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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Kidney International (2021) **100,** 700–702; https://doi.org/10.1016/j.kint.2021.07.002

Reasons for COVID-19 vaccination hesitancy in hemodialysis patients

To the editor: We read the excellent series of reports and editorial on the effectiveness of vaccination in patients on dialysis.[1] We would concur that although vaccination is less effective in these high-risk patients it remains critical to ensure our at-risk population remains as protected as possible. We would draw attention to the other significant challenge in such a population, namely hesitancy toward vaccination in patients on maintenance dialysis. Vaccine hesitancy is defined by the World Health Organization as a delay in acceptance or refusal of safe vaccines despite availability of vaccine services. We have completed vaccination of our large cohort of patients on renal replacement therapy and have found that while a substantial portion agreed to vaccination, hesitancy still exists in approximately 3% (12 of 378) of our patients. Various reasons for declining the vaccination by these patients are detailed in Table 1. Because others have reported even higher rates of unvaccinated patients on dialysis (and between 8% and 41% may display vaccine hesitancy, depending on ethnicity, sex, age, and deprivation[2]), this represents a significant risk to the remaining cohort of patients and staff as we approach considering booster vaccinations this winter to minimize further COVID-19 disease spikes. A mandatory vaccination is a potential solution for minimizing the risk but could be considered a controversial approach that may interfere with patients' autonomy and choice. The nephrology community needs to provide recommendations that involve a universal thoughtful process.

Table 1 | Reasons given by patients on hemodialysis for not being vaccinated with any of the available COVID-19 vaccines

No. of patients	Reason
2	"Their choice"—no faith in the COVID-19 vaccines.
1	Noncompliant with all treatments and did not wish additional treatment.
1	Refused to give reason for not accepting a COVID-19 vaccine.
1	Verbally aggressive to staff when offered and not prepared to give reasons.
1	Believes COVID-19 is just flu and so will not have it—does not take flu vaccine.
1	Refused to consider COVID-19 vaccine and does not want to be approached. Again a patient who has general noncompliance.
3	We are young and we believe the media reports that it is all overhyped and we are not convinced of the benefit.
1	Recovery from a recent long-term illness but may consider it.
1	Stated they are allergic to vaccines, but this is not substantiated.

COVID-19, coronavirus disease 2019.

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Kidney International (2021) **100,** 702; https://doi.org/10.1016/j.kint.2021.07.003

Humoral response after 3 doses of the BNT162b2 mRNA COVID-19 vaccine in patients on hemodialysis

To the editor: Dialysis patients are at increased risk of severe coronavirus disease 2019 (COVID-19) infections.[1] Therefore, they are considered as being a priority population for COVID-19 vaccination. Because immune responses against vaccines are considerably reduced in this population,[2] a vaccination strategy including 3 doses of vaccine has been recommended for dialysis patients. However, few data exist concerning humoral response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination with 3 doses of BNT162b2 (Pfizer–BioNTech) in patients on hemodialysis (HD). Moreover, about 90% of HD patients exhibit antibody positivity after 2

