

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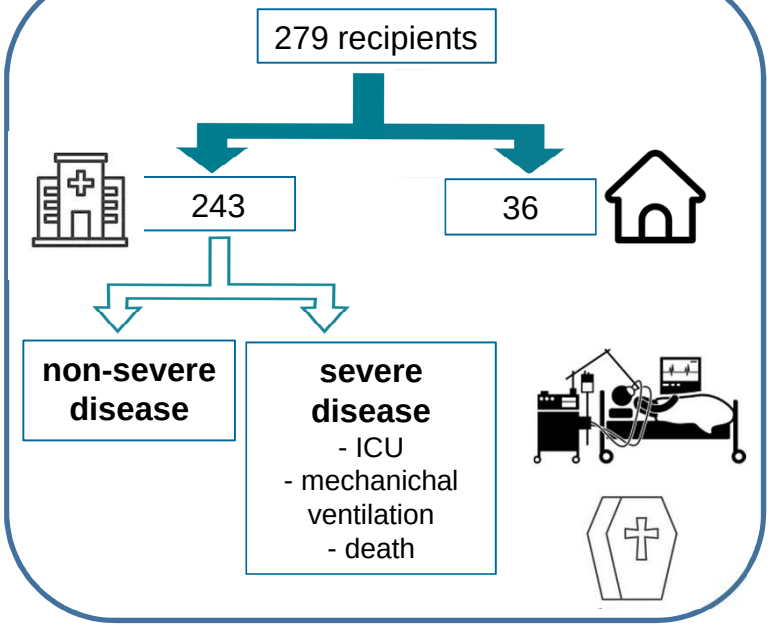
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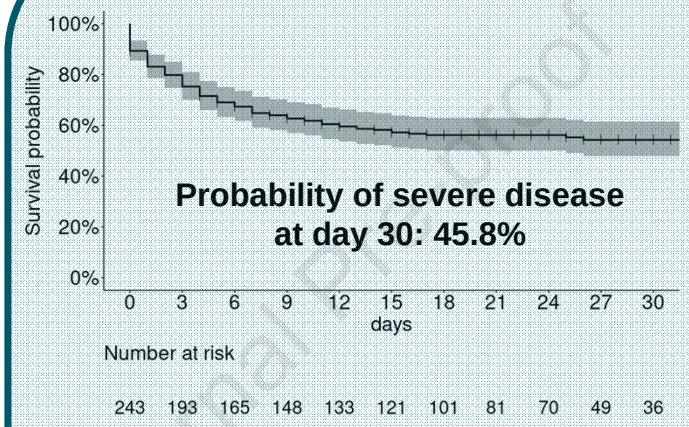
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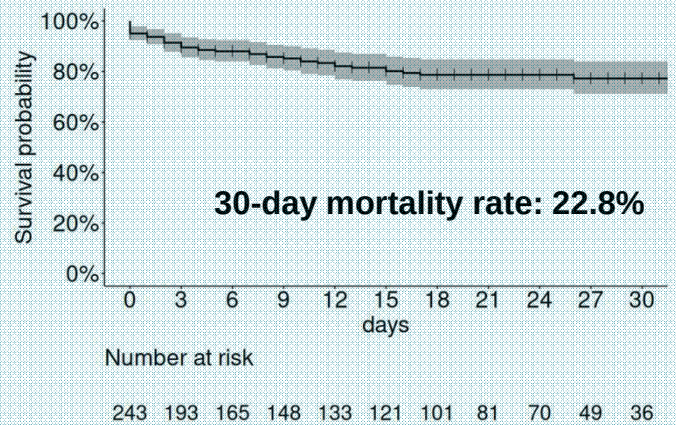
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An initial report from the French SOT COVID Registry suggests high mortality due to Covid-19 in recipients of kidney transplants.

A registry-based observational study to explore the characteristics and clinical outcomes of kidney transplant recipients included in the French nationwide Registry







Risk factors for severe disease

- BMI>25 kg/m²: 1.65 [1.05-2.60], p=0.03
- Fever: 2.01 [1.09-3.71], p=0.03
- Dyspnea: 2.23 [1.47-3.39], p<0.001

Risk factors for death

- Age>60 years: 3.81 [1.56-9.31], p=0.003
- Cardiovasc.Dis.: 2.04 [1.07-3.90], p=0.031
- Dyspnea: 2.35 [1.23-4.49], p<0.01

CONCLUSION:

Covid-19 in KT recipients portends a high mortality rate. Risk factors for severe disease are closed to those of the general population. Proper management of immunosuppression and tailored treatment of this population remain challenging.

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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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Abstract

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 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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Key words: Covid-19, kidney transplantation, immunosuppression, prognosis, mortality

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INTRODUCTION

Coronavirus disease-2019 (Covid-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is 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[1,2] and other countries.[3,4] Although preexistent kidney disease is a predisposing factor for Covid-19 morbidity and mortality,[5] information on its clinical presentation and prognosis in kidney transplant (KT) recipients under immunosuppressive therapy remains scanty. Published data are limited to case reports[6-9] and small single-center case series.[10-21] On March 1, 2020, a French nationwide registry of patients with Covid-19 and a history of solid organ transplantation has been 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 RT-PCR in 93% of cases. The diagnosis in the remaining 7% of the study participants was based on clinical presentation and pulmonary CT findings (7%). A total of 243 patients were admitted to 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

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hydroxychloroquine. Antimetabolites and mTOR inhibitors were stopped in 13 patients (36%). The general characteristics of hospitalized patients are summarized in the Table 1. The median age was 61.6 years (IQR: 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 (IQR: 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 (IQR: 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 (CRP) and procalcitonin were 62 mg/L and 0.20 ng/mL, respectively (Table 2). The median lymphocyte count was 0.66 $\times 10^9$/L, whereas thrombocytopenia was identified in 54 (29%) patients. Lung infiltrates on chest CT 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%) of patients were on mTOR inhibitors and belatacept, respectively. During hospitalization (Table 2), antimetabolites, CNIs, and mTOR inhibitors were withdrawn in 70.8% (136/192), 28.7% (58/202), and 62.1% (18/29) of patients, respectively. Moreover, belatacept administration was postponed in seven of the 15 participants taking this drug. Of note, changes in immunosuppressive drugs other than withdrawn were not recorded.

Treatment and clinical course

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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 seven 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. MV 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 ICU care either on admission (n = 25) or during hospitalization (n = 63). In the latter subgroup, the median interval between hospitalization and transfer to 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, of whom four of them died. The composite endpoint of severe Covid-19 within 30 days of hospital admission was reached by 46% of the study patients (Figure 2 panel A).

