Incidence, Risk Factors, and Outcomes of COVID-19 Infection in a Large Cohort of Solid Organ Transplant Recipients

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Background. Solid organ transplant recipients (SOTr) are at increased risk for severe disease from coronavirus disease 2019 (COVID-19) compared with non-SOTr. Methods. We performed a retrospective cohort study between March 1, 2020, and March 30, 2021, in an integrated healthcare system with 4.3 million members aged ≥18 y including 5126 SOTr. Comparisons in COVID-19 mortality, hospitalization, and incidence were made between SOTr and non-SOTr, and between different SOTr organs. Multivariate analysis was performed to identify risk factors for COVID-19 mortality and hospitalization. Results. There were 600 SOTr (kidney, liver, heart, and lung) with COVID-19. Per person-year incidence of COVID-19 among SOTr was 10.0% versus 7.6% among non-SOTr (P < 0.0001). Compared with uninfected SOTr, infected SOTr were older (57.1 ± 14.0 versus 45.7 ± 17.9 y, P < 0.001), predominantly Hispanic/Latino (58.8% versus 38.6%, P < 0.0001), hypertensive (77.0% versus 23.8%, P < 0.0001), and diabetic (49.6% versus 13.0%, P = 0.0009). Compared with non-SOTr, infected SOTr had higher hospitalization (39.5% versus 6.0%, P < 0.0001), intensive care unit admission (29.1% versus 15.5%, P < 0.0001), and mortality (14.7% versus 1.8%, P < 0.0001) from COVID-19. Older age (hazard ratio [HR], 1.07; 95% confidence interval [CI], 1.05-1.10), male gender (HR, 1.79; 95% CI, 1.11-2.86), and higher body mass index (HR, 1.04; 95% CI, 1.00-1.09; P = 0.047) were associated with increased mortality from COVID-19, whereas race, diabetes, and number/type of immuno-suppressive medications were not. Among the different SOTr, COVID-19 mortality risk was lowest in liver recipients (HR, 0.34; 95% CI, 0.16-0.73) and highest in lung recipients (HR, 1.74; 95% CI, 0.68-4.42). Conclusions. SOTr have higher rates of hospitalization and mortality from COVID-19 compared with the general population. Among the SOTr, the incidence and outcomes were distinct among different transplantation types.

INTRODUCTION

Severe acute respiratory syndrome coronavirus virus 2 (SARS-CoV-2), the cause of the coronavirus disease 2019 (COVID-19), led to a global pandemic as declared by World Health Organization in March 2020. Since the emergence of SARS-CoV-2 in December 2019, across the globe >520 million people have been affected, with 6 million deaths. In the United States, 82 million people have...
been infected with SARS-CoV-2, with 1 million deaths.\textsuperscript{1,2} The hallmark of the SARS-CoV2 is its ability to mutate rapidly, generating multiple variants of concern, the most recent being the Delta and Omicron variants leading to surges around the globe.\textsuperscript{3}

Most infected persons with SARS-CoV-2 are asymptomatic or have mild disease and serve as the silent spreaders, whereas populations at high risk for complications may more likely develop moderate to severe illness.\textsuperscript{4} These high-risk groups, as defined by the Centers for Disease Control and Prevention, include persons aged ≥65 y; those with comorbidities, such as obesity and diabetes mellitus (DM); and those who are immunocompromised, including solid organ transplant recipients (SOTr).\textsuperscript{5} SOT patients on chronic immunosuppression and with other medical comorbidities may be at higher risk of complications from COVID-19.\textsuperscript{6} A recent study found that SOTr admitted for COVID-19 have higher odds of mortality compared with SOTr admitted for non–COVID-19 reasons.\textsuperscript{7}

Although the impact of COVID-19 on SOTr has been reported, these have primarily been small case series of hospitalized SOTr.\textsuperscript{8-13} In Europe and the United States, the incidence of COVID-19 has been shown to be higher in SOTr than non-SOTr patients.\textsuperscript{10,13-15}

Kaiser Permanente Southern California (KPSC) is the largest integrated health system in California and represents >16% of the population in the coverage area that reflects the socioeconomic diversity of the Southern California census population.\textsuperscript{16} With a single, comprehensive electronic health records (EHRs) system and access to medical care for all members, KPSC is an ideal population to evaluate the impact of COVID-19 on recipients of different SOTr compared with the general population. We report our findings from a large cohort of SOTr with different organs at the point of care diagnosis of COVID-19 to identify risk factors for hospitalization and death from COVID-19. The outcomes of the SOTr infected with SARS-CoV-2 were compared with the general population who were also infected.

