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An initial report from the French SOT COVID Registry suggests high mortality due to COVID-19 in recipients of kidney transplants

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Notwithstanding the ongoing coronavirus disease-2019 (Covid-19) pandemic, information on its clinical presentation and prognosis in recipients of a kidney transplant remain scanty. The aim of this registry-based observational study was to explore characteristics and clinical outcomes of recipients of kidney transplants included in the French nationwide Registry of Solid Organ Transplant Recipients with Covid-19. Covid-19 was diagnosed in symptomatic patients who had a positive PCR assay for SARS-CoV-2 or having typical lung lesions on imaging. Clinical and laboratory characteristics, management of immunosuppression, treatment for Covid-19, and clinical outcomes (hospitalization, admission to intensive care unit, mechanical ventilation, or death) were recorded. Risk factors for severe disease or death were determined. Of the 279 patients, 243 were admitted to hospital and 36 were managed at home. The median age of hospitalized patients was 61.6 years; most had comorbidities (hypertension, 90.1%; overweight, 63.8%; diabetes, 41.3%; cardiovascular disease, 36.2%). Fever, cough, dyspnea, and diarrhea were

Editor’s Note
This is one of several articles we think you will find of interest that are part of our special issue of Kidney International addressing the challenges of dialysis and transplantation during the COVID-19 pandemic. Please also find additional material in our commentaries and letters to the editor sections. We hope these insights will help you in the daily care of your own patients.
the most common symptoms on admission. Laboratory findings revealed mild inflammation frequently accompanied by lymphopenia. Immunosuppressive drugs were generally withdrawn (calcineurin inhibitors: 28.7%; antimetabolites: 70.8%). Treatment was mainly based on hydroxychloroquine (24.7%), antiviral drugs (7.8%), and tocilizumab (5.3%). Severe Covid-19 occurred in 106 patients (46%). Forty-three hospitalized patients died (30-day mortality 22.8%). Multivariable analysis identified overweight, fever, and dyspnea as independent risk factors for severe disease, whereas age over 60 years, cardiovascular disease, and dyspnea were independently associated with mortality. Thus, Covid-19 in recipients of kidney transplants portends a high mortality rate. Proper management of immunosuppression and tailored treatment of this population remain challenging.

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Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has created an ongoing global pandemic of major concern. Frail patients with comorbidities are at high risk of developing severe disease, as shown by initial reports from China and other countries. Although preexisting kidney disease is a predisposing factor for COVID-19 morbidity and mortality, information on its clinical presentation and prognosis in kidney transplant (KT) recipients under immunosuppressive therapy remains scant. Published data are limited to case reports and small single-center case series.

On March 1, 2020, a French nationwide registry of patients with COVID-19 and a history of solid organ transplantation was established under the auspices of the French-Speaking Society of Transplantation. As of April 21, 2020, a total of 598 patients were included in the registry—of whom 426 were KT recipients, 61 heart transplant recipients, 72 liver transplant recipients, and 39 lung transplant recipients. Here, we describe the disease presentation, immunosuppression management, clinical outcomes, and independent prognostic variables in a large sample of 279 KT recipients with COVID-19.

RESULTS
Patient characteristics
Of the 279 KT recipients included in the registry, COVID-19 was diagnosed by reverse transcriptase–polymerase chain reaction in 93% of cases. The diagnosis in the remaining 7% of the study participants was based on clinical presentation and pulmonary computed tomography findings (7%). A total of 243 patients were admitted to the hospital, and 36 were managed at home following assessment by a transplant physician (Table 1). In brief, the latter group consisted of younger patients with a lower frequency of dyspnea, fever, and gastrointestinal manifestations. One patient received home treatment with hydroxychloroquine. Antimetabolites and mammalian target of rapamycin (mTOR) inhibitors were stopped in 13 patients (36%). The general characteristics of hospitalized patients are summarized in Table 1. The median age was 61.6 years (interquartile range: 50.8–69.0 years; range: 19–93 years), and two-thirds were men. Most of them were overweight (63.8%), and the most common comorbidities were hypertension (90.1%), cardiovascular disease (36.2%), diabetes (41.3%), and a history of respiratory disease (14.8%). SARS-CoV-2 infection was identified after a median of 74.1 months (interquartile range: 27.6–138.7 months; range: 1–1943 months) from KT. The median delay between the onset of symptoms and hospital admission was 5 days (interquartile range: 3–8 days; range: 0–34 days). The most frequent symptom on admission was fever (80%), followed by cough (63.6%), diarrhea (43.5%), dyspnea (40.3%), and anosmia (14.1%). Median levels of C-reactive protein and procalcitonin were 62 mg/L and 0.20 ng/mL, respectively (Table 2). The median lymphocyte count was 0.66 × 10^9/L, whereas thrombocytopenia was identified in 54 (29%) patients. Lung infiltrates on chest computed tomography images were detected in 87% of cases.

