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protect dialysis patients, for the time being we cannot let our guard down, even after vaccination.

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Experience with SARS-CoV-2 BNT162b2 mRNA vaccine in dialysis patients



see commentary on page 1275

To the editor: The immune system is profoundly affected by uremia. Patients with end-stage kidney disease (ESKD) may be more vulnerable to infections and may have suboptimal response to vaccination.¹ Patients with ESKD and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease 2019 [COVID-19]) are at increased risk of infection and mortality.^{2–4} The first emergency-use authorizations for COVID-19 vaccines were granted by the Food and Drug Administration in December 2020, and clinical trials for the approval of more vaccines are ongoing. However, the representation of patients with chronic kidney disease and ESKD in these trials is low or unreported.⁵ The Pfizer BioNTech trial of the BNT162b2 vaccine included 256 patients with renal disease with no further details on the

Table 1 | Participants and response to BNT162b2 mRNA vaccine

Variable	Dialysis patients (n = 160)	Control group (n = 132)	P value
Age, median [IQR], yr	69 [62–78]	50.5 [41–60]	<0.001
Male	101 (63)	67 (51)	0.022
Female	59 (37)	65 (49)	
Hemodialysis	127 (79)	—	—
Peritoneal dialysis	33 (21)	—	—
Dialysis vintage, median [IQR], yr	3.21 [1.60–5.39]	—	—
Anti-spike antibody negative (<15 AU/ml)	16 (10)	0	<0.001
Anti-spike antibody level, median [IQR], AU/ml	116.5 [66.0–160.0]	176.5 [142–235]	<0.001
COVID-19 infection after complete vaccination	6 (3.75)	0	0.033

AU, arbitrary unit; COVID-19, coronavirus disease 2019; IQR, interquartile range. Data are given as n (%), unless otherwise indicated.

stages of the chronic kidney disease.⁶ We investigated dialysis patients and a control group who had completed 2 doses of vaccination with the mRNA BNT162b2 vaccine for anti-spike protein antibody response (LIAISON SARS-CoV-2 S1/S2 IgG; DiaSorin) and observed them for up to 10 weeks (for detailed methods, see the [Supplementary Methods](#)).

A total of 160 chronic dialysis patients (127 hemodialysis and 33 peritoneal dialysis patients) and 132 control group persons were analyzed (Table 1). The median age of the dialysis group was 69 years (interquartile range [IQR], 62–78 years), and of the control group, 50.5 years (IQR, 41–60 years; $P < 0.001$). A total of 63% in the dialysis group and 51% in the control group were men ($P = 0.022$). In the dialysis group, 79% were on hemodialysis and 21% were on peritoneal dialysis. The median dialysis vintage was 3.2 years (IQR, 1.6–5.4 years).

A total of 90% of the dialysis group and 100% of the control group were positive for anti-spike antibodies ($P < 0.0001$). The median level of anti-spike antibody was 116.5 arbitrary unit (AU)/ml (IQR, 66–160 AU/ml) in the dialysis group and 176.5 AU/ml (IQR, 142–235 AU/ml) in the control group ($P < 0.001$).

In the dialysis group, in patients aged ≥ 75 years, the median anti-spike antibody level was 99.5 AU/ml (IQR, 28.75–139.5 AU/ml), and in patients aged < 75 years, the median level was 122 AU/ml (IQR, 72.8–167.0 AU/ml; $P = 0.035$) (Supplementary Figure S1).

In the dialysis group, we compared the lowest anti-spike antibody level quartile group (antibody level, < 3.8 to 66 AU/ml) with the highest anti-spike antibody level quartile (160 to > 400 AU/ml); the median age in the lowest quartile was 72 years (IQR, 66.25–81.00 years), and in the highest quartile, 67 years (IQR, 56.25–74.00 years; $P = 0.02$). These 2 subgroups did not differ in dialysis modality, dialysis vintage, and sex distribution (Supplementary Table S1).

