Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

BioNTech) received a third vaccine dose (mRNA-1273; Moderna), which was well-tolerated. For a description of the employed methods, see the Supplementary Methods. The third vaccination induced seroconversion in 6 subjects (60%) with a median antibody titer concentration of 542 (interquartile range, 478–923) U/ml and neutralizing capacity (Figure 1a and b). Correspondingly, a strong increase in the magnitude of SARS-CoV-2 spike (S)-protein–reactive T-cell immunity (median, 0.08%) was observed in 9 subjects (90%; Figure 1c and d and Supplementary Table S1) with T-cell frequencies comparable to healthy individuals.[2] Increased frequencies of cytokine-producing T cells and follicular T-helper cells indicated a gain of antiviral functionality (Figure 1e–i).

Compared with recent data showing increased SARS-CoV-2 S-protein antibody levels in transplant patients after 3-dose SARS-CoV-2 mRNA vaccination,[4,5] our study provides a deeper immunologic characterization of vaccination-specific immunity, as demonstrated by antibody neutralizing capacity and spike-reactive T-cell immunity.

In summary, a third dose of an mRNA vaccine elicits a humoral and cellular response in 60% and 90% of RTR patients, respectively, who failed the primary vaccination. Although larger cohort studies with longer observation time are needed to confirm our results, the exceptionally high risk of fatal COVID-19 in RTRs supports consideration of a third vaccination in clinical practice.

DATA STATEMENT

Data will be available on request.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Study population. Description of the demographic and clinical characteristics of the cohort, including information on the anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) humoral immune response after the first, second, and third doses and corresponding cellular immune response.

Supplementary Methods. Concise description of the employed methods.

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[1]Medical Department I, Marien Hospital Herne, University Hospital of the Ruhr-University Bochum, Herne, Germany; [2]Center for Translational Medicine and Immune Diagnostics Laboratory, Marien Hospital Herne, University Hospital of the Ruhr-University Bochum, Herne, Germany; [3]Berlin Center for Advanced Therapies, Charité–Universitätsmedizin Berlin, Corporate Member of Freie Universität, Berlin, Humboldt-Universität, Berlin, Germany; [4]Department of Molecular and Medical Virology, Ruhr-University Bochum, Bochum, Germany; [5]Medizinische Klinik und Poliklinik III, Universitätsklinikum Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany; and [6]Department of Surgery, University Hospital Knappschaftskrankenhaus Bochum, Ruhr-University Bochum, Bochum, Germany

Correspondence: *Nina Babel, Marien Hospital Herne, University Hospital of the Ruhr-University Bochum, Hölkeskampring 40, 44625 Herne, Germany. E-mail: timm.westhoff@elisabethgruppe.de; and Timm Westhoff, Marien Hospital Herne, University Hospital of the Ruhr-University Bochum, Hölkeskampring 40, 44625 Herne, Germany. E-mail: nina.babel@charite.de*

[7]THW, FSS, US and NB have contributed equally to this manuscript.

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Anti–SARS-CoV-2 spike protein S1 receptor-binding domain antibody after vaccination with inactivated whole-virus SARS-CoV-2 in end-stage kidney disease patients: an initial report

To the editor: Patients with end-stage kidney disease (ESKD) are at greater risk for morbidity and mortality following coronavirus disease 2019 (COVID-19) than the general population.[1] Vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) for this vulnerable population is the main priority to prevent COVID-19 and mitigate unfavorable or severe complications. However, the immune responses to vaccination in patients with ESKD may be altered by accumulation of uremic toxins and comorbidities.[2] Currently, the effectiveness and safety

profiles of immunization with SARS-CoV-2 vaccines in patients on maintenance dialysis remain poorly understood.

Several studies reported variable humoral and cellular responses to different platforms of the approved SARS-CoV-2 vaccine in chronic dialysis patients.[3–7] Preliminary studies revealed that most patients with ESKD receiving maintenance dialysis developed decent seroconversion after the second vaccine dose. However, most immunogenicity and safety data against SARS-CoV-2 in these susceptible individuals mainly derived from the mRNA or adenoviral-vectored vaccines. Presently, the effects of immunization with an inactivated whole-virus SARS-CoV-2 vaccine among patients on maintenance dialysis have not been evaluated.