Management of immunosuppression
On admission, calcineurin inhibitors (CNIs), antimetabolites, and steroids were being taken by 83.1%, 79.8%, and 72.8% of patients, respectively. Of note, 29 (12%) and 15 (6.2%) patients were on mammalian target of rapamycin inhibitors and belatacept, respectively. During hospitalization (Table 2), antimetabolites, CNIs, and mammalian target of rapamycin inhibitors were withdrawn in 70.8% (136 of 192), 28.7% (58 of 202), and 62.1% (18 of 29) of patients, respectively. Moreover, belatacept administration was postponed in 7 of the 15 participants taking this drug. Of note, changes in immunosuppressive drugs other than those withdrawn were not recorded.

Treatment and clinical course
Most patients received nasal oxygen therapy (72.4%) and antibiotics other than azithromycin (63%). Hydroxychloroquine and azithromycin were given to 60 (24.7%) and 71 (29.2%) patients, respectively (Table 2). CNIs were stopped in 7 of the 11 patients treated with lopinavir/ritonavir. Tocilizumab was administered to 13 (5.3%) cases. Bacterial coinfections were identified in 57 (23.5%) participants. Mechanical ventilation was required for approximately 30% of cases. Acute kidney injury occurred in 43.6% of patients, with renal replacement therapy being necessary in 11.1% of cases. A total of 88 patients (36%) required intensive
care unit (ICU) care either on admission (n = 25) or during hospitalization (n = 63). In the latter subgroup, the median interval between hospitalization and transfer to the ICU was 4 days (range: 1–25 days). The 30-day mortality rate of hospitalized patients was 22.8% (Figure 1). Nine patients lost their graft during hospitalization, 4 of whom died. The composite endpoint of severe COVID-19 within 30 days of hospital admission was reached by 46% of the study patients (Figure 2a).

**Risk factors for severe COVID-19**

Table 3 compares the general characteristics of hospitalized patients who developed severe COVID-19 (n = 109) versus those who did not (n = 137). Patients aged >60 years who were overweight or had diabetes were significantly over-represented in the former group. Fever and dyspnea on admission—but not cough—were associated with severe disease. However, the time elapsed between symptom onset and hospitalization was similar in the 2 groups (5 days). C-reactive protein levels >60 mg/L, procalcitonin concentrations >0.2 g/L, and a partial pressure of oxygen <95% on admission were significantly associated with severe COVID-19. No similar associations were observed with lymphocyte count, platelet count, or creatinine levels. Treatment modalities and management of immunosuppression (Table 4) were slightly different in the 2 study groups in relation to disease
presentation and the clinical evolution over time. These differences were especially evident with respect to CNI withdrawal (52% and 11% in patients with severe and nonsevere disease, respectively, \( P < 0.001 \)). Kaplan–Meier plots of severe COVID-19–free survival according to different risk factors are provided in Figure 2b–i. Multivariable analysis identified overweight, fever, and dyspnea as independent risk factors for severe disease (Figure 3a).

### Risk factors for mortality

Table 5 compares the general characteristics of hospitalized patients who died (n = 43) versus those who did not (n = 200). Patients aged >60 years, who had cardiovascular disease, were receiving immunosuppressive drugs different from CNIs, and who presented with dyspnea or a partial pressure of oxygen <95% on admission, were significantly over-represented in the former group. Multivariable analysis identified age >60 years, cardiovascular disease, and dyspnea as independent risk factors for death in hospitalized patients (Figure 3b).

Subgroup analyses conducted in patients who tested negative on reverse transcriptase-polymerase chain reaction (7%) yielded similar results both in terms of severe disease and mortality (data not shown). The median follow-up time was 22 days; a total of 66 patients were still in the ICU at the time the manuscript was written.