**MATERIALS AND METHODS**

**Study Setting**

This study was conducted at KPSC, with a population of 4.3 million active members aged ≥18 y across 15 large medical center areas and 235 medical offices that use a single EHR that collates demographic, services, diagnosis, and procedure data from outpatient, emergency room, and inpatient settings. KPSC members receive organ transplant surgeries at transplant centers in California and other states across the country. The care preceding and after organ transplantation is centralized within KPSC transplant physicians, nurses, and pharmacists. SARS-CoV-2 testing criteria at KPSC followed national Centers for Disease Control and Prevention guidelines—first with symptomatic patients then at will. During the pandemic, care was delivered to patients with COVID-19 remotely and in-person depending on the severity of illness. Patients with COVID-19 who were not hospitalized were followed by the KPSC COVID-19 home monitoring program.\textsuperscript{17} This study was approved by the Institutional Review Board at KPSC.

**Study Design**

A retrospective cohort study was conducted on KPSC members aged ≥18 y who received SOT (defined kidney, liver, heart, or lung transplants) before December 31, 2020, and who were infected with SARS-CoV-2 between March 1, 2020, and March 31, 2021, after transplantation. Laboratory data and International Classification of Diseases 10th Revision codes were used to identify patients who tested positive for SARS-CoV-2. SARS-CoV-2 infection was defined as any patient with a positive polymerase chain reaction (PCR) testing for the SARS-CoV-2 virus regardless of the presence of symptoms. Date of SARS-CoV-2 infection was based on the first positive PCR test. SARS-CoV-2 PCR testing data were extracted from EMR. Immunosuppression regimen recorded was at the time of COVID-19 diagnosis. The denominator used to calculate incidence included all active SOTr aged ≥18 y who had received SOT before December 31, 2020. Follow-up data for outcomes were collected until July 31, 2021, for all patients. Information on time between the date of transplant and the onset of SARS-CoV-2 infection was captured. For SOTr without SARS-CoV-2 infection, December 31, 2020, was used as the reference date to calculate time from transplant.

Data for SARS-CoV-2 infection of the general KPSC population aged ≥18 y during the study period were also collected for comparison. Demographic and clinical data for the general population were extracted from the EHR. Clinical data for SOTr cohort were obtained by chart review and KPSC transplant registry. Comparisons were made between KPSC general population and SOT populations without and with SARS-CoV-2 infection. Further comparisons were made between the different SOTr by organ type. Subgroup analysis was performed on hospitalized patients.

**Outcomes**

The primary outcome was mortality from COVID-19 as determined by death registry information and clinical documentation. Mortality rate was defined as number of deaths per number of total confirmed cases. All-cause mortality was calculated separately. Secondary outcomes included hospitalization and intensive care unit (ICU) admission. Admission to the hospital was defined as hospitalization for COVID-19–related issues (determined by the admitting or primary hospital teams) that was extracted by chart review for SOTr and from the EHR for the general population. Patients who were admitted for other causes (eg, fall, cellulitis) with incidental asymptomatic COVID-19 as determined by the primary hospital providers were not counted as hospitalized for COVID-19. The first wave of COVID-19 was defined between March 1, 2020, and September 30, 2020, and the second wave of COVID-19 beginning October 1, 2020, until the end of the study period at March 31, 2021. Outcomes between the 2 waves of COVID-19 were compared.

**Statistical Analysis**

Statistical analysis was performed using univariate and multivariate analyses. Descriptive data were presented as number (percentage) for categorical variables and as mean (standard deviation) or median (interquartile range) for
continuous variables. The Kruskal-Wallis test was used to
detect the means difference for continuous variables and
chi-square or Fisher exact test was applied to evaluate the
difference in incidence of categorical variables among SOTr
and general KPSC population with or with COVID-19
and, lastly, among different types of organ transplantation.

**Covariates**

Individual-level factors included age at diagnosis, gen-
der, race/ethnicity, primary organ transplanted, number of
immunosuppressive drugs used, time from transplant, and
comorbidities including body mass index (BMI), hyperpres-
sion, and DM. Subgroup analysis was conducted among
SOTr who were hospitalized to evaluate clinical data such
as laboratory markers and treatments received.

