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BRIEF COMMUNICATION

Changing trends in mortality among solid organ transplant recipients hospitalized for COVID-19 during the course of the pandemic

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Abbreviations: BMI, body mass index; CNI, calcineurin inhibitor; COVID-19, coronavirus disease 2019; ICU, intensive care unit; mTOR, mammalian target of rapamycin; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SOTR, solid organ transplant recipients.

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Mortality among patients hospitalized for COVID-19 has declined over the course of the pandemic. Mortality trends specifically in solid organ transplant recipients (SOTR) are unknown. Using data from a multicenter registry of SOTR hospitalized for COVID-19, we compared 28-day mortality between early 2020 (March 1, 2020–June 19, 2020) and late 2020 (June 20, 2020–December 31, 2020). Multivariable logistic regression was used to assess comorbidity-adjusted mortality. Time period of diagnosis was available for 1435/1616 (88.8%) SOTR and 971/1435 (67.7%) were hospitalized: 571/753 (75.8%) in early 2020 and 402/682 (58.9%) in late 2020 ($p < .001$). Crude 28-day mortality decreased between the early and late periods (112/571 [19.6%] vs. 55/402 [13.7%]) and remained lower in the late period even after adjusting for baseline comorbidities (aOR 0.67, 95% CI 0.46–0.98, $p = .016$). Between the early and late periods, the use of corticosteroids (≥6 mg dexamethasone/day) and remdesivir increased (62/571 [10.9%] vs. 243/402 [61.5%], $p < .001$ and 50/571 [8.8%] vs. 213/402 [52.2%], $p < .001$, respectively), and the use of hydroxychloroquine and IL-6/IL-6 receptor inhibitor decreased (329/571 [60.0%] vs. 4/492 [1.0%], $p < .001$ and 73/571 [12.8%] vs. 5/402 [1.2%], $p < .001$, respectively). Mortality among SOTR hospitalized for COVID-19 declined between early and late 2020, consistent with trends reported in the general population. The mechanism(s) underlying improved survival require further study.

KEYWORDS
clinical research/practice, infection and infectious agents - viral, infectious disease, organ transplantation in general, quality of care/care delivery

1 | INTRODUCTION

During the early portion of 2020, short-term mortality among solid organ transplant recipients (SOTR) hospitalized for COVID-19 was high, with estimates ranging from approximately 18%–30%.[1–3] Multiple recent studies of hospitalized adults (general population) with COVID-19 have reported that mortality has declined substantially since the start of the pandemic in the United States and Europe, from 20% to 25% during March and April 2020 to less than 10% during July through November 2020.[4–7] The overall decline in mortality has been attributed to various factors including earlier diagnosis due to greater access of testing, improvements in the supportive management, and the potential impact of therapies such as corticosteroids and remdesivir.[4] Whether similar decreases in mortality have occurred in SOTR has not been reported.

We previously described the 28-day outcomes of SOTR hospitalized for COVID-19 who were enrolled in a multicenter registry between March 1 and April 15, 2020.[1] This registry accrued additional cases diagnosed between April 15 and December 31, 2020. Here, we compare outcomes by 28 days among SOTR hospitalized for COVID-19 during the first half of 2020 to those diagnosed during the second half of 2020, to determine whether reductions in mortality reported among the general population have similarly occurred among SOTR.

2 | MATERIALS AND METHODS

2.1 | Study design and patients

We performed a multicenter observational cohort study of SOTR with laboratory-confirmed SARS-CoV-2 infection, as described previously.[1] This study was approved by the institutional review board (IRB) at the University of Washington with a waiver of informed

consent (STUDY00009698). The University of Washington IRB issued a "no human subjects research" designation for local sites contributing de-identified patient data. Individual sites sought local IRB approval as needed.

2.2 | Data collection

Data were collected using an online data collection tool, REDCap (Research Electronic Data Capture), as described previously.[1,8] A summary of all collected variables is shown in Table S1. Only patients who were hospitalized within 28 days of diagnosis, and for whom 28-day follow-up forms were completed, were included in this analysis. Patients were excluded if they were hospitalized for another indication prior to or concurrent with their first positive SARS-CoV-2 test (Figure S1). For example, a patient admitted to the hospital for a hip fracture with a positive SARS-CoV-2 screening test on admission would have been excluded. Patient race and ethnicity were collected as distinct variables and reported by the contributor based on observations or documentation in the electronic medical record. Race and ethnicity were collected as part of the registry to characterize the study population.