### DISCUSSION

Despite the growing literature focusing on the clinical manifestations and prognosis of COVID-19, data on certain selected clinical populations that merit special consideration—including immunocompromised patients with a history of solid organ transplantation—remain scant. To address this knowledge gap, herein we report the general characteristics and the main risk factors for adverse outcomes—including severe disease and mortality—of a large nationwide French cohort consisting of 279 KT recipients with COVID-19.

First, we demonstrate that the clinical presentation of COVID-19 in KT recipients is similar to that reported in the general population—with fever and cough being the 2 more common symptoms. These findings are in line with those from initial large reports showing fever in 77%–94% and cough in 68%–79% of cases, respectively.\(^1\) However, the occurrence of gastrointestinal symptoms (mainly diarrhea) was as high as 42% in our patients (i.e., significantly more frequent than that previously reported in general population studies conducted in both China [3%–5%]\(^2\)^ and the United States [24%]).\(^3\) Patients with a history of solid organ transplantation are at high risk of gastrointestinal disorders—which may be exacerbated by immunosuppressive drugs. Importantly, anosmia was present in 14% of our patients, and in accordance with previous findings obtained in the general population,\(^22\) tended to be associated with more favorable survival figures. We also demonstrate that some immunocompromised patients with COVID-19 were manageable at home with a favorable outcome, as described in an Italian cohort from Brescia.\(^23\) This decision was made on a case basis and was chiefly implemented for young patients without

### Table 2 | Laboratory data, management of immunosuppression, treatment modalities, and outcomes of kidney transplant recipients hospitalized with COVID-19

| Variable                              | Value       | n   |
|----------------------------------------|-------------|-----|
| Laboratory data                        |             |     |
| CRP, mg/l                              | 62 [27–114] | 186 |
| Procalcitonin, ng/ml                   | 0.20 [0.14–0.48] | 90  |
| Lymphocyte count, \( \times 10^9/\text{l} \) | 0.66 [0.40–0.96] | 184 |
| Platelet count, \( \times 10^9/\text{l} \) | 178 [145–238] | 188 |
| Thrombocytopenia \(<150 \times 10^9/\text{l} \) | 54 [29]    | 188 |
| SaO_2                                  | 96 [91–98]  | 176 |
| Creatinine, µmol/l                     | 176 [131–244] | 200 |
| Immunosuppression management           |             |     |
| CNI withdrawal                         | 58 (28.7)   | 202 |
| Antimetabolite withdrawal              | 136 (70.8)  | 192 |
| mTOR inhibitor withdrawal              | 18 (62.1)   | 29  |
| Belatacept withdrawal                  | 7 (46.7)    | 15  |
| COVID-19 treatment modalities          |             |     |
| Azithromycin                           | 71 (29.2)   | 243 |
| Other antibiotics                      | 153 (63.0)  | 243 |
| Antifungal drugs                       | 6 (2.5)     | 243 |
| Remdesivir                             | 2 (0.8)     | 243 |
| Lopinavir/ritonavir                    | 11 (4.5)    | 243 |
| Oseltamivir                            | 6 (2.5)     | 243 |
| Hydroxychloroquine                     | 60 (24.7)   | 243 |
| Tocilizumab                            | 13 (5.3)    | 243 |
| Outcome                                |             |     |
| Bacterial coinfection                  | 57 (23.5)   | 243 |
| Viral coinfection                      | 5 (2.1)     | 243 |
| Fungal coinfection                     | 6 (2.5)     | 243 |
| Oxygen therapy                         | 152 (72.4)  | 210 |
| Mechanical ventilation                 | 72 (29.6)   | 243 |
| Vasopressor support                    | 27 (11.1)   | 243 |
| Acute kidney injury                    | 106 (43.6)  | 243 |
| Renal replacement therapy              | 27 (11.1)   | 243 |

CNIs, calcineurin inhibitors; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; mTOR, mammalian target of rapamycin; SaO_2, arterial oxygen saturation. Data are expressed as median [interquartile range] or count (%), as appropriate, unless otherwise indicated. Laboratory tests were performed on admission.
dyspnea and high fever. This patient subgroup was offered daily teleconsultation surveillance until disease resolution, a strategy that has been successfully implemented in a recent report from the United States.\textsuperscript{21} The laboratory findings of our patients on admission are also in line with previous studies. In general, there was evidence of mild inflammation—with lymphopenia being present in most patients, and thrombocytopenia in approximately one third. Notably, high procalcitonin levels were identified in 16\% of our study participants—a markedly lower prevalence compared with that previously reported in KT recipients (42\%).\textsuperscript{13}

