, although inpatient COVID-19 mortality did not significantly differ.

THE ongoing coronavirus disease 2019 (COVID-19) pandemic is an outbreak of historic proportions. As of January, 2021, there are over 23 million cases and over 390,000 deaths reported in the United States alone and over 94 million cases and 2 million reported deaths globally [1,2]. The progression of the pandemic has generated an understanding of the varied clinical presentations of COVID-19 and factors that increase morbidity and mortality in the general population, including older age and comorbidities [3-9]. Solid organ transplant (SOT) recipients are a complex immunocompromised

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population for which the full impact of COVID-19 remains to be determined. Mortality in SOT recipients has been reported to be higher than that in the general population, with rates of 10% to 28% seen in symptomatic patients and up to 50% to 75% in those requiring intubation [10-13].

SOT recipients often have comorbidities, such as older age, obesity, diabetes, hypertension, renal dysfunction, cardiovascular disease, and chronic lung disease, that lead to or are a result of their organ transplants and are also likely to increase the risk for a more severe COVID-19 clinical course. SOT recipients are unique in their regular use of immunosuppressant medications, however, potentially impacting presentation, clinical course, and outcomes in COVID-19. A high proportion of transplant recipients infected during previous coronavirus outbreaks had severe disease [14]. It is currently not known whether immunosuppressive therapy impacts susceptibility to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or the severity of inflammation in COVID-19.

Our study aims to describe the clinical features and clinical course of COVID-19 in SOT recipients seen in our region during the first COVID-19 wave. We compare subgroups of SOT recipients with severe and nonsevere illness and compare SOT recipients with our health care system's general patients with COVID-19. Through reporting our findings, we aim to further the understanding of COVID-19 in the SOT recipient population as transplant centers continue with patient care and transplantation surgery during the ongoing surge in COVID-19 cases anticipated through 2021.

METHODS

Study Design

This was a retrospective cohort study of 58 SOT recipients diagnosed with first-wave COVID-19 in our health care system located in Philadelphia, Pennsylvania and southern New Jersey and including 4 multihospital locations. The primary study objective was to compare SOT recipients with severe and nonsevere infection. A secondary objective was to compare SOT recipients with COVID-19 with general patients with COVID-19 in our health care system during the study period. The study protocol was reviewed and approved by our center's institutional review board.

Definitions

Thomas Jefferson University's COVID-19 Data Mart is an electronic medical record–based data resource established for tracking ambulatory patients and inpatients with COVID-19 and facilitating research. The Data Mart definition of COVID-19 includes a positive SARS-CoV-2 polymerase chain reaction test within 21 days, a confirmed charted COVID-19 infection status within 21 days, or having U07.1 (COVID-19 virus identified) as a discharge diagnosis for hospitalized patients. SOT status was identified using relevant *International Statistical Classification of Diseases and Related Health Problems*, 10th Revision codes for organ transplantation [15]. SOT recipients were categorized as having severe disease if they had a COVID-19 related hospitalization ≥10 days, required intensive care unit (ICU) admission, or died of COVID-19.

Patient Characteristics

We identified patients with a history of SOT and COVID-19 diagnosed between March 15 and September 16, 2020 using Jefferson's COVID-19 Data Mart. Patients without an active transplant or a new diagnosis of COVID-19 were excluded. Given incomplete data with automated extraction, manual chart review was performed to identify COVID-19 symptoms, comorbidities, presence of bacteremia, COVID-19 management, and graft dysfunction.

Statistical Analysis

Analysis was performed on available data. All data points were not available for each patient and the adjusted number of patients for each variable is noted. Continuous data are presented as mean values with calculated standard deviations and *t* tests performed against severe disease status for the primary outcome. Categorical data are presented as proportions with χ^2 tests performed against severe disease status for the primary outcome. A P value <.05 was considered significant. Testing was not performed when the total N was less than 9.

