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Effectiveness of SARS-CoV-2 vaccination in fully vaccinated solid organ transplant recipients

To the Editor:

The COVID-19 pandemic has disproportionately impacted immunosuppressed patients, including solid organ transplant recipients (SOTR). COVID-19-associated mortality among SOTR was estimated at 20.5% in the early phase of the pandemic.[1] SARS-CoV-2 vaccination may help reduce the morbidity and mortality of COVID-19 among SOTR. Under the emergency use authorization, the US Food Drug Administration approved two SARS-CoV-2 messenger RNA vaccines (BNT162b2 [Pfizer], mRNA-1273 [Moderna]), and an adenovirus vector-based vaccine (Ad26.COV2.S [Johnson and Johnson]). The efficacy of the mRNA vaccines and Ad26.COV2.S is >95% and 66% in the general population, respectively, but little is known about efficacy in SOTR due to their exclusion from clinical trials.[2–4]

A retrospective, observational study of SOTR who received SARS-CoV-2 vaccine was conducted at Yale New Haven Hospital by chart review. This study was approved by the Yale University Institutional Review Board (HIC#2000027876). A total of 2197 adult SOTR are engaged in care. As of May 18, 2021, 557 SOTR (388 kidney, 105 liver, 50 heart, 14 combined organ transplants) (Table S1) without documented SARS-CoV-2 infection received ≥1 dose of a SARS-CoV-2 vaccine (Figure 1). Three-hundred and twenty-four (58%) and 206 (37%) SOTR received ≥1 dose of BNT162b2 and mRNA-1273, respectively. Twenty-seven (5%) SOTR received Ad26.COV2.S. Four hundred and eighty-two SOTR (86%) completed vaccination, and 459 (82%) were fully vaccinated (i.e., ≥14 days postcompletion of vaccine series). Of those who received ≥1 dose, 9 (1.6%) tested positive using SARS-CoV-2

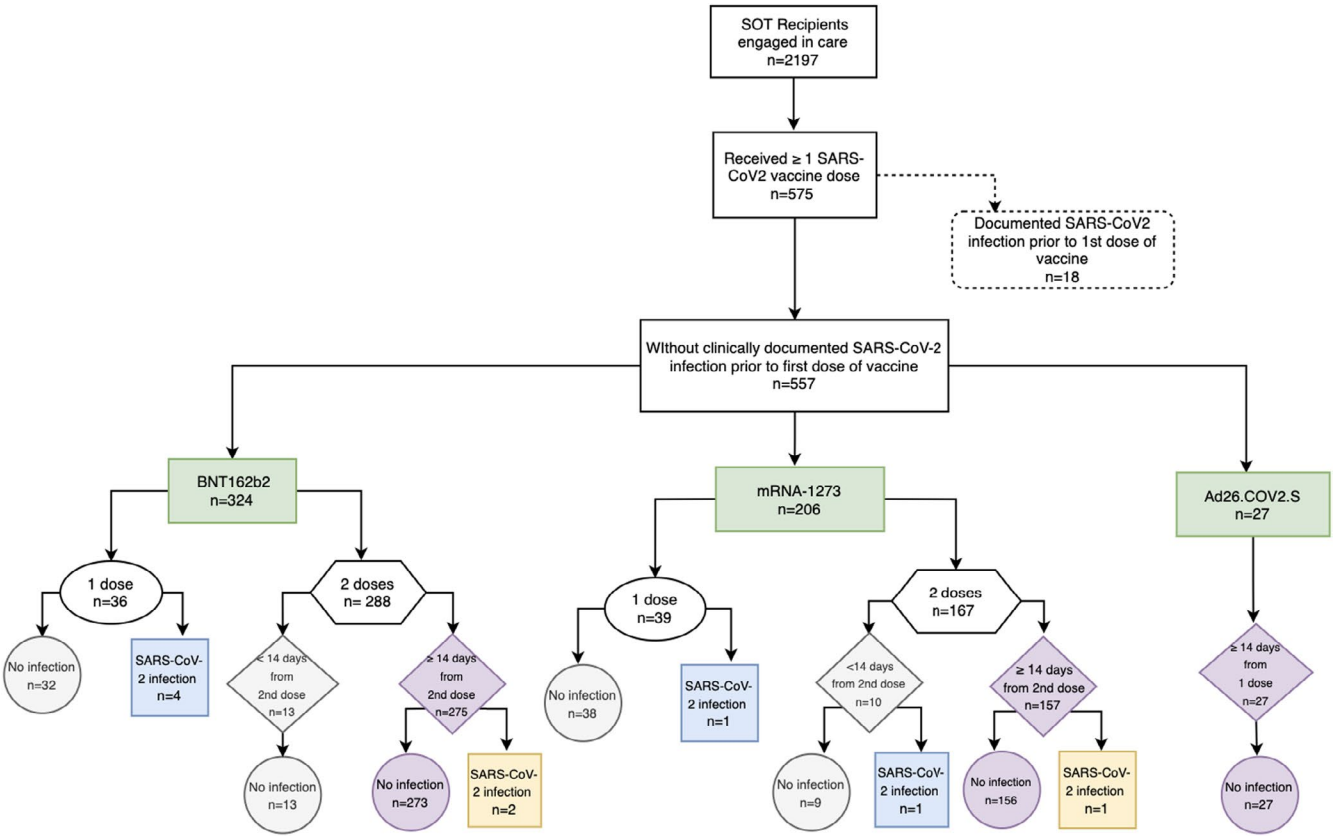

FIGURE 1 Solid organ transplant recipients at Yale New Haven Transplant Center who received SARS-CoV-2 vaccine [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Clinical characteristics of solid organ transplant recipients who developed SARS-CoV-2 infection after vaccination