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 overrepresented 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 two groups (5 days). CRP 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 two study groups in relation to disease presentation and the clinical evolution

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over time. These differences were especially evident with respect to CNIs withdrawal (52% and 11% in patients with severe and non-severe disease, respectively, p<0.001).

Kaplan-Meier plots of severe Covid-19-free survival according to different risk factors are provided in Figure 2 (panels B-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 overrepresented 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 RT-PCR (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 ICU at the time when the manuscript was written.

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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 scanty. 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 two 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.[1-3] 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 both in China (3−5%)[1,2] and in the USA (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 favorable outcome as described in an Italian cohort from Brescia.[23] This decision was taken on a case-basis and was chiefly implemented for young patients without 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.[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

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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%).[13]

The initially reported mortality rate for Covid-19 in the general population of Wuhan, China, was 1.4%.[1] Higher mortality figures have been published for hospitalized patients in New York (10%)[3] and for Italian patients admitted to ICU (26%).[4] Previous data obtained in small-sized series of transplanted patients reported a death rate similar to that observed in our cohort.[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 ICU.[4] 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 those reported for immunocompetent subjects (16−33%).[2,3]

Male sex has been previously linked to severe Covid-19.[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.[3] In our study, age, cardiovascular disease, and dyspnea were independent risk factors for mortality. Age[2, 25] and comorbidities have been reported to have an 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,[2,3] severe inflammation on admission was found to have an adverse prognostic significance. Procalcitonin and CRP levels were higher in USA patients

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requiring MV,[3] whereas procalcitonin levels were an unfavorable predictor of mortality in Chinese patients.[2] However, differently from previous studies, [2,26] 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.[27] Published case reports and small-sizes series of KT recipients diagnosed with Covid-19 have consistently documented a reduction in maintenance immunosuppression[6-14] and this approach is currently being recommended by guidelines.[28] However, precise guidance on the management of CNIs, antimetabolites, and steroids is still 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 USA case series.[11,13] 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*,[29,30] 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 in 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 mTOR inhibitors, which have been related to the onset of acute renal failure in solid organ transplant recipients.[9,10,12] Only 25% of our patients received hydroxychloroquine. The lower usage of this drug compared with other cohorts[13,10] may be explained by low-quality evidence on its effectiveness[31,32] and potential risk of severe adverse events in KT recipients. The potential

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benefits of interleukin (IL)-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. [33] Because IL-6 plays a central role in the cytokine storm, IL-6 targeting therapies have been proposed to tackle its occurrence.[34,35] Trials of tocilizumab have been already attempted in non-transplanted[36] and transplanted patients,[10-13] 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, non-randomized nature of our study, our results are in line with those by Alberici *et al.*[10] who demonstrated a 50% reduction in 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 are aware that the follow-up time is limited and 88 patients were still being hospitalized at the time of analysis. We cannot exclude 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 intensive care. 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

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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 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: 1) evidence of SARS-CoV-2 infection on reverse transcriptase-polymerase chain reaction (RT-PCR) testing performed on nasopharyngeal swab specimens or 2) presence of typical respiratory symptoms accompanied by evocative pulmonary lesions on low-dose chest computed tomography (CT) even when RT-PCR 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 two groups according to their need for hospitalization (admitted to hospital *versus* managed at home). Severe COVID-19 was defined as admission (or transfer) to an intensive care unit (ICU), need for mechanical ventilation (MV) or death. All other patients

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were considered non-severe cases. Acute kidney injury (AKI) 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 the 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 (IQRs) 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 MV, or death), whereas the second was a hard endpoint consisting of death only. Survival curves were plotted with the Kaplan-Meier method and compared with the log-rank test. Cox proportional hazard univariable and multivariable models were constructed to identify predictors of the study endpoints. All variables showing an association with a $P<0.1$ in univariable analysis were included as covariates in the multivariable model using a backward conditional selection procedure. The optimal model was selected according to the highest concordance value. Results are expressed as hazard ratios (HRs) with their 95% confidence intervals. All analyses were conducted in the R environment (R Foundation for Statistical Computing, Vienna, Austria), and two-tailed P values <0.05 were considered statistically significant.

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Authors' contributions

Sophie Caillard and Marc Hazzan had full access to all the data of the cohort study and takes responsibility for the integrity of the data and the accuracy of the analyses

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***French SOT COVID Registry**

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References

1. Guan WJ, Ni ZY, Hu Y, et al. China medical treatment expert group for Covid-19: Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* doi:10.1056/ NEJMoa2002032
2. Zhou F, Yu T, Du R, et al.: Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: A retrospective cohort study. *Lancet*. 2020 Mar 28;**395**:1054-1062
3. Goyal P, Choi JJ, Pihneiro LC, et al. Clinical Characteristics of Covid-19 in New York City *N Engl J Med* 2020 Apr 17 doi: 10.1056/NEJMc2010419
4. Grasselli G, Zangrillo A, Zanella A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA* 2020 Apr 6. doi: 10.1001/jama.2020.5394
5. Arentz M, Yim E, Klaff L, et al. Characteristics and Outcomes of 21 Critically Ill Patients With COVID-19 in Washington State. *JAMA*. 2020 Mar 19. doi: 10.1001/jama.2020.4326
6. Guillen E, Pineiro GJ, Revuelta I, et al.: Case report of COVID-19 in a kidney transplant recipient: Does immunosuppression alter the clinical presentation? *Am J Transplant* doi:10.1111/ajt.158744
7. Zhu L, Xu X, Ma K, et al. Successful recovery of COVID-19 pneumonia in a renal transplant recipient with long-term immunosuppression. *Am J Transplant* doi:10.1111/ajt.15869

Journal Pre-proof

8. Zhong Z, Zhang Q, Xia H, et al. Clinical characteristics and immunosuppressants management of coronavirus disease 2019 in solid organ transplant recipients. *Am J Transplant* doi: 10.1111/ajt.15928

9. Gandolfini I, Delsante M, Fiaccadori E, et al. COVID-19 in Kidney Transplant Recipients. *Am J Transplant* doi:10.1111/ajt.15891

10. Alberici F, Delbarba E, Manenti C, et al.
A single center observational study of the clinical characteristics and short-term outcome of 20 kidney transplant patients admitted for SARS-CoV2 pneumonia Kidney Int. 2020 Apr 9. doi: 10.1016/j.kint.2020.04.002

11. The Columbia University Transplant Program. Early Description of Coronavirus 2019 Disease in Kidney Transplant Recipients in New York. *J Am Soc Nephrol* 2020;ASN.2020030375. doi:10.1681/ASN.2020030375

12. Fernandez Ruiz M, Andres A, Lopez-Medrano F, San Juan R. COVID-19 in solid organ transplant recipients: a single-center case series from Spain. *Am J Transplant* doi:10.1111/AJT.15929

13. Akalin E, Azzi Y, Bartash R, et al. Covid-19 and Kidney Transplantation. *N Engl J Med* DOI: 10.1056/NEJMc2011117

14. Pereira M, Mohan S, Ali Husain S, et al. Covid-19 in Solid Transplant Organ Recipients: initial report of the US epicenter. *Am J Transplant* doi: 10.1111/AJT.15941

15. Banerjee D, Popoola J, Shah S, Ster IC, Quan V, Phanish M. COVID-19 infection in kidney transplant recipients. *Kidney Int.* 2020 Jun;97(6):1076-1082.