A pilot, multicenter, prospective study of patients with ESKD on maintenance dialysis who received a 2-dose immunization, administered at a 4-week interval, of an inactivated whole-virus SARS-CoV-2 vaccine, CoronaVac (Sinovac Biotech Ltd), was conducted from April 2021 to July 2021. SARS-CoV-2–specific humoral response was measured at baseline before administering the vaccine, 4 weeks after the first dose, and 2 weeks after the second dose, using a semiquantitative SARS-CoV-2 IgG assay (Abbott Diagnostics), which detects IgG antibodies against the receptor-binding domain (RBD) of the S1 spike antigen of SARS-CoV-2. The level of anti-RBD antibody was reported in arbitrary units per milliliter (AU/ml). Those humoral responses were also referenced to healthy controls. The study was approved by the Institutional Review Board of the Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand (MURA2021/242). All patients provided written informed consent before participation.

A total of 60 patients with ESKD on maintenance dialysis, and 30 healthy controls, aged between 18 and 59 years, were recruited into the study. A total of 29 and 31 patients received peritoneal dialysis (PD) and regular maintenance hemodialysis (HD) treatment, respectively. Of patients with ESKD, 67% were men, with a mean age (SD) of 42.1 (10.4) years. The median dialysis vintage for the PD and HD groups was 32.2 months (interquartile range, 7.0–55.1 months) and 32.6 months (interquartile range, 17.3–83.5 months; $P = 0.35$), respectively. The median Charlson Comorbidity Index scores of both groups were 3 (interquartile range, 2–4). A total of 45% in the HD group and 24% in the PD group carried underlying diabetes mellitus. The per-session average dialyzer urea clearance (Kt/V_{urea}) was 1.6 for the HD group, and the total average weekly Kt/V_{urea} was 2.0 for the PD group. A total of 36% of the HD group and 51% of the PD group used either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers as an antihypertensive medication, respectively. At 2 weeks after the second dose of vaccine, a median (95% confidence interval [CI]) of anti-RBD IgG antibody was significantly greater in the healthy controls than patients with ESKD: 1767 (95% CI, 312–7870) versus 590 (95% CI, 219–1427) AU/ml ($P < 0.01$; Figure 1).

In comparison, the median anti-RBD IgG antibody response elicited by a 2-dose form of an inactivated whole-virus SARS-CoV-2 vaccine was comparable between the HD and the PD groups: 601 (95% CI, 20–4145) versus 537 (95% CI, 20–1783) AU/ml ($P = 0.10$; Figure 2). Seroconversion rates, defined by anti-RBD IgG level >50 AU/ml, were slightly

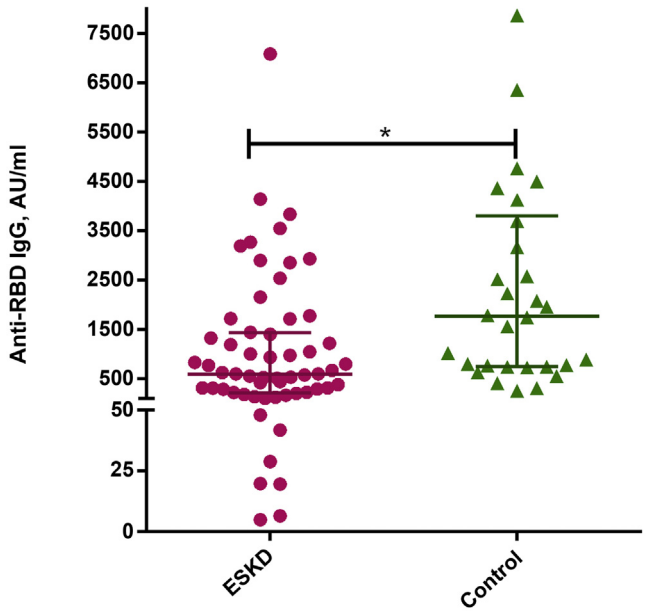

Figure 1 | A median with an interquartile range of anti–receptor-binding domain (RBD) IgG antibody in patients with end-stage kidney disease (ESKD) and healthy controls at 2 weeks after the second dose of inactivated whole-virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine. *$P < 0.05$. AU, arbitrary unit.

