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Humoral Response to Third Dose of SARS-CoV-2 Vaccines in the CKD Spectrum

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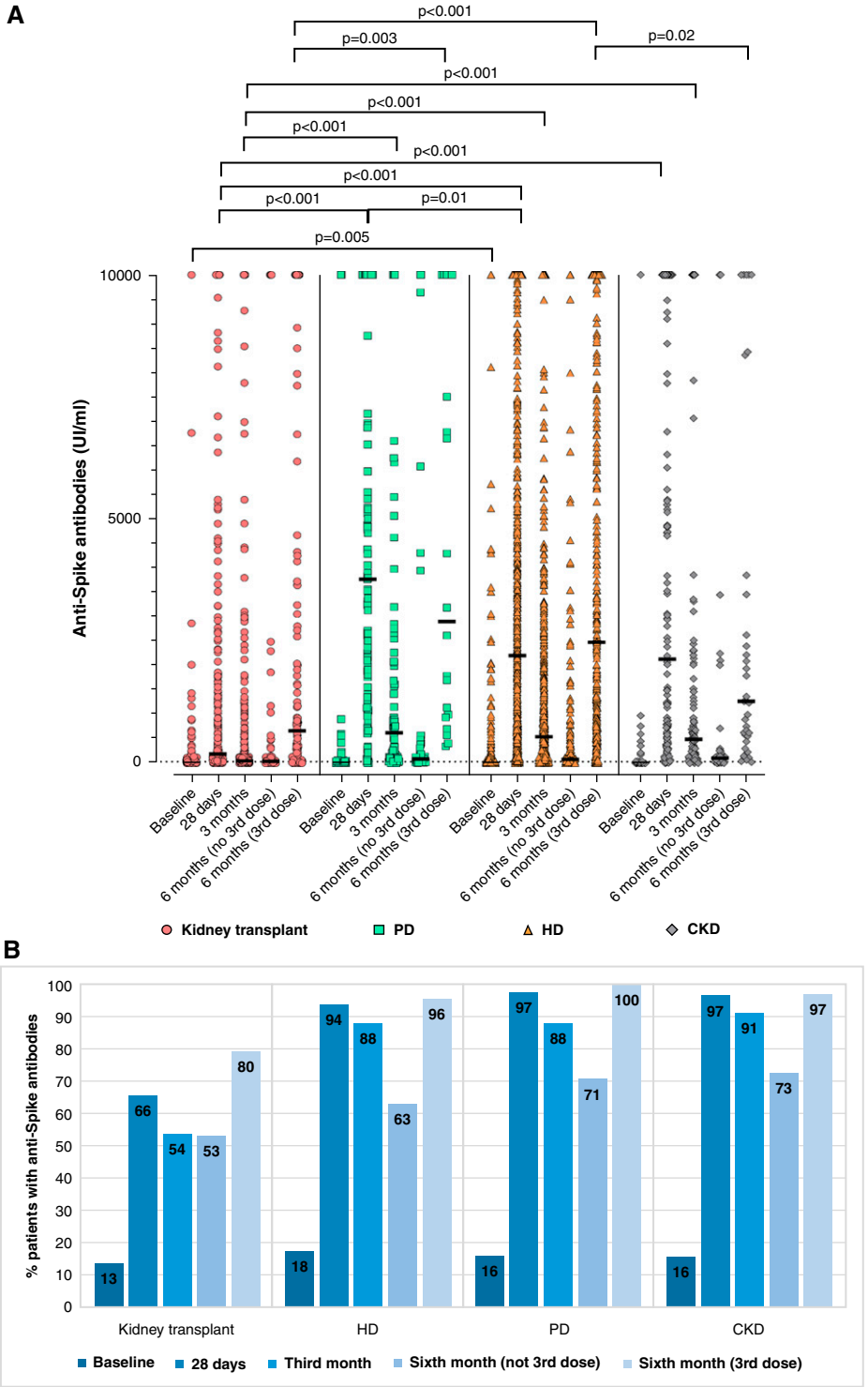
Information on the effect of a third dose of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine in advanced CKD is incomplete (1). We assessed the humoral response up to 6 months after receipt of two or three doses of the SARS-CoV-2 vaccine across the CKD spectrum. SENCOVAC is a prospective, multicentric study of four cohorts of patients with CKD: kidney transplant, hemodialysis (HD), peritoneal dialysis (PD), and nondialysis CKD (eGFR <30 ml/min per 1.73 m^2) (2,3). Patients were vaccinated against SARS-CoV-2 during routine clinical care. Some patients received a third dose of an mRNA vaccine. This depended on the timing of vaccination drives by local health authorities. We assessed anti-Spike antibodies (CLIA, Covid-19 Spike Quantitative Virclia IgG Monotest; Vircell SL, Spain) kinetics at a prespecified 6-month time point after completing the original vaccination schedule (2,3). The study was approved by the ethics committee of Instituto de Investigación Sanitaria-Fundación Jiménez Díaz (IIS-FJD) (February 2021).