The initially reported mortality rate for COVID-19 in the general population of Wuhan, China, was 1.4\%.\textsuperscript{1} Higher mortality figures have been published for hospitalized patients in New York (10\%),\textsuperscript{1} and for Italian patients admitted to the ICU (26\%).\textsuperscript{1} Previous data obtained in small-sized series of transplanted patients indicated a death rate similar to that observed in our cohort.\textsuperscript{24} Here, the 30-day mortality rate of our hospitalized KT recipients with COVID-19 was 22.8\%, a value similar to that reported for Italian patients admitted to the ICU.\textsuperscript{1} The high mortality rate observed in these patients may reflect the frailty of KT recipients and/or a high burden of comorbidities. Mechanical ventilation and ICU transfer were required in 36\% of our patients—a slightly higher percentage than that reported for immunocompetent subjects (16\%—33\%).\textsuperscript{1,3}

Male sex has been previously linked to severe COVID-19.\textsuperscript{25} However, no significant association between male sex and severe disease or mortality was observed in our cohort—possibly because of the high burden of comorbidities. Conversely, overweight, fever, and dyspnea were independent risk factors for severe disease in our cohort. The association between overweight/obesity and severe COVID-19—which has been shown here for the first time in transplant recipients—is in accordance with previous data obtained in the general population.\textsuperscript{1} In our study, age, cardiovascular disease, and dyspnea were independent risk factors for mortality. Age\textsuperscript{2,25} and comorbidities have been reported to have an

Figure 2 | Probability of reaching the composite endpoint of severe disease. (a) The 30-day severe disease–free survival in the entire study cohort was 54.2\% (48\%—61.4\%). Kaplan–Meier plots stratified according to (b) age (<60 years vs. >60 years), (c) diabetes (yes vs. no), (d) body mass index (BMI; <25 kg/m\textsuperscript{2} vs. >25 kg/m\textsuperscript{2}), (e) fever on admission (yes vs. no), (f) dyspnea on admission (yes vs. no), (g) arterial oxygen saturation (SaO\textsubscript{2}) on admission (>95\% vs. <95\%), (h) C-reactive protein (CRP) level on admission (<60 mg/l vs. >60 mg/l), and (i) procalcitonin level on admission (<0.2 ng/ml vs. >0.2 ng/ml). PCT, procalcitonin.
adverse prognostic significance in previous general population studies. The lack of prognostic significance of hypertension in our sample may be explained by its high prevalence (90%). In accordance with previous studies, severe inflammation on admission was found to have an adverse prognostic significance. Procalcitonin and C-reactive protein levels were higher in patients in the United States requiring mechanical ventilation, whereas procalcitonin levels were an unfavorable predictor of mortality in Chinese patients. However, in contrast to previous studies, lymphopenia did not predict severe COVID-19 or mortality in our sample. A potential explanation may lie in the fact that lymphopenia occurs commonly in KT patients and thus might not be invariably linked to SARS-CoV-2 infection. The debate on the management of immunosuppression in transplant recipients following SARS-CoV-2 infection remains unresolved. Published case reports and small-size series of KT recipients diagnosed with COVID-19 have consistently documented a reduction in maintenance immunosuppression, and this approach is currently being recommended by guidelines. However, precise guidance on the management of CNIs, antimetabolites, and steroids is still

Table 3 | Baseline characteristics of kidney transplant recipients with severe versus nonsevere COVID-19