16. Yi SG, Rogers AW, Saharia A, et al. Early Experience With COVID-19 and Solid Organ Transplantation at a US High-volume Transplant Center. *Transplantation*. 2020 Jun 1:10.1097/TP.0000000000003339. doi: 10.1097/TP.0000000000003339.

Journal Pre-proof

17. Nair V, Jandovitz N, Hirsch JS, et al. COVID-19 in kidney transplant recipients. *Am J Transplant.* 2020 Jul;20(7):1819-1825. doi: 10.1111/ajt.15967. Epub 2020 May 27.

18. Zhu L, Gong N, Liu B, et al. Coronavirus Disease 2019 Pneumonia in Immunosuppressed Renal Transplant Recipients: A Summary of 10 Confirmed Cases in Wuhan, China. *Eur Urol.* 2020 Jun;77(6):748-754. doi: 10.1016/j.eururo. 2020.03.039. Epub 2020 Apr 18.

19. Chen TY, Farghaly S, Cham S, et al. COVID-19 Pneumonia in Kidney Transplant Recipients: Focus on Immunosuppression Management. *Transpl Infect Dis.* 2020 Jun 23:e13378. doi: 10.1111/tid.13378

20. Hoek RAS, Manintveld OC, Betjes MGH, et al for the Rotterdam Transplant Group. COVID-19 in solid organ transplant recipients: a single-center experience. *Transpl Int.* 2020 May 27:10.1111/tri.13662

21. Husain SA, Dube G, Morris H, et al. Early Outcomes of Outpatient Management of Kidney Transplant Recipients with Coronavirus Disease 2019. *Clin J Am Soc Nephrol.* May 2020, CJN.05170420

22. Kim GU, Kim MJ, Ra SH, et al. Clinical characteristics of asymptomatic and symptomatic patients with mild COVID-19. *Clin Microbiol Infect.* 2020 Jul;26(7):948.e1-948.e3.

23. Bossini N, Alberici F, Delbarba E et al. Kidney transplant recipients with SARS Cov2 infection: the Brescia Renal Covid Task force experience. Am J Transplant 2020, DOI: 10.1111/ajt.16176

24. Maggiore U, Abramowicz D, Crespo M, et al. How should I manage immunosuppression in a kidney transplant patient with COVID-19? An ERA-EDTA DESCARTES expert opinion. *Nephrol Dial Transplant.* 2020 Jun 1;35(6):899-904.

Journal Pre-proof

25. Shi Y, Yu X, Zhao H, et al. Host susceptibility to severe COVID-19 and establishment of a host risk score: findings of 487 cases outside Wuhan. *Critical care*. doi.org/10.1186/s13054-020-2833

26. Chen Z, Hu J, Zhang Z, et al. Efficacy of hydroxychloroquine in patients with COVID-19: results of a randomized clinical trial. *MedRvix* doi.org/10.1101/2020.03.22.20040758.

27. Willicombe M, Thomas D, McAdoo S. COVID-19 and Calcineurin Inhibitors: Should They Get Left Out in the Storm? *J Am Soc Nephrol* 31: ccc–ccc, 2020. doi.org/10.1681/ASN.2020030348

28. French guidelines for COVID-19 management in solid organ transplant recipients. A collegial statement endorsed by the « Société Francophone de Transplantation » (SFT), the « Société Francophone de Néphrologie, Dialyse et Transplantation » (SFNDT) the « Groupe Infection et Immunodépression », and the « Société de pathologie infectieuse de langue française » (SPILF). https://www.transplantation-francophone.org/images/public/COVID19_et_transplantees_d_organes_solides_Guide_pratiquev1_SFT_SFNDT_SP.pdf

29. De Wilde AH, Zevenhoven-Dobbe JC, Van der Meer Y, et al. Cyclosporin A inhibits the replication of diverse coronaviruses. *J Gen Virol* 2011; **92**: 2542–2548

30. Carbajo-Lozoya J, Müller MA, Kallies S, et al: Replication of human coronaviruses SARS-CoV, HCoVNL63 and HCoV-229E is inhibited by the drug FK506. *Virus Res* 2012; **165**: 112–117

31. Cao B, Wang Y, Wen D, et al. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med.* 2020 Mar 18. doi: 10.1056/NEJMoa2001282

Journal Pre-proof

32. Tang W, Cao Z, Han M, et al. Hydroxychloroquine in patients with COVID-19: an open-label, randomized, controlled trial. *MedRvix* doi.org/10.1101/2020.04.10.20060558

33. Blanco-Melo D, Nilsson-Payant BE, Liu WC, et al. Imbalanced host response to SARS-CoV-2 drives development of COVID-19. *Cell* doi: 10.1016/j.cell.2020.04.026

34. Fu B, Xu X, Wei H. Why tocilizumab could be an effective treatment for severe COVID-19? *J Transl Med* 2020 Apr 14;18(1):164. doi: 10.1186/s12967-020-02339-3

35. Mehta P, McAuley DF, Brown M, et al. COVID-19: Consider cytokine storm syndromes and immunosuppression. *Lancet* 2020; **395**: 1033–1034

36. Di Giambenedetto S, Ciccullo A, Borghetti A, et al. Off-label Use of Tocilizumab in Patients with SARS-CoV-2 Infection. *J Med Virol.* 2020 Apr 16. doi: 10.1002/jmv.25897

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Table 1. Baseline characteristics of kidney transplant recipients with Covid-19 managed at home *versus* in-hospital