Antibody titers were assessed at 28 days in 1736 patients, 3 months in 1371 patients, and 6 months in 1008 patients. At 6 months, 175 (17%) were kidney transplant recipients, 64 (6%) were on PD, 698 (70%) were on HD, and 71 (7%) were patients with CKD. Patients had received two doses of BNT162b2 (Pfizer-BioNTech; 305, 30%) or mRNA-1273 (Moderna; 703, 70%). Additionally, 624 (65%) patients received a third dose (26% BNT162b2, 74% mRNA-1273): 118 (71%) kidney transplant recipients, 20 (37%) patients on PD, 451 (67%) patients on HD, and 35 (51%) patients with CKD. The third dose was given a median of 144 (111–170) days after the second dose (125 [85–156] days in kidney transplant recipients, 145 [125–183] days in patients on PD, 147 [115–174] days in patients on HD, and 148 [125–188] days in patients with CKD).

Six months after completing the initial vaccination schedule, anti-Spike titers were lower in kidney transplant recipients than in patients on HD ($P<0.001$) (Figure 1A). Similarly, among patients with negative baseline anti-Spike antibodies, kidney transplant recipients had lower anti-Spike antibodies titers at 6 months than patients on HD ($P<0.001$). Anti-Spike antibody titers were lower in patients on PD than in those on HD ($P=0.001$). At 6 months, patients who had received a third vaccine dose had higher anti-Spike antibody titers than those without the third dose ($P<0.001$) in all CKD cohorts. Among patients who did not receive a third dose, antibody titers decreased significantly from 3 to 6 months ($P<0.001$).

According to the manufacturer, a positive humoral response was defined as anti-Spike IgG titers >36 U/ml. A positive response at 6 months among those receiving versus not receiving a third dose, by CKD subgroup, was as follows: 94 of 118 (80%) versus 25 of 47 (53%; $P=0.002$) kidney transplant recipients, respectively; 20 of 20 (100%) versus 24 of 34 (71%; $P=0.01$) patients on PD, respectively; 432 of 451 (96%) versus 138 of 217 (64%; $P<0.001$) patients on HD, respectively; and 34 of 35 (97%) versus 24 of 33 (73%; $P=0.02$) patients with CKD, respectively (Figure 1B). These responses were higher than in patients without a third dose ($P<0.001$). Among patients without humoral response at 3 months, 72 (69%) seroconverted after the third dose. The percentage of seroconverted patients was numerically higher with a third dose of mRNA-1273 (58%) than of BNT162b2 (38%; $P=0.07$). Among the CKD cohorts, 36 of 58 (62%) kidney transplant recipients, 34 of 45 (76%) patients



Sample size of each CKD group	Baseline (n=1126)	28 days (n=1736)	Third month (n=1371)	Sixth month (not 3rd dose) (n=331)	Sixth month (3rd dose) (n=624)
Kidney transplant	289	350	302	47	118
HD	622	155	894	217	451
PD	129	1091	75	34	20
CKD	86	140	100	33	35

Figure 1. | **Anti-Spike antibodies during follow-up in CKD cohorts.** (A) Anti-Spike antibodies titers during follow-up in different CKD cohorts. Data show anti-Spike antibodies titers of all patients irrespective of their baseline anti-Spike antibody titers. (B) Presence of anti-Spike antibodies during follow-up in the different CKD cohorts. Data are expressed as the percentage of patients with the presence of anti-Spike antibodies (*i.e.*, titer >36 IU/ml). The table shows the sample size of each CKD group across each time point. Only significant *P* values are shown. HD, hemodialysis; PD, peritoneal dialysis.

on HD, and two of two (100%) patients with CKD seroconverted after the third dose.

In an adjusted multivariable model using logistic regression, a positive humoral response at 6 months was associated with initial mRNA-1273 vaccine (hazard ratio [HR], 1.78; 95% confidence intervals [95% CI], 1.11 to 2.88; $P=0.02$), a positive humoral response at 3 months (HR, 26.2; $P<0.001$), having received a third dose (HR, 22.9; 95% CI, 8.06 to 65.2; $P<0.001$), and not being a kidney transplant recipient (HR for kidney transplant recipients, 0.26; 95% CI, 0.09 to 0.73; $P=0.01$). In patients with 3-month negative humoral response, a third dose (HR, 27.8; 95% CI, 5.12 to 150.0; $P<0.001$) and not being a kidney transplant recipient (HR for kidney transplant recipients, 0.11; 95% CI, 0.02 to 0.74; $P=0.02$) were associated with a humoral response at 6 months in a model adjusted for age, type of initial and subsequent mRNA vaccine, and baseline anti-Spike antibodies.

The limitations are a small sample size, especially for some of the CKD subgroups that did not receive a third dose; that the timing of the third dose (between the third and sixth months) was variable and not accounted for in describing these results; and that the study did not assess cellular immunity or clinical efficacy (4).

In conclusion, the pragmatic analysis of the SENCOVAC study reveals that anti-Spike antibodies continue to decrease from 3 to 6 months after vaccination in patients with CKD. A third dose of SARS-CoV-2 vaccine induces seroconversion in a high percentage of antibody-negative patients with CKD after two doses, although responses were poorer in kidney transplant recipients.

Disclosures

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Data Sharing Statement

The data underlying this article will be shared on reasonable request to the corresponding authors.

Supplemental Material

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Supplemental Summary 1. A list of the SENCOVAC collaborative network nonauthor contributors.

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