Given our sample size, 2 to 4 independent variables were estimated in multivariable models with the binary outcome variable of severe disease. Variables from the multivariable regression models with a P value <.1 on analysis were considered significant. The signs of estimated parameters with the smallest P values are reported from 10 multivariable models to understand risk factor correlation with outcome. Given our sample size, true correlation effects (or odds ratios) could not be controlled for all confounding factors.

RESULTS

Patient Characteristics

A total of 129 SOT recipients were identified as having COVID-19 between March 15 and September 16, 2020. Seventy-one patients were excluded: 8 for no active transplant and 63 for duplicate entries unrelated to initial COVID-19, leaving 58 patients for analysis.

Summarized baseline characteristics (Table 1) and COVID-19 clinical course (Table 2) are provided. Transplants included 38 kidneys, 8 livers, 5 hearts, and 3 pancreases. Four patients had multiorgan transplants and were included based on the organ driving their level of immunosuppression. Two patients were transplanted during the COVID-19 pandemic and 16 were transplanted during or after 2018. The earliest transplant year was 1981. The average patient age was 57.4 years, average patient body mass index (BMI) was 30.4, 62% were male, 46.6% were African American, and 36.2% were white. Patients resided in 46 ZIP codes, of which 37 ZIP codes included 1 patient, 6 ZIP codes included 2 patients, and 3 ZIP codes included 3 patients. Eighty-six percent of patients had hypertension, 86.2% had chronic kidney disease, 50% had diabetes mellitus, 25.9% had coronary artery disease, and 13.8% had chronic obstructive pulmonary disease (COPD). Presenting symptoms included fever (46.3%), cough (46.3%), dyspnea (37%), fatigue (20.4%), diarrhea/vomiting (18.5%), pharyngitis (9.3%), and loss of taste or smell (3.7%). One-third of patients presented with a white blood cell count <4/L, 42% had a platelet count <150/μL, and 47% had a C-reactive protein (CRP) >10 mg/L. Acute kidney injury was reported in 46.3% of cases.

Table 1. COVID-19 SOT Recipient Characteristics

Characteristics	All Patients (n = 58)	Nonsevere COVID-19 (n = 38)	Severe COVID-19 (n = 20)	*P* Value
Age, mean (SD), y	57.4 (14)	53.7 (13)	64.5 (13.2)	.0042
Male sex, n (%)	36 (62)	25 (65.7)	11 (55)	.4209
Race, n (%)	n = 58	n = 38	n = 20	
African American	27 (46.6)	18 (47.4)	9 (45)	.8635
White	21 (36)	11 (28.9)	10 (50)	.1128
Hispanic	8 (14)	8 (21)	0 (0)	*
Asian	1 (1.7)	0 (0)	1 (5)	*
American Indian/Alaskan Native	1 (1.7)	1 (2.6)	0 (0)	*
Organ transplant, n (%)	n = 54	n = 35	n = 19	
Kidney	38 (70.4)	24 (68.6)	14 (73.7)	.1544
Liver	8 (14.8)	5 (14.3)	3 (15.8)	*
Heart	5 (9.3)	3 (8.6)	2 (10.5)	*
Pancreas	3 (5.6)	3 (8.6)	0 (0)	*
Multiorgan†	4 (7.4)	3 (8.6)	1 (5.3)	*
Time from transplant, mean (SD), y	n = 54 7.7 (7.4)	n = 35 8.0 (7.9)	n = 19 7.1 (6.5)	.6589
Baseline immunosuppression, n (%)	N = 54	n = 35	n = 19	
CNI	50 (92.6)	33 (94.3)	17 (89.5)	.8467
MMF	37 (68.5)	23 (65.7)	14 (73.7)	.4755
Low-dose glucocorticoid‡	26 (48)	16 (45.7)	10 (52.6)	.5655
mTORi	5 (9.3)	3 (8.6)	2 (10.5)	*
Azathioprine	3 (5.6)	3 (8.6)	0 (0)	*
Body mass index, mean (SD), kg/m^2	30.4 (5.5)	30.8 (5.7)	29.4 (5.2)	.3800
Comorbidities, n (%)	n = 58	n = 38	n = 20	
Chronic kidney disease	50 (86.2)	31 (81.6)	19 (95)	.1589
Hypertension	50 (86.2)	30 (78.9)	20 (100)	.0271
Diabetes mellitus	29 (50)	18 (47.3)	11 (55)	.5806
Coronary artery disease	15 (25.9)	9 (23.7)	6 (30)	.6016
Chronic obstructive pulmonary disease	8 (13.8)	3 (7.9)	5 (25)	0.0726