	Home (n = 36)	In-hospital (n = 243)	p	n
Baseline characteristics				
Median age [IQR], years	55.6 [48.0-61.1]	61.6 [50.8-69.0]	0.002	279
Men, n (%)	20 (55.6%)	162 (66.7%)	0.263	279
Median BMI [IQR], kg/m^2	25.0 [23.4-28.9]	26.1 [23.0-30.7]	0.608	270
BMI >25 kg/m^2, n (%)	18 (51.4%)	150 (63.8%)	0.221	270
Blood group, n (%)			0.691	275
A	18 (50.0%)	105 (43.9%)		
AB	1 (2.8%)	12 (5.0%)		
B	6 (16.7%)	29 (12.1%)		
O	11 (30.6%)	93 (38.9%)		
Transplanted organ, n (%)			0.525	279
Kidney	35 (97.2%)	233 (95.9%)		
Kidney-heart	0 (0.0%)	4 (1.6%)		
Kidney-liver	1 (2.8%)	2 (0.8%)		
Kidney-pancreas	0 (0.0%)	4 (1.6%)		
Time from Tx to Covid-19 [IQR], months	58.9 [25.0-118.9]	74.1 [27.6-	0.626	279
Time Tx to COVID stratified (mo) -			0.827	279
<6	3 (8.3%)	20 (8.2%)		
6-12	1 (2.8%)	15 (6.2%)		
12-60	14 (38.9%)	73 (30.0%)		
60-120	9 (25.0%)	60 (24.7%)		
>120	9 (25.0%)	75 (30.9%)		
Hypertension, n (%)	24 (82.8%)	201 (90.1%)	0.213	252
RAS blockers, n (%)	15 (55.6%)	97 (44.5%)	0.377	245
Cardiovascular disease, n (%)	6 (20.0%)	81 (36.2%)	0.122	254
Respiratory disease, n (%)	5 (16.7%)	33 (14.8%)	0.786	253
Diabetes, n (%)	12 (40.0%)	92 (41.3%)	1.000	253
Cancer, n (%)	4 (13.3%)	35 (15.5%)	1.000	256
Smoking, n (%)	3 (13.0%)	30 (15.5%)	1.000	217
Baseline immunosuppression				
CNIs, n (%)	28 (77.8%)	202 (83.1%)	0.581	279
Mycophenolate acid, n (%)	29 (80.6%)	183 (75.3%)	0.632	279
Azathioprine, n (%)	1 (2.8%)	11 (4.5%)	1.000	279
mTOR inhibitors, n (%)	5 (13.9%)	29 (11.9%)	0.784	279
Steroids, n (%)	25 (69.4%)	177 (72.8%)	0.822	279
Belatacept, n (%)	1 (2.8%)	15 (6.2%)	0.703	279
Clinical presentation				
Cough, n (%)	20 (55.6%)	145 (63.6%)	0.459	264
Rhinitis, n (%)	6 (16.7%)	20 (9.3%)	0.231	251
Dyspnea, n (%)	2 (5.6%)	98 (40.3%)	<0.00	279
Anosmia, n (%)	10 (29.4%)	29 (14.1%)	0.046	240
Fever, n (%)	15 (41.7%)	180 (80.0%)	<0.00	261
Headache, n (%)	11 (30.6%)	39 (17.5%)	0.106	259
Diarrhea, n (%)	9 (25.0%)	97 (43.5%)	0.056	259

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Abbreviations: IQR, interquartile range; BMI, body mass index; Ref, reference; Tx, transplantation; RAS, renin-angiotensin system; CNIs, calcineurin inhibitors; mTOR, mammalian target of rapamycin. Data are expressed as medians (IQRs) or counts (percentages), as appropriate.

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Table 2. Laboratory data, management of immunosuppression, treatment modalities, and outcomes of kidney transplant recipients hospitalized with Covid-19

Variable	*Value*	*n*
Laboratory data		
Median CRP [IQR], mg/L	62 [27-114]	186
Median procalcitonin [IQR], ng/mL	0.20 [0.14-0.48]	90
Median lymphocyte count [IQR], $\times 10^9$/L	0.66 [0.40-0.96]	184
Median platelet count [IQR], $\times 10^9$/L	178 [145-238]	188
Thrombocytopenia < 150 $\times 10^9$/L, n (%)	54 (29%)	188
Median SaO_2 [IQR], n (%)	96 [91-98]	176
Median creatinine [IQR], µmol/L	176 [131-244]	200
Immunusuppression management		
CNIs withdrawal, n (%)	58 (28.7%)	202
Antimetabolite withdrawal, n (%)	136 (70.8%)	192
mTOR inhibitors withdrawal, n (%)	18 (62.1%)	29
Belatacept withdrawal, n (%)	7 (46.7%)	15
~~**Covid-19**~~ **Treatment modalities**		
Azithromycin, n (%)	71 (29.2%)	243
Other antibiotics, n (%)	153 (63.0%)	243
Antifungal drugs, n (%)	6 (2.5%)	243
Remdesivir, n (%)	2 (0.8%)	243
Lopinavir/ritonavir, n (%)	11 (4.5%)	243
Oseltamivir, n (%)	6 (2.5%)	243
Hydroxychloroquine, n (%)	60 (24.7%)	243
Tocilizumab, n (%)	13 (5.3%)	243
Outcome		
Bacterial coinfection, n (%)	57 (23.5%)	243
Viral coinfection, n (%)	5 (2.1%)	243
Fungal coinfection, n (%)	6 (2.5%)	243
Oxygen therapy, n (%)	152 (72.4%)	210
Mechanical ventilation, n (%)	72 (29.6%)	243
Vasopressor support, n (%)	27 (11.1%)	243
Acute kidney injury, n (%)	106 (43.6%)	243
Renal replacement therapy, n (%)	27 (11.1%)	243

Abbreviations: IQR, interquartile range; CRP, C-reactive protein; SaO_2, arterial oxygen saturation; CNIs, calcineurin inhibitors; mTOR, mammalian target of rapamycin. Data are expressed as medians (IQRs) or counts (percentages), as appropriate. Laboratory tests were performed on admission.

