SARS-CoV-2 Messenger RNA Vaccine Immunogenicity in Solid Organ Transplant Recipients With Prior COVID-19

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Immunocompetent people with prior severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (convalescent individuals) have been shown to have a more robust antibody response to the first SARS-CoV-2 mRNA vaccine dose compared with previously uninfected people (naive individuals).[1] Given limited immunogenicity of SARS-CoV-2 vaccines in solid organ transplant recipients,[2,3] we sought to quantify the antibody response to vaccination among convalescent versus naive transplant recipients.

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Leveraging our ongoing prospective cohort of transplant recipients who underwent SARS-CoV-2 mRNA vaccination December 18, 2020–April 1, 2021,[4] we compared antispike antibody titers after dose 1 in convalescent transplant recipients with prior polymerase chain reaction-confirmed SARS-CoV-2 infection at a median (interquartile range [IQR]) of 3.5 mo (2.6–5.3 mo) before vaccination (n = 28) versus naive recipients (n = 1012) using weighted-by-the-odds Poisson regression. As previously reported, serologic testing was conducted on the Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay (range, <0.4 to >250 U/mL [positive ≥0.8 U/mL]), which tests for antibodies against the receptor-binding domain of the spike protein, or the EUROIMMUN enzyme immunoassay (positive ≥1.1 AU), which tests for immunoglobulin G to the S1 domain of the spike protein. This study was approved by the Johns Hopkins Institutional Review Board.

Convalescent vaccinees were more likely to have a positive antibody response to dose 1 compared with naive vaccinees (89% versus 18%, $P < 0.001$) (Table 1). After weighting to adjust for age, antimetabolite therapy, and organ transplant type, prior SARS-CoV-2 infection was associated with a 6.28-fold higher chance of a positive antibody response (weighted incidence rate ratio = ${}_{5.23}6.28_{7.54}$, $P < 0.001$). Convalescent vaccinees also had a higher post–dose 1 antispike antibody titer than naive vaccinees (median [IQR], 250 [250–250] versus 7.63 [2.02–28.97], $P < 0.001$ [Roche] and 7.62 [7.44–9.14] versus 3.42 [2.3–5.16], $P = 0.02$ [EUROIMMUN]). In a sensitivity analysis restricting to only those with a confirmed prevaccine negative antibody result, convalescent recipients were still more likely to have a positive antibody response to dose 1 (75% versus 19%, $P < 0.001$).

Prevaccine antispike antibody testing was available in 12 of the 28 convalescent recipients and detectable in 8 of 12 (67%). In this population, postvaccine titers were higher than those prevaccine (>250 versus 223.3 U/mL [Roche]; 9.14 versus 5.5 AU [EUROIMMUN]).

Limitations include a convenience sample, which may limit generalizability; inclusion of late entries, which limited the availability of prevaccination titers; self-report of SARS-CoV-2, which may have led to information bias; and lack of data on whether antimetabolite immunosuppression was held at the time of SARS-CoV-2 infection.

In this study of transplant recipients with prior SARS-CoV-2 infection, antibody response to vaccination was much stronger than in SARS-CoV-2 naive recipients.

TABLE 1.

Demographics of study population stratified by prior SARS-CoV-2 infection status

	Previously uninfected	Previously infected	*P*
n	1012	28	
Kidney recipient	476 (48.0%)	14 (50.0%)	0.83
Age, median (IQR)	60.0 (45.7–68.1) (n = 1002)	56.6 (50.6–66.3) (n = 28)	0.45
Transplant type			0.88
Kidney	476 (47.0%)	14 (50.0%)	
Liver	215 (21.2%)	5 (17.9%)	
Pancreas	12 (1.2%)	0 (0.0%)	
Heart	145 (14.3%)	4 (14.3%)	
Lung	107 (10.6%)	3 (10.7%)	
Other	8 (0.8%)	0 (0.0%)	
Kidney/pancreas	29 (2.9%)	2 (7.1%)	
Not available	20 (2.0%)	0 (0.0%)	
Years since transplant, median (IQR)	6.2 (2.7–13.6) (n = 992)	6.1 (3.8–14.1) (n = 28)	0.56
White	889 (89.4%)	26 (92.9%)	0.56
Antimetabolite	699 (69.1%)	24 (85.7%)	0.059
Tacrolimus	813 (80.3%)	19 (67.9%)	0.15
Prevaccine antibody result			<0.001
Positive	3 (0.3%)	8 (28.6%)	
Negative	495 (48.9%)	4 (14.3%)	
Not available	514 (50.8%)	16 (57.1%)	
Post–dose 1 testing platform			0.19
EUROIMMUN	264 (26.1%)	4 (14.3%)	
Roche	748 (73.9%)	24 (85.7%)	
Days between dose 1 and post-D1 Ab testing, median (IQR)	21 (19–26) (n = 1003)	21 (19–24.5) (n = 28)	0.93

Ab, antibody; IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Furthermore, even in this population with some natural immunity, antibody titers were substantially boosted by 1 dose of a SARS-CoV-2 mRNA vaccine. Prior COVID-19 infection may prime the immune system in a similar way to the intended effect of dose 1 in uninfected patients.[5]

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