Antibody Kinetics and Durability in SARS-CoV-2 mRNA Vaccinated Solid Organ Transplant Recipients

Brian J. Boyarsky, MD, PhD,[1] Teresa P.-Y. Chiang, MD, MPH,[1] Aura T. Teles, BS,[1] Ross S. Greenberg, BA,[1] Michelle R. Krach, BA,[1] Michael T. Ou, BS,[1] Allan B. Massie, PhD,[1] Aaron A. R. Tobian, MD, PhD,[2] Jacqueline M. Garonzik-Wang, MD, PhD,[1] Dorry L. Segev, MD, PhD,[1,3] and William A. Werbel, MD[4]

Decline in severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antispike antibodies over time following natural infection and vaccination have been reported,[1–3] though kinetics and durability of antispike antibodies in vaccinated transplant recipients are unknown. We sought to quantify antispike antibody titers over a 3 mo period in transplant recipients who completed the mRNA vaccine series.

Received 10 June 2021.

Accepted 11 June 2021.

[1] Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD.

[2] Department of Pathology, Johns Hopkins School of Medicine, Baltimore, MD.

[3] Department of Epidemiology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD.

[4] Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD.

B.J.B., W.A.W., T.P.C., A.T.T., R.S.G., M.R.K., M.T.O., A.B.M., A.A.R.T., D.L.S., and J.M.G.-W. contributed substantially to the conception or design of the work; the acquisition, analysis, or interpretation of data for the work; drafting the work or revising it critically for important intellectual content; final approval of the version to be published; and agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

This research was made possible with generous support of the Ben-Dov family. This work was supported by grants F32DK124941 (B.J.B.), K23DK115908 (J.M.G.-W.), and K01DK101677 (A.B.M.) from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); K24AI144954 (D.L.S.) from National Institute of Allergy and Infectious Diseases (NIAID); and gSAN-201C0WW from the Transplantation and Immunology Research Network of the American Society of Transplantation (W.A.W.). The analyses described here are the responsibility of the authors alone and do not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the US Government.

D.L.S. has the following financial disclosures: consulting and speaking honoraria from Sanofi, Novartis, CSL Behring, Jazz Pharmaceuticals, Veloxis, Mallinckrodt, and Thermo Fisher Scientific. The remaining authors of this manuscript have no financial disclosures or conflicts of interest to disclose as described by Transplantation.

Correspondence: Dorry L. Segev, MD, PhD, Associate Vice Chair, Department of Surgery, Johns Hopkins Medical Institutions, Director, Epidemiology Research Group in Organ Transplantation, 2000 E Monument St, Baltimore, MD 21205. (dorry@jhmi.edu).

ISSN: 0041-1337/21/10510-e137

DOI: 10.1097/TP.0000000000003863

As previously reported,[4,5] serologic testing was undertaken on the Roche Elecsys anti-SARS-CoV-2 S enzyme immunoassay (range <0.4–>250 U/mL [positive ≥0.8 U/mL]) which tests for antibodies against the receptor-binding domain of the spike protein or EUROIMMUN enzyme immunoassay (positive ≥1.1 arbitrary units) which tests for IgG to the S1 domain of the spike protein at 3 time points: before dose 2, 1 mo and 3 mo after dose 2. Participants underwent vaccination between 16 December 2020 and 13 March 2021, and this study was approved by the Johns Hopkins Institutional Review Board.

Overall, 40/305 (13%) had detectable antibody at median (interquartile range [IQR]) 21 (18–25) d after dose 1; 169/305 (55%) had detectable antibody at median (IQR) 29 (28–31) d after dose 2; and 203/305 (67%) had detectable antibody at median (IQR) 90 (88–92) d after dose 2.

Among the participants with detectable antibody at 1 mo, 6/169 (4%) fell below the threshold of positivity at 3 mo (Table 1). Titers decreased in 59/169 (35%), increased in 74/169 (43%), and remained constant in 36/169 (21%).

