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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

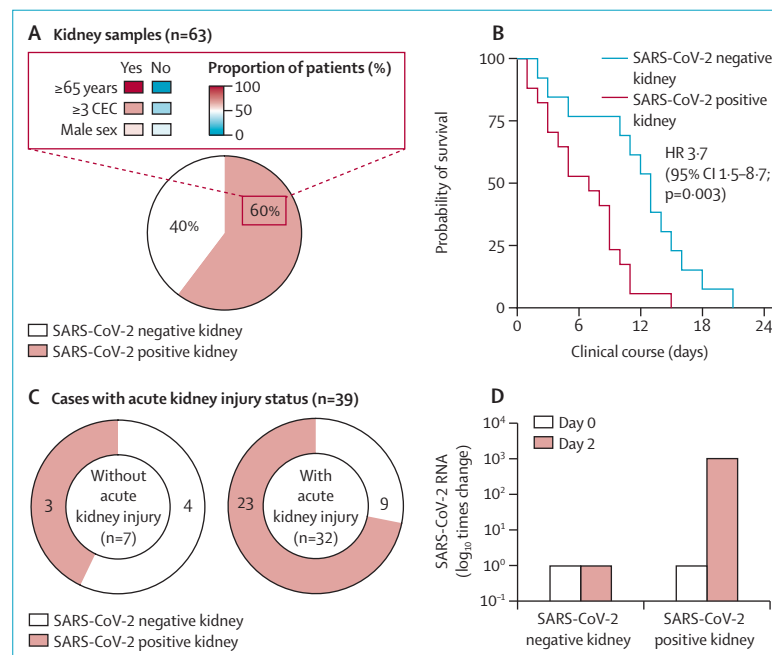


Figure: Association between SARS-CoV-2 renal tropism, disease severity, and acute kidney injury

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.

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.

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See Online for appendix

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Back to basics: the outbreak response pillars

The Global Outbreak Alert and Response Network (GOARN), with more than 250 technical partner organisations across the world, has undertaken 150 operations in response to disease outbreaks during the past 20 years.

We read with interest the Editorial entitled, *COVID-19: the worst may be yet to come*.¹ GOARN has learned that the worst can be avoided through rapid and robust action to minimise the transmission of severe acute respiratory syndrome coronavirus 2. This prevention and control involves the core pillars of the outbreak response: surveillance and contact tracing, testing, case management, infection prevention and control, epidemiological and outbreak analytics, logistics, risk communication, and community engagement. Lockdowns and border

closures are not a desirable long-term strategy; these measures should be used to gain time for building up capacities for a public health response.

To this end, the GOARN Steering Committee urges all governments and partners at a local level to (1) engage communities to build trust for evidence-based public health and encourage local ownership of outbreak control response measures; (2) discourage the politicisation of the COVID-19 response because politicisation is counterproductive and leads to poor strategic decisions; (3) leverage in-country expertise of experienced outbreak responders, including GOARN partners and emergency medical teams, because current decisions can be strengthened by expanding the advisory pool; (4) invest in the rapid expansion of the public health workforce for this response; (5) make decisions on the basis of a comprehensive strategy, the latest evidence, and the epidemiological situation (eg, supervised isolation for infectious patients and mandated mask wearing have been shown to improve outcomes), and explain these decisions clearly;^{2–4} (6) ensure equitable access to diagnostic tests, therapeutics, and vaccines, which should be allocated according to sound public health criteria and needs; and (7) champion multilateral action and international solidarity. WHO is key to the international response as the organisation offers both a global direction to each nation and tailored technical assistance to responders.

We declare no competing interests.

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SARS-CoV-2 PCR testing of skin for COVID-19 diagnostics: a case report

Understanding the disease course and prevalence of COVID-19 is important not only for medical, but also for socioeconomic reasons. So far, COVID-19 has been understood as a multisystem disease, mainly affecting the lungs, kidneys, and heart.¹ In the past few months, different cutaneous manifestations, such as chilblain-like, vasculitis-like, or urticaria-like lesions, have been described in patients with COVID-19.² Colmenero and colleagues³ detected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in endothelial cells of cutaneous chilblain lesions via immunohistochemistry methods in seven paediatric patients with negative nasopharyngeal swabs.³

Here, we report the case of an 81-year-old woman who presented at the Department of Dermatology at the University Hospital of Basel, Basel, Switzerland, with a temperature of up to 39°C and a generalised macular eruption with partial vasculitis-like patterns and palmo-plantar accentuation (appendix pp 1–2). Infection with SARS-CoV-2 was suspected and laboratory assessments of blood samples showed increased C-reactive protein (248 mg/L), decreased lymphocyte

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