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Table 3. Baseline characteristics of kidney transplant recipients with severe *versus* non-severe Covid-19

	Non-severe (n =137)	**Severe** (n = 106)	**HR [95%**	**p**	**n**
Baseline characteristics					
Median age [IQR], years	59.5 [48.7-67.8]	63.5 [54.7-69.6]	1.02 [1.00-1.04]	0.013	243
Age >60 years, n (%)	67 (48.9%)	67 (63.2%)	1.63 [1.10-2.43]	0.015	243
Men, n (%)	90 (65.7%)	72 (67.9%)	1.07 [0.71-1.61]	0.740	243
BMI > 25 kg/m^2, n (%)	78 (57.8%)	72 (72.0%)	1.80 [1.16-2.79]	0.008	235
Blood group, n (%)					239
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, n (%)					243
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 [IQR], months	73.4 [30.9-151]	77.8 [25.4-131]	1.00 [1.00-1.00]	0.660	243
Tx within 1 year, n (%)	19 (13.9%)	16 (15.1%)	0.97 [0.57-1.65]	0.912	243
Hypertension, n (%)	112 (89.6%)	89 (90.8%)	1.14 [0.57-2.25]	0.717	223
RAS blockers, n (%)	58 (47.2%)	39 (41.1%)	0.83 [0.55-1.25]	0.377	218
Cardiovascular disease, n (%)	41 (32.5%)	40 (40.8%)	1.32 [0.88-1.98]	0.176	224
Respiratory disease, n (%)	19 (15.2%)	14 (14.3%)	0.96 [0.54-1.69]	0.885	223
Diabetes, n (%)	42 (33.6%)	50 (51.0%)	1.73 [1.16-2.57]	0.007	223
Cancer, n (%)	17 (13.4%)	18 (18.2%)	1.33 [0.80-2.21]	0.276	226
Smoking, n (%)	16 (14.8%)	14 (16.3%)	0.99 [0.56-1.76]	0.977	194
CNIs, n (%)	115 (83.9%)	87 (82.1%)	0.96 [0.58-1.58]	0.868	243
Mycophenolate acid, n (%)	102 (74.5%)	81 (76.4%)	1.08 [0.69-1.69]	0.743	243
Azathioprine, n (%)	5 (3.65%)	6 (5.66%)	1.32 [0.58-3.01]	0.509	243
mTOR inhibitors, n (%)	15 (10.9%)	14 (13.2%)	1.08 [0.62-1.90]	0.785	243
Steroids, n (%)	96 (70.1%)	81 (76.4%)	1.24 [0.79-1.94]	0.347	243
Belatacept, n (%)	8 (5.84%)	7 (6.60%)	1.08 [0.50-2.33]	0.844	243
Characteristics on admission					
Cough, n (%)	81 (62.3%)	64 (65.3%)	1.20 [0.79-1.82]	0.390	228
Rhinitis, n (%)	12 (9.76%)	8 (8.70%)	0.82 [0.40-1.69]	0.592	215
Dyspnea, n (%)	42 (30.7%)	56 (52.8%)	2.28 [1.55-3.34]	<0.001	243
Anosmia, n (%)	19 (16.1%)	10 (11.4%)	0.71 [0.37-1.38]	0.315	206
Fever, n (%)	98 (75.4%)	82 (86.3%)	1.77 [0.99-3.19]	0.055	225
Headache, n (%)	25 (19.5%)	14 (14.7%)	0.75 [0.43-1.32]	0.322	223
Diarrhea, n (%)	59 (46.1%)	38 (40.0%)	0.86 [0.57-1.30]	0.486	223
Time from symptom onset to admission	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, n (%)	51 (46.4%)	49 (64.5%)	2.07 [1.29-3.31]	0.003	186
Procalcitonin > 0.2 ng/mL, n (%)	21 (37.5%)	23 (67.6%)	3.19 [1.55-6.57]	0.002	90
Median lymphocyte count [IQR], $\times 10^9$/L	0.70 [0.40-0.95]	0.60 [0.40-0.96]	1.10 [0.74-1.64]	0.627	184
Median platelet count [IQR], $\times 10^9$/L	178 [146-229]	178 [145-247]	1.00 [1.00-1.00]	0.742	188
Thrombocytopenia < 150 $\times 10^9$/L, n (%)	31 (28.7%)	23 (28.7%)	0.98 [0.60-1.58]	0.923	188
SaO_2 < 95%, n (%)	26 (26.8%)	40 (50.6%)	2.47 [1.59-3.84]	<0.001	176

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	Non-severe (n =137)	Severe (n = 106)	HR [95%	p	n
Median creatinine [IQR], µmol/L	173 [126-230]	182 [132-251]	1.00 [1.00-1.00]	0.378	200

Abbreviations: IQR, interquartile range; BMI, body mass index; Ref, reference; Tx, transplantation; RAS, renin-angiotensin system; CNIs, calcineurin inhibitors; mTOR, mammalian target of rapamycin. Data are expressed as medians (IQRs) or counts (percentages), as appropriate.

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Table 4. Treatment modalities and immunosuppression management in kidney transplant recipients hospitalized for COVID-19 according to the presence of severe *versus* non severe disease

	Non-severe ***N=137***	**Severe** ***N=106***	**p**	**n**
Covid-19 treatment				
Azithromycin – n (%)	38 (27.7%)	33 (31.1%)	0.790	243
Other antibiotics – n (%)	81 (59.1%)	72 (67.9%)	0.190	243
Antifungal drugs – n (%)	1 (0.7%)	5 (4.7%)	0.060	243
Remdesivir – n (%)	0 (0.0%)	2 (1.9%)	0.035	243
Lopinavir/Ritonavir – n (%)	2 (1.5%)	9 (8.5%)	0.002	243
Oseltamivir – n (%)	3 (2.2%)	3 (2.8%)	0.708	243
Hydoxychloroquine – n (%)	28 (20.4%)	32 (30.2%)	0.168	243
Tocilizumab – n (%)	4 (2.9%)	9 (8.5%)	0.077	243
Immunosuppression management				
CNI withdrawal – n (%)	13 (11.3%)	45 (51.7%)	<0.001	202
Antimetabolite withdrawal – n (%)	73 (68.2%)	63 (74.1%)	0.376	192
mTOR inhibitor withdrawal – n (%)	8 (53.3%)	10 (71.4%)	0.187	29
Belatacept withdrawal – n (%)	4 (50.0%)	3 (42.9%)	0.549	15

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Table 5. Baseline characteristics of kidney transplant recipients with Covid-19 who died *versus* those who did not