t tests were used for age-related continuous measures. χ^2 tests were used for categorical variables.

CNI, calcineurin inhibitor; COVID-19, coronavirus disease 2019; MMF, mycophenolate mofetil; mTORi, mammalian target of rapamycin inhibitor; SD, standard deviation; SOT, solid organ transplant.

* Test was not performed when N < 9.

† Four patients had multiorgan transplants, included as organ dictating level of immunosuppression (2 kidney/pancreas as pancreas, 1 kidney/liver as liver, 1 heart/kidney as heart).

‡ Prednisone 5 mg/d or methylprednisolone 4 mg/d.

Seventy percent of patients were hospitalized, with an average inpatient length of stay of 11.1 days, and 34% were readmitted within 3 months of discharge. Total mortality for our patient population was 17.2%, with 2 patients dying outside of the hospital: 1 at home and 1 in a long-term care facility.

Severe vs Nonsevere COVID-19

Twenty patients had severe disease (34.5%) and 38 had nonsevere disease (65.5%). As shown in Table 1, there were no significant differences in patient sex, race, type of transplant, time from transplant, baseline immunosuppressive therapy, or month of diagnosis among patients with severe and nonsevere COVID-19. Patients with severe disease were older than those with nonsevere disease, with an average age of 64.5 vs 53.7 years ($P = .0042$). Severe disease affected only 1 out of 11 patients aged <50 years but 8 out of 12 in those aged >71 years. Patients with severe disease were more likely to have hypertension (100% vs 78.9%, $P = .0271$) and/or COPD (25% vs 7.9%, $P = .0726$).

As shown in Table 2, those with severe illness were more likely to present with cough (84.2% vs 25.7%, $P < .0001$) and/or dyspnea (57.9% vs 25.7%, $P < .0171$) and to receive a diagnosis of pneumonia (100% vs 42%, $P < .0001$). They were also more likely to have a CRP >10 mg/L (84.6% vs 23.8%, $P = .0007$) and/or a platelet count <150/μL (64.7% vs 28.6%, $P = .0088$). Sixty-five percent of patients received an adjustment in immunosuppressive therapy, more commonly those with severe illness (84.2% vs 55.6%, $P = .0412$). Twenty-seven patients received antiviral therapy (46.6%), with severely ill patients more likely to receive remdesivir (31.6%) and convalescent plasma (31.6%). Ten patients were treated with corticosteroids initiated for COVID-19, 9 of whom had severe illness. Severely ill patients had a significantly longer hospital length of stay (average 19 days) than those admitted and nonseverely ill (average 5 days, $P = .0003$). Critical illness included those admitted to the ICU (12 patients), mechanically ventilated (10 patients), and on extracorporeal membrane oxygenation (2 patients). Mortality was 17.2% in the total SOT cohort,