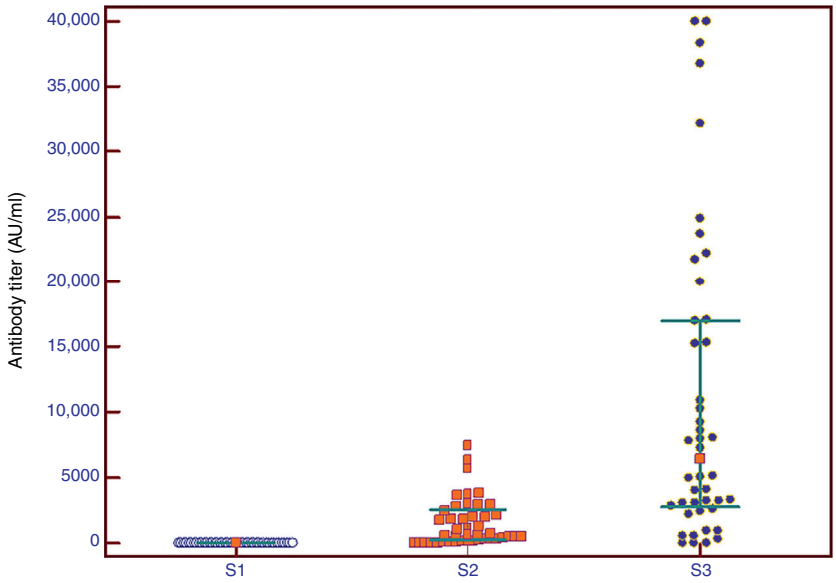

Figure 1 | Antibody titers (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] immunoassay, which Abbott designed to detect IgG antibodies to the receptor-binding domain of the S1 subunit of the spike protein of SARS-CoV-2) before vaccine and after 2 and 3 doses of BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine. AU, arbitrary unit; S1, serology 1 = before vaccine; S2, serology 2 = after 2 doses; S3, serology 3 = after the third dose.

injections of vaccine,[3–6] and the relevance of a third dose is questionable. Nevertheless, only 75% exhibit robust responses after 2 doses, and a vaccine booster may be useful.[7]

We studied vaccine response in 50 HD patients who were COVID-19–naïve (no clinical history, negative serology) having received the BNT162b2 mRNA COVID-19 vaccine

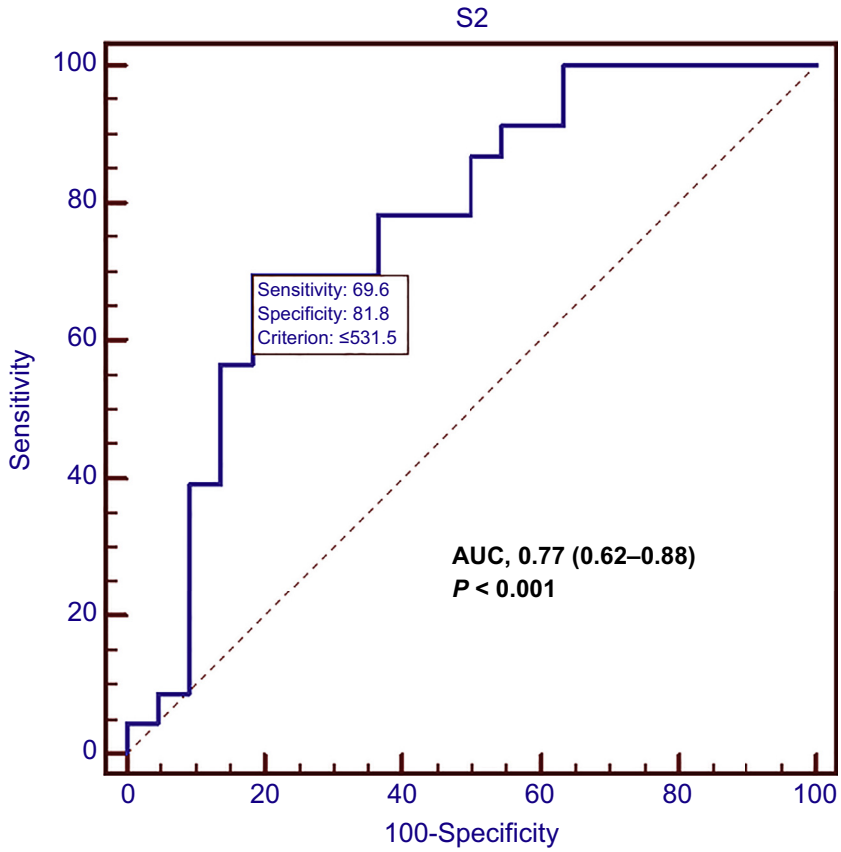

Figure 2 | Receiver operating characteristic curve illustrating the ability of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serology after 2 doses of BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine to predict the increase in antibody titers after a third dose. Data in parentheses are interquartile range. AUC, area under the curve.

