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Postvaccine Anti–SARS-CoV-2 Spike Protein Antibody Development in Kidney Transplant Recipients

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Solid organ transplant recipients are at an elevated risk of severe coronavirus disease 2019 (COVID-19), and early reports also suggest impaired response after the first dose of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mRNA vaccine series.[1–3] Because of concerns about vaccine immunogenicity, all kidney transplant recipients at our center are recommended to undergo anti–SARS-CoV-2 spike protein IgG ("anti-spike antibody") testing 2 to 6 weeks after completing their vaccination series in full.

As of March 29, 2021, 28 recipients at our center have undergone such testing, with median age of 66 years and a median time since transplant of 8.7 years (range 1.0–15.8 years; Table 1). Only 3 patients had a history of polymerase chain reaction–positive SARS-CoV-2 infection. Antibody testing was performed using anti-spike IgG immunoassay (Liaison assay [DiaSorin, Saluggia, Italy], n = 5, or Elecsys [Roche Diagnostics, Indianapolis, IN], n = 23). Each of these clinical assays initially was designed to identify the presence of an adaptive immune response to SARS-CoV-2 infection. The Roche assay has a reported sensitivity of 96.6% (95% confidence interval [CI] 93.4%–98.3%) and specificity of 100% (95% CI 99.7%–100%).[4] The DiaSorin Liaison assay has a reported sensitivity of 97.6% (95% CI 87.4%–99.6%) and specificity of 99.3% (95% CI 98.6%–99.6%).[4]

Among included patients, only 7 (25%) had detectable anti-spike IgG ("antibody-positive"), whereas 21 (75%) did not have detectable antibodies ("antibody-negative"). Demographics and clinical characteristics, including kidney function, of antibody-positive and antibody-negative patients were similar, although the small sample size precluded formal comparisons (Table 1).

Most patients were taking tacrolimus at the time of vaccination (86% antibody-positive, 71% antibody-negative). However, only 2 of 17 patients (12%) using mycophenolate at the time of vaccination were antibody-positive, including 1 with a previous COVID-19 infection and 1 taking low-dose mycophenolate mofetil (250 mg twice daily). Notably, none of the 6 patients receiving belatacept were antibody-positive.

These findings suggest that transplant recipients do not demonstrate the near-complete antibody response to anti–SARS-CoV-2 mRNA vaccines observed in clinical trials, which excluded immunosuppressed patients and those with impaired kidney function,[5,6] and are consistent with early evidence of limited immunogenicity of the first dose of these vaccines.[2] Consequently, patients should continue to exercise caution after vaccination with the understanding that published vaccine efficacy data derived from the general population cannot necessarily be inferred to apply to them. Other clinical implications of these findings remain unclear until additional data are available. Our findings of impaired antibody response in patients on regimens that included belatacept and mycophenolate are consistent with data from influenza vaccinations.[7] However, the value and implications of short-term changes in immunosuppression management around the time of vaccination remain uncertain, and modifying maintenance immunosuppression to enhance vaccine responsiveness cannot be recommended empirically without further studies because of the risk of precipitating antiallograft immune responses.

Table 1. Characteristics of kidney transplant recipients included in the analysis, stratified by postvaccination anti-spike antibody status

	All, n = 28 (100%)	Undetectable anti-spike antibody, n = 21 (75%)	Detectable anti-spike antibody, n = 7 (25%)
Age, yr, median (range)	66 (42–87)	67 (42–87)	60 (48–76)
Female, n (%)	11 (39)	9 (43)	2 (29)
Time since transplant, yr, median (range)	8.0 (1.0–15.8)	8.7 (1.0–15.8)	7.3 (1.8–12.0)
Hypertension, n (%)	18 (64)	14 (67)	4 (57)
Diabetes, n (%)	12 (43)	10 (48)	2 (29)
Most recent creatinine, mg/dl, median (range)	1.3 (0.9–4.2)	1.3 (0.9–4.2)	1.4 (1.0–2.3)
Maintenance immunosuppression, n (%)			
Tacrolimus	21 (75)	15 (71)	6 (86)
Belatacept	6 (21)	6 (29)	0 (0)
Prednisone	9 (32)	5 (24)	4 (57)
Mycophenolate mofetil/mycophenolic acid	17 (61)	15 (71)	2 (29)
Azathioprine	3 (11)	2 (10)	1 (14)
Leflunomide	1 (4)	0 (0)	1 (14)
Sirolimus/everolimus	4 (14)	2 (10)	2 (29)
Rejection within year before vaccine, n (%)	2 (7)	1 (5)	1 (14)
History of COVID-19, n (%)	3 (11)	1 (5)	2 (29)
Vaccine brand, n (%)			
Moderna	12 (43)	9 (43)	3 (43)
Pfizer-BioNTech	16 (57)	12 (57)	4 (57)
Time between second vaccine dose and antibody testing, d, median (range)	29 (12–59)	28 (12–59)	30 (14–47)

Limitations of this report include a small study population and a lack of patients receiving other approved vaccines. We are also unable to draw conclusions about vaccine efficacy. It is possible that some protection against infection and/or severe COVID-19 is conferred through other mechanisms, including T cell reponse.[8] Alternative explanations for our findings include a lack of longitudinal antibody testing or the development of IgM/IgA not detected by IgG immunoassays. In addition, patients were not tested for the presence of anti-spike antibodies before vaccination. It therefore remains possible that some antibody-positive patients developed anti-spike antibodies because of unrecognized previous SARS-CoV-2 infection rather than as a result of vaccination. Further, we relied on clinical assays designed to detect an anti-spike immune response to SARS-CoV-2 infection rather than research assays designed to measure viral binding or neutralization.

Our findings underscore the need to evaluate COVID-19 incidence among completely vaccinated transplant recipients to determine whether the failure to develop anti-spike antibodies portends continued SARS-CoV-2 susceptibility. Confirmation of a poor response to SARS-CoV-2 vaccination in transplant recipients and other immunosuppressed populations might require enhanced vaccination strategies, which may include different dosing, alternative schedules, or vaccines with a different mechanism of action.

DISCLOSURE

All the authors declared no competing interests.

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