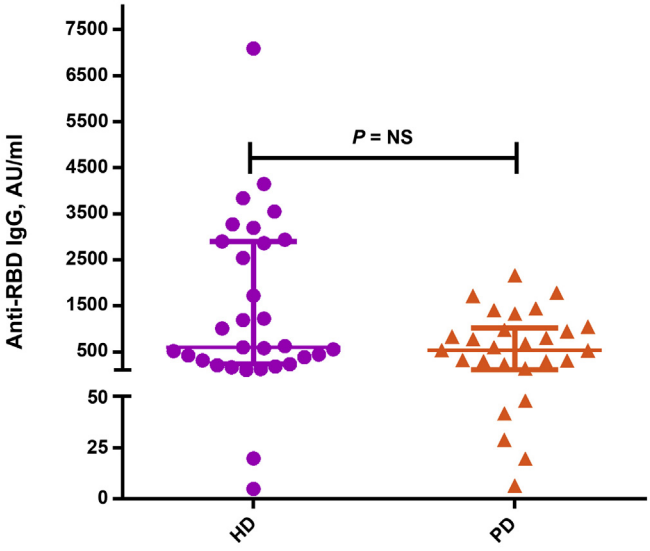

Figure 2 | A median with an interquartile range of anti–receptor-binding domain (RBD) IgG antibody in patients requiring maintenance hemodialysis (HD) and peritoneal dialysis (PD) treatment at 2 weeks after the second dose of inactivated whole-virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine. AU, arbitrary unit; NS, not significant.

better in patients on maintenance HD in comparison to patients on PD treatment, at 94% and 83%, respectively ($P = 0.25$). There was also a marginally significant trend of greater seroconversion rates among healthy controls than patients with ESKD (100% vs. 88%; $P = 0.051$). There were 12 (60%) patients in the control group and 21 (35%) patients in the ESKD group who reported mild adverse reactions in the early postvaccination period. Those adverse reactions included low-grade fever, headache, myalgia, and pain around the injection site.

Our preliminary report suggests that patients with ESKD requiring maintenance dialysis raised satisfactory humoral seroconversion response rates at 2 weeks after the second dose of an inactivated whole-virus SARS-CoV-2 vaccine. However, patients with ESKD developed lower levels of anti-RBD antibodies compared with healthy individuals. Adverse reactions were infrequent and relatively mild. Although obtained in a small number of patients, these data suggest that the immune response to CoronaVac is comparable to that achieved with mRNA and adenoviral-vectored vaccines. Further study including neutralizing antibody and cell-mediated immunity, is encouraged to better explore immunogenicity in these specific populations (Thai Clinical Trials Registry, TCTR20210226002).

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[1]Division of Nephrology, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; [2]Banphaeo-Charoenkrung Peritoneal Dialysis Center, Banphaeo Dialysis Group, Banphaeo Hospital, Bangkok, Thailand; [3]Division of Infectious Diseases, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand; and [4]Immunology Laboratory, Department of Pathology, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Correspondence: *Jackrapong Bruminhent, Division of Infectious Diseases, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, 270 Rama VI Road, Ratchathewi, Bangkok 10400, Thailand. E-mail: jackrapong.brm@mahidol.ac.th*

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Angiotensin-converting enzyme 2 decreased expression during kidney inflammatory diseases: implications to predisposing to COVID-19 kidney complications

To the editor: Although angiotensin-converting enzyme 2 (ACE2) is the receptor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) entry into target cells, it has a major anti-inflammatory role by hydrolyzing angiotensin II, a proinflammatory mediator, to angiotensin 1-7, an anti-inflammatory molecule.

Kidneys are a common target of SARS-CoV-2 infection. Both roles for direct viral infection and downstream effects of a cytokine storm syndrome have been suggested as mechanisms driving kidney injury in patients with coronavirus disease 2019 (COVID-19).[1]

It was recently reported that patients with glomerulonephritis have higher mortality and risk of acute kidney injury associated with SARS-CoV-2 infection.[2] We hypothesize that downregulation of the ACE2/angiotensin 1-7 pathway may account for higher kidney complications in these patients. We found both mRNA and protein expression of ACE2 is reduced in models of inflammation targeting glomeruli (anti–glomerular basement glomerulonephritis) and the tubulointerstitium (tubulointerstitial nephritis) compared with a normal kidney (Figure 1a–c). This is consistent with reduced ACE2 mRNA and protein expression in human kidney inflammatory diseases, including diabetic and IgA nephropathies.[3] We also identified that angiotensin 1-7, the product of ACE2, inhibits macrophage migration to C-X-C Motif Chemokine Ligand 16 (CXCL16), C-C Motif Chemokine Ligand 2 (CCL2)/Monocyte chemoattractant protein-1 (MCP-1), and C-C Motif Chemokine Ligand 5 (CCL5)/Regulated upon Activation, Normal T-Cell Expressed and Presumably Secreted (RANTES) chemokines (Figure 1d). Angiotensin 1-7 also suppresses glomerular endothelial cell CXCL10/interferon-γ–inducible protein 10 (IP10)–angiotensin II dependent induction (Figure 1e). Notably, angiotensin 1-7 infusion in rats with anti–glomerular basement glomerulonephritis