	Alive (n = 200)	Dead (n = 43)	HR [95% CI]	p	n
Baseline characteristics					
Median age [IQR], years	59.8 [49.8-67.5]	68.9 [61.7-75.1]	1.07 [1.04-1.10]	<0.001	243
Age >60 years, n (%)	99 (49.5%)	35 (81.4%)	3.98 [1.85-8.59]	<0.001	243
Men, n (%)	137 (68.5%)	25 (58.1%)	0.68 [0.37-1.25]	0.215	243
BMI > 25 kg/m^2, n (%)	122 (61.9%)	28 (73.7%)	1.65 [0.80-3.39]	0.177	235
Blood group, n (%)					239
A	89 (45.2%)	16 (38.1%)	Ref.	Ref.	
AB	11 (5.58%)	1 (2.38%)	0.58 [0.08-4.40]	0.601	
B	23 (11.7%)	6 (14.3%)	1.36 [0.53-3.48]	0.521	
O	74 (37.6%)	19 (45.2%)	1.42 [0.73-2.77]	0.299	
Transplanted organ, n (%)					243
Kidney	190 (95.0%)	43 (100%)	Ref.	Ref.	
Kidney-heart	4 (2.00%)	0 (0.00%)	0.00 [0.00]	0.997	
Kidney-liver	2 (1.00%)	0 (0.00%)	0.00 [0.00]	0.998	
Kidney-pancreas	4 (2.00%)	0 (0.00%)	0.00 [0.00]	0.997	
Time from Tx to Covid-19 [IQR],	72.5 [27.7-147]	83.7 [25.7-116]	1.00 [1.00-1.00]	0.933	243
Tx within 1 year, n (%)	29 (14.5%)	6 (14.0%)	0.95 [0.40-2.26]	0.914	243
Hypertension, n (%)	165 (89.7%)	36 (92.3%)	1.39 [0.43-4.53]	0.580	223
RAS blockers, n (%)	80 (44.4%)	17 (44.7%)	1.07 [0.56-2.03]	0.836	218
Cardiovascular disease, n (%)	59 (31.9%)	22 (56.4%)	2.74 [1.45-5.17]	0.002	224
Respiratory disease, n (%)	28 (15.2%)	5 (12.8%)	0.77 [0.30-1.96]	0.577	223
Diabetes, n (%)	69 (37.5%)	23 (59.0%)	2.27 [1.20-4.29]	0.012	223
Cancer, n (%)	28 (15.0%)	7 (17.9%)	1.17 [0.52-2.65]	0.708	226
Smoking, n (%)	25 (15.5%)	5 (15.2%)	0.97 [0.38-2.52]	0.953	194
CNIs, n (%)	172 (86.0%)	30 (69.8%)	0.46 [0.24-0.88]	0.019	243
Mycophenolate acid, n (%)	152 (76.0%)	31 (72.1%)	0.83 [0.43-1.62]	0.586	243
Azathioprine, n (%)	8 (4.00%)	3 (6.98%)	1.41 [0.43-4.55]	0.569	243
mTOR inhibitors, n (%)	22 (11.0%)	7 (16.3%)	1.38 [0.61-3.10]	0.439	243
Steroids, n (%)	147 (73.5%)	30 (69.8%)	0.81 [0.42-1.56]	0.533	243
Belatacept, n (%)	12 (6.00%)	3 (6.98%)	1.15 [0.36-3.71]	0.817	243
Characteristics on admission					
Cough, n (%)	123 (64.4%)	22 (59.5%)	0.81 [0.42-1.56]	0.521	228
Rhinitis, n (%)	16 (8.89%)	4 (11.4%)	1.24 [0.44-3.51]	0.687	215
Dyspnea, n (%)	74 (37.0%)	24 (55.8%)	1.99 [1.09-3.63]	0.025	243
Anosmia, n (%)	28 (16.0%)	1 (3.23%)	0.20 [0.03-1.45]	0.110	206
Fever, n (%)	151 (79.9%)	29 (80.6%)	1.05 [0.46-2.41]	0.901	225
Headache, n (%)	35 (18.6%)	4 (11.4%)	0.59 [0.21-1.68]	0.323	223
Diarrhea, n (%)	84 (44.7%)	13 (37.1%)	0.75 [0.38-1.48]	0.401	223
Time from symptom onset to	6.00 [3.00-9.00]	4.00 [2.75-6.00]	0.94 [0.88-1.02]	0.138	219
CRP > 60 mg/L, n (%)	82 (51.9%)	18 (64.3%)	1.69 [0.78-3.66]	0.185	186
Procalcitonin > 0.2 ng/mL, n (%)	34 (44.7%)	10 (71.4%)	2.79 [0.87-8.89]	0.083	90
Median lymphocyte count [IQR],	0.70 [0.40-0.97]	0.60 [0.44-0.96]	0.80 [0.38-1.65]	0.538	184
Median platelet count [IQR], ×10^9/L	178 [144-232]	178 [155-257]	1.00 [1.00-1.00]	0.894	188

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	Alive (n = 200)	Dead (n = 43)	HR [95% CI]	p	n
Thrombocytopenia < 150 ×10^9/L, n	48 (30.8%)	6 (18.8%)	0.54 [0.22-1.32]	0.176	188
SaO_2 < 95%, n (%)	47 (32.2%)	19 (63.3%)	3.39 [1.61-7.14]	0.001	176
Median creatinine [IQR], µmol/L	176 [131-249]	184 [131-230]	1.00 [1.00-1.00]	0.864	200

Abbreviations: IQR, interquartile range; BMI, body mass index; Ref, reference; Tx, transplantation; RAS, renin-angiotensin system; CNIs, calcineurin inhibitors; mTOR, mammalian target of rapamycin. Data are expressed as medians (IQRs) or counts (percentages), as appropriate.

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Figure legends

Figure 1

Kaplan-Meier plot of survival in KT recipients who were hospitalized with Covid-19. The 30-day mortality rate after admission was 22.8% (16.1-28.9%)

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 *versus* >60 years), C) diabetes (yes *versus* no), D) body mass index (<25 *versus* >25 kg/m²), E) fever on admission (yes *versus* no), F) dyspnea on admission (yes *versus* no), G) SaO2 on admission (>95 *versus* <95%); H) C-reactive protein on admission (<60 *versus* >60 mg/L), and I) procalcitonin on admission (<0.2 *versus* >0.2 ng/mL).

Figure 3

Multivariable analysis of risk factors for A) severe disease (intensive care unit admission/need for mechanical ventilation/mortality) or B) mortality. Concordance for the severe disease model: 0.66; concordance for the mortality model: 0.76.