The univariate and multivariate Cox proportional haz-
ard models were performed to detect factors associated
with time to COVID-19–related death for infected SOTr.
Crude and adjusted hazard ratios (HRs) with confidence
intervals (CIs) were presented for each covariate listed
above and the Wald P values were calculated. The forest
plot was produced to display the result graphically for the
multivariate Cox model. All analyses are 2-sided and per-
fomed using SAS EG 7.13 (Cary, NC). P values of <0.05
were considered statistically significant.

**RESULTS**

**General Population (Non-SOT) and SOT Populations**

Within the KPSC general population, 4.3 million adult
patients without SOT and 5126 adult patients who received
SOT before December 31, 2020 were identified (Figure 1).
The demographic characteristics of the SOTr and the
KPSC general population are shown in Table 1. SOTr were
older (57.1 ± 14.0 versus 45.7 ± 17.9 y; P < 0.0001) with a
lower proportion of females compared with the general
population (40.7% versus 51.7%; P = 0.0001). Hispanic/
Latino and Whites represented the majority in the general
population and SOTr groups.

Between March 1, 2020, and March 30, 2021, 1342481
(31.5%) of general population and 2731 (53.3%) of SOTr
underwent COVID-19 testing (P < 0.0001) with positive test
rates of 23.2% in the general population and 21.9% in SOTr
(P = 0.116). Of the general patient population, 312011 indi-
viduals and 600 SOTr developed COVID-19 with incidences
of 7.6 per 100 person-years and 10.0 per 100 person-years
(P < 0.0001), respectively (Table 1). In the general population
with COVID-19, there was a higher proportion of Hispanics
(60.9% versus 38.1%; P < 0.0001) and a lower propor-
tion of Whites (19.3% versus 30.6%; P < 0.0001) compared
with those without COVID-19. Similarly, in the SOTr popula-
tion with COVID-19, there was a higher proportion of Hispanics
(58.8% versus 38.6%; P < 0.0001) compared with other
racial groups versus uninfected SOTr. Compared with unin-
fected SOTr, infected SOTr were younger compared with
uninfected SOTr (median 57.0 versus 60.0 y; P = 0.0006).

Hospitalization rate was significantly higher for infected
SOTr compared with infected general population (39.5%
versus 6.0%, P < 0.001; Table 2). Among those hospital-
ized, 99.4% of non-SOTr were given supplemental oxygen
compared with 86.1% of SOTr (P < 0.0001). Remdesivir
was given to 66.0% of hospitalized non-SOTr compared
with 57.0% of hospitalized SOTr (P = 0.004). ICU hospi-
talization was higher in SOTr compared with non-SOTr
(29.1% versus 15.5%; P < 0.0001). Overall mortality
rate of COVID-19 in SOTr was higher compared with

![Figure 1](https://example.com/figure1.png)

**FIGURE 1.** Cohort selection. KPSC, Kaiser Permanente Southern California; SARS-CoV-2, severe acute respiratory syndrome coronavirus virus 2; SOTr, solid organ transplant recipient.
the general population (14.7% versus 1.8%;  P<0.0001). Among hospitalized patients, the mortality rate was 34.2% among SOTr compared with 17.3% in the general population ( P<0.0001). Mortality rate in patients admitted to the ICU was also higher among SOTr compared with 17.3% in the general population (14.7% versus 1.8%;  P<0.0001).

**SOTr With COVID-19**

The baseline characteristics of SOTr with and without COVID-19 are shown in Tables 3 and 4. The SOT cohort with COVID-19 had an average BMI of 29.2 ± 5 kg/m². The mean Charlson Comorbidity Index was 4.9 ± 2.4. SOTr with COVID-19 were more likely to have hypertension ( P<0.0001) and DM ( P<0.0001) compared with those without COVID-19. The majority of SOTr (55.8%) were on ≥3 immunosuppressive medications (including prednisone), whereas only 10.7% were on a single immunosuppressive agent. The most common baseline immunosuppressive agents at the time of COVID-19 diagnosis were tacrolimus (79.0%), prednisone (71.0%), and mycophenolate mofetil (68.8%). At the time of diagnosis with COVID-19, 82.4% were symptomatic, with most common symptoms being cough (47.9%), fever (33.0%), myalgias (23.4%), and dyspnea (21.6%; Table S1, SDC, http://links.lww.com/TP/C584).