| Characteristics                      | Nonsevere (n = 137) | Severe (n = 106) | HR [95% CI] | P     | n |
|--------------------------------------|---------------------|------------------|-------------|-------|---|
| **Baseline**                         |                     |                  |             |       |   |
| Age, yr                              | 59.5 [48.7–67.8]    | 63.5 [54.7–69.6] | 1.02 [1.00–1.04] | 0.013 | 243 |
| Age >60 yr                           | 67 (48.9)           | 67 (63.2)        | 1.63 [1.10–2.43] | 0.015 | 243 |
| Male                                 | 90 (65.7)           | 72 (67.9)        | 1.07 [0.71–1.61] | 0.740 | 243 |
| BMI > 25 kg/m²                       | 78 (57.8)           | 72 (72.0)        | 1.80 [1.16–2.79] | 0.008 | 235 |
| **Blood group**                      |                     |                  |             |       |   |
| A                                    | 65 (48.5)           | 40 (38.1)        | Ref         | Ref   |     |
| AB                                   | 6 (4.48)            | 6 (5.71)         | 1.52 [0.64–3.59] | 0.340 |     |
| B                                    | 16 (11.9)           | 13 (12.4)        | 1.27 [0.68–2.38] | 0.449 |     |
| O                                    | 47 (35.1)           | 46 (43.8)        | 1.32 [0.86–2.02] | 0.198 |     |
| **Transplanted organ**               |                     |                  |             |       |   |
| Kidney                               | 129 (94.2)          | 104 (98.1)       | Ref         | Ref   |     |
| Kidney–heart                         | 2 (1.46)            | 2 (1.89)         | 1.36 [0.34–5.51] | 0.668 |     |
| Kidney–liver                         | 2 (1.46)            | 0 (0.00)         | 0.00 [-]     | 0.997 |     |
| Kidney–pancreas                      | 4 (2.92)            | 0 (0.00)         | 0.00 [-]     | 0.996 |     |
| **Time from Tx to COVID-19, mo**     | 73.4 [30.9–151.1]   | 77.8 [25.4–131.1] | 1.00 [1.00–1.00] | 0.660 | 243 |
| Tx within 1 yr                       | 19 (13.9)           | 16 (15.1)        | 0.97 [0.57–1.65] | 0.912 | 243 |
| Hypertension                         | 112 (89.6)          | 89 (90.8)        | 1.14 [0.57–2.25] | 0.717 | 223 |
| RAS blockers                         | 58 (47.2)           | 39 (41.1)        | 0.83 [0.55–1.29] | 0.377 | 218 |
| Cardiovascular disease               | 41 (32.5)           | 40 (40.8)        | 1.32 [0.88–1.98] | 0.176 | 224 |
| Respiratory disease                  | 19 (15.2)           | 14 (14.3)        | 0.96 [0.54–1.69] | 0.865 | 223 |
| Diabetes                             | 42 (33.6)           | 50 (51.0)        | 1.73 [1.16–2.57] | 0.007 | 223 |
| Cancer                               | 17 (13.4)           | 18 (18.2)        | 1.33 [0.80–2.21] | 0.276 | 226 |
| Smoking                              | 16 (14.8)           | 14 (16.3)        | 0.99 [0.56–1.76] | 0.977 | 194 |
| CNIs                                 | 115 (83.9)          | 87 (82.1)        | 0.96 [0.58–1.58] | 0.868 | 243 |
| Mycophenolate acid                   | 102 (74.5)          | 81 (76.4)        | 1.08 [0.69–1.69] | 0.743 | 243 |
| Azathioprine                         | 5 (3.65)            | 6 (5.66)         | 1.32 [0.58–3.01] | 0.509 | 243 |
| mTOR inhibitors                      | 15 (10.9)           | 14 (13.2)        | 1.08 [0.62–1.90] | 0.785 | 243 |
| Steroids                             | 96 (70.1)           | 81 (76.4)        | 1.24 [0.79–1.94] | 0.347 | 243 |
| Belatacept                           | 8 (5.84)            | 7 (6.60)         | 1.08 [0.50–2.33] | 0.844 | 243 |
| **On admission**                     |                     |                  |             |       |   |
| Cough                                | 81 (62.3)           | 64 (65.3)        | 1.20 [0.79–1.82] | 0.390 | 228 |
| Rhinitis                             | 12 (9.76)           | 8 (8.70)         | 0.82 [0.40–1.69] | 0.592 | 215 |
| Dyspnea                              | 42 (30.7)           | 56 (52.8)        | 2.28 [1.55–3.34] | >0.001 | 243 |
| Anosmia                              | 19 (16.1)           | 10 (11.4)        | 0.71 [0.37–1.38] | 0.315 | 206 |
| Fever                                | 98 (75.4)           | 82 (86.3)        | 1.77 [0.99–3.19] | 0.055 | 225 |
| Headache                             | 25 (19.5)           | 14 (14.7)        | 0.75 [0.43–1.32] | 0.322 | 223 |
| Diarrhea                             | 59 (46.1)           | 38 (40.0)        | 0.86 [0.57–1.30] | 0.486 | 223 |
| Time from symptom onset to admission, d| 5.00 [3.00–9.00]   | 5.00 [3.00–7.00] | 1.00 [0.96–1.04] | 0.873 | 219 |
| C-reactive protein >60 mg/l          | 51 (46.4)           | 49 (64.5)        | 2.07 [1.29–3.31] | 0.003 | 186 |
| Procalcitonin > 0.2 ng/ml            | 21 (37.5)           | 23 (67.6)        | 3.19 [1.55–6.57] | 0.002 | 90  |
| Lymphocyte count, ×10³/l             | 0.70 [0.40–0.95]    | 0.60 [0.40–0.96] | 1.10 [0.74–1.64] | 0.627 | 184 |
| Platelet count, ×10⁹/l               | 176 [146–229]       | 178 [145–247]    | 1.00 [1.00–1.00] | 0.742 | 188 |
| Thrombocytopenia < 150 × 10⁹/l       | 31 (28.7)           | 23 (28.7)        | 0.98 [0.60–1.58] | 0.923 | 188 |
| SăO₂ < 95%                           | 26 (26.8)           | 40 (50.6)        | 2.47 [1.59–3.84] | <0.001 | 176 |
| Creatinine, μmol/l                   | 173 [126–230]       | 182 [132–251]    | 1.00 [1.00–1.00] | 0.378 | 200 |