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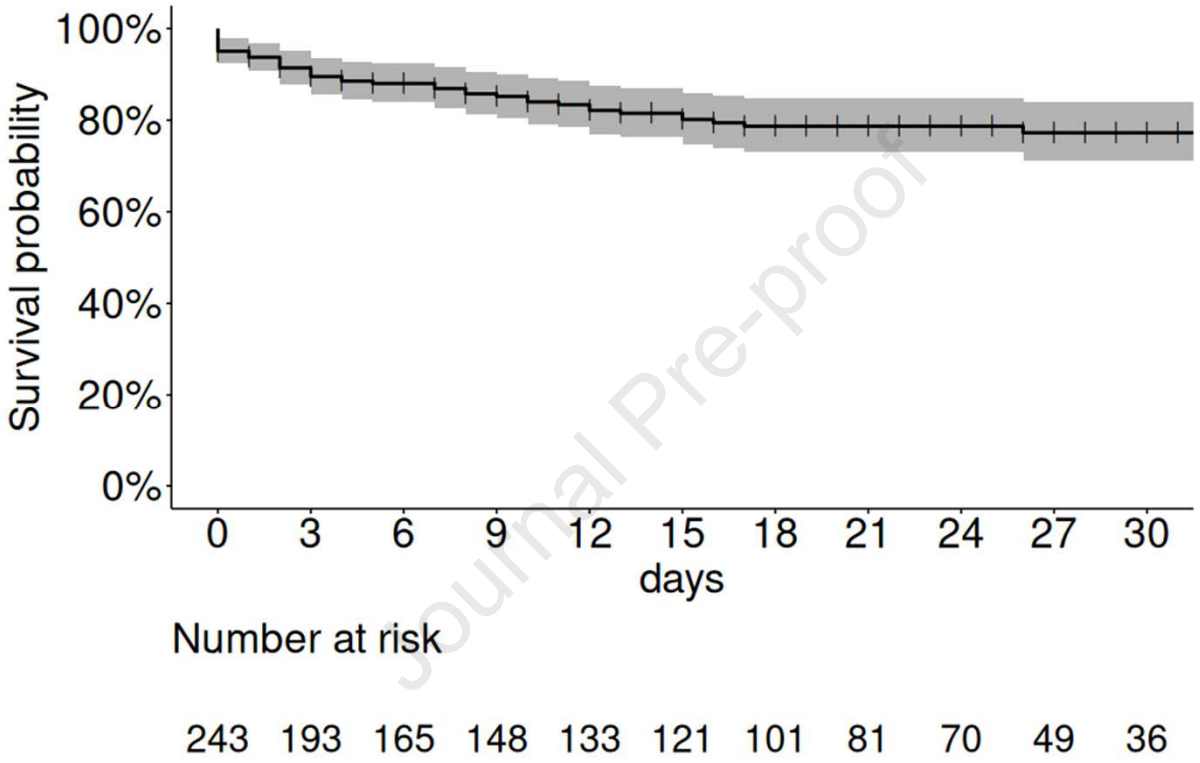
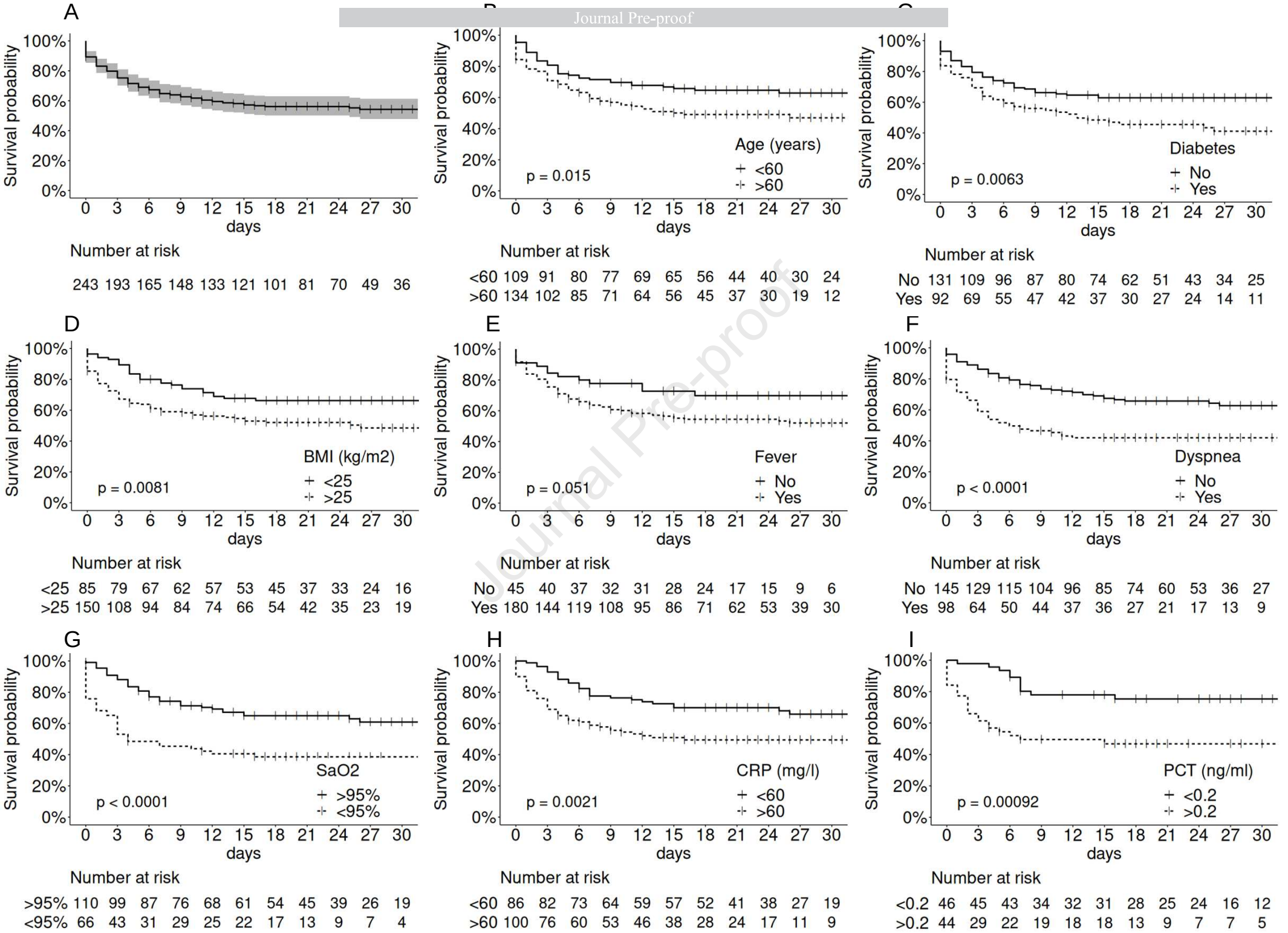


Figure 1:
Kaplan-Meier plot of survival in KT recipients who were hospitalized with Covid-19. The 30-day mortality rate after admission was 22.8% (16.1-28.9%)