Patients with symptomatic COVID-19 were recommended to hold their mycophenolate. Corticosteroids were administered to 30.7% of the infected SOTr cohort (either as new treatment or increased dosage from baseline dose), 22.0% received remdesivir, 6.2% received convalescent plasma, 3.2% received anakinra, and 1.2% received monoclonal antibodies against SARS-CoV-2.

COVID-19 incidence by transplant era was highest in SOTr transplanted >5 y before infection (13.6%) compared with those transplanted <5 y (9.8%;  P=0.0006; Table 3). COVID-19 incidence per 100 000 person-years was highest among SOTr transplanted >5 y before infection (83.9) compared with those transplanted <5 y (33.3;  P<0.0001).

### Table 1.

| KSACS General Population vs All SOTr Age ≥18 During 3/1/2020–3/31/2021 |
|---------------------------|-----------------------------|-----------------------------|
| Age, y, mean (SD)         | 45.7 (17.9)                 | 57.1 (14.0)                 |
| Sex, male, n (%)          | 2 060 251 (48.3)            | 3 025 931 (69.0)            |
| Race, n (%)               |                             |                             |
| Hispanic                  | 1 626 505 (38.1)            | 2 099 409 (40.9)            |
| White                     | 1 304 380 (30.6)            | 1 605 313 (31.3)            |
| Asian and Pacific Islander| 472 635 (11.1)              | 726 (14.2)                  |
| Black                     | 317 224 (7.4)               | 619 (12.1)                  |
| Unknown                   | 438 777 (10.3)              | 0 (0.0)                     |
| Other                     | 107 451 (2.5)               | 77 (1.5)                    |

### Table 2.

| KSACS with COVID-19 vs SOT with COVID-19 |
|----------------------------------------|----------------------------------------|
| Age, y, mean (SD)                      | 57.3 (14.1)                            |
| Sex, male, n (%)                       | 142 329 (45.6)                         |
| Race/ethnicity, n (%)                  | 23 009 (7.4)                           |
| Hispanic                               | 189 861 (60.9)                         |
| Black                                  | 60 247 (19.3)                          |
| Asian/Pacific Islander                 | 2891 (15.5)                            |
| White                                  | 61 292 (19.6)                          |
| Hypertension                           | 7 600 (11.7)                           |
| Diabetes mellitus                      | 7 600 (11.7)                           |
| COVID-19 mortality                     | 61 292 (19.6)                          |
| All-cause mortality                    | 72 697 (13.4)                          |

### Table 3.

| SOTr Without COVID-19 vs with COVID-19 |
|---------------------------------------|---------------------------------------|
| N (Y)                                 |
| Age, y, mean (SD)                     | 57.3 (14.1)                            |
| Sex, male, n (%)                      | 142 329 (45.6)                         |
| Race/ethnicity, n (%)                 | 23 009 (7.4)                           |
| Hispanic                               | 189 861 (60.9)                         |
| Black                                  | 60 247 (19.3)                          |
| Asian/Pacific Islander                 | 2891 (15.5)                            |
| White                                  | 61 292 (19.6)                          |
| Hypertension                           | 7 600 (11.7)                           |
| Diabetes mellitus                      | 7 600 (11.7)                           |

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Figure S1, SDC, http://links.lww.com/TP/C584). There were no differences in mortality rate based on time from transplant relative to COVID-19 infection (P = 0.56).

Of the 600 infected SOTr, 110 and 490 were infected during the first and second COVID-19 surges, respectively. Infected SOTr during the first surge were more likely to be hospitalized (51.8% versus 36.7%; P = 0.01), but there were no differences in ICU admission (29.8% versus 28.8%; P = 0.885) or mortality rates (17.3% versus 14.1%; P = 0.39).

### Disaggregated SOT Data

The clinical characteristics of SOTr by organ are shown in Table 4. The majority of SOTr were kidney (73%) or liver (19%) transplant recipients. The incidence of COVID-19 infection was highest among kidney (11.8%) and lowest among liver recipients (8.2%) and intermediate among lung (8.9%) and heart transplant recipients (9.0%; P = 0.0016). Lung (61 y) and liver recipients (62 y) were the older, whereas heart recipients (57 y) were the younger (P = 0.004). Hispanic/Latinos was the predominant ethnic group among all organ types with the highest proportion in liver transplant (63.2%) and lowest in heart transplant (42.4%; P = 0.003). There was no significant difference in BMI between organ types (P = 0.48). Majority of the SOTr were on multiple immunosuppressive agents: 55.3% liver, 67.1% kidney, 90.9% heart, and 93.3% lung transplants.