Contributors were instructed to submit cases of COVID-19 in SOTR that were diagnosed between March 1 and December 31, 2020. Because dates are considered potentially identifiable protected health information, the month and day of COVID-19 diagnosis could not be reported. Instead, season of diagnosis (the Northern Hemisphere's winter, spring, summer, or fall) was captured. Cases were considered to have occurred during the early period of 2020 if they were diagnosed in the winter or spring (corresponding to March 1–June 19, 2020) and were considered to have occurred during the late period of 2020 if they occurred during the summer or fall (corresponding to June 20–December 31, 2020). The time cutoff in June 2020 was used in accordance with a mortality inflection point observed in the general population[4,5] and because it closely coincided with two major advances for COVID-19: evidence supporting the use of corticosteroids for patients requiring supplemental oxygen and the emergency use authorization of remdesivir in the United States.[9]

2.3 | Statistical analysis

Demographic and baseline characteristics were assessed as counts and percentages for categorical values and as a mean (standard deviation) or median (interquartile range) for continuous variables. χ^2 and Fisher's exact tests were used to assess proportions of categorical variables. Continuous variables were assessed using Student's *t*-test or the Wilcoxon rank-sum test. Death by 28 days was the primary outcome, and admission to the intensive care unit (ICU), use of mechanical ventilation, initiation of renal replacement therapy, pathogen-proven bacterial and fungal pneumonia, bloodstream infection, acute cellular rejection, and duration of hospitalization were secondary outcomes. Age, sex, organ transplanted, geographic location, comorbidities, and features related to immunosuppression were evaluated as potential risk factors for mortality using univariable logistic regression (Table S2). These covariates were selected *a priori* based on hypotheses and/or prior studies showing a relationship with COVID-19 mortality.[10,11] A multivariable logistic regression model was constructed using covariates with at least a prevalence of 5% and a $p < .2$ in the univariable analysis. The final multivariable model included age, receipt of lung transplant hypertension, diabetes mellitus, heart failure, obesity, chronic kidney disease, coronary artery disease, and chronic lung disease. Age was assessed as a dichotomous variable (age ≤ 65 years vs. >65 years) based on clinical relevance and in accordance with prior studies.[5,12] Stata version 16.1 (StataCorp) and R version 4.0.2 were used to perform statistical analyses.

3 | RESULTS

3.1 | Study population

Of 1616 SOTR with COVID-19 in 2020, the time period of diagnosis was available for 1435 patients (88.8%). Of these 1435 patients, 973 (67.8%) were hospitalized for COVID-19 within the 28 days following diagnosis: 571/753 (75.8%) during the early period and 402/682 (58.9%) during the late period ($p < .001$, Figure S1). Overall, the baseline characteristics of hospitalized patients excluded due to an unknown period of diagnosis were similar to those of the included population with an available time period of diagnosis (Table S3).

The mean age was similar in the early (57 ± 13 years) and late (58 ± 14 years) periods ($p = .28$). The proportions of cases from the Northeastern and Midwestern United States were higher in the early period compared to the late period (284/571 [49.7%] vs. 74/402 [18.4%], $p < .001$ and 97/571 [17.0%] vs. 7/402 [1.7%], $p < .001$), and the proportions of cases from the Southern and Western United States were lower in the early period compared to the late cohort (100/571 [17.5%] vs. 194/402 [48.3%], $p < .001$ and 74/571 [13.0%] vs. 119/402 [29.6%], $p < .001$). Black patients accounted for a higher proportion of cases in the early period than the later period (221/523 [42.3%] vs. 113/375 [30.1%], $p < .001$). Hispanic or Latinx patients accounted for a lower proportion of cases in the early period than in the late period (151/545 [27.7%] vs. 142/293 [36.2%], $p = .006$). There was a higher proportion of kidney recipients and a lower proportion of lung recipients in the early cohort compared to the late cohort (383/571 [67.1%] vs. 225/402 [56.0%], $p = .001$, and 41/571 [7.2%] vs. 63/402 [15.7%], $p < .001$, respectively). The proportion of patients with absolute lymphopenia on presentation increased from the early to the late periods (150/535 [28.0%] vs. 131/365 [35.9%], $p = .01$). The proportion with abnormal chest imaging at presentation was similar between time periods (450/541 [83.2%] vs. 294/362 [81.2%], $p = .45$). Additional baseline characteristics of hospitalized patients in each time period are shown in Table 1.

