





FORUM

Undoubtedly, kidney transplant recipients have a higher mortality due to COVID-19 disease compared to the general population

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This Forum discusses the paper by Hugo et al: Solid organ transplantation is not a risk factor for COVID-19 disease outcome. *Transpl Int.* 2021;34; 378.

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With interest, we read the article of Hugo et al, who described a mortality of 8.7% in 46 solid organ transplant recipients after COVID-19 infection [1]. Because a misinterpretation may have detrimental implications for solid organ transplant recipients regarding COVID-19 vaccine prioritization, we think it is important to comment on the misleading title and the limitations of their conclusions due to an obvious selection bias in the control group.

In the Berlin-Brandenburg region, we serve an area of 6.1 million people and approximately 2500 kidney transplant recipients. Here, 209.960 cases of COVID-19 (3.4% of the total population) and 6002 deaths due to COVID-19 (2.9% of registered COVID-19 cases) were documented up to March 7 [2]. During the last year, we observed 114/2500 (4.6%) cases of COVID-19 in kidney transplant recipients and 10/114 (8.8%) deaths due to COVID-19. Hence, mortality was strikingly similar in our cohort compared to Hugo et al. [1] and lower as compared to previously described kidney transplant cohorts with mortality rates between 12% and

32% (see Table 1). In summary, mortality of kidney transplant recipients is at least three- to fourfold higher than in the general population, supporting the thorough analysis from the United Kingdom with a four-time higher hazard ratio of death for solid organ transplant recipients [3].

In our view, a meaningful comparator should represent the general population, which was not the case in the recently published paper [1], where the control group exhibited a mortality of 17.5%, far exceeding the overall mortality from COVID-19 in Germany (70.800 deaths in 2.445 Mio infected people; 2.9%) [2], and suggesting a strong selection bias for controls. The control group was selected from the LEOSS registry of hospitalized COVID-19 cases, which are treated in large part at tertiary university hospitals [4]. This can lead to selection bias for higher mortality, since these hospitals are referral centers for severe and complicated ICU cases. As a consequence, the control group had a substantial higher rate of complicated and critical cases (23.9% vs. 29.5% and 4.4% vs 8.6%, respectively). Unfortunately, the proportion of patients requiring an ICU stay was not reported in the study. Another major risk factor for mortality, namely age, appears highly unmatched, as the proportion of patients >65 years is almost twice as high in the control group (47.5% vs. 23.9%), which additionally distorts the conclusions.

We acknowledge the authors' ambition to gain insights about the risk attributable to immunosuppression and transplantation independent of the comorbidities of transplant recipients. However, because the control group does not reflect the general population, the conclusions in the article [1] are misleading and may have detrimental effects on the decision-making process regarding risk stratification and immunization,

Table 1. Summary of 8 studies investigating the clinical outcome of kidney transplant recipients and solid organ transplant recipients with COVID-19. We analyzed the studies for data about sample size, patient characteristics, comorbidities, clinical outcomes, predictors of mortality, and data about the study design

| Patients | Comorbidities | Clinical Outcome | Predictors of Mortality | Reference and Study Design |
|---------------------|--|---|--|---|
| 144 KTR | Mean age 62y Hypertension 95% Diabetes 52% Obesity 49% Heart disease 28% Lung disease 19% | Mortality 32% Hospitalization 100% ICU/MV 30%/29% AKI 52% | Age > 60 RR > 20/min PCT LDH Dyspnea | Cravedi et al. [5] Multicentric, TANGO Registry (US, Spain, Italy) March–May 2020 |
| 286 KTR | Mean age 60y | Mortality 19% Hospitalization 94% ICU 9% | Older age Pneumonia | Sanchez-Alvarez et al. [6] Multicentric, Registry of Spanish Society of Nephrology March - April 2020 |
| 104 KTR | Mean age 60y Hypertension 86% Diabetes 31% Obesity 27% Heart Disease 30% Lung Disease 15% | Mortality 27% Hospitalization 100% ICU 23% AKI 47% | Older age ARDS at admission Lung disease LDH | Fava et al. [7] Multicentric, Spain March–April 2020 |
| 482 SOTR 318 KTR | Median age 57.5y Hypertension 77% Diabetes 51% Obesity 35% Heart disease 30% Lung disease 10% | Mortality - SOTR 19% Mortality - KTR 18% Hospitalization 78% ICU/MV 34%/27% AKI/RRT 38%/12% | Age > 65 years Congestive heart failure Lung disease Obesity Diabetes | Kates et al. [8] Multicentric, UW SOT COVID Registry March–May 2020 |
| 36 KTR | Median age 60y Hypertension 94% Diabetes 69% Heart disease 17% Lung disease 11% | Mortality 28% Hospitalization 78% MV 39% | – | Akalin et al. [9] Monocentric, Montefiore Medical Center, New York, United States March–April 2020 |
| 1013 KTR | Median age 61y Heart disease 17% Lung disease 11% | Mortality 20% | Older Age Male Sex | Jager et al. [10] Multicentric, ERA-EDTA Registry Feb–April 2020 |
| 46 KTR | Diabetes 11% | Mortality 14% Hospitalization 80% ICU/MV 21%/12% | – | De Meester et al. [11] Multicentric, Belgium March–May 2020 |
| 250 KTR | Median age 43y Hypertension 84% Diabetes 32% Adipositas 24% Heart disease 12% Lung disease 4% | Mortality 12% Hospitalization 80% ICU/MV 21%/12% AKI/RRT 48%/10% | Older age Dyspnea Disease severity Allograft dysfunction Obesity CRP, IL-6, PCT Chest XR abnormality ICU/MV | Kute et al. [12] Multicentric, India March–Sep 2020 |
| 2197 KTR | – | Pooled mortality for KTR: 19% (420/2197) | – | – |

AKI, acute kidney injury; CRP, C-reactive protein; ICU, intensive care unit; IL-6, interleukin-6; KTR, kidney transplant recipients; LDH, lactate dehydrogenase; MV, mechanical ventilation; PCT, procalcitonin; RR, respiratory rate; RRT, renal replacement therapy; SOTR, solid organ transplant recipients; XR, X-ray; y, years.

as all published data clearly demonstrate a much higher mortality from COVID-19 in solid organ transplant recipients.

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Conflict of interest

The authors declare no conflicts of interest.

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Response to Invited Commentary "Undoubtedly, kidney transplant recipients have a higher mortality due to COVID-19 disease compared to the general population"

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This is a Response to Forum: Bilgin Osmanodja, Manuel Mayrdorfer, Fabian Halleck, Mira Choi & Klemens Budde. Undoubtedly, kidney transplant recipients have a higher mortality due to COVID-19 disease compared to the general population. *Transplant International* 2021;34; 769

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We appreciate the opportunity to have this scientific discussion regarding the important question, whether