Symptoms were similar among the different SOT groups except for dyspnea that was mostly reported by lung recipients (60%; P = 0.0029). Lung transplant recipients had the highest rate of hospitalization (93.3%; P = 0.0002) and need for ICU care (46.7%; P < 0.0001) compared with other SOTs, compared with liver transplant recipients (7.0%; P < 0.0001). The mortality rates from COVID-19 among SOTr were highest in lung recipients (46.7%) and lowest in liver recipients (8.8%; P = 0.0013). The mortality rate among those hospitalized was highest among heart

### TABLE 4

Baseline and clinical characteristics of SOTr with COVID-19 by organ transplant types

| Primary organ | Heart (N = 33) | Kidney (N = 438) | Liver (N = 114) | Lung (N = 15) | Total (N = 600) | P value |
|---------------|----------------|-----------------|----------------|---------------|----------------|---------|
| Age, y, median (IQR) | 57.0 (42.0–71.0) | 56.0 (47.0–64.0) | 62.0 (53.0–67.0) | 61.0 (57.0–68.0) | 57.0 (47.0–66.0) | 0.0035⁶ |
| Sex, male, n (%) | 27 (81.8) | 267 (61.0) | 55 (48.2) | 7 (46.7) | 356 (59.3) | 0.0026⁷ |
| Race/ethnicity, n (%) | 0.003⁴ ⁷ |
| Asian | 0 (0.0) | 48 (11.0) | 6 (5.3) | 0 (0.0) | 54 (9.0) |
| Black/African American | 7 (21.2) | 55 (12.6) | 6 (5.3) | 1 (6.7) | 69 (11.5) |
| Hispanic/Latino | 14 (42.4) | 254 (58.0) | 72 (63.2) | 9 (60.0) | 349 (58.2) |
| White | 12 (36.4) | 81 (18.5) | 30 (26.3) | 5 (33.3) | 128 (21.3) |
| Body mass index, mean (SD) | 28.4 (5.6) | 29.3 (5.7) | 29.4 (6.3) | 27.3 (2.6) | 29.2 (5.8) | 0.480⁶ |
| Charlson Comorbidity Index, median (IQR) | 6.0 (2.0–8.0) | 4.0 (3.0–6.0) | 6.0 (3.0–8.0) | 5.0 (3.0–6.0) | 5.0 (3.0–6.0) | <0.0001⁵ |
| Hypertension, n (%) | 25 (75.8) | 413 (94.3) | 76 (66.7) | 8 (53.3) | 522 (87.0) |
| Diabetes mellitus, n (%) | 17 (51.5) | 224 (51.1) | 58 (50.9) | 11 (73.3) | 310 (51.7) |
| Number of Immunosuppressants, median (IQR) | 2.0 (2.0–3.0) | 3.0 (2.0–3.0) | 2.0 (1.0–2.0) | 3.0 (3.0–3.0) | 3.0 (2.0–3.0) | <0.0001⁰ |
| Immunosuppression type, n (%) | 0.003⁴ |
| Tacrolimus | 24 (72.7) | 333 (76.0) | 103 (90.4) | 14 (83.3) | 474 (79.0) | 0.003² |
| Cyclosporine | 5 (15.2) | 63 (14.4) | 10 (8.8) | 0 (0.0) | 78 (13.0) | 0.177⁴ |
| Mycophenolate | 26 (78.6) | 329 (75.1) | 46 (40.4) | 12 (80.0) | 413 (68.8) | <0.0001⁵ |
| Sirolimus | 8 (24.2) | 27 (6.2) | 0 (0.0) | 2 (13.3) | 37 (6.2) | <0.0001⁷ |
| Everolimus, n (%) | 1 (3.0) | 0 (0.0) | 1 (0.0) | 1 (6.7) | 3 (0.5) | 0.000⁴ |
| Prednisone | 10 (30.3) | 369 (84.2) | 32 (28.1%) | 15 (100.0) | 426 (71.0) | <0.0001⁰ |
| COVID-19 | 0.0016 |
| Incidence | 33 (9.0) | 433 (11.8) | 114 (8.2) | 15 (8.9) | 0.016 |
| Hospitalized for COVID-19 | 12 (36.4) | 172 (39.3) | 39 (34.2) | 14 (93.3) | 237 (39.5) |
| Admitted to ICU for COVID-19 | 6 (18.2) | 48 (11.0) | 8 (7.0) | 7 (46.7) | 69 (11.5) |
| COVID-19 mortality | 6 (18.2) | 65 (14.8) | 10 (8.8) | 7 (46.7) | 88 (14.7) |
| Among hospitalized | 6 (50.0) | 55 (32.0) | 10 (25.6) | 7 (50.0) | 78 (32.9) |
| Among ICU | 6 (100) | 41 (65.4) | 6 (57.0) | 7 (100) | 60 (67.0) |
| Time from transplant, y, n (%) | 0.553⁴ |
| <1 | 5 (15.2) | 35 (8.0) | 19 (16.7) | 2 (13.3) | 61 (10.2) |
| 1–<5 | 9 (27.3) | 134 (30.6) | 35 (30.7) | 8 (53.3) | 186 (31.0) |
| 5–<10 | 8 (24.2) | 129 (29.5) | 25 (21.9) | 3 (20.0) | 165 (27.5) |
| ≥10 | 11 (33.3) | 140 (32.0) | 35 (30.7) | 2 (13.3) | 188 (31.3) |