Table 2. COVID-19–SOT Recipient Symptoms, Lab Results, and Treatments

Measure	All Patients	Nonsevere COVID-19	Severe COVID-19	*P* Value
Month of first positive COVID test, n (%)	n = 58	n = 38	n = 20	
March	6 (10.3)	4 (10.5)	2 (10)	*
April	21 (36.2)	14 (36.8)	7 (35)	.8897
May	13 (22.4)	7 (18.4)	6 (30)	.3148
June	5 (8.6)	1 (2.6)	4 (20)	*
July	10 (17.2)	7 (18.4)	3 (15)	.3430
August	2 (3.4)	1 (2.6)	1 (5)	*
September	1 (1.7)	1 (2.6)	0 (0)	*
Presenting symptoms, n (%)	n = 54	n = 35	n = 19	
Fever	25 (46.3)	15 (42.9)	10 (52.6)	.4416
Cough	25 (46.3)	9 (25.7)	16 (84.2)	< .0001
Dyspnea	20 (37)	9 (25.7)	11 (57.9)	.0071
Fatigue, myalgias	11 (20.4)	7 (20)	4 (21)	.8841
Diarrhea, vomiting	10 (18.5)	8 (22.9)	2 (10.5)	.2895
Pharyngitis	5 (9.3)	5 (14.3)	0 (0)	*
Loss of taste/smell	2 (3.7)	2 (5.7)	0 (0)	*
Labs at presentation, n (%)	n = 45	n = 28	n = 17	
WBC <4 (4.0-10.8 × 10^3/mL)	15 (33.3)	13 (46.4)	2 (11.8)	.0453
Platelets <150 (130-400 × 10^3/mL)	19 (42.2)	8 (28.6)	11 (64.7)	.0088
AST >40 (18-54 U/L)	10 (22.2)	5 (17.9)	5 (29.4)	.2564
ALT >40 (10-50 U/L)	7 (15.6)	2 (7)	5 (29.4)	*
CRP >10 (<5.0 mg/L)	n = 34	n = 21	n = 13	
	16 (47)	5 (23.8)	11 (84.6)	.0007
Diagnosis of pneumonia	n = 57	n = 38	n = 19	
	35 (61.4)	16 (42)	19 (100)	.0001
Hospitalized, n	n = 41	n = 23	n = 18	
Length of stay, mean (SD), d	11.1 (12.7)	5.0 (2.7)	19.0 (16.1)	.0003
ICU admission, n (%)	12 (29.3)	0 (0)	12 (66.7)	< .0001
Mechanical ventilation	10 (24.4)	0 (0)	10 (55.6)	< .0001
ECMO	2 (4.9)	0 (0)	2 (11)	*
Readmitted within 3 months, n (%)	14 (34)	9 (39)	5 (27.8)	
COVID treatment, n (%)	n = 55	n = 36	n = 19	
Hydroxychloroquine	14 (25.5)	10 (27.8)	4 (21)	.5932
Remdesivir	6 (10.9)	0 (0)	6 (31.6)	*
Convalescent plasma	7 (12.7)	1 (2.8)	6 (31.6)	*
Corticosteroids	10 (18)	1 (2.8)	9 (47.4)	.0000
Tocilizumab	2 (36.3)	0 (0)	2 (10.5)	*
Adjustment in IS	36 (65.5)	20 (55.6)	16 (84.2)	.0412
MMF held	27 (50)	15 (42.9)	12 (63)	.1363
Acute kidney injury, n (%)	n = 54	n = 35	n = 19	
	25 (46.3)	14 (40)	11 (58)	.1844
Mortality (inpatient + outpatient), n (%)	n = 58	n = 38	n = 20	
	10 (17.2)	0 (0)	10 (50)	< .0001

t tests were used for age-related continuous measures. χ^2 tests were used for categorical variables.

ALT, alanine aminotransferase; AST, aspartate transaminase; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IS, immunosuppression; MMF, mycophenolate mofetil; SD, standard deviation; SOT, solid organ transplant; WBC, white blood cell.

* Test was not performed when N < 9.

19.5% in those hospitalized, and 50% in patients with severe infection.

As shown in Table 3, most multivariate analysis results were consistent with bivariable analyses, although kidney as the transplanted organ was marginally negatively correlated with severe disease and a BMI value 30 kg/m^2 or higher was negatively correlated with severe disease. Age >71, COPD, a diagnosis of pneumonia, and CRP >10 mg/L were positively correlated with severe disease.