Six hemodialysis patients (3.75%) and none in the control group developed a new COVID-19 infection (confirmed by positive COVID-19 reverse transcriptase–polymerase chain reaction) > 7 days after completion of the recommended vaccination regimen ($P = 0.033$). Epidemiological investigation

indicated that the infection was acquired from family members in 2 patients, at the dialysis facility in the other 2 patients, in a religious gathering in another patient, and from an unknown source for 1 patient. The virus variant was determined in 2 patients, and the B.1.1.7 – UK (L5F[S]) variant was confirmed. All 6 patients had symptoms compatible with COVID-19 infection. The clinical course was severe for 1 patient, moderate for 3 patients, and mild for 2 patients. All of them recovered (Supplementary Table S2). Of these 6 patients, 4 had an anti-spike antibody level in the lowest quartile (<3.8–66 AU/ml); in the other 2 patients, blood samples for antibody levels were not obtained before the diagnosis of COVID-19 infection. One patient in this group received long-term steroid treatment and had a history of kidney transplant.

Sixteen patients (10%) in the dialysis group were negative for anti-spike antibodies. When compared with the dialysis patients who were positive for anti-spike antibodies, there was no difference in age, sex, dialysis modality, and dialysis vintage (Supplementary Table S3). Two patients in this group had had a past kidney transplant, and 1 patient had active malignancy. None of these patients received recent immunosuppressive therapy. All the patients in this group had adequate dialysis dose: KT/V (according to Daugirdas' formula) ≥ 1.2 for the hemodialysis patients and ≥ 1.7 weekly KT/V for the peritoneal dialysis patients.

In this study, our main findings are (i) a lower response rate to the vaccine, (ii) a lower anti-spike antibody level, and (iii) a higher rate of COVID-19 infection after vaccination in the dialysis group. We found a lower anti-spike antibody response rate in dialysis patients compared with a control group representative of the general population. In the group of 16 patients with negative antibody response, we did not find a difference in age, sex, dialysis modality, and dialysis vintage when compared with dialysis patients who developed anti-spike antibodies in response to the vaccine. All 16 patients had adequate dialysis dose. Only 3 patients had other medical conditions that could have contributed to the blunt antibody response. Similar findings of decreased antibody response to vaccination in the dialysis population are reported also for other vaccines^{1,7} and may be explained by the aberrations in immune response characterizing ESKD. The median anti-spike antibody level was lower in the dialysis group when compared with the control group. Older age in our dialysis group was associated with lower anti-spike antibody levels. It is not yet clear if higher level of antibodies after COVID-19 infection correlates with better protection,^{8,9} and there are no reports of a correlation between the level of antibodies following vaccination and protection from future COVID-19 infection.

Six hemodialysis patients, comprising 3.75% of this group, developed a new COVID-19 infection >7 days after completion of the 2-dose vaccination. This rate is higher than that reported (0.043%) of new infection in the phase 3 clinical trial of BNT162b2⁶ and is also higher than 0 events in our control group. It is possible that evolving SARS-CoV-2 variants may be associated with different rates of protection of the vaccine, but the participants in both of our groups live in the same area and were vaccinated and investigated at the same time. Therefore, different virus

variants are less likely to contribute to the between-group difference. The anti-spike antibody levels in patients who developed COVID-19 infection after vaccination were in the lowest quartile. The assumption of a correlation between antibody levels and protection from future COVID-19 infection should be further investigated.

Some important issues remain unanswered: What is the immunogenicity pattern for other vaccines? Should we routinely determine antibody response in dialysis patients following vaccination against COVID-19? Should we give a booster dose(s) when the antibody level is low?

Considering the results of our study, and although many limitations related to COVID-19 are expected to ease in the near future, we may consider maintaining physical distancing and other recommended measures in place for protection of the dialysis population.

Our findings are limited by a relatively small number of participants and a short-term follow-up.

SUPPLEMENTARY MATERIAL

Supplementary File (Word)

Supplementary Methods.

Figure S1. Anti-spike antibody levels in dialysis patients, patients aged <75 years and ≥ 75 years.

Table S1. Comparisons of dialysis patients in the lowest and highest antibody-level quartiles.

Table S2. Details of 6 patients with COVID-19 infection after vaccination.

Table S3. Comparison of dialysis patients with negative and positive antibody responses.