⁶Kruskal-Wallis P value.
⁷Chi-Square P value.
⁸Fisher Exact P value.

COVID-19, coronavirus disease 2019; ICU, intensive care unit; IQR, interquartile range; SOTr, solid organ transplant recipient.
TABLE 5.
Risk factors for COVID-19 mortality

| Parameter                      | Survived (n = 512) | Died (n = 88) | Univariate analysis | Multivariate analysis |
|--------------------------------|--------------------|--------------|---------------------|----------------------|
|                                | Median (IQR)       | Median (IQR) | HR (95% CI)         | P value              |
| Age (per 1-y increase)         | 55.5 (46.0–64.0)   | 66.0 (58.0–71.0) | 1.06 (1.05–1.09)    | <0.0001              |
| Time from transplant (per 1-y increase) | 6.3 (2.7–11.8)   | 7.6 (3.4–15.7)     | 1.03 (1.00–1.05)    | 0.0644               |
| Female gender (reference: male) | 214 (41.8%)         | 30 (34.1%)     | 0.74 (0.48–1.16)    | 0.1895               |
| Race/ethnicity (reference: White) | 108 (21.1%)        | 20 (22.7%)   | 1.17 (0.55–2.50)    | 0.1895               |
| Primary organ (reference: kidney) | 373 (72.9%)      | 65 (73.9%)   | 2.50 (0.19–33.9)    | 0.0062               |
| Hypertension                   | 445 (86.9%)        | 77 (87.5%)     | 1.06 (0.56–1.99)    | 0.0062               |
| Diabetes mellitus              | 251 (49.0%)        | 59 (67.0%)     | 1.99 (1.28–3.11)    | 0.0062               |
| Shortness of breath            | 88 (17.2%)         | 43 (48.9%)     | 3.92 (2.58–5.95)    | <0.0001              |
| Number of immunosuppressants   | 3.0 (2.0–3.0)      | 3.0 (2.0–3.0)   | 1.05 (0.81–1.38)    | 0.7087               |
| Tacrolimus                     | 415 (81.1%)        | 59 (67.0%)     | 0.51 (0.32–0.79)    | 0.0027               |
| Cyclosporine                   | 60 (11.7%)         | 18 (20.5%)     | 1.80 (1.07–3.01)    | 0.0262               |
| Mycophenolate                  | 354 (69.1%)        | 59 (67.0%)     | 1.11 (0.71–1.72)    | 0.6596               |
| Prednisone                     | 357 (69.7%)        | 69 (78.4%)     | 1.52 (0.92–2.53)    | 0.104                |

P values calculated by Wald test.
Cl, confidence interval; COVID-19, coronavirus disease 2019; HR, hazard ratio; IQR, interquartile range.

