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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References

1. Cheng X, Wu B, Liu Y, Mao H, Xing C. Incidence and diagnosis of acute kidney injury in hospitalized adult patients: a retrospective observational study in a tertiary teaching hospital in Southeast China. *BMC Nephrol*. 2017;18:203.
2. Al-Jaghbeer M, Dealmeida D, Bilderback A, Ambrosino R, Kellum JA. Clinical decision support for in-hospital AKI. *J Am Soc Nephrol*. 2018;29:654-660.
3. Park S, Baek SH, Ahn S, et al. Impact of Electronic Acute Kidney Injury (AKI) Alerts With Automated Nephrologist Consultation on Detection and Severity of AKI: A Quality Improvement Study. *Am J Kidney Dis*. 2018;71:9-19.
4. Carli D, Fahrni G, Bonnabry P, Lovis C. Quality of Decision Support in Computerized Provider Order Entry: Systematic Literature Review. *JMIR Med Inform*. 2018;6:e3.
5. Kidney Disease: Improving Global Outcomes (KDIGO) Work Group. KDIGO clinical practice guildeline for acute kidney injury. *Kidney Int Suppl*. 2012;2:1-138.

Immunogenicity of BNT162b2 SARS-CoV-2 Vaccine in a Multicenter Cohort of Nursing Home Residents Receiving Maintenance Hemodialysis

To the Editor:

We recently reported that almost all maintenance hemodialysis (MHD) patients mount specific antibodies within a month of COVID-19 onset.[1] However, evidence concerning the immunogenicity of SARS-CoV-2 vaccines in this immunodeficient population is scarce.[2]

We prospectively assessed the response to BNT162b2, a messenger RNA vaccine encoding the spike protein, in a multicenter cohort of MHD patients living in nursing homes and compared their antibody response with that observed in a group of nondialyzed nursing home residents.

Following approval by the European Medicines Agency of mRNA vaccines developed by Pfizer-BioNTech and Moderna, Belgian health authorities prioritized nursing home residents for vaccination. We included all nursing home residents on in-center HD at 5 UCLouvain network hospitals. A cohort of nondialyzed nursing home residents, matched for COVID-19 history, served as controls. All participants received 2 BNT162b2 doses, 21 days apart. Serum samples were taken on day 28 after the first dose (the time of peak neutralizing antibodies in phase 1 trials)[3] and on days 49 and 77, the latter only in MHD patients. Comorbidities listed by the Centers for Disease Control as risk factors for severe COVID-19 were recorded.[4]

Serum samples were tested with 2 electrochemiluminescent assays from Roche Elecsys for SARS-CoV-2 antibodies: a qualitative immunoassay using a recombinant nucleocapsid antigen (anti–SARS-CoV-2 N), and a quantitative immunoassay using the spike receptor-binding domain (anti–SARS-CoV-2 RBD). Both tests have a very high sensitivity and specificity, and the anti-RBD immunoassay correlates well with neutralization tests (Item S1).

Groups were compared using Mann-Whitney, Kruskal-Wallis, or χ^2 tests, as appropriate. Statistical analyses used Stata (v16) and GraphPad Prism (v8). All tests were 2-tailed and $P < 0.05$ was considered significant.

Thirty-four MHD patients and 45 controls were included. SARS-CoV-2 infection was previously diagnosed in 10 MHD patients (by qPCR on a nasopharyngeal swab) and 12 controls (by periodic serologic testing); controls were significantly older and had fewer comorbidities than MHD patients (Table 1). On day 28, anti-N antibodies were detected in all but 3 MHD patients with prior COVID-19, 2 of whom were first qPCR positive the day of the first vaccine dose. All participants without known prior COVID-19 were seronegative for anti-N antibodies.

On day 28, proportions of those without a history of COVID-19 who developed anti-RBD antibodies were similar ($P = 0.6$) in MHD patients (19/24 [79%]) and controls (28/33 [85%]). All participants with prior COVID-19 mounted an anti-RBD response, except 1 MHD patient who was first qPCR positive on the day of first vaccination. Anti-RBD levels were not statistically different in MHD patients and controls, both in groups with and without prior COVID-19 (Table 2). The humoral response in MHD patients was sustained until day 77. Responders to the vaccine did not differ from nonresponders in demographics and comorbidities (Table 1, Table S1), except for the presence of anti-N antibodies (more prevalent in responders, $P = 0.04$) and liver disease (more prevalent in nonresponders, $P = 0.007$). By June 1, 2021, no case of

Table 1. Baseline Characteristics

	Controls (n = 45)	MHD (n = 34)	*P*
Age, years	88 [85-90]	81 [74-87]	<0.001
Female sex	29 (64%)	19 (56%)	0.4
Hypertension	23 (51%)	25 (74%)	0.04
Diabetes	2 (4%)	14 (41%)	<0.001
Obesity	4 (9%)	6 (18%)	0.3
Cardiovascular disease	10 (22%)	14 (41%)	0.07
Stroke	2 (4%)	10 (29%)	0.002
COPD or asthma	4 (9%)	5 (15%)	0.4
Liver disease	0 (0%)	3 (9%)	0.04
Dementia	0 (0%)	6 (18%)	0.003
History of cancer	7 (16%)	4 (12%)	0.6
Active cancer	2 (4%)	4 (12%)	0.2
Immunosuppressive therapy	4 (9%)	0 (0%)	0.07
HIV infection	2 (4%)	0 (0%)	0.2
History of COVID-19	12 (27%)	10 (29%)	0.8

Age given as median [interquartile range]; other values as count (%). Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019.

