Letter Regarding "Association Between CKD, Obesity, Cardiometabolic Risk Factors, and Severe COVID-19 Outcomes"

Volbeda, Meint; Jou-Valencia, Daniela; van den Heuvel, Marius; Moser, Jill; van Meurs, Matijs; Franssen, Casper F M

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To the Editor: In the 2023 April issue of KI Reports, Sorling *et al.*[1] reported that chronic kidney disease (CKD) is a critical risk factor for severe COVID-19 and death. We would like to further emphasize the negative impact of CKD on outcome in patients with a severe COVID-19 course by showing that preexisting CKD is often not diagnosed in these patients. CKD is under-recognized in the general population because only the more severe CKD stages lead to clinical symptoms. In hospitalized patients, baseline serum creatinine levels are often unknown and elevated creatinine levels are usually interpreted as a sign of acute kidney injury, whereas at least part of the supposedly acutely impaired renal function may in fact be due to preexisting CKD. In addition, pre-existing CKD might be missed in patients with anuric acute kidney injury because albuminuria cannot be assessed. Moreover, a normal estimated glomerular filtration rate and the absence of albuminuria do not rule out histopathological kidney damage, because renal functional reserve can be large enough to avoid a significant rise in serum creatinine.[2]

We recently reviewed the renal histopathological findings of patients with COVID-19 at an individual patient level from various published studies to increase our understanding of acute kidney injury in COVID-19.[3] This allowed us to investigate the incidence of CKD based on renal histology in hospitalized patients with COVID-19. We analyzed the individual patient characteristics including data on the presence or absence of CKD in medical history and post-mortem renal biopsy results from 88 patients with COVID-19 from 8 studies.[S1–S8] Strikingly, the incidence of CKD based on medical history was only 17% (15 of the 88 patients), whereas 93% of patients (82 of the 88 patients) showed histopathological features of CKD (Figure 1), such as glomerulosclerosis (46 of the 82 patients), atherosclerosis (75 of the 82 patients), and nephrocalcinosis (4 of the 82 patients). In addition, several patients showed histopathological features compatible with diabetic nephropathy (7 of the 82 patients) or focal segmental glomerulosclerosis (3 of the 82 patients).[4] Our findings suggest that the association between CKD and severe COVID-19 might be even stronger than previously thought.

DISCLOSURE

All the authors declared no competing interests.

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Availability of Data and Materials

The data underlying this article will be shared upon reasonable request to the corresponding author.

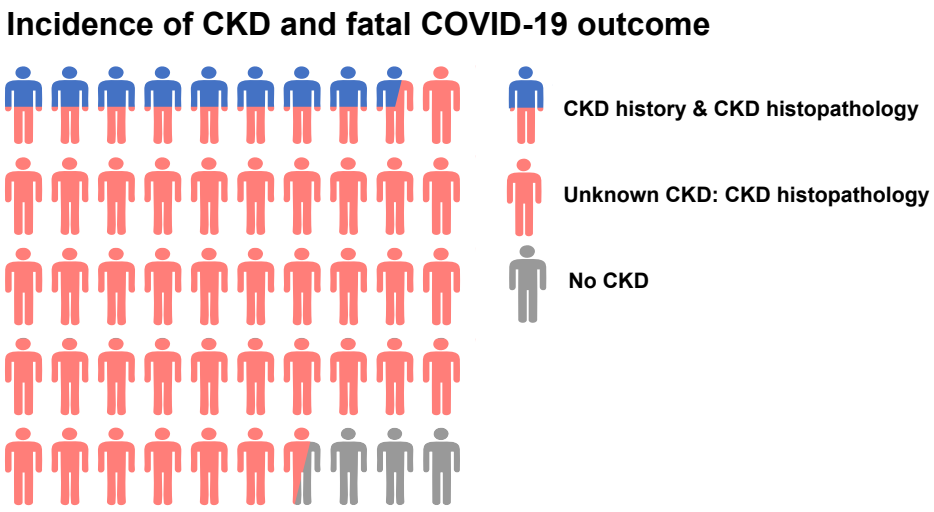

Figure 1. Incidences of CKD based on medical history and CKD based on renal histology. All patients with a medical history of CKD (15 patients) also had CKD based on renal histology. In contrast, most patients without a medical history of CKD actually did have CKD based on renal histology (67 of the 73 patients). CKD, chronic kidney disease.

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AUTHOR CONTRIBUTIONS

MV, MvM, and CFMF contributed to the conception and the design of the study. MV, DJ-V, and MvdH contributed to the interpretation of data. MV and DJ-V organized the database. JM made the Figure. MV, DJ-V, MvdH, CFMF, JM, and MvM contributed to the drafting and revising of the article and provided intellectual content of critical importance.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary References.

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Meint Volbeda[1], Daniela Jou-Valencia[1] Marius C. van den Heuvel[2], Jill Moser[1,3], Matijs van Meurs[1,3] and Casper F.M. Franssen[4]

[1]Department of Critical Care, University of Groningen, University Medical Center Groningen, The Netherlands; [2]Department of Pathology and Medical Biology, Pathology Section, University of Groningen, University Medical Center Groningen, The Netherlands; [3]Department of Pathology and Medical Biology, Medical Biology Section, Laboratory for Endothelial Biomedicine and Vascular Drug Targeting Research, University of Groningen, University Medical Center Groningen, The Netherlands; and [4]Department of Nephrology, University of Groningen, University Medical Center Groningen, The Netherlands

Correspondence: Meint Volbeda, Department of Critical Care, University of Groningen, University Medical Center Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands. E-mail: m.volbeda@umcg.nl

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Response to Letter from Dr. Volbeda and Colleagues Regarding COVID-19 and CKD

The Author Replies: We would like to thank Dr. Volbeda and colleagues for showing interest in our article[1] and for putting our findings in the context of their interesting findings in which a vast majority of patients with severe COVID-19 had histopathological signs of chronic kidney disease (CKD).[2] We can just agree that CKD is a key risk factor for severe COVID-19 and the main question here is whether milder CKD is underestimated and to a larger extent explains a severe course of COVID-19.

Surely, our study that is based on registered diagnosis from health care episodes in a national patient register underestimates the true prevalence of CKD in particular among those with milder stages of CKD. However, some major differences in study designs should be considered. First, we studied a nationwide sample of patients with severe COVID-19 treated with ventilator in Swedish intensive care units, whereas Volbeda *et al*.[2] report findings from case series of patients with renal biopsies either with a clinical indication or biopsied postmortem. Therefore, patients with an indication for biopsy (acute kidney injury) or deceased patients were selected, and it is reasonable to assume that their sample is enriched with other risk factors that are shared between CKD and the most severe course of COVID-19. Therefore, the higher prevalence of CKD in the case series could partly be explained by that the deceased were older and had more underlying conditions leading to CKD. In fact, we have recently showed that CKD is not only a risk factor in the population for being admitted to the intensive care unit with severe COVID-19 but also for mortality after admission to the intensive care unit.[3] Most importantly, we can compare characteristics among patients with severe COVID-19 to matched control subjects and report associations between CKD and severe COVID-19 outcomes. Although underestimation of milder CKD by health care diagnosis is likely, this will occur both among patients with COVID-19 and control subjects and is unlikely to affect the relative risk. Although Volbeda *et al*.[2] suggest that the association between CDK and severe COVID-19 might be stronger, this is an interesting hypothesis, but such a conclusion cannot be supported by data from case series. To study whether the association between histopathological