SARS-CoV-2 renal tropism associates with acute kidney injury

Acute kidney injury is a commonly described complication of COVID-19 that has been linked to increased morbidity and mortality. Although severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been found in the kidney,[1] the clinical effect remains unclear.[2] Here, we present data from a post-mortem series of 63 patients who had SARS-CoV-2 respiratory infection (appendix pp 2–3), linking SARS-CoV-2 renal tropism to clinical outcome and acute kidney injury.

In this cohort, SARS-CoV-2 RNA was found in 38 (60%) of 63 patients. Presence of SARS-CoV-2 RNA in the kidney was associated with older age and an increased number of coexisting conditions (figure). Furthermore, SARS-CoV-2 RNA was associated with a reduction in patients' survival time, obtained by calculating the time interval between COVID-19 diagnosis and date of death (figure). These findings support a potential correlation between extra-respiratory viral tropism, disease severity, and increased risk of premature death within the first 3 weeks of disease.

Previous studies have identified an increased risk of acute kidney injury in patients with COVID-19.[3] Within our cohort, clinical kidney status was defined in 39 (62%) patients during the course of their disease progression (appendix pp 4–5). SARS-CoV-2 RNA was detected in the kidneys of 23 (72%) of 32 patients with acute kidney injury. By contrast, patients without acute kidney injury showed a lower frequency of SARS-CoV-2 renal tropism, with viral RNA only found in three (43%) of seven patients (figure).

SARS-CoV-2-mediated acute kidney injury might be explained by indirect factors (eg, cytokine-mediated injury) and by direct viral infection and replication in kidney epithelial cells.[4] We isolated SARS-CoV-2 from an autopsied kidney, which produced a 1000-times increase in viral RNA after 48 h of cell infection in vitro (figure; appendix p 1), thus confirming the presence of infective virus in the kidney, even under post-mortem conditions. Furthermore, we found that patient-derived SARS-CoV-2 replicates in non-human primate kidney tubular epithelial cells (the main cellular target of acute kidney injury) using indirect immunofluorescence imaging of SARS-CoV-2 non-structural protein 3, one of the SARS-CoV replicase cleaving products (appendix p 5).[5]

Our findings indicate that SARS-CoV-2 renal tropism is associated with disease severity (ie, premature death) and development of acute kidney injury. This suggests that SARS-CoV-2 is able to target the kidney, pointing towards the importance of early urinary testing and eventual therapeutic prevention of kidney infection.