BMI, body mass index; CNI, calcineurin inhibitor; COVID-19, coronavirus disease 2019; HR, hazard ratio; mTOR, mammalian target of rapamycin; RAS, renin–angiotensin system; Ref, reference; Tx, transplantation.

Data are expressed as median [interquartile range] or count (%), as appropriate, unless otherwise indicated.
lacking. In our registry, CNIs and antimetabolites were withdrawn in 28.7% and 70.8% of the study patients, respectively. Similar figures have been reported in United States case series. These management strategies have been chiefly informed by alterations in T-cell responses induced by SARS-CoV-2. Although CNIs may exert an inhibitory effect against the replication of coronaviruses in vitro, whether or not this effect can have clinical implications is arguable. In our study, patients who were free from CNIs on admission had a lower risk of mortality in univariable but not multivariable analysis (probably because of their older age; data not shown). No firm conclusions can therefore be drawn on the potential beneficial or detrimental effects of CNIs in KT recipients with COVID-19.

A minority of our patients received specific antiviral drugs. The lopinavir/ritonavir combination has strong pharmacological interactions with CNIs and mammalian target of rapamycin inhibitors, which have been related to the onset of acute renal failure in solid organ transplant recipients. Only 25% of our patients received hydroxychloroquine. The lower usage of this drug compared with the usage level in other cohorts may be explained by low-quality evidence on its effectiveness and the potential risk of severe adverse events in KT recipients. The potential benefits of interleukin-6 inhibition merit comment. A hyperinflammatory state characterized by the release of massive amounts of cytokines (cytokine storm) has been reported in patients with severe or catastrophic forms of COVID-19. Because interleukin-6 plays a central role in the cytokine storm, interleukin-6–targeting therapies have been proposed to tackle its occurrence. Trials of tocilizumab have been already attempted in nontransplanted and transplanted patients, and this drug was given to 13 patients included in our registry. Of them, 11 had favorable outcomes despite severe COVID-19. Although no firm conclusions can be drawn because of the retrospective, nonrandomized nature of our study, our results are in line with those by Alberici et al. who demonstrated a 50% reduction in the oxygen therapy requirement and a significant improvement in imaging features of pulmonary lesions upon tocilizumab administration.

