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Commentary

COMMENTARY

Long-term effects of Covid-19 on the kidney

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Acute kidney injury (AKI) is a common complication of Covid-19 and one associated with increased mortality, especially when requiring renal replacement therapy.[1,2] AKI affects over 20% of hospitalized patients and over 50% of patients in the ICU.[3] Varying rates of recovery of renal function on discharge are described. Unsurprisingly, pre-existing CKD is a risk factor for dialysis dependence on discharge.[4] Previous studies have found that AKI, regardless of cause, results in pre-disposition to progressive CKD and the risk increases with the severity of AKI;[5] this will likely be the case with Covid-19 infection as well. Understanding the long-term impact of Covid-19 on the kidney is vital for planning and resource allocation for nephrology services.[6]

At this stage of the pandemic, the renal consequences of Covid-19 infection after 3–6 months have been described in three studies; the patient demographics differ, as do the renal parameters examined. Hultström *et al.* describe the outcomes of a group discharged following ICU admission of whom 10% required RRT.[7] Prior to admission 10% of this group had CKD stage 3 or higher. After 3–6 months, 16% (10/60) of the patients had progressed to a higher CKD stage, including one who became dialysis dependent. CKD stage progression was associated with AKI lasting for longer than 7 days as well as with more severe AKI (KDIGO stage 3); it was not associated with baseline renal function.

Stockmann *et al.* describe the outcomes of 74 patients admitted to ICU who developed severe AKI requiring RRT.[8] 98.6% of these patients were mechanically ventilated and 39.2% required ECMO. Of the 50% that survived, 21.6% of patients (8/37) had pre-existing CKD stage 3 or higher. After a median follow-up of 5 months, three surviving patients (8.1%) were dialysis dependent, while the remaining 91.9% of patients had achieved variable degrees of renal recovery, including 62.2% with full renal recovery. This study does not stratify outcomes based on pre-existing CKD but shows good rates of recovery from severe AKI.

Finally, Huang *et al.* describe outcomes 6 months after diagnosis in a cohort of 1733 patients discharged from hospital, of which 4% were admitted to ICU, with low rates of AKI (6%) and no mention of RRT requirement.[9] At follow-up, 13% (107/822) of patients with normal eGFR at the acute phase and without AKI during their admission, were found to have reduced GFR (<90 ml/mi/1.73 m2). However, 29.7% (142/478) of the patients with a reduced eGFR at the acute phase who did not have an AKI as defined in the study were then found to have normal renal function. This may be accounted for by the fact that baseline creatinine was not used to diagnose AKI and thus the diagnosis was inaccurate. Additionally, 8.6% (213/2469) of the original cohort were excluded from the analysis due to various co-morbid conditions; the exclusion of these frailer patients may have led to bias.

The data available are necessarily preliminary and describe outcomes from the early stages of the pandemic. Current, improved management of the disease may help prevent multisystem deterioration leading to renal injury. Conversely, as treatment strategies evolve to enhance patient survival, more patients with co-morbidities recover and are discharged who may have lower potential for long-term recovery of renal function. Another key consideration is that Covid-19 infection has been found to lead to severe weight loss, more severe in patients with reduced renal function.[10] The ensuing sarcopenia may lead to an over-estimation of GFR.

There are multiple ways, pathologically, in which Covid-19 infection could affect the kidney via both the systemic inflammatory response and the effects of critical illness. Direct infection of renal cells has been debated: positive PCR tests of renal tissue have been described,[11] however recent biopsy series have not found evidence of infection using immunohistochemistry or RNA *in situ* hybridization. Biopsies have shown various findings in addition to the non-specific finding of acute tubular

injury. In some patients with nephrotic range proteinuria, collapsing glomerulopathy has been observed.[12] This has been found in patients of African ancestry, and is strongly associated with a high risk *APOL1* genotype. An additional repeated finding in biopsy series is thrombotic microangiopathy, found in one series in 6/17 cases and in 2/10 cases in another.[13,14] A recent study found an increased incidence of anti GBM disease during the first wave.[15]

The immediate impact of Covid-19 on patients with pre-existing renal disease has been severe, with high mortality rates;[16] analysis of large prospective cohorts of patients that have survived Covid-19, such as the PHOSP-COVID study, will allow us to understand the proportion of all patients who have survived with long-term renal impairment and the risk factors that pre-dispose to it. The integration of genetic and proteomic data from such studies may also identify biomarkers for recovery or chronicity and point to the mechanisms involved.