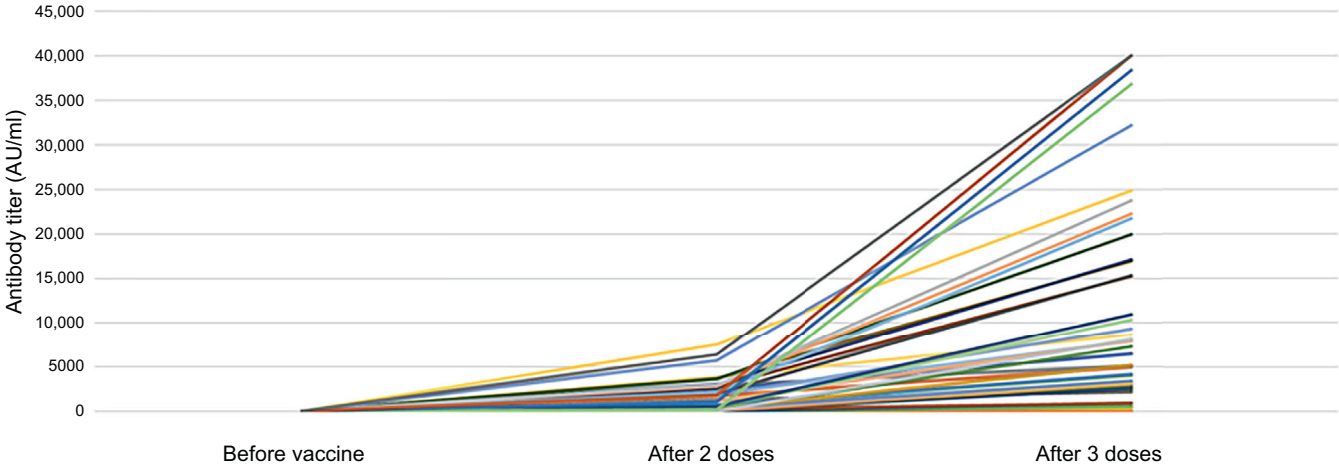

Figure 3| Individual variations in antibody titers (severe acute respiratory syndrome coronavirus 2 [SARS-Cov-2] immunoassay, which Abbott designed to detect IgG antibodies to the receptor-binding domain of the S1 subunit of the spike protein of SARS-CoV-2) during the vaccine scheme. AU, arbitrary unit.

and 15 HD patients with a history of COVID-19 infections. Three doses of vaccine were proposed for naïve patients, and 2 were proposed for those previously exposed to COVID-19.

Forty-five naïve patients received 3 doses, whereas 5 received only 2 doses (refusal of patients). Humoral response was studied using the SARS-CoV-2 immunoassay, Abbott designed to detect IgG antibodies to the receptor-binding domain of the S1 subunit of the spike protein of SARS-CoV-2. As a relevant threshold cannot be determined, we used that provided by the manufacturer.

Among 45 naïve patients having received the 3 doses of vaccine, 40 (89%) had an antibody titer >50 arbitrary units [AU]/ml after 2 doses and 42 (93%) after 3 doses. Among the 5 nonresponders after 2 doses (antibody titer, <50 AU/ml), 2 had a robust response after the third dose (568 vs. 17 AU/ml and 923 vs. 35 AU/ml, respectively). Values of antibody titers were not normally distributed. Median values of antibody titers were 672 AU/ml (interquartile range [IQR]: 213–2528 AU/ml) and 6435 AU/ml (IQR: 2790–17,014 AU/ml) 1 month after the second and the third dose, respectively (Figure 1). After 3 doses, 92% of patients had antibody titers above the median antibody titer observed after 2 doses. Five patients denied a third dose of vaccine. There was no variation in antibody titers in 3 and a significant decline in 2.

Median increase in antibody titers after the third dose was 580%. Explosive response (increase in titer >580%) was inversely related to antibody titer 1 month after the second dose ($R^2 = 0.373$; $P < 0.001$). Those with an antibody titer <531 AU/ml after the second dose had better improvement in response (receiver operating curve characteristics, area under the curve, 0.77 [0.62–0.88]; $P < 0.001$; Figure 2).

Antibody responses after 3 doses of vaccine in those not previously infected were similar to those after prior infection and 2 vaccine doses (5156 AU/ml [1502–21,569 AU/ml]).

We report in a single-center study that 90% of dialysis patients have a vaccine response after 2 doses of BNT162b2 mRNA COVID-19 vaccine. A third dose enhances humoral response in almost all patients (Figure 3), but especially in those with lower antibody titers after 2 doses. Moreover, a fraction of nonresponders after 2 doses develops a strong response after the third dose. Dialysis patients with low humoral response may benefit from a third dose of BNT162b2 mRNA COVID-19 vaccine.

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Kidney International (2021) **100,** 702–704; https://doi.org/10.1016/j.kint.2021.06.025