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Low immunization rates among kidney transplant recipients who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine



see commentary on page 1275

To the editor: The efficacy rates of vaccines to prevent infection with severe acute respiratory syndrome coronavirus

2 (SARS-CoV-2) have not been specifically investigated in kidney transplant recipient (KTRs). Preliminary results suggest that among KTRs who received the first injection of an mRNA-based vaccine, the antibody response is weak.^{1,2} This study reports on the immunization rates of KTRs who received 2 doses of the mRNA-1273 SARS-CoV-2 vaccine (Moderna).³

All participants had a negative history for coronavirus disease 2019 (COVID-19) and tested negative for anti-SARS-CoV-2 antibodies on the day of first injection. Serologic response was assessed on the day of the second injection and 1 month thereafter using the ARCHITECT IgG II Quant test (Abbott). Titers >50 arbitrary units (AUs)/ml were considered positive (detection range, 6.8–80,000 AUs/ml). This assay is reported to correlate with *in vitro* virus neutralization.⁴

The study sample consisted of 205 KTRs (Table 1). Only 98 patients displayed a positive serology 28 days after the second dose. The median antibody titer was 803.2 AUs/ml (interquartile range, 142.6–4609.6 AUs/ml). Compared with patients who did not respond after the first injection, patients with a positive serology after the first dose (n = 24 [11.7%]) displayed a higher antibody titer after the second injection (104 vs. 9415 AUs/ml, respectively; $P = 7.3^{-11}$). Antibody titers measured 1 month after the first and second

Table 1 | Characteristics of kidney transplant recipients stratified according to the serologic response after 2 doses of the mRNA-1273 SARS-CoV-2 vaccine

Characteristics	Entire cohort (n = 204) ^a	SARS-CoV-2-seronegative patients (n = 106)	SARS-CoV-2-seropositive patients (n = 98)	P	Missing data
Age, yr	57.7 (49.4–67.5)	58 (51–67.7)	57.3 (46.9–66.2)	0.45	0
Male sex	130 (63.8)	66 (62.3)	64 (65.3)	0.66	0
BMI, kg/m ²	25.6 (22.4–28.5)	25.4 (22.3–27.6)	25.9 (22.6–29.9)	0.3	2
Time from kidney transplantation, yr	6.2 (3–12.8)	5.4 (2.4–12)	7.1 (3.8–14.7)	0.04	1
First transplantation	170 (83.3)	80 (75.5)	90 (91.8)	0.002	0
Deceased donor	163 (79.9)	84 (79.3)	79 (80.6)	0.86	0
ABO group				0.1	2
O	84 (41.6)	38 (36.5)	46 (46.9)		
A	86 (42.6)	48 (46.2)	38 (38.8)		
B	11 (10.9)	15 (14.4)	7 (7.1)		
AB	10 (5)	3 (2.9)	7 (7.1)		
Induction treatment				0.5	9
Anti-thymocyte globulin	118 (60.5)	63 (61.8)	55 (59.1)		
Anti-CD25	70 (35.9)	37 (36.3)	33 (35.5)		
No induction	7 (3.6)	2 (2)	5 (5.4)		
CNI				0.13	0
Tacrolimus	115 (56.4)	67 (63.2)	48 (49)		
Cyclosporine	73 (35.8)	32 (30.2)	41 (41.8)		
No CNI	16 (7.8)	7 (6.6)	9 (9.2)		
MMF/MPA	161 (78.9)	91 (85.9)	70 (71.4)	0.02	0
Azathioprine	6 (2.9)	0	6 (6.12)	0.01	0
mTOR inhibitors	27 (13.2)	9 (8.5)	18 (18.4)	0.04	0
Steroids	122 (59.8)	69 (65.1)	53 (54.1)	0.12	0
Tacrolimus + MMF/MPA	98 (48)	60 (56.6)	38 (38.8)	0.001	0
Tacrolimus + MMF/MPA + steroids	64 (31.3)	46 (43.4)	18 (18.4)	0.0001	0
Belatacept	5 (2.5)	4 (3.8)	1 (1)	0.37	0
eGFR, ml/min per 1.73 m ²	57.1 (42.4–70.6)	54.4 (38.1–67.5)	62.5 (47.8–72.5)	0.004	1
Serum creatinine, μmol/L	120 (100–161)	137 (109–173)	110 (96–141)	0.0003	1

BMI, body mass index; CNI, calcineurin inhibitor; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; MMF, mycophenolate mofetil; MPA, mycophenolic acid; mTOR, mammalian target of rapamycin; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Continuous variables are presented as medians (interquartile ranges), whereas categorical variables are given as n (%).

^aThe patient who developed COVID-19 was excluded from the analysis.