Multivariate analysis was performed to evaluate factors associated with mortality in the SOTr cohort with COVID-19 as shown in Table 5 and Figure 2. Every 1-y increase in age at diagnosis (HR, 1.07; 95% CI, 1.05–1.10; P < 0.0001) was associated with a 7% increased risk of mortality from COVID-19. BMI (HR, 1.04; 95% CI, 0.04–0.58; P = 0.006), and Blacks (HR, 0.21; 95% CI, 0.07–0.69; P = 0.01) had lower risk of COVID-19 mortality. Hispanic/Latino race (HR, 0.63; 95% CI, 0.25–1.54; P = 0.31) was not associated with increased risk of mortality compared with other races. In addition, the duration of time to onset of COVID-19 diagnosis and the transplant date were not associated with an increased risk of mortality (HR, 1.02; 95% CI, 0.99–1.05; P = 0.20). Patients who received remdesivir trended toward a lower risk of COVID-19 mortality (HR, 0.51; 95% CI, 0.26–1.01; P = 0.05). Gender, BMI, DM, and number of immunosuppressive agents were not found to be significant risk factors in subgroup multivariate analysis in hospitalized patients. Using an alternative multivariate model with individual immunosuppressant agents (Table S3, SDC, http://links.lww.com/TP/C584), tacrolimus (HR, 0.49; 95% CI, 0.24–1.02; P = 0.06) had decreased risk of mortality but did not reach significance.

DISCUSSION
KPSC is the largest healthcare system in southern California, with uniform processes that provide equal access to all members for medical care. We compared the incidences and outcomes of all SOTr and the general population infected with SARS-CoV-2. To our knowledge, this

(50.0%) and lung (50.0%) transplants and lowest in liver transplants (25.6%; P = 0.013).
is the largest single-center study in the United States of disaggregated SOTr who were infected with SARS-CoV-2 during the initial 2 surges of the pandemic. Although SOTr were more likely to be tested for COVID-19 compared with the general population, the positive test rates were similar. However, SOTr had a significantly higher incidence of COVID-19 compared with the nontransplant population that has also been reported in Europe and the United States.\textsuperscript{10,13-15} There were differences in the incidences of COVID-19 among various SOTr, highest among kidney recipients and lowest among liver transplant recipients that was found in studies from Spain,\textsuperscript{15} Italy,\textsuperscript{14} and the National COVID Cohort Collaborative.\textsuperscript{18} In our study, incidence of COVID-19 among liver recipients was comparable with the general population. The reasons for the different incidences of COVID-19 among the different SOTr are not apparent.

In the SOTr, rates of hospitalization were 6-fold higher, ICU admission was almost 2-fold higher, and the mortality was 8-fold higher compared with the general population, which is similar to a smaller study.\textsuperscript{19} In contrast, a greater proportion of non-SOTr received supplemental oxygen and remdesivir, inferring that they likely had more dyspnea and elevated inflammatory markers compared with SOTr. This may also reflect a lower threshold to admit SOTr because of their immunocompromised status but did not meet national guidelines criteria for remdesivir treatment. As reported by Jerring et al,\textsuperscript{7} SOTr hospitalized for COVID-19 had 2-fold higher mortality compared with the general population. This may be because of the immunosuppressed state and comorbidities, although number and type of immunosuppressive medications used in our cohort were not identified as risk factors for COVID-19–related mortality. However, the number of immunosuppressive medications may not reflect the net state of immunosuppression.

The association of older age with increased mortality from COVID-19 was also confirmed within our cohort. Longer time from transplant to diagnosis of COVID-19 trended toward higher risk of COVID-19 mortality but did not reach statistical significance. Although few studies report associations between time from transplant and mortality, 2 multicenter studies in the United States and the United Kingdom also found that older age rather than time from transplant was associated with mortality.\textsuperscript{20,21} However, a study in Spain of hospitalized infected SOTr found more favorable outcomes in those closer to their transplant.\textsuperscript{22} This suggests that other clinical factors such as age and comorbidities may contribute toward COVID-19 mortality in the SOTr cohort.\textsuperscript{23,24}

Among the different SOTr, highest mortality occurred in lung and heart transplants, whereas lowest mortality

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Forest plot for risk factors for COVID-19 mortality. BMI, body mass index; CI, confidence interval; COVID-19, coronavirus disease 2019.}
\end{figure}
occurred in liver transplant recipients. This is not surprising as COVID-19 is a respiratory viral illness, and similar to other community respiratory viral infections carry high mortality in lung transplant patient population.\textsuperscript{25-27} Our findings are similar to other reports in their disaggregated SOTr populations with the highest mortality rates, ranging from 14% to 46% in lung transplant recipients with COVID-19 compared with other SOTr.\textsuperscript{13,21,25,28-30} Heart recipient mortality was significantly lower than in lung recipients in our cohort, which is similar to other reports.\textsuperscript{31,33}

