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.

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SARS-CoV-2–reactive cellular and humoral immunity in hemodialysis population

see commentary on page 1275

To the editor: The outcome of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in patients receiving hemodialysis (HD) is significantly worse compared with the general population.[1–3] Whether the SARS-CoV-2–specific immunity in patients with coronavirus disease 2019 (COVID-19) receiving dialysis is impaired as a possible cause for the inferior outcome is not known so far.

We performed an observational case-control study comparing the frequencies and functionality of SARS-CoV-2–reactive T cells as well as antibody titers in 14 COVID-19 convalescent patients receiving HD with 14 age-, sex-, and COVID-19–presentation matched patients with normal renal function (Supplementary Table S1).

In general, the frequencies of SARS-CoV-2 spike, nucleocapsid, and membrane protein-reactive T cells in patients receiving HD and patients with normal renal function were similar (Table 1; Supplementary Figure S1A). Spike-specific antibody titers were also comparable in both groups (Supplementary Figure S1B). Frequencies of SARS-CoV-2–reactive $CD4^+$ and $CD8^+$ T cells producing effector cytokines granzyme B, interleukin-2, tumor necrosis factor, and interferon-γ were similar or, for certain cytokines, even significantly higher in patients receiving HD compared with patients with normal renal function (Table 1; Supplementary Figure S1C). Patients receiving dialysis demonstrated higher frequencies of memory SARS-CoV-2–reactive T cells (Supplementary Figure S2).

To our knowledge, this exploratory study suggests for the first time that patients receiving dialysis are able to generate efficient T-cell immunity, as demonstrated by their multiple cytokine production. The magnitude and functionality of SARS-CoV-2–reactive T cells was comparable or even higher than in patients with normal renal function. Further larger studies are required to confirm our observation.

SUPPLEMENTARY MATERIAL

Supplementary File (Word)

Supplementary Methods.

Table S1. Cohort characteristics.

Figure S1. Frequency of SARS-CoV-2–reactive T cells. Isolated PBMCs from dialysis (n = 14) and nondialysis patients with normal renal function (n = 14) after a SARS-CoV-2 infection were stimulated for 16 hours with 1 μg/ml of SARS-CoV-2 OPPs from the M (n = 13/14), N (n = 13/14), or S (n = 14/14) protein. SARS-CoV-2–reactive T helper cells were identified as Life/Dead-Marker$^-$CD3$^+$CD4$^+$CD137$^+$CD154$^+$, and SARS-CoV-2–reactive cytotoxic T cells were identified as Life/Dead-Marker$^-$CD3$^+$CD8$^+$CD137$^+$. (**A**) Frequencies of total SARS-CoV-2–reactive CD4$^+$CD137$^+$CD154$^+$ and CD8$^+$CD137$^+$ T cells reactive to the M, N, or S protein combined are shown. (**B**) Comparison of the relative titers of SARS-CoV-2 Spike-protein–specific IgG antibodies of

Table 1 | Frequency of SARS-CoV-2–reactive T cells in dialysis and nondialysis patients

		$CD4^+CD154^+CD137^+$			
Group, %	$CD4^+CD154^+CD137^+$	+Granzyme B^+	+IFN-γ^+	+IL-2^+	+TNF^+
Dialysis	0.7745 (0.057–1.57)	0.02029 (0–0.134)	0.1538 (0.017–0.437)	0.42 (0.054–0.651)	0.282 (0.02–0.588)
Nondialysis	0.237 (0.031–0.734)	0 (0–0.025)	0.0255 (0–0.195)	0.1165 (0.023–0.3)	0.0705 (0.012–0.223)
		$CD8^+CD137^+$			
Group, %	$CD8^+CD137^+$	+Granzyme B^+	+IFN-γ^+	+IL-2^+	+TNF^+
Dialysis	0.355 (0.187–1.21)	0.2795 (0.08–0.61)	0.0225 (0–0.1665)	0.0225 (0–0.096)	0.085 (0–0.15)
Nondialysis	0.1325 (0–0.33)	0.0205 (0–0.107)	0 (0–0.06)	0 (0–0.018)	0 (0–0.045)

IFN-γ, interferon-γ; IL-2, interleukin-2; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TNF, tumor necrosis factor.
Frequency of SARS-CoV-2–reactive $CD4^+$ or $CD8^+$ T cells among all $CD4^+$ or $CD8^+$ T cells. Data are given as median (95% confidence interval).