TABLE 1 Baseline characteristics and treatments among hospitalized patients by season for those with season of diagnosis available (N = 973)

Covariate, *n* (%)	Early period (n = 571)	Late period (n = 402)	*p*-value
Male	366 (64.1)	244 (60.9)	.3
Race[a]			
Asian	28 (5.4)	18 (4.8)	<.001
Black	221 (42.3)	113 (30.1)	
Indigenous People	4 (0.8)	10 (2.7)	
Pacific Islander	1 (0.2)	3 (0.8)	
White	269 (51.4)	231 (61.6)	
Hispanic or Latinx ethnicity[b]	151 (27.7)	142 (36.2)	.006
Age > 65 year	167 (29.3)	135 (33.6)	.15
Mean age (SD), years	57.0 (13.5)	57.6 (14.1)	.47
Geographic location			
Northeastern U.S.	284 (49.7)	74 (18.4)	<.001
Midwestern U.S.	97 (17.0)	7 (1.7)	<.001
Southern U.S.	100 (17.5)	194 (48.3)	<.001
Western U.S.	74 (13.0)	119 (29.6)	<.001
International	16 (2.8)	8 (2.0)	.42
Organ[c]			
Kidney	383 (67.1)	225 (56.0)	<.001
Liver	76 (13.3)	62 (15.4)	.35
Heart	68 (11.9)	52 (12.9)	.63
Lung	41 (7.2)	63 (15.7)	<.001
Other	3 (0.5)	0 (0.0)	
Underlying comorbidities			
Hypertension	458 (80.2)	296 (73.6)	.02
Diabetes mellitus	301 (54.3)	191 (47.5)	.04
Heart failure	47 (8.2)	18 (4.5)	.02
Obesity (BMI ≥ 30 kg/m^2)[d]	201 (35.8)	135 (35.1)	.81
Chronic kidney disease	202 (35.4)	125 (31.1)	.16
Coronary artery disease	124 (21.7)	58 (14.4)	.004
Chronic lung disease	52 (9.1)	15 (3.7)	.001

(Continues)

TABLE 1 (Continued)

Covariate, *n* (%)	Early period (*n* = 571)	Late period (*n* = 402)	*p*-value
Baseline immunosuppression			
Induction in the past 3 months[e]	28 (7.0)	30 (5.3)	.27
CNI, antimetabolite, corticosteroids	305 (53.4)	204 (50.8)	.41
Any CNI[f]	528 (92.5)	368 (91.5)	.6
Any antimetabolite[f]	406 (71.1)	313 (77.8)	.02
Any corticosteroid[g]	438 (76.7)	277 (68.9)	.01
Any mTOR inhibitor	32 (5.6)	23 (5.7)	.94
Presenting features			
Lymphopenia (ALC $< 0.5 \times 10^9$/L)[h]	150 (28.0)	131 (35.9)	.01
Abnormal chest imaging[i]	450 (83.2)	294 (81.2)	.49

Abbreviations: ALC, absolute lymphocyte count; BMI, body mass index; CNI, calcineurin inhibitor, mTOR, mammalian target of rapamycin; SD, standard deviation, U.S., United States.

[a]Race was available for 523 patients in the early period and 375 patients in the late period.

[b]Ethnicity was available for 545 patients in the early period and 293 patients in the late period.

[c]Kidney includes 16 kidney/pancreas recipients. Liver includes 28 liver/kidney and 1 liver/pancreas/small bowel recipients. Heart includes 13 heart kidney and 1 heart/kidney/small bowel recipients. Lung includes 2 heart/lung, 1 liver/lung, and 1 lung/kidney/islet cell recipients. Other organ recipients include 2 small bowel recipients and 1 vascular composite allograft recipient.

[d]BMI was available for 561 patients in the early period and 385 patients in the early period.

[e]Induction immunosuppression refers to polyclonal antilymphocyte globulin (early period, *n* = 16; late period, *n* = 17), alemtuzumab (early period, *n* = 2; late period, *n* = 0), basiliximab (early period, *n* = 9; late period, *n* = 6), pulse steroids at ≥500 mg methylprednisolon e/day for ≥3 days (early period, *n* = 6; late period, *n* = 14), rituximab (early period, *n* = 1; late period, *n* = 2), and plasmapheresis (early period, *n* = 0; late period, *n* = 1). Some patients received more than one induction agent.

