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Immunogenicity of SARS-CoV-2 BNT162b2 vaccine in solid organ transplant recipients

To the Editor:

Solid organ transplant (SOT) recipients represent a high-risk group for all SARS-CoV-2 infection-related adverse outcomes.[1] Therefore, most European countries have established prioritization of SOT recipients in their vaccination programs. Suboptimal vaccine efficacy to the SARS-CoV-2 vaccines is anticipated; however, they have been excluded from vaccination trials. Overall response rates to other vaccines, such as influenza vaccine, have demonstrated high, though acceptable, variability.[2] Herein we report preliminary results of the humoral immune response in 34 SOT recipients and 116 matched health-care workers (HCW) after vaccination with the BNT162b2 mRNA vaccine.

The first 34 SOT (10 kidney and 24 heart) recipients who were vaccinated in the country with BNT162b2 and 116 age- and sex-matched HCW were included. The study was approved by the Ethics committee of the "Onassis Cardiac Surgery Center" and all the participants had signed written informed consent. Postvaccination antibodies were tested by an anti-SARS-CoV-2-RBD IgG assay (Abbott SARS-CoV-2 IgG II Quant). It quantifies IgG antibodies against the receptor-binding domain (RBD) of the S1 subunit of the spike protein of SARS-CoV-2 by a chemiluminescent microparticle immune assay (CMIA). The linear range is between 21.0 and 40 000 AU/ml and according to the manufacturer, the clinical specificity is estimated at 99.55% and the clinical sensitivity at 98.81% in samples collected >=15 days following a positive PCR at a cut-off value of 50 AU/ml. Anti-SARS-CoV-2 RBD IgG assays have shown an excellent correlation with neutralizing antibodies.[3]

Antibodies were measured at a median of 10 (IQR: 9–10) days from the second vaccination dose. We evaluated the associations among demographic and clinical characteristics and positive antibody response using modified Poisson regression with a robust variance estimator.

A total of 34 SOT recipients were analyzed. There was a male predominance (79.4%). The median age was 60 (IQR: 49.1–68.4) years, and median time from transplantation was 11.1 (IQR: 7.3–15.8) years. Almost all (94%) SOT recipients received a calcineurin inhibitor-based immunosuppressive regimen, 44% an antimetabolite, 15% corticosteroids, and 62% (all the heart and a minority of kidney recipients) a mTOR inhibitor. Anti-SARS-CoV-2 RBD-IgG antibodies were detected in 20 of the 34 SOT recipients (58.8%). From the covariates assessed, antimetabolite-containing immunosuppression was the only factor that negatively influenced immune response: 33% in those receiving MPA versus 79% in those who did not (adjusted incidence ratio IRR 0.42, p = .027) (Table 1). The study was underpowered for the assessment of immunogenicity by transplantation type. When SOT recipients were compared to HCW, antibody response rates (58.8% vs. 100%, p < .001), median (1370 vs. 11 710, p < .001), and geometric mean titers (948 vs. 11 300, p < .001) of anti-SARS-CoV-2 RBD IgG titers were all highly significant (Figure 1).

TABLE 1 Prevalence of anti-SARS-CoV-2 RBD IgG after second dose of BNT162b2 vaccine in organ transplant recipients (OTR). Samples with anti-SARS-CoV-2 RBD IgG concentration ≥50 AU/ml were considered positive

	Prevalence of anti-SARS-CoV-2 RBD IgG			
Covariates	***N***	***n/N***	**IRR (95% CI)[a]**	***p*[b]**
Total	34	20 (58.8)		
Age (years), *n* (%)				
≤60	17	11 (64.7)	1	
>60	17	9 (52.9)	0.82 (0.46–1.46)	.496
Sex, *n* (%)				
Male	27	16 (59.3)	1	
Female	7	4 (57.1)	0.96 (0.47–1.99)	.922
Type of transplant, *n* (%)				
Heart	24	18 (75.0)	1	
Kidney	10	2 (20.0)	0.27 (0.07–0.96)	.043
Time since transplant (years), median (25th–75th)				
≤11	17	9 (52.9)	1	
>11	17	11 (64.7)	1.22 (0.69–2.18)	.496
Antimetabolite maintenance immunosuppression, *n* (%)[c]				
No	19	15 (79.0)	1	
Yes	15	5 (33.3)	0.42 (0.20–0.91)	.027

[a]95% CI: 40.7–75.4.

[b]We evaluated the associations among demographic and clinical characteristics and positive antibody response using modified Poisson regression with a robust variance estimator.

[c]Includes mycophenolate mofetil and mycophenolate acid.

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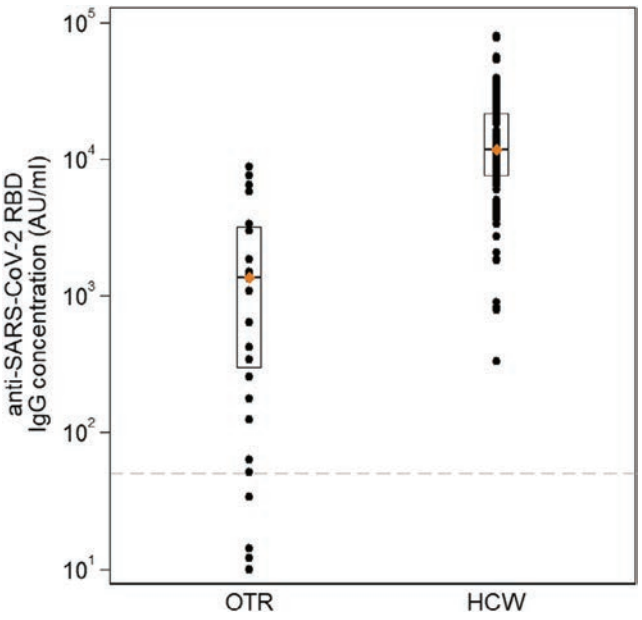

FIGURE 1 Anti-SARS-CoV-2 RBD IgG concentration (AU/ml) in organ transplant recipients (OTR) in comparison with healthcare workers (HCW). Diamonds and endpoints of the rectangles represent median concentration and 25th–75th percentile, respectively. Dashed horizontal line indicates the assay limit of detection (LOD) 50 AU/ml [Color figure can be viewed at wileyonlinelibrary.com]

These preliminary results demonstrated a reduced humoral immune response to the BNT162b2 mRNA vaccine in SOT recipients compared to their healthy counterparts. Our study further confirms a recent study by Boyarsky et al,[4] describing an anti-RBD IgG prevalence of 31% in 223 SOT recipients after the first vaccination dose. Our study included 34 SOT recipients who had completed their immunization with both vaccine doses, and the immunogenicity was assessed at a time where antibody titers are considered highest.[5] We found low antibody response rates and low antibody titers in immunocompromised individuals (58.5%). The study limitations include: the small sample size, the single measurement of antibodies, sole use of the BNT162b2 vaccine, and assessment only of the humoral component and not the T-cell immune response. Our findings, however, may be significant. They indicate that a substantial proportion of SOT recipients are expected to develop antibody titers below the protective threshold, which may eventually wane faster. Subsequently, immunocompromised individuals may remain at infection risk even after complete vaccination. Furthermore, if confirmed by large-scale studies, alternative approaches to improve vaccine response may be indicated in patients receiving lifelong immunosuppression.

KEYWORDS

clinical research/practice, heart transplantation/cardiology, infection and infectious agents – viral, infectious disease, kidney transplantation/nephrology, vaccine

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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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