Among those with any positive titer after dose 2, median (IQR [range]) change between 1 mo and 3 mo antibody levels was 0 (0–75 [−166.8.1 to 247.12]; Roche) and −1.19 (−2.04 to 0.55, [−4.2 to 3.02]; EUROIMMUN). Among those with low-positive titers at 1 mo, 35/75 (47%) remained in the low-positive range and 35/75 (47%)

TABLE 1.

Antispike antibody sero-response 3 mo following SARS-CoV-2 vaccine dose 2 in transplant recipients, stratified by antibody response 1 mo after 2-dose mRNA vaccine series

		Sero-response after 3 mo		
		Negative	Low-positive	High-positive
Sero-response after 1 mo	Negative	96 (70)	31 (23)	9 (7)
	Low-positive	5 (7)	35 (47)	35 (47)
	High-positive	1 (1)	18 (19)	75 (80)

Negative sero-response was defined per manufacturer data as EUROIMMUN anti-S1 IgG <1.1 arbitrary units (AU) or Roche Elecsys anti-RBD pan Ig <0.8 units/mL. Low-positive sero-response was defined as anti-S1 IgG 1.1–4 AU or anti-RBD pan Ig 0.8–50 units/mL. High-positive sero-response was defined as anti-S1 IgG >4 AU or anti-RBD pan Ig >50 units/mL.
IgG, immunoglobulin G; RBD, receptorbinding domain; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

<zdoi;10.1097/TP.0000000000003863>

became high-positive. Among those with high-positive titers at 1 mo, 18/94 (19%) dropped to the low-positive range and 75/94 (80%) remained high-positive.

In this study of antibody kinetics and durability following SARS-CoV-2 mRNA vaccination, 43% experienced an increase antibody titer, 35% decreased, and 21% remained stable between 1 and 3 mo postvaccination. Though only a small minority (4%) who had detectable antibody at 1 mo fell below the threshold of detectability at 3 mo, 19% with high-positive titers at 1 mo dropped to low-positive.

In the mRNA-1273 trial, binding antibody levels declined slightly over time, but remained elevated at 3 mo after the completion of the 2-dose series.[1] It is unknown if antibody decline over time results in higher risk of SARS-CoV-2 infection; however, these results raise the suggestion that additional booster dosing may help augment lower antibody responses in transplant recipients.

This study is limited by convenience sampling, lack of immunocompetent control group, and lack of exploration of neutralizing antibody and memory B immune response. Also, despite clinical screening for incident symptomatic coronavirus disease 2019, antinucleocapsid testing was not performed, precluding analysis of asymptomatic exposure.

In conclusion, we found that antispike antibody seroresponse 3 mo following the mRNA vaccine series was largely stable. Understanding longitudinal kinetics of antibody decline among transplant recipients in the context of thresholds for protection may inform need and timing for booster vaccinations.

REFERENCES

1. Widge AT, Rouphael NG, Jackson LA, et al; mRNA-1273 Study Group. Durability of responses after SARS-CoV-2 mRNA-1273 vaccination. *N Engl J Med*. 2021;384:80–82.
2. Patel MM, Thornburg NJ, Stubblefield WB, et al. Change in antibodies to SARS-CoV-2 over 60 days among health care personnel in Nashville, tennessee. *JAMA*. 2020;324:1781–1782.
3. Pegu A, O'Connell S, Schmidt SD, et al. Durability of mRNA-1273-induced antibodies against SARS-CoV-2 variants . *bioRxiv*. Preprint posted online May 16, 2021. doi:10.1101/2021.05.13.444010
4. Boyarsky BJ, Werbel WA, Avery RK, et al. Immunogenicity of a single dose of SARS-CoV-2 messenger RNA vaccine in solid organ transplant recipients. *JAMA*. 2021;325:1784–1786.
5. Boyarsky BJ, Werbel WA, Avery RK, et al. Antibody response to 2-dose SARS-CoV-2 mRNA vaccine series in solid organ transplant recipients. *JAMA*. 2021;325:2204–2206.