[f]Includes tacrolimus and cyclosporine.

[g]Includes mycophenolate mofetil, mycophenolic acid, azathioprine, and leflunomide.

[h]Dose of baseline corticosteroids consistent of ≤5 mg/day of prednisone or equivalent (early period, *n* = 414; late period, *n* = 267) or >5 mg/day of prednisone (early period, *n* = 24; late period, *n* = 10).

[i]Absolute lymphocyte count was measured in 535 patients in the early period and 365 patients in the late period.

[j]Chest imaging was performed in 541 patients in the early period and 362 patients in the late period. Refers to changes from baseline for patients with abnormal chest imaging prior to COVID-19.

3.2 | Outcomes by 28 days during study periods

Among SOTR hospitalized for COVID-19, crude mortality by 28 days declined between the early and late periods (112/571 [19.6%] vs. 55/402 [13.7%], respectively, $p = .016$). Unadjusted survival curves are shown in Figure 1. After adjusting for differences in baseline comorbidities between time periods, the odds of death remained lower in the late period (aOR 0.67, 95% CI 0.46–0.98, $p = .04$). The proportion of patients admitted to the ICU was similar in early and late periods (213/551 [38.6%] vs. 152/388 [39.2%], $p = .87$, respectively). The proportion of patients who required any form of supplemental oxygen increased between the early and late periods (395/571 [71.0%] vs. 303/394 [76.9%], $p = .04$, respectively), but the use of mechanical ventilation declined between the early and late periods (171/554 [30.9%] vs. 93/394 [23.6%], $p = .014$, respectively). Initiation of renal replacement therapy among patients who did not require dialysis prior to admission declined between the early and late periods (89/528 [17.8%] vs. 48/402 [12.9%], $p = .051$). The median length of hospitalization was similar in the early and late periods (10 days [IQR: 5–19] and 8 days [IQR: 5–18], $p = .08$, respectively). The proportion of patients who developed bacterial pneumonia, bloodstream infections, and acute cellular rejection were similar between the two time periods (Table 2).

3.3 | Therapeutic interventions used during study periods

The use of hydroxychloroquine and monoclonal antibodies targeting interleukin 6 (IL-6) or the IL-6-receptor (IL-6R) declined between the early and late periods (Table 3). The use of corticosteroids (at a dose equivalent to ≥6 mg dexamethasone/day) and remdesivir increased between the early and late periods (62/571 [10.9%] vs. 243/402 [61.4%], $p < .001$, and 50/571 [8.8%] vs. 213/402 [53.0%], $p < .001$, respectively). Twenty patients in the early period and four patients in the late period received both corticosteroids and anti-IL6/IL-6R monoclonal antibody. Three hospitalized patients in the late period received a monoclonal antibody targeting the SARS-CoV-2 spike protein during their clinical course; no patients in the early period were treated with anti-SARS-CoV-2 monoclonal antibodies. In both the early and late periods, immunosuppression was reduced in over 70% of patients (Table 3). In patients taking antimetabolites at the time of COVID-19 diagnosis, cessation of the antimetabolite was common in both the early and late periods (270/406 [66.5%] vs. 206/313 [66.5%], respectively, $p = .87$). In patients taking calcineurin inhibitors at the time of COVID-19 diagnosis, reduction of target calcineurin troughs was more common in the early period compared to the late period (160/571 [30.3%] vs. 49/402 [13.3%], respectively, $p < .001$).