Conflict of interest. None declared.

References

1. Chan L, Chaudhary K, Saha A, Chauhan K, Vaid A, Zhao S, *et al.*; Mount Sinai COVID Informatics Center (MSCIC). AKI in hospitalized patients with COVID-19. *J Am Soc Nephrol* 2021; **32**:151–60.
2. Gupta S, Coca SG, Chan L, Melamed ML, Brenner SK, Hayek SS, *et al.*; The STOP-COVID Investigators. AKI treated with renal replacement therapy in critically ill patients with COVID-19. *J Am Soc Nephrol* 2021; **32**:161–76.
3. Nadim MK, Forni LG, Mehta RL, Connor MJ, Liu KD, Ostermann M, *et al.* COVID-19-associated acute kidney injury: consensus report of the 25th acute disease quality initiative (ADQI) workgroup. *Nat Rev Nephrol Nat Res* 2020; **16**:747–64.
4. Ng JH, Hirsch JS, Hazzan A, Wanchoo R, Shah HH, Malieckal DA, *et al.*; Northwell Nephrology COVID-19 Research Consortium. Outcomes among patients hospitalized with COVID-19 and acute kidney injury. *Am J Kidney Dis* 2021; **77**:204–215 e1.
5. Chawla LS, Eggers PW, Star RA, Kimmel PL. Acute kidney injury and chronic kidney disease as interconnected syndromes. *N Engl J Med* 2014; **371**:58–66.
6. Bruchfeld A. The COVID-19 pandemic: consequences for nephrology. *Nat Rev Nephrol Nat Res* 2021; **17**:81–2.
7. Hultström M, Lipcsey M, Wallin E, Larsson I-M, Larsson A, Frithiof R. Severe acute kidney injury associated with progression of chronic kidney disease after critical COVID-19. *Crit Care* 2021; **25**:37.
8. Stockmann H, Hardenberg J-HB, Aigner A, Hinze C, Gotthardt I, Stier B, *et al.* High rates of long-term renal recovery in survivors of COVID-19-associated acute kidney injury requiring kidney replacement therapy. *Kidney Int* 2021; **99**(4):1021–1022.
9. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, *et al.* 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021; **397**:220–32.
10. Di Filippo L, De Lorenzo R, D'Amico M, Sofia V, Roveri L, Mele R, *et al.* COVID-19 is associated with clinically significant weight loss and risk of malnutrition, independent of hospitalisation: a post-hoc analysis of a prospective cohort study. *Clin Nutr* 2020 ;S0261–5614(20)30589-6.
11. Puelles VG, Lütgehetmann M, Lindenmeyer MT, Sperhake JP, Wong MN, Allweiss L, *et al.* Multiorgan and renal tropism of SARS-CoV-2. *N Engl J Med* 2020; **383**:590–2.
12. Velez JCQ, Caza T, Larsen CP. COVAN is the new HIVAN: the re-emergence of collapsing glomerulopathy with COVID-19. *Nat Rev Nephrol Nat Res* 2020; **16**:565–7.
13. Akilesh S, Nast CC, Yamashita M, Henriksen K, Charu V, Troxell ML, *et al.* Multicenter clinicopathologic correlation of kidney biopsies performed in COVID-19 patients presenting with acute kidney injury or proteinuria. *Am J Kidney Dis* 2021; **77**:82–93 e1.
14. Sharma P, Uppal NN, Wanchoo R, Shah HH, Yang Y, Parikh R, *et al.*; Northwell Nephrology COVID-19 Research Consortium. COVID-19–associated kidney injury: a case series of kidney biopsy findings. *J Am Soc Nephrol* 2020; **31**:1948–58.
15. Prendecki M, Clarke C, Cairns T, Cook T, Roufosse C, Thomas D, *et al.* Anti–glomerular basement membrane disease during the COVID-19 pandemic. *Kidney Int Elsevier B.V.* 2020; **98**:780–1.
16. ERA-EDTA Council; ERACODA Working Group. Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA. *Nephrol Dial Transplant* 2021; **36**: 87–94.