dialysis patients (n = 10) and nondialysis patients with normal renal function (n = 14), measured by ELISA and evaluated as the ratio to an internal control for samples with SARS-CoV-2–specific $CD4^+$ T cells. (**C**) Identification of cytokine-expressing T cells reactive to the M, N, or S protein combined: expression of Th1 cytokines IFNγ, IL-2, or TNF and granzyme B among antigen-reactive $CD4^+CD137^+CD154^+$ (upper panels) and $CD8^+CD137^+$ (lower panels) among all $CD4^+$ or $CD8^+$ cells, respectively. Groups were compared using a 2-sided, unpaired Mann–Whitney U test. *P* values ≤ 0.05 were defined as significant and are marked by an asterisk.

Figure S2. SARS-CoV-2–reactive memory T-cell phenotypes. Isolated PBMCs from dialysis (n = 14) and nondialysis patients with normal renal function as the control (n = 14) with SARS-CoV-2 infection were stimulated for 16 hours with 1 μg/ml of SARS-CoV-2 OPPs from the M (n = 13/14), N (n = 13/14), or S (n = 14/14) protein. Presented are frequencies directed against all proteins combined. (**A**) Identification of antigen-reactive memory T cells: After gating on SARS-CoV-2–reactive $CD4^+CD137^+CD154^+$ and $CD8^+CD137^+$ T cells, memory cells were identified by the expression of CD45RA and CCR7 as naïve ($CD45RA^+CCR7^+$), central-memory (CM, $CD45RA^-CCR7^+$), effector-memory (EM, $CD45RA^-CCR7^-$), and TEMRA ($CD45RA^+CCR7^-$) cells. Comparison of overall SARS-CoV-2–reactive naïve and memory (**B**) $CD4^+CD137^+CD154^+$ and (**C**) $CD8^+CD137^+$ T cells. (**D**) Distribution of naïve and memory SARS-CoV-2–memory T-cell populations. Groups were compared using a 2-sided, unpaired Mann–Whitney U test. *P* values ≤ 0.05 are marked by an asterisk.

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Antibody response to the BNT162b2 vaccine in maintenance hemodialysis patients

see commentary on page 1275

To the editor: Patients receiving maintenance hemodialysis (MHD) may have altered vaccine responses.[1] Although mRNA vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have demonstrated dramatic efficacy in preventing symptomatic forms of coronavirus disease 2019 (COVID-19) in the nondialysis population,[2] the characterization of vaccine response in patients receiving MHD remains a major unmet need.

We studied the humoral response after the BNT162b2 mRNA vaccine using anti–spike(S)1 IgG antibody (Beckman Coulter Access; reference range for antibody positivity signal-to-cutoff >1; gray zone, 0.8–1) in a single-center cohort of 69 patients receiving MHD.

Three hundred seventy-eight samples were analyzed (Figure 1). Thirteen patients (19%) had a history of previous COVID-19 or positive baseline serology. Samples until week 6 to 7 were available for 64 patients. Overall seropositivity rate at last follow-up was 55 of 64 (86%) (Supplementary Table S1). Patients aged >70 years were less likely to reach seropositivity at last follow-up (28 of 37 [75%]; $P = 0.01$; Supplementary Table S1). Conversely, immunocompromised status did not influence the seroconversion rate (7 of 8 [87%] seropositive among immunocompromised patients). The rate of early seropositivity was associated with a history of COVID-19 (Supplementary Table S2). Since week 2, the mean anti-S1 levels of these patients were significantly higher than those of infection-naïve individuals, even after both injections (Supplementary Table S3; Figure 1a). No difference in patient characteristics was observed between both groups (Supplementary Table S3). Among infection-naïve patients, anti–S1 IgG levels progressively increased among time (Figure 1b). The seropositivity rate was 10 of 56 (18%) before the second injection and 43 of 52 (82%) at last follow-up (Supplementary Tables S3–S5). Older age was associated with a reduced late seropositivity rate (Supplementary Table S5). Interestingly, 2 infection-naïve patients developed paucisymptomatic SARS-CoV-2 infection 5 and 6 weeks after first vaccine dose. Anti-S1 titers were 0.5 and 1.4, respectively, in these patients.

In this analysis of postvaccine humoral response, patients receiving MHD have an overall anti-S1 seropositivity rate