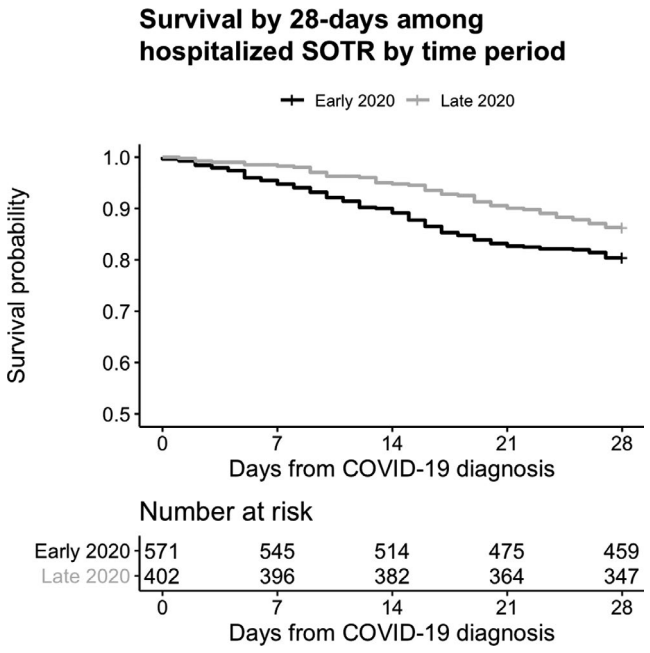

FIGURE 1 Unadjusted survival curves in solid organ transplant recipients hospitalized for COVID-19 in early and late 2020

4 | DISCUSSION

In this large multicenter observational cohort study, mortality among SOTR hospitalized for COVID-19 declined during the pandemic, even when controlled for baseline comorbidities, similar to trends reported in the general population.

We explored potential explanations for the observed reduction in mortality during the most recent study period. We noted key differences in patient characteristics between the study periods: the prevalence of heart and lung disease, high-risk comorbidities that are strongly associated with mortality in SOTR with COVID-19,[1] was significantly lower in the late, more recent period. However, mortality remained lower in the late period after adjusting for these confounding conditions, consistent with findings from the general population demonstrating decreased mortality among persons of all ages and in those with multiple medical comorbidities.[4,13] Thus, differences in underlying comorbidities between study periods are unlikely to fully explain the observed decrease in mortality and suggest that other factors were likely contributory.

We also assessed COVID-19 illness severity between time periods as a possible explanation for the observed decline in mortality. SARS-CoV-2 testing availability increased significantly throughout 2020,[14] potentially facilitating earlier detection of milder cases of COVID-19 during the late study period. Indeed, we observed a significantly lower rate of hospitalization after diagnosis in the late (more recent) period. To minimize the impact of potential variations in baseline severity of illness between time periods, we limited our analysis to hospitalized patients with the rationale that indications for hospitalization likely remained similar between periods. Importantly, surrogate markers of disease severity among hospitalized patients included in the analysis did not vary substantially between time periods. There was no difference in the prevalence of abnormal chest imaging or ICU admission between time periods, and absolute lymphopenia at illness presentation was more common in the later

TABLE 2 Outcomes by 28 days in solid organ transplant recipients hospitalized for COVID-19 during early and late 2020

Outcomes, *n* (%)	Early period (*n* = 571)	Late period (*n* = 402)	Unadjusted OR (95% CI)[a]	*p*-value[a]	Adjusted OR (95% CI), *p*-value[b]
Death	112 (19.6)	55 (13.7)	0.7 (0.5–0.9)	.016*	0.67 (0.46–0.98), *p* = .037
ICU admission[c]	213 (38.7)	152 (39.2)	1.0 (0.8–1.3)	.87	
Any supplemental oxygen[d]	395 (71.0)	303 (76.9)	1.4 (1.0–1.8)	.04*	
Nasal cannula or simple facemask	167 (30.0)	152 (38.5)	1.5 (1.1–1.9)	.01*	
High flow nasal cannula	43 (7.7)	49 (12.4)	1.7 (1.1–2.6)	.02*	
Noninvasive positive pressure ventilation	14 (2.5)	9 (2.3)	0.9 (0.4–2.1)	.82	
Mechanical ventilation	171 (30.9)	93 (23.6)	0.7 (0.5–0.9)	.014	
New RRT[e]	89 (17.8)	48 (12.9)	0.7 (0.5–1.0)	.051	
Infection[f]					
Bacterial pneumonia	43 (7.5)	34 (8.5)	1.2 (0.7–1.8)	.60	
Fungal pneumonia	2 (0.4)	5 (1.3)	3.6 (0.7–18.5)	.13	
Bloodstream infection	37 (6.5)	28 (7.0)	1.1 (0.6–1.8)	.77	
Acute cellular rejection	4 (0.7)	6 (1.5)	2.1 (0.6–7.7)	.29	
Median length of hospitalization, days (IQR)[g]	10 (5–19)	8 (5–18)		.08	

Abbreviations: CI, confidence interval; ICU, intensive care unit; IQR, interquartile range; OR, odds ratio; RRT, renal replacement therapy.