Kidney transplants had a higher mortality rate compared with liver transplants but lower compared with heart and lung transplants. In a large European database study where 89% of post–kidney transplant recipients were hospitalized for COVID-19, the mortality rate of 21.3% was observed in kidney recipients and 23.6% among those who were hospitalized.\textsuperscript{34} In another multicenter study of 144 hospitalized kidney recipients with COVID-19 in the United States and Europe, 32% died.\textsuperscript{35}

Our results show that although liver transplants had a higher incidence of COVID-19 and COVID-19–related hospitalizations compared with the general population, the hospitalization and mortality were significantly lower compared with other SOTr. This is similar to 2 reports of matched-cohort liver recipients that reported a wide range of hospitalization rates from 29% to 86.5%, with both reporting a mortality rate of 18%,\textsuperscript{36,37} whereas others report no difference in mortality between liver recipients and general populations with COVID-19.\textsuperscript{38,39} Immunosuppressive regimens with kidney, heart, and lung recipients that may include T cell–depleting agents, higher use of corticosteroids, and mycophenolate rendering these 3 transplant groups at higher risk for complications.\textsuperscript{40}

Overall, our cohort had a lower hospitalization rate compared with other studies that report hospitalization rates as high as 82% in SOTr.\textsuperscript{20} This is likely because of the COVID-19 home monitoring program within KPSC that was implemented in which mild cases of COVID-19 were triaged to reduce hospitalizations.\textsuperscript{17} This may explain the higher hospital mortality rate in this study because only high-risk patients were hospitalized. The overall mortality rate of 14.7% among all patients (regardless of hospitalization status) is lower compared with the other large-scale studies with multiorgan SOTr reporting mortality rates of 18.7% to 30.6%.\textsuperscript{14,15,21,41}

We also observed higher incidence of COVID-19 infection in Hispanic/Latinos among SOTr and the general population.\textsuperscript{52-55} Unequal incidence and outcomes in the Hispanic/Latino populations could be attributed to work conditions, housing situation with multigenerational dwellings, healthcare access, coexisting medical conditions, language barriers, and immigration status.\textsuperscript{43,44,46} However, our SOTr population, regardless of race/ethnicity, has equal access to medical care although the many aforementioned socioeconomic factors may be present. In this study, ethnicity was not identified as a risk factor for COVID-19–related mortality. Our SOTr cohort may have more experience navigating through the healthcare system and have ongoing relationships with their transplant teams with no disparity in access to healthcare.\textsuperscript{12,47} A centralized group of transplant coordinators provides close follow-up to patients in assisting with routine care and follow-up. A higher number of patients with COVID-19 were recorded during the second surge, which can be attributed to increased transmissibility of SARS-CoV-2 variants and improvement in the testing capabilities. Improved medical management of COVID-19 over time may explain the trend toward better survival observed in our cohort during the second surge. For example, remdesivir was available during the latter portion of the first surge but was used more in the second surge (data not shown). Further analysis of the impact of novel COVID-19 treatments will be investigated in a follow-up study. Coll et al\textsuperscript{48} observed a higher risk of death during the first wave compared with the second wave among SOTr, but not among those hospitalized. Data on the KPSC population suggest that the epsilon (B.1.427 and B.1.429) and alpha (B.1.1.7) strains were the predominant strains at the end of our study period.\textsuperscript{19}

A major strength of our study is that relevant demographic and clinical data for all SOTr and non-SOT patients within the integrated KPSC healthcare system who tested positive for SARS-CoV-2 were captured in both inpatient and outpatient settings. Care provided to all COVID-19 patients, including SOTr, was standardized without disparity of access to healthcare, which may have mitigated the variability of clinical outcomes related to therapeutic interventions.\textsuperscript{50} The comparison between the general non-SOT and SOT population in this cohort was within the same community with similar racial/ethnic distribution that eliminates variance that may be observed in other studies with patients from diverse geographical areas and ethnic distribution.

The limitations of this study include the inherent issues of a retrospective design.\textsuperscript{51} Vaccination status was not included in this study but will be a focus of investigation in future studies. Because vaccination only became available toward the end of the study period, few patients in this cohort were likely vaccinated. Behavioral data that may be associated with COVID-19 infection were not included in this study.

We observed higher rates of COVID-19 and attributable mortality in the SOTr compared with the non-SOT population. Hispanics/Latinos were disproportionately affected with COVID-19; however, mortality related to COVID-19 was not impacted by race/ethnicity. Infected SOTr were more likely to be hospitalized, require ICU level of care, and have higher COVID-19–related mortality. Incidence and outcomes of COVID-19 were distinct among the different transplant types.

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