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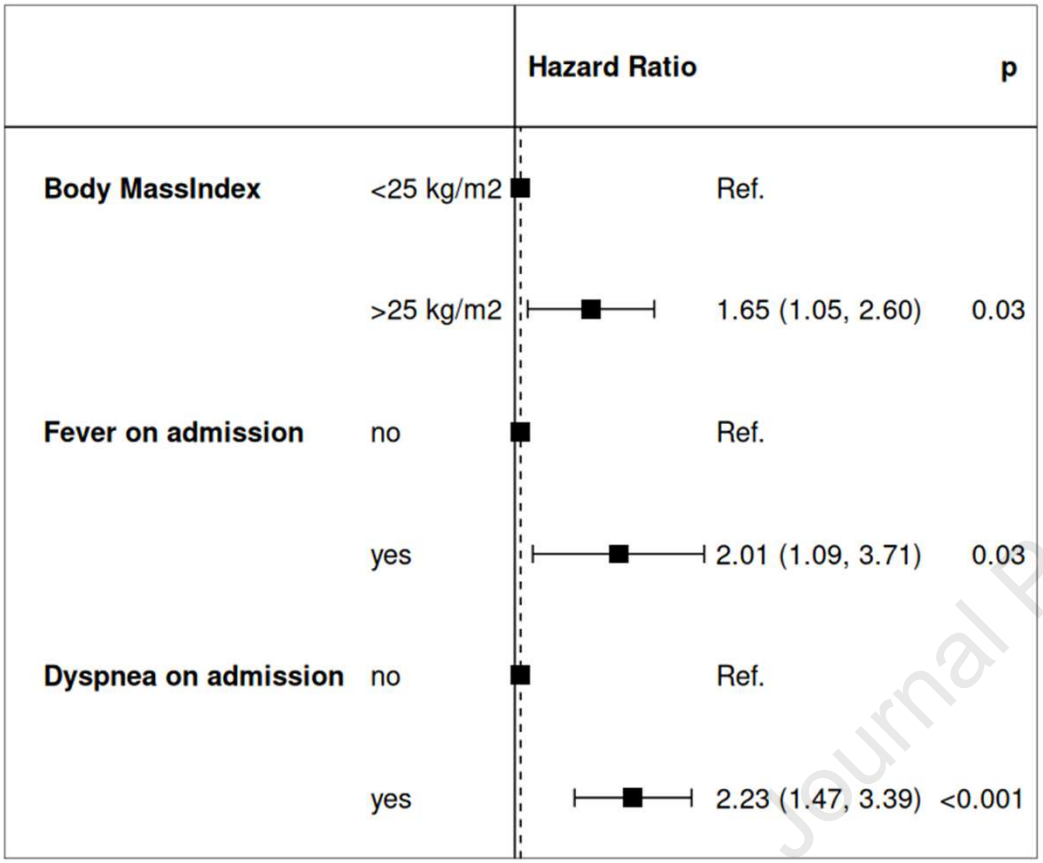
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Figure 2. Probability of reaching the composite endpoint of severe disease. A) The 30-day severe disease-free survival in the entire study cohort was 54.2% (48-61.4%). Kaplan-Meier plots stratified according to B) age (<60 *versus* >60 years), C) diabetes (yes *versus* no), D) body mass index (<25 *versus* >25 kg/m²), E) fever on admission (yes *versus* no), F) dyspnea on admission (yes *versus* no), G) SaO2 on admission (>95 *versus* <95%); H) C-reactive protein on admission (<60 *versus* >60 mg/L), and I) procalcitonin on admission (<0.2 *versus* >0.2 ng/mL).

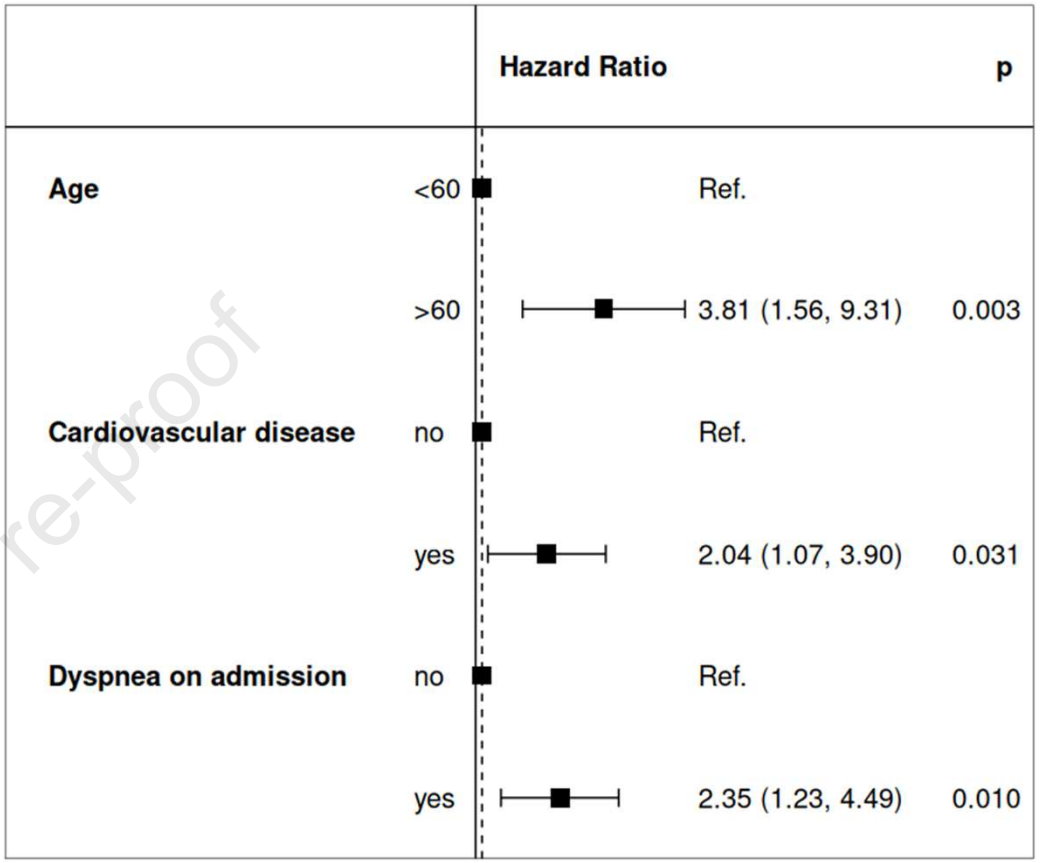
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A



B



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Figure 3: Multivariable analysis of risk factors for A) severe disease (intensive care unit admission/need for mechanical ventilation/mortality) or B) mortality. Concordance for the severe disease model: 0.66; concordance for the mortality model: 0.76.