[a]Reference is early period.

[b]*P*-values reflect χ^2 and Fisher's exact tests for heterogeneity for dichotomous outcomes and Wilcoxon rank-sum test for the continuous outcome (length of hospitalization). *Indicates statistical significance at $\alpha = .05$.

[c]Adjusted odds ratio is based on multivariable logistic regression for the primary outcome (death). The multivariable model adjusted for age (> 65 years vs. ≤65 years), receipt of lung transplant hypertension, diabetes mellitus, heart failure, obesity, chronic kidney disease, coronary artery disease, and chronic lung disease.

[d]ICU admission status available for 551 patients in the early period and 388 patients in the late period.

[e]Highest level of respiratory support and need for mechanical ventilation was available for 554 patients in the early period and 394 patients in the late period. In the early period, eight patients who required mechanical ventilation also required extracorporeal membrane oxygenation (ECMO). In the late period, two patients who required mechanical ventilation required ECMO.

[f]Refers to initiation of renal replacement therapy among those who were not receiving renal replacement therapy prior to COVID-19 diagnosis (528 patients in the early period and 386 patients in the late period).

[g]Infections include bacterial pneumonia, fungal pneumonia, and bloodstream infections. Only pathogen-proven infections were included. Some patients experienced more than one infection.

[h]Length of hospital stay was available for 547 patients in the early period and 391 patients in the late period. The number of days refer to the number of days hospitalized during the first 28 days following Covid-19 diagnosis.

period when mortality was lower. Therefore, the observed decrease in mortality over time among SOTR hospitalized for COVID-19 also does not appear to be fully explained by a shift towards lower baseline illness severity in the later study period. Although we did not collect data on all presenting features that have been associated with death in COVID-19, abnormal chest imaging, lymphopenia, and ICU admission are established predictors of mortality in COVID-19 and likely correlated with other predictors of baseline disease severity, including baseline oxygen saturation.[15–17] A higher proportion of patients in the late period required some form of supplemental oxygen despite lower mortality in the late period, further suggesting that the variations in disease severity do not explain the observed decline in mortality.

Based on our findings of decreased mortality despite unchanged surrogates of illness severity and controlling for baseline comorbidities between study periods, we speculate that general improvements in care and COVID-specific treatments may explain the improved survival in SOTR between the first and second portions of 2020. The adoption of therapeutic corticosteroids, prone positioning to improve oxygenation without mechanical ventilation, and overall adaptation of health care systems to the pandemic have been cited as potential reasons for lower contemporary mortality in the general population.[4,5,7,18] The decrease in use of renal replacement therapy observed in this cohort is consistent with findings from the general population and may reflect changes in the approach to volume management over the course of the pandemic.[19] We observed a decline in the use of mechanical ventilation, despite an increase in the proportion of patients requiring any form of supplemental oxygen. The observed decrease in mechanical ventilation likely reflects global changes in the approach to the management of COVID-19 over time, as early intubation at the onset of hypoxemia was a frequent practice early but became less common over time.[20] The current observational study design does not allow for definitive testing of these hypotheses and associations between specific interventions and outcomes should be interpreted with caution. Substantial confounding by indication, whereby sicker patients were more likely to receive therapeutic interventions, precludes meaningful assessment of the association between various treatments and outcomes on

TABLE 3 Treatments for Covid-19 in solid organ transplant recipients hospitalized for Covid-19 during early and late 2020

Treatment, *n* (%)	Early period (*n* = 571)	Late period (*n* = 402)	*p*-value[a]
Corticosteroids[a]	62 (10.9)	243 (61.4)	<.001*
Remdesivir	50 (8.8)	213 (53.0)	<.001*
Anti-IL−6/IL−6R agents	73 (12.8)	5 (1.2)	<.001*
Hydroxychloroquine	329 (60.0)	4 (1.0)	<.001*
Convalescent plasma	48 (8.4)	119 (29.6)	<.001*
Monoclonal antibodies targeting SARS-CoV−2	0 (0.0)	3 (0.8)	.07
Any decrease in maintenance of immunosuppression[b]	322 (79.1)	265 (65.9)	.05*
Hold antimetabolite[c]	270 (66.5)	206 (65.8)	.87
Decrease antimetabolite[c]	51 (12.6)	31 (9.9)	.27
Decrease CNI trough goal[d]	160 (30.3)	49 (13.3)	<.001*

Abbreviations: CNI, calcineurin inhibitor; CI, confidence interval; IL-6R, interleukin-6 (IL-6), interleukin-6 receptor; OR, odds ratio.