	Organ	Age (years)	Race	Ethnicity	Sex	Induction IS	Maintenance IS	Co-morbidities	BMI (kg/m^2)	SARS-CoV–2 Vaccine	Dose received	Last dose of SARS-COV–2 Vaccine to first positive SARS-CoV–2 NAAT (days)	Time from TXP to first SARS-CoV–2 positive NAAT (years)	Severity of COVID–19[a]	Hospitalized	Treatment received for COVID-19	Follow-up days after SARS-CoV2 positive NAAT (days)[b]	Status at last follow-up day[b]
Infections after partial vaccination																		
1	Kidney	44	White	Latinx	Female	Alemtuzumab	TAC,MMF, Prednisone	HTN Obesity	47.26	mRNA–1273	1	16	3.7	Moderate	No	Bamlavinimab	103	Alive
2	Kidney/ Pancreas	49	White	Latinx	Male	ATG	TAC, MMF, Prednisone	DM HTN	25.24	BNT162b2	1	5	6.8	Severe	Yes	Remdesivir Dexamethasone	18	Alive
3	Heart	58	Black	Non-Latinx	Male	Basiliximab	TAC,MMF	HTN Obesity	30.61	BNT162b2	1	36	4.0	Severe	Yes	Bamlavinimab/ etesevimab	19	Alive
4	Kidney	61	White	Non-Latinx	Male	Alemtuzumab	Belatacept, MMF, Prednisone	HTN Obesity	32.75	BNT162b2	1	4	6.4	Mild	No	Bamlavinimab	26	Alive
5	Kidney	64	White	Non-Latinx	Male	Alemtuzumab	TAC, MMF, Prednisone	DM	20.61	BNT162b2	1	16	4.6	Severe	Yes	Bamlavinimab/ etesevimab Dexamethasone	39	Alive
6	Kidney	71	White	Latinx	Male	Unknown	TAC, MMF, Prednisone	HTN	20.85	mRNA–1273	2	7	14.5	Severe	Yes	Remdesivir Dexamethasone	41	Alive
Breakthrough infections ≥14 days after last dose of vaccine series																		
7	Kidney	65	White	Non-Latinx	Female	Alemtuzumab	Belatacept, MMF, Prednisone	HTN	27.95	mRNA–1273	2	18	2.2	Mild	No	Bamlavinimab/ etesevimab	30	Alive
8	Liver	66	White	Non-Latinx	Female	None	TAC, Prednisone	DM HTN	22.65	BNT162b2	2	35	1.9	Mild	Yes	Bamlavinimab/ etesevimab	32	Alive
9	Kidney	80	Asian	Non-Latinx	Female	Alemtuzumab	Belatacept	DM HTN	28.75	BNT162b2	2	63	6.3	Mild	No	Bamlavinimab/ etesevimab	30	Alive

Abbreviations: ATG, antithymocyte globulin; BMI, body mass index; DM, diabetes mellitus; HTN, hypertension; IS, immunosuppression; MMF, mycophenolate mofetil; NAAT, nucleic acid amplification test; TAC, tacrolimus; TXP, transplant.

[a]Severity of COVID-19 was based on the National Institute of Health definition (https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/). Mild disease: Individuals with symptoms but no respiratory symptoms nor abnormal chest imaging. Moderate disease: Individuals with evidence of lower respiratory disease by clinical assessment or imaging and who have oxygen saturation ≥94% on room air at sea level. Severe disease: Individuals who have oxygen saturation <94% on room air at sea level, respiratory rate of 30 breaths/min or lung infiltrates >50%.

[b]As of May 18, 2021.

nucleic acid amplification testing (NAAT) postvaccination. Six of 98 (6.12%) partially vaccinated SOTR developed SARS-CoV-2 infection. Breakthrough infection, defined as positive SARS-CoV-2 NAAT ≥14 days postvaccine series completion, occurred in 3 of 459 (0.65%) fully vaccinated SOTR (Table S2). Clinical characteristics of the SOTR who developed SARS-CoV-2 infection postvaccination are summarized in Table 1. All three had mild COVID-19, received bamlanivimab/etesevimab, and survived. Only one (patient 8) had an available cycle threshold, which was reported 15.5 and was hospitalized for a reason unrelated to COVID-19.

A recently published study demonstrated poor immunogenicity of mRNA SARS-CoV-2 vaccine among SOTR, measured by antispike antibody responses after completion of vaccination.[4] Though discouraging, such a finding was not unexpected given known reduced antibody responses to other vaccines posttransplant. Determining what antibody levels are protective against SARS-CoV-2, the role of the cellular immune responses and the utility of additional boosters in potentiating immune responses require further investigation. Despite concerns of poor humoral response, breakthrough SARS-CoV-2 infection was infrequent in our cohort. However, this rate is relatively higher compared to the general population reported by the CDC (i.e., 0.001%).[5] Future prospective studies are needed to define the long-term effectiveness and immunogenicity of SARS-CoV-2 vaccines in SOTR and to determine the impact of variants on outcomes of vaccinated SOTR. As we wait for more studies, SOTR and their household members are strongly encouraged to be vaccinated and practice safety measures that include mask-wearing and social distancing.

KEYWORDS

clinical research/practice, infection and infectious agents – viral, infectious disease, organ transplantation in general, vaccine

DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

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SUPPORTING INFORMATION

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