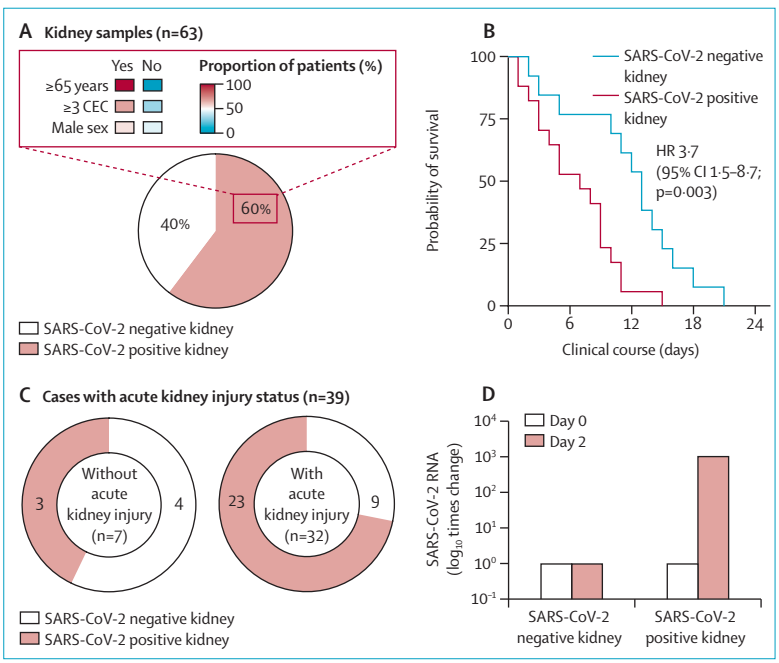

Figure: **Association between SARS-CoV-2 renal tropism, disease severity, and acute kidney injury**
SARS-CoV-2 tropism was associated with older age and a number of coexisting conditions (A). Survival graph comparing patients with (n=19) and without (n=13) SARS-CoV-2 renal tropism (B). High frequency of SARS-CoV-2 renal tropism in patients with acute kidney injury (C). Successful isolation of infectious SARS-CoV-2 from a post-mortem kidney tissue sample (D). SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. CEC=coexisting conditions. HR=hazard ratio.

Published **Online**
August 17, 2020
https://doi.org/10.1016/
S0140-6736(20)31759-1

See **Online** for appendix

FB reports grants and personal fees from Amicus Therapeutics; personal fees from Takeda/Shire; and travel support from Sanofi Genzyme and Astellas, unrelated to this Correspondence. TBH reports grants from the German Research Foundation (CRC/1192, HU 1016/8-2, HU 1016/11-1, HU 1016/12-1), the Federal Ministry of Education and Research (STOP-FSGS-01GM1518C), and the European Research Council (grant 616891) during the study; grants and personal fees from Fresenius Medical Care; grants from Amicus Therapeutics and Sanofi Genzyme; and personal fees from Boehringer Ingelheim, Goldfinch Bio, Novartis Pharma, DaVita Germany, and Bayer Vital, unrelated to this Correspondence. SK reports grants and personal fees from Pfizer; personal fees from Biotest, Cytosorbents, Gilead, Merck Sharp & Dohme, Bayer, Astellas, Baxter, and Fresenius, unrelated to this Correspondence. VGP reports grants from the German Research Foundation (DFG: CRC/1192) and the Federal Ministry of Education and Research (BMBF: eMed Consortia Fibromap) during the study. All other authors declare no competing interests. FB, ML, SP, MNW, CE, MA, VGP, and TBH contributed equally as co-first or senior authors.

Fabian Braun, Marc Lütgehetmann, Susanne Pfefferle, Milagros N Wong, Alexander Carsten, Maja T Lindenmeyer, Dominik Nörz, Fabian Heinrich, Kira Meißner, Dominic Wichmann, Stefan Kluge, Oliver Gross, Klaus Pueschel, Ann S Schröder, Carolin Edler,

*Martin Aepfelbacher, Victor G Puelles, *Tobias B Huber*
t.huber@uke.de

Department of Medicine (FB, MNW, MTL, VGP, TBH), Institute of Medical Microbiology, Virology and Hygiene (ML, SP, AC, DN, MA), Department of Legal Medicine (FH, KM, KP, ASS, CE), and Department of Intensive Care Medicine (DW, SK), University Medical Center Hamburg-Eppendorf, Hamburg 20246, Germany; and Clinic of Nephrology and Rheumatology, University of Gottingen, Gottingen, Germany (OG)

1 Puelles VG, Lütgehetmann M, Lindenmeyer MT, et al. Multi-organ and renal tropism of SARS-CoV-2. *N Engl J Med* 2020; published online May 13. https://doi.org.10.1056/NEJMc2011400.

2 Gross O, Moerer O, Weber M, Huber TB, Scheithauer S. COVID-19-associated nephritis: early warning for disease severity and complications? *Lancet* 2020; **395:** e87–88.

3 Selby NM, Forni LG, Horne KL, et al. Covid-19 and acute kidney injury in hospital: summary of NICE guidelines. *BMJ* 2020; **369:** m1963.

4 Batlle D, Soler MJ, Sparks MA, et al. Acute kidney injury in COVID-19: emerging evidence of a distinct pathophysiology. *JASN* 2020; **31:** 1380–83.

5 Kim D, Lee J-Y, Yang J-S, Kim JW, Kim VN, Chang H. The architecture of SARS-CoV-2 transcriptome. *Cell* 2020; **181:** 914–21.