[a]*p*-values reflect χ^2 and Fisher's exact tests for heterogeneity.

*Indicates statistical significance at $\alpha = .05$.

[b]Dosed at ≥6 mg dexamethasone equivalents per day.

[c]Complete cessation or reduction in the dose or goal trough of at least one maintenance immunosuppressive agent. Some patients had more than one change. In the early period, corticosteroids were stopped in 2/438 (0.5%) patients taking steroids at baseline. In the late periods, steroids were stopped in 1/277 (0.3%) and decreased in 1/277 (0.3%) patients taking steroids at baseline.

[d]Refers to percentage of patients taking and antimetabolite at the time of Covid-19 diagnosis (406 patients in the early period and 313 patients in the late period).

[e]Refers to percentage of patients taking a calcineurin inhibitor at baseline (528 patients in the early period and 368 patients in the late period).

[f]Refers to percentage of patients taking a corticosteroid at baseline (438 patients in the early period and 277 patients in the late period). Corticosteroid dose was decreased in one patient in the late period; all other steroid decrease involved complete cessation.

the individual level. Thus, our data provide only indirect evidence that contemporary management of COVID-19 may similarly benefit SOTR and the general population.

The strengths of this study include the relatively large sample size, institutional and geographic diversity, standardized data collection and follow-up, and inclusion of cases of COVID-19 diagnosed throughout the entire course of the year 2020. Nonetheless, there are several important limitations including the lack of precise diagnosis dates, observational design leading to inability to detect the impact of specific interventions on outcomes, and reliance on voluntary reporting of cases. This study was restricted to de-identified patient information, a practical strategy that circumvented the need for local IRB approval at many participating institutions, facilitating prompt accumulation of data during a global pandemic. This practical study design did not allow for evaluation of month-by-month variations in mortality. However, we defined study periods using a logical cutoff time that corresponded with the timing of treatment paradigm shifts and data from the general population demonstrate stable mortality throughout our study's later period.[4] The voluntary nature of participation and reporting of cases makes it challenging to understand the extent to which the study cohort represents the entire SOT population. We minimized the potential impact of reporting biases by limiting the analysis to patients hospitalized for COVID-19, which created a more homogeneous study population. Although there were geographic differences between the two study periods, there was no difference in mortality across regions in the univariable analysis, suggesting that any regional differences in care, including threshold for hospitalization, were unlikely to explain the observed mortality trends.

There were significant differences in the racial and ethnic composition of patients between time periods. Social determinants of health and structural racism have placed racial and ethnic minority groups at a higher risk for SARS-CoV-2 acquisition as well as the medical comorbidities that are associated with poor outcomes from COVID-19.[21–23] As such, Black and Hispanic or Latinx patients account for a disproportionately high percentage of COVID-19 cases and deaths, and mortality among waitlisted Black kidney transplant candidates increased disproportionately after the start of the COVID-19 pandemic.[23-25] However, among all patients who are hospitalized for COVID-19, neither racial nor ethnic minority status has been independently associated with an increased risk of death, and comorbidity-adjusted analyses suggest that hospitalized Black and Hispanic or Latinx patients with COVID-19 may be less likely to die than non-Hispanic White patients.[24,26,27] These observations support the definition of race and ethnicity as social constructs that reflect risk factors for COVID-19 exposure and underlying comorbidities without independent biological implications for disease progression following infection.[28] In our cohort of SOT recipients hospitalized for COVID-19, neither race nor ethnicity were associated with death. Therefore, it is unlikely that the temporal variation in the racial and ethnic composition of our cohort is related to the observed trends in mortality.

In conclusion, this large multicenter study demonstrates that mortality among hospitalized SOTR with COVID-19 decreased over the course of the pandemic, reflecting trends observed in the general population. These data provide indirect evidence of a benefit of advances in care and COVID-19 therapies in the general population to SOTR. Future studies to define the mechanism(s) and their relative contributions to improvements in short-term survival in SOTR hospitalized for COVID-19 are warranted.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

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