Our findings need to be interpreted in the context of several limitations. First, we acknowledge that some baseline clinical, laboratory, and imaging data were missing. Similarly, information on the exact management of immunosuppression (i.e., dose reduction) and changes in laboratory parameters over time is lacking. Second, we

| Therapy | Nonsevere | Severe | P | n |
|---------|-----------|--------|---|---|
| Azithromycin | 38 (27.7) | 33 (31.1) | 0.790 | 243 |
| Other antibiotics | 81 (59.1) | 72 (67.9) | 0.190 | 243 |
| Antifungal drugs | 1 (0.7) | 5 (4.7) | 0.060 | 243 |
| Remdesivir | 0 (0.0) | 2 (1.9) | 0.035 | 243 |
| Lopinavir/ritonavir | 2 (1.5) | 9 (8.5) | 0.002 | 243 |
| Oseltamivir | 3 (2.2) | 3 (2.8) | 0.708 | 243 |
| Hydroxychloroquine | 28 (20.4) | 32 (30.2) | 0.168 | 243 |
| Tocilizumab | 4 (2.9) | 9 (8.5) | 0.077 | 243 |

Immunosuppression management

| CNI withdrawal | 13 (11.3) | 45 (51.7) | <0.001 | 202 |
| Antimetabolite withdrawal | 73 (68.2) | 63 (74.1) | 0.376 | 192 |
| mTOR inhibitor withdrawal | 8 (53.3) | 10 (71.4) | 0.187 | 29 |
| Belatacept withdrawal | 4 (50.0) | 3 (42.9) | 0.549 | 15 |

COVID-19, coronavirus disease 2019; CNI, calcineurin inhibitor; mTOR, mammalian target of rapamycin.

Values are n (%), unless otherwise indicated.
are aware that the follow-up time is limited, and 88 patients were still being hospitalized at the time of analysis. We cannot exclude the possibility that some of these cases will ultimately develop severe disease and eventually die. We also acknowledge that some patients with severe disease did not qualify for admission to the intensive care unit. Third, we are aware that representativeness can affect the generalizability of our registry data and that our findings need external validation. However, efforts to address potential sources of bias in our registry included the prospective data collection and the controlling for potential confounders in multivariable analysis. Notwithstanding the potential caveats, this study is by far the largest so far to provide a comprehensive description of KT recipients with COVID-19.

### Conclusion

COVID-19 in KT recipients portends a high risk of mortality. Proper management of immunosuppression and tailored treatment of this fragile population remain challenging. Overweight, fever, and dyspnea were independent risk factors for severe COVID-19 in this patient group, whereas age >60 years, cardiovascular disease, and dyspnea were independently associated with mortality.
PATIENTS AND METHODS

Patients
Data from all French patients with COVID-19 and a history of KT included in a nationwide registry—termed French Solid Organ Transplant (SOT) COVID—between March 4 and April 21, 2020, were retrieved. Inclusion criteria were age ≥18 years at the diagnosis of COVID-19 and presence of a functioning kidney graft. Patients who received double solid organ transplantation (kidney with pancreas, liver, or heart transplantation) were deemed eligible. The diagnostic criteria for COVID-19 were as follows: (i) evidence of SARS-CoV-2 infection on reverse transcriptase–polymerase chain reaction testing performed on nasopharyngeal swab specimens; or (ii) presence of typical respiratory symptoms accompanied by evocative pulmonary lesions on low-dose chest computed tomography even when reverse transcriptase–polymerase chain reaction yielded negative results. Clinical and laboratory variables were extracted from medical records. In case of hospitalization, data on presentation and other clinical and biological variables (including ongoing immunosuppressive therapy) were collected on admission. Changes in immunosuppression during the course of hospitalization were thoroughly recorded. Patients were divided into 2 groups according to their need for hospitalization (admitted to hospital vs. managed at home). Severe COVID-19 was defined as admission (or transfer) to an intensive care unit (ICU), need for mechanical ventilation, or death. All other patients were considered nonsevere cases. Acute kidney injury was defined according to the Kidney Disease Improving Global Outcomes guidelines as an increase in serum creatinine of >50%. The creation of the French SOT COVID Registry was approved by the Institutional Review Board of Strasbourg University (approval number 02.26) and registered at clinicaltrials.gov (NCT04360707). The need for informed consent was waived. However, all patients were informed about their inclusion in the registry.

Statistical analysis
Categorical data are presented as counts and percentages. Continuous variables are expressed as medians and interquartile ranges upon verification of their skewed distribution with the Shapiro-Wilk test. Two time-dependent variables served as the outcome measures. The first was a composite endpoint of severe COVID-19 (including admission/transfer to an ICU, need for mechanical ventilation, or death), whereas the second was a hard endpoint consisting of death, stroke, acute kidney failure, or unplanned hospitalization.

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