COVID-19 SOT Recipients vs Patients With COVID-19

In comparison to general patients with COVID-19 at our health care system during the study period, SOT recipients with COVID-19 were more likely to be male (62% vs 45%, P = .0094) and/or Hispanic (13.8% vs 4.9%, P = .0018), as shown in Table 4. Seventy percent of SOT recipients were admitted to the hospital with COVID-19 compared with 27.2% of general patients (P < .00001). Inpatient progression measures were examined for SOT recipients and general inpatients

Table 3. Multivariate Results for COVID-19 Severe Disease Outcome in SOT Recipients

Measure	Estimate	*P* Value
Race (white)	+	.0408
Age ≥71 years	+	.0038
BMI 30 kg/m^2 or higher	−	.0142
Inpatient length of stay	+	.0157
Organ (kidney)	−	.0864
COPD/asthma	+	.0717
Pneumonia	+	.0029
CXR CT abnormal	+	.0766
CRP >10 mg/L	+	.0006
Steroid given for COVID-19	+	.0012
Adjustment in immunosuppression	+	.0583

BMI, body mass index; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; CXR CT, chest radiograph computed tomography scan; SOT, solid organ transplant.

with COVID-19. SOT recipients had a higher mechanical ventilation rate (24.4% vs 14.3%, $P = .070$). They trended toward a longer average inpatient length of stay (11.1 vs 8.7 days), a higher ICU admission rate (29.3% vs 24.3%), and a higher inpatient mortality rate (19.5% vs 14.8%) without a significant difference in comparison to general patients.

DISCUSSION AND REVIEW OF COVID-19 IN SOT

This article provides a profile analysis of 58 SOT recipients diagnosed with COVID-19 between March and September 2020, comparing those with and without severe infection. SOT recipients are also compared with general patients with COVID-19.

The Centers for Disease Control and Prevention identifies organ transplant recipients as at increased risk of severe COVID-19 [16]. Reported mortality in SOT recipients has been higher than that in the general population, with rates of 10% to 28% in symptomatic patients and up to 50% to 75% in those requiring intubation [10-13,17-19]. Notably, 70% of our SOT recipients were hospitalized compared with 27.2% of general patients with COVID-19 in our health care system. This difference likely reflects a lower threshold for hospitalization in SOT recipients as well as concerning clinical markers. A greater percentage of our SOT recipients required mechanical ventilation than general patients, though the inpatient metric comparisons of length of stay, need for ICU admission, and inpatient mortality (19.5% in SOT recipients and 14.8% in general patients) did not significantly differ. Once hospitalized for COVID-19, progression in SOT recipients may be similar to that in the general population. One-third of our SOT recipients were readmitted to the hospital within 3 months of discharge, however, speaking to frailty and an often complicated recovery. Mortality in general patients has declined with progression of the pandemic likely in part because of improved management [20,21]. Accordingly, only 1 patient in our series with a fatal outcome was admitted after June 1, 2020. Fifteen of our patients recovered at home with supportive care and further investigation into the heterogeneity of COVID-19 in immunocompromised hosts is warranted.

The risk of severe COVID-19 in SOT recipients is likely multifactorial, with the direct contribution of immunosuppression challenging to assess. Other centers have not found transplant-related immunosuppression surrogates to contribute to increased COVID-19 morbidity and mortality, though age and medical comorbidities have been independently associated with worse outcomes [13,18,19]. Most SOT-related factors did not correlate with severity of infection differences among our transplant recipients. Time from transplant, baseline immunosuppressive therapy, and graft dysfunction did not differ among those with severe and nonsevere infection. Better general health in kidney transplant recipients may explain the observed negative correlation of kidney as the transplanted organ with severe disease on multivariate analysis.