Table 2. Immune Response to SARS-CoV-2 Vaccination Among MHD Patients and Controls

	Comparison Between Groups on Day 28 After First Dose			Longitudinal Follow-up in MHD Patients	
	Controls	MHD	*P*	Day 49	Day 77
No history of COVID-19					
No. of participants	33	24		24	22
Presence of anti-N antibodies	0 (0%)	0 (0%)	–	0 (0%)	0 (0%)
Presence of anti-RBD antibodies	28 (85%)	19 (79%)	0.6	21 (88%)	20 (91%)
Anti-RBD antibodies, U/mL	199 [9-250]	25 [5-250]	0.4	190 [33-250]	118 [26-250]
History of COVID-19					
No. of participants	12	10[a]		10	10
Presence of anti-N antibodies	12 (100%)	7 (70%)[a]	0.04	9 (90%)	9 (90%)
Anti-N antibodies[b]	94 [34-158]	25 [1-56]	0.8	50 [13-64]	44 [31-59]
Presence of anti-RBD antibodies	12 (100%)	9 (90%)	0.3	10 (100%)	10 (100%)
Anti-RBD antibodies, U/mL	250 [250-250]	250 [250-250]	0.6	250 [250-250]	250 [250-250]

Values given as count (%) or median [interquartile range].
[a]Including the 2 MHD patients who tested positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by quantitative polymerase chain reaction (qPCR) on a nasopharyngeal swab on the day of the first vaccine dose.
[b]Cut-off index (chemiluminescent signal of sample/cut-off value).

severe COVID-19 was observed in MHD patients or in controls.

Around 80% of the included nursing home residents on MHD mounted anti-RBD antibodies 1 week after the second BNT162b2 dose, despite advanced age and multiple comorbidities. Moreover, the humoral response was sustained until day 77 after the first dose. Nevertheless, although this did not reach statistical significance (likely owing to the small sample size), anti-RBD level on day 28 was lower in MHD patients than in controls without COVID-19 history (25 and 199, respectively). Yet, no severe COVID-19 was observed among MHD patients by June 1, 2021; however, their lower peak antibody titers may be associated with a shorter duration of clinical efficacy, as observed with other vaccines.[5] Grupper et al[6] recently documented a humoral response in 54 of 56 (96%) vaccinated MHD patients. However, their patients were younger (mean age 74) and did not have serologic testing for prior COVID-19, and the level of anti-RBD antibodies was measured 1 month after the second vaccine dose, all factors potentially complicating comparison with our results.[3,7] In a recent nationwide mass-vaccination study, the clinical effectiveness of BNT162b2 was similar across age groups (with >70,000 participants aged >70 years).[8]

Our results demonstrate the immunogenicity of the vaccine in elderly patients on MHD with extensive comorbidities. Since the immunogenicity of other vaccines and duration of specific immunity is lower in MHD patients than in the general population,[5] serological follow-up may help determine optimal immunization schedules.

As recently documented in the general population,[7] anti-RBD levels are 10-fold higher in vaccinated MHD patients with preexisting COVID-19 than in those without. Moreover, 8 out of 10 seropositive MHD patients elicited rapid and maximal immune responses, with anti-RBD levels above the upper level of measurement (>250 U/mL), even 7-13 days after the first dose in 2 of them.

A definite strength of this study is its multicentric design. Clear limitations are the small sample size, and the focus on a specific population of frail and very ill patients.

In conclusion, around 80% of nursing home residents on MHD develop anti-spike antibodies 1 week after the second dose of the Pfizer-BioNTech mRNA SARS-CoV-2 vaccine, and this response is sustained over 2 months after the second dose. Follow-up studies are needed to assess the durability of the vaccine response in this high-risk population.

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Supplementary Material

Supplementary File (PDF)

Item S1; Table S1.

Article Information

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References

1. Labriola L, Scohy A, Seghers F, et al. A longitudinal, 3-months serologic assessment of SARS-CoV-2 infections in a Belgian hemodialysis facility. *Clin J Am S Nephrol*. 2021;16(4):613-614.
2. Glenn DA, Hegde A, Kotzen E, et al. Systematic review of safety and efficacy of COVID-19 vaccines in patients with kidney disease. *Kidney Int Rep*. 2021;6(9):1407-1410.
3. Walsh EE, Frenck RW, Falsey AR, et al. Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. *N Engl J Med*. 2020;383(25):2439-2450.
4. Centers for Disease Control and Prevention. People with certain medical conditions. Accessed March 5, 2021. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html
5. Labriola L, Jadoul M. The decades-long fight against HBV transmission to dialysis patients: slow but definite progress. *Nephrol Dial Transplant*. 2010;25(7):2047-2049.
6. Grupper A, Sharon N, Finn T, et al. Humoral response to the Pfizer BNT162b2 vaccine in patients undergoing maintenance hemodialysis. *Clin J Am Soc Nephrol*. 2021;16(7):1037-1042.
7. Krammer F, Srivastava K, Alshammary H, et al. Antibody responses in seropositive persons after a single dose of SARS-CoV-2 mRNA vaccine. *N Engl J Med*. 2021;384(14):1372-1374.
8. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 vaccine in a nationwide mass vaccination setting. *N Engl J Med*. 2021;384(15):1412-1423.