Table 4. Comparison of SOT Recipients With COVID-19 and General Population With COVID-19

Measure	SOT Recipients With COVID-19	Patients With COVID-19	*P* Value*
Sample size (inpatients and outpatients)	n = 58	n = 14,975†	
Male	62%	45.0%	.0094
Race			
White	36.2%	51.6%	.3895
African American	46.6%	31.0%	.4457
Hispanic	13.8%	4.9%	.0018
Asian	1.7%	4.5%	.3040
Age (years)	57.4	52.3	.6734
Sample size (inpatient)	n = 41	n = 2495‡	
Percentage hospitalized	70.7%	27.2% of 9169‡ patients	< .00001
BMI (kg/m^2)	30.4	29.5	.3276
Length of stay (days)	11.1	8.7	.2266
Intensive care unit	29.3%	24.3%	.4575
Mechanical ventilation	24.4%	14.3%	.0702
Inpatient mortality	19.5%	14.8%	.3992

BMI, body mass index; COVID-19, coronavirus disease 2019; SOT, solid organ transplant.

* χ^2 tests were used for all categorical measures except age, BMI, and length of stay, for which an unequal variance *t* test was used.

† All health care system patients with COVID-19.

‡ Health care system locations with inpatient and outpatient data available for all patients with COVID-19 (n = 9169) and inpatients with COVID-19 (n = 2495).

Advanced age, comorbidities, racial and ethnic minority identification, and male sex have been shown to increase COVID-19 morbidity and mortality in the general population [5,22-25]. In contrast to the 2009 influenza A (H1N1) pandemic in which severe illness was less common among the elderly, lack of pre-existing or cross-reactive adaptive immunity to SARS-CoV-2 in the general population has contributed to its impact on older adults [26-28]. Longstanding systemic health and social inequities have contributed to the disproportionate burden of COVID-19 experienced by Americans of color, those of lower socioeconomic status, and those residing in population-dense regions [23,29,30]. A majority of our SOT recipients with COVID-19 had demographic or medical risk factors for worse outcomes. Those with severe infection had an increased prevalence of hypertension and/or COPD and were significantly older than those with nonsevere infection. We did not observe BMI or nonwhite race to be associated with severity of COVID-19 or clustering of cases by ZIP code. Transplant recipients are well connected to the health care system given their chronic conditions. This could potentially increase SARS-CoV-2 exposure given frequent contact with health care facilities while also facilitating support when confronted with infection. Differences in demographic characteristics as well as high rates of comorbidities reflect the SOT population's risk factors for organ failure requiring a transplant as well as increased risk for COVID-19 complications [16,23,31,32].

Despite the potential for confounding medication toxicity and organ rejection, available literature has demonstrated that SOT recipients exhibit symptoms and laboratory abnormalities similar to those of general patients [6,9,12,13,33-38]. Presentation similar to that of general patients allows clinicians to use similar illness scripts and case definitions when determining which SOT recipients require further investigation for COVID-19 and those at higher risk for progression. Our SOT recipients with severe COVID-19 presented more often with cough, dyspnea, a diagnosis of pneumonia, higher CRP values, and lower platelet counts. Only 2 patients reported loss of taste or smell, both of whom had a nonsevere clinical course as has been portended in other cases [39]. Acute kidney injury, found in 46% of our patients, is likely multifactorial in COVID-19, especially in severe illness, with the roles of hypotension, viral-mediated nephrotoxicity, complement deposition, and microvascular thrombosis contributing [40,41].

Because T-cell immunity, a key component of the immune response to viral pathogens, is hampered by immunosuppressive transplant therapy, reduction of maintenance immunosuppression strategies in COVID-19 are understandable and were used in the majority of our patients. Presentation with lymphopenia in many patients with COVID-19 indirectly supports this approach [42]. However, cytokine release syndrome with amplification of viral cytopathic lung injury has been proposed as an underlying mechanism for severe COVID-19, supported by increases in interleukin 6 and other inflammatory markers [28,43-45]. Improved mortality in patients treated with corticosteroids supports this proposed mechanism and suggests potential benefits of immunosuppression [46-48]. Immunosuppressive therapy poses the risk of prolonged viral replication and co-infections, with the benefits of decreased inflammation and lower rates of transplant rejection. Practices of decreasing or discontinuing cell cycle inhibitors, reducing calcineurin inhibitor levels, and continuing maintenance corticosteroids are in use with variation based on the type of transplant, especially for calcineurin discontinuation given the risk of acute rejection in those with a lifesaving organ [12,19,28,49-51].

The need for therapies directed against SARS-CoV-2 and its inflammatory and hypercoagulable complications continues with tremendous collaborative efforts to conduct randomized controlled trials (RCTs) of treatments and vaccines undertaken during the pandemic thus far. Though extrapolation from general treatment guidelines is advised, COVID-19 therapeutics pose unique challenges in transplant recipients given the potential for drug-drug interactions and overlapping toxicities [52]. Antiviral therapies, received by almost half of our SOT recipients, target the early viral phase of infection. Remdesivir, an antiviral, is the only drug currently approved by the US Food and Drug Administration (FDA) for treatment of COVID-19 with a decreased symptomatic period found in RCTs [53,54]. Convalescent plasma and 2 monoclonal antibody therapies, also antivirals, have received emergency use authorization from the FDA for inpatients and outpatients, respectively [55,56]. Whether immunosuppressed patients with delayed adaptive immunity will benefit from early passive antibody therapy remains a consideration [54-60]. Hydroxychloroquine, chloroquine, and lopinavir/ritonavir are no longer recommended owing to negative data [61-63]. With the mortality benefit of corticosteroids in patients with COVID-19 who are mechanically ventilated or requiring supplemental oxygen established [46,47], other immunomodulators have been used off-label in transplant recipients for treatment of the inflammatory stage of illness [64]. Baricitinib, a signal transduction (Janus-associated kinase inhibitor) inhibitor, received FDA emergency use authorization based on improved outcomes in combination with remdesivir in an RCT, and studies of tocilizumab, an interleukin 6 receptor inhibitor, have demonstrated mixed results [64-66]. Of note, SOT recipients have been excluded from many clinical trials of immunomodulator therapies.

Vaccines present opportunities for protection of SOT recipients from SARS-CoV-2–related illness, with 2 inactivated mRNA candidates from manufacturers Pfizer BioNtech and Moderna having demonstrated safety and efficacy in RCTs and granted emergency use authorization from the FDA as of January, 2021. Authorization of 2 adenovirus vector vaccines from Johnson & Johnson and AstraZenica is anticipated [67,68]. Because of high-risk status, patients with organ failure awaiting transplant and SOT recipients will be prioritized for COVID-19 vaccination [69]. Additional research is required to fully determine the safety and efficacy of SARS-CoV-2 vaccination in transplant recipients. Considerations include the potential for a lower antibody response, a more rapid decline in antibody titer, reduced protection posttransplant, and immune stimulation [70]. Although acknowledging these gaps in knowledge, the benefits of vaccination in SOT recipients are thought to outweigh the risks. Transplant candidates should optimally receive vaccination 2 or more weeks before transplantation. Unvaccinated transplant recipients should delay vaccination for 1 to 6

Table 5. Solid Organ Transplant Candidate and Donor SARS-CoV-2 Testing Recommendations

Population	General Recommendations	Population Subgroup	Additional Guidance
Transplant candidates	NAT for SARS-CoV-2 from the upper respiratory tract if signs or symptoms of COVID-19		NAT for SARS-CoV-2 from the upper respiratory tract shortly before transplantation surgery
		Transplant candidate with SARS-CoV-2 exposure within 14 days	Consider delaying surgery even if asymptomatic
		Transplant candidate with SARS-CoV-2 infection	Consider delaying surgery until symptom resolution and negative NAT for SARS-CoV-2
Deceased donors	NAT for SARS-CoV-2 of at least 1 respiratory tract sample within 3 days of organ procurement		When feasible, a second test is recommended 24 hours after initial test and within 24-48 hours of procurement
		Thoracic organ donors	As feasible, 1 out of 2 screening NATs for SARS-CoV-2 should be performed on a lower respiratory tract sample (eg, bronchoalveolar lavage or tracheal aspirate)
		Deceased donor with prior SARS-CoV-2 infection	Consider organ acceptance if repeat NAT for SARS-CoV-2 negative (upper and lower respiratory tract samples both negative in lung donors) and symptom resolution occurred at least 21-90 days prior to evaluation
Living Donors	NAT for SARS-CoV-2 of at least 1 upper respiratory tract sample as close to donation as possible and within 3 days of surgery		
		Living donor with known SARS-CoV-2 exposure within 14 days	Consider delaying transplant even if asymptomatic
		Living donor with SARS-CoV-2 infection	Consider organ donation if repeat NAT for SARS-CoV-2 negative and symptom resolution/infection at least 21-90 days prior to evaluation

Recommendations based on solid organ donor testing guidelines from the American Society of Transplantation [81].
COVID-19, coronavirus disease 2019; NAT, nucleic acid testing; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

months after transplant including 3 months after anti-thymocyte globulin therapy. Vaccination is recommended after COVID-19 recovery with the option to postpone for up to 90 days [71,72].

Though our study demonstrates that SOT recipients face morbidity and mortality from COVID-19, the impact of the pandemic on the operation of transplant centers also harms patients awaiting transplant. Over 113,000 patients are on the US national transplant waiting list. A patient is added to the waitlist every 9 minutes, and 17 patients die every day waiting for a transplant [73,74]. Early in the pandemic, transplant surgery was markedly reduced throughout the United States owing to concerns about safety and lack of center capacity [49,75,76]. In communities with circulating SARS-CoV-2, transplant centers must weigh resource availability, in particular intensive care resources, with the need for continuation of organ transplantation. Per the Centers for Medicare and Medicaid Services, organ transplants are considered Tier 3b procedures that should not be postponed in high-acuity or unhealthy patients [77].

Strategies for donor and candidate screening, appropriate personal protective equipment, general COVID-19 prevention practices, and the use of telemedicine have allowed centers to continue patient care and resume organ transplantation at levels similar to prior years [24,78]. Living donors and candidates should be counseled on prevention strategies, the need to report COVID-19 symptoms and contacts, and the need to self-quarantine leading up to organ donation as feasible. SARS-CoV-2 organ transplant testing recommendations have been developed by the American Association for the Study of Liver Diseases, the International Society for Heart and Lung Transplantation, the American Society of Transplantation, and the Association of Organ Procurement Organizations, as outlined in Table 5 [79-84]. Additional considerations for transplant centers include COVID-19–related renal dysfunction in potential kidney donors, non-lung organ utilization in SARS-CoV-2 positive donors, and the roles of antigen and antibody testing.

Our study has several limitations, including a small sample size and the fact that 70% of patients were kidney transplant recipients, limiting full extrapolation to other organs. In addition, some data points were not available for all patients or the general COVID-19 cohort and longer follow-up could identify additional outcomes.

In summary, SOT recipients in our health care system have been significantly impacted by the SARS-CoV-2 pandemic. The majority of those infected required hospitalization and over one-third had a severe clinical course. Once hospitalized for COVID-19, however, outcomes were similar for SOT recipients and general patients. Risk factors for severe infection in SOT recipients appear to be similar to those in the general population, advanced age and comorbidities in particular, and the contribution of immunosuppressive therapy remains to be determined. As circulation of SARS-CoV-2 continues, with an unknown impact of variant viral strains, transplant centers may experience ongoing straining of resources, facing similar challenges to those seen in the spring of 2020. The challenges confronting organ transplant recipients and transplant centers, however, are now faced with improved access to testing, best practices on infection control, expanded treatment interventions, SARS-CoV-2 vaccines, and a growing body of literature contributing to our understanding of SARS